Carmen Rottenberg,
USDA Acting Deputy Under
Secretary of Food Safety

Good morning. I'm Carmen Rottenberg. I'm the Acting Deputy Undersecretary for Food Safety, and on behalf of USDA I want to welcome you all here to our building and the joint public meeting on the use of animal cell culture technology to develop food products from livestock and poultry. We're very pleased to see such a diverse group of stakeholders that have registered for the event. We have approximately 600 people who are expected to be here between today and tomorrow, either in person or through the webcast. Today, to open the two-day public meeting we're honored to have Secretary Perdue and Commissioner Gottlieb here to deliver some opening remarks. We have a very full two-day agenda, so with that, it's my pleasure to introduce the 31st Secretary of Agriculture, the Honorable Sonny Perdue.

Sonny Perdue,
USDA Secretary of Agriculture

Have you all had your coffee yet? Good morning!

[Good morning!]

So good to see all of you. We appreciate you coming out so early to talk about an important topic. This may be one of the more robust meetings we've had here at USDA and we want to welcome our guests on stage, Commissioner of FDA, Dr. Scott Gottlieb and his team, all of you in the audience, and people who are viewing from around the world who are interested. We've got a lot of international interest as well, so we're happy that you're here and we hope that we'll have a great informed panel over the next day or so.

I want to thank, frankly, everyone in both agencies who came together to work together to pull this meeting together. These things just don't happen, it takes long hours and very dedicated to detail work to put together.

Essentially, what we're trying to accomplish here today is a stakeholder meeting as we begin to frame how the new technology of cell cultured meat is regulated by the federal government. I'm glad to see the excitement over new technology and it's always important to have good, informed, interested stakeholders. As we begin to talk about this and listen to your comments, as it informs our decisions on public policy going forward. So, that's why we're here today. I think Dr. Gottlieb will also comment in the spirit of collaboration with various government officials, our scientists, our consumers, and members of our industry - making decisions together as we move along.

Obviously here in this room today, it's filled with individuals who have an interest in ensuring that the food on America's tables remains safe, wholesome, and accurately labeled – and these are challenges as new technologies that never have been thought about in the past come to fruition. It's very important that we have a framework that encourages innovation and encourages new technology while we provide the responsibility of a public, safe, wholesome, and nutritious food supply.

Industry innovators and consumers alike can help determine the roles of USDA and FDA. Simply put, we're here to talk about how we decide who does what in this arena, how do we come together as one federal government to make the best decisions for the public at large, and how do we make a regulatory framework and protocols that are clear and concise and easily be complied with. There needs to be a clear understanding of the roles and responsibilities of both the Federal Drug Administration as well as the USDA in the production and commercialization of this new technology.

I think it's also interesting to note that the industry is many times already ahead of us. I note that the North American Meat Institute, along with one of our innovators in this area, Memphis Meats, agreed in a letter to President Trump a few weeks ago, that they envision a role for both agencies in this new technology. Both the industry, and as I said, the consumers - the public - have a right to know and expect clear, concise regulations and bright lines. It's important to keep in mind, that right now, also as the United States is leading in this area to see how we are looking and see how we handle this issue from a regulatory standpoint, and we want to be true world leaders on this topic as we have a challenge to feed the world.

Our new motto at USDA, you may have heard, is to “Do right and feed everyone.” That's pretty profound. “Do right” has a lot of connotations but “feeding everyone” is a little bit like our energy independence. I like to think about the approach, “all the above.” While it sounds like a very lofty goal, to do right and feed everyone, it has real world meaning and we know, demographically, that there are projected to be nine billion people on this planet by the year 2050.

That means they're going to be nine billion hungry souls and that means we must feed them, wherever they are, by whatever means are available and necessary. So, as I said, we here are talking about a “whatever it takes and all of the above” technology, including new technology like cell cultured meat. New proteins should be treated in the same fashion, as we believe, past products. There must be safe processing and safe production for consumers, as well as safe

innovation, making sure that these things have no unsafe or unhealthy aspects to them. It's my view that both of our agencies need to be open to innovation and welcoming of innovation that will help to feed people. The projected population of our planet demands it, so we'll need to produce the same amount of food, this is startling, over the next 50 years as we have in the history of civilization. That's the exponential result of demographic change. To do that, I believe in our motto, we must “Do right and feed everyone.” In order to continue that conversation of collegiality, cooperation, collaboration I want to welcome my friend and colleague Dr. Scott Gottlieb, Commissioner of the Food and Drug Administration. [Applause]

Scott Gottlieb,
FDA Commissioner

Thanks a lot and thanks for hosting us here too. I want to thank the Secretary for his collegiality and the work that he's done in collaboration with FDA. We've worked on a lot of important issues together to advance the public health and advance the interest of growers all over the country and we’re grateful for that collaboration with the Secretary and with his team. I'd like to thank all the participants for joining us here in this room and also those who are tuning-in online today. I’d also like to thank the Secretary and his team for hosting this.

We're here over the next two days to discuss cell culture technology in the food industry. Adoption of this technology has advanced rapidly over the past few years and numerous companies are currently working to harness this technology to develop new products. In recent years, FDA has been contacted by firms interested in developing foods using cultured animal cells from various species and we've had several stakeholder engagements on this topic. It's clear to us from these meetings that cell culture products will take many forms.

Products derived from livestock and poultry will be the focus of this meeting, but cell cultured seafood is also on the horizon and at FDA we foresee that this technology could be used for a variety of multi-component foods and in development of innovative food products that can only be imagined right now in the present moment. It won't be long before these products reach wide scale and wide marketplace. Reports indicate that the cost of using cell culture technology to develop food products derived from livestock is one fiftieth of what was just a few years ago and while I don't have a crystal ball to see the future, I wouldn't be surprised to see cell culture burgers on restaurant menus in the coming years.

This meeting today presents an opportunity for the FDA and for USDA to hear from stakeholders about the potential hazards, oversight

considerations, and labeling of cell cultured food products. We fully anticipate that both FDA and USDA will have active roles in the regulatory oversight of cell culture products. The feedback we hear from you today will help us to advance this interagency cooperation and these discussions, as they go forward. Our two agencies take very seriously our shared mission of protecting the public health, and while there are many considerations regarding proper oversight of the use of cell culture technology to produce food, consumer safety will always be at the forefront of our work.

One of my priorities as Commissioner, is enabling innovation and consumer choice while supporting public health and safety and for the FDA, these products stands at an interesting intersection of medical technology and food technology. As many of you know, the field of animal derived cell culture technology began in the medical product space. Today, animal cell culture technology, along with human cell culture technology, is used to create products such as recombinant protein, cell therapies, gene therapies for human and veterinary use, and, in the near future, we expect this technology will also be expanded to produce products such as regenerative medicine products derived from stem cells. It will also be used for tissue engineering products such as tissue grafts and solid organs created from the living cells of *ex vivo* culturing techniques.

FDA has already approved many novel medical products that use different cell culture technologies. And these novel products manufactured using various cell culture technologies emerged. As they emerged, our scientists recognized unique risks introduced by these technologies. We require proper controls needed to prevent the introduction of hazards into these products while helping these tools, these innovative tools, advance. As a result, we've issued a number of guidance documents for the production of these products and I believe that our technical and our scientific work has assured the safety of these products and provided life-changing novel therapies to patients, and our consistent regulatory approach provides certainty to companies currently making these medical products or considering entering the market in the future.

That's our medical product experience, but now we're grappling with the challenge of determining how to ensure that food products derived from these same technologies are also safely produced. Cell culture derived tissues that are inserted into the human body and become part of living tissues are very different applications than cell culture products that are ingested and we want to define the aspects of our medical products experience that are pertinent to food products and identify those pieces that are different. We also need to examine whether

existing food safety oversight tools are sufficient for these products or whether more is needed, and these are the questions that we're all actively discussing in collaboration and I hope we will have a robust discussion on all of these issues here today.

We also have a long history of ensuring the safety of the country's food supply and this encompasses our oversight of food additives, added substances, and dietary supplements, and you'll hear more about FDA's broad regulatory authorities for foods later today, so here, I'd like to just say a few words about the work we're doing to implement the Food Safety Modernization Act, or FSMA.

FSMA is transformative because of the tools it gives FDA to help prevent foodborne outbreaks before they occur. The law requires facilities that manufacture, process, pack, or hold human food to create and maintain food safety plans. Among other components, this plan must include a hazard analysis of known or reasonably foreseeable hazards, controls to prevent allergen or sanitation issues, and plans in the event of a recall. FSMA also provides the FDA with new enforcement authorities and it gives us important new tools to hold imported food to the same standards as domestic foods.

The risk-based prevention-oriented food safety framework that the FDA is working hard to strengthen lends itself well to evaluating and ensuring the continued safety of new food technologies, such as cell culturing. The USDA, of course, has their own safety framework for foods under their jurisdiction and there's no question that our two agencies working together have the right regulatory tools in our tool boxes to ensure the safety of new food products. This includes cell cultured food but deciding whether and how to use available tools is the art of regulation. I know that our success will depend on and help secure consumer and stakeholder support, and confidence, and buy-in of these new products.

Yesterday, FDA science board walked through some of the basics of animal cell culture. Our board provided their input to a series of questions aimed at understanding potential hazards in the source materials and the culture media and the structural materials. They also provided us with valuable insight into questions of the nutritional properties of the future state of finished products. This public meeting today, helps build on those discussions. First, it gives FDA and USDA a chance to walk you through our current safety and labeling frameworks, but more importantly, FDA and USDA will learn from you about the potential hazards you anticipate as well as hear your suggestions on possible ways and strategies to address them. We also look forward to hearing from you on the labeling of these products, both in terms of

naming and what claims can be appropriate to some of these new products.

Cell cultured food sits at the nexus of many constituencies and includes tech start-ups, consumer advocates, producers of traditional food products. Everyone in this room might have a different view on the regulatory considerations for these products, depending on a profession or their personal conviction, and that's one of the reasons cell cultured foods are so exciting, but also very challenging for us. We don't pretend to have all the answers yet. You'll help us identify the best path forward and the FDA and our partners at USDA know the value of this sort of stakeholder input. Whether you provide your opinion or expertise or just raise related issues we may not have thought of, we welcome your continued engagement in today's meeting, and also, in the future.

Throughout this process, FDA is committed to working with USDA and with you to determine the most efficient and most effective regulatory oversight framework for these novel products. We want to advance these promising technologies, but to be clear, regulatory efficiencies won't come at the expense of consumer safety and that's why USDA and FDA are holding the meeting together today. Partnership and coordination between our two agencies will be critical as we work together, leveraging our respective expertise in considering these novel technologies, and so, I look forward to hearing your thoughts and concerns today and in the coming months, and I look forward to continuing work with USDA and with the Secretary on these challenging questions and issues. I want to thank you for joining us today and for your interest and your participation. Thanks a lot.

Carmen Rottenberg,
USDA Acting Deputy Under Secretary of Food Safety

Thank you very much, Secretary Perdue and Commissioner Gottlieb. I have a few housekeeping announcements before we get started here today. As a reminder, the meeting is being webcast live today and tomorrow and will be available for viewing after the meeting today and tomorrow, so it will be immediately available for those that want to watch after it's been recorded. As a result of it being a public meeting and being webcast and recorded to video, if you’re publicly speaking or in the auditorium you may be part of those recordings and there's no expectation of privacy. I would say to our friends in the media - who it looks like are exiting stage left over there - that out of courtesy and out of respect for our speakers, we'd ask that media members remain seated while speakers are presenting and can have an opportunity to ask speakers questions during the breaks.

The meeting format is designed to create a number of opportunities for the public to make comment, and throughout the two-day meeting, USDA and FDA will be giving presentations on each of the topics - as Commissioner Gottlieb outlined - oversight considerations, potential hazards, and labeling. After each topic we have several open public comment sessions, as well as formal comment sessions, so you'll have opportunities to comment in either of those spaces, either in response to the questions in each segment or at the end of the day for open formal comment. The way this will work is, if you wish to make a comment you'll come to the front of the stage where we have two microphones here to give your comments and you'll be limited to three minutes. We have a timer up here that you all can't see from back there, but the speakers can see from the front. Then, as I mentioned, the final session of each day will have a formal public comment session and we would just ask, so that we can move people along, that folks come up to the microphones and sort of be staged up while the other person is speaking.

The formal sessions have been scheduled in advance and pre-registered commenters have received notification of their group number to come forward and give that public comment and we want to give anyone who's interested and here in person a chance to speak, so again, you'll be limited to three minutes. We also would encourage you to submit your written comments to us on regulations.gov or you can mail your comments to the docket clerk. The comment period is open until November 26. We would encourage those who are watching on the webcast to submit their comments in writing by mail or electronically. We have a great team of USDA staff here to assist, many of whom you met on your way in, so please feel free to ask them if you need anything - and with that I would like to start the formal section of our segment of our program and introduce Dr. David Goldman, Chief Medical Officer here at FSIS. Dr. Goldman. [Applause]

Dr. David Goldman,
USDA FSIS Chief Medical Officer

Well, good morning and as Carmen said, I'm the Chief Medical Officer here at FSIS. As Secretary Perdue and Commissioner Gottlieb have both said, today and previously, both USDA and FDA expect to have a role in the oversight of food products cultured from the cells of livestock and poultry; that's what this meeting is about. I attended yesterday's FDA Science Board meeting that Dr. Gottlieb referred to, where this was a prominent focus of discussion - this topic. You'll hear more about the Science Board meeting a bit later this morning during the meeting today, but that meeting reflected the considerable complexity of cell culture technology, and so to inform the agency's presentations later today and tomorrow, we thought it would be important to provide you

at the beginning of this meeting a broad foundational overview of cell culture technology. This has been presented before. It was presented yesterday, and I think it will be informative for those of you who may not have heard this presentation at the FDA's public meeting in the summer or were present yesterday. So, to do this I'd like to introduce Leah Stitz, an FDA Public Affairs Specialist in the Food and Cosmetic Information Center at CFSAN, who will be providing you a brief overview of this technology based in large part on FDA's experience with biologic products. Leah Stitz. [Applause]

Leah Stitz,
FDA Center for Food
Safety and Applied Nutrition

Thank you, Dr. Goldman and thank you for everyone in the audience who has chosen to participate today. I am going to give you a brief overview, this won't take a lot of your time. I'm going to provide this to you first with a schematic or a definition of animal cell culture food technology. It is referred to in the *Federal Register* notice for this meeting as “the controlled growth of animal cells from livestock, poultry, fish, and other animals, their subsequent differentiation into various cell types, and their collection and processing into food.”

Next, I have an overview, a schematic of the entire process from the cell procurement and qualification through to final post-harvest processing using traditional food processing techniques. Animal cell culture begins with tissue collection. You go to the live animal, you take a biopsy, you place the collected muscle or tissue in some type of solutions - such as Hank’s balance salts - to maintain physiological osmotic pressure and pH. Next, you liberate the cells from the tissue. In muscle, which is what I'm going to focus on for this presentation, you have to digest away the extracellular matrix to liberate the cells; to do so, enzyme treatment is typically used. The enzyme could be classically derived or recombinantly produced. If one desires to avoid the use of enzymes, there are other ways to liberate the cells. From these liberated cells, you're now selecting for the cells that are known as satellite cells or myoblasts. These are uninucleate cells that are capable of proliferating. Now you have a seed cell sample.

This seed sample can be possibly used for the establishment of master cell banks. Qualifying a master cell bank, usually 10 to 200 vials, involves quality control testing for the presence of viruses, bacteria, yeast, and mycoplasma, as well as cell line authentication. There are not many established master cell banks and cell lines for the animal species humans typically use for meat and poultry, so, we may only have a qualified vial of cells to begin.

Now we begin the proliferation phase where we multiply the cells. Cells

require growth factors, such as cytokines, hormones, and signaling molecules; nutrients, such as sugars, fats, minerals, amino acids, and vitamins; gases, such as oxygen and carbon dioxide, to grow. Cell culture media is a solution that contains nutrients, growth factors, pH buffers, and other components necessary to grow cellular structures. Currently, the primary cell culture media used contains fetal bovine serum. Serum-free formulas do exist for cell culture, but they are very expensive. We have read that firms working in this space have a heavy focus on research to eliminate the use of animal serum and create economical serum-free media. Currently, sourcing, sterilizing, and certification requirements for cell culture media are established for biomedicine use. It is hoped by the firms in the industry that the requirements for cell culture media use for food production will be focused on food safety requirements, rather than on biomedical requirements.

At this time, the technologies used for creation of food products from animal cell technology are on a laboratory scale, with cells being cultured in flasks or in small bioreactors. To optimize cell attachment, plasticware for cell culture is generally coded by the manufacturer, or if not, often by the end user. Choices include collagen, fibronectin, laminin, gelatin, or other extracellular components. Bioreactors for proliferation do not require cell attachment necessarily and will likely be stirred tank reactors, which are already developed and in use for things, such as vaccine production. Removal of cellular waste products is also an additional requirement during this phase.

Next, we move to the differentiation phase. In the differentiation phase, the cultured cells are now manually seated onto scaffolds and allowed to grow, differentiate, and mature. Firms that are working to commercialize these products are currently working on scale-up and automation of this phase, so that it will be viable on an industrial level. As in the proliferation phase, the cells still need nutrients, they still need gases, and they need growth factors. Now the growth factors are specifically selected for their role in helping the cells to differentiate. For most structured food product applications, scaffolding is required in order to grow the cells and have them adhere to each other in any sort of 3-D manner. Scaffolding and structural elements are additional areas of research and innovation and going forward we may see both animal and plant derived scaffolding used for these products. We anticipate that scaffolding may be developed through 3-D cell printing, recombinant microbes, hydrogels, or yet undiscovered structural elements. Because the scaffolding may be consumed as part of the product, depending on its function as a perhaps a bone, which likely wouln’t be eaten, or connective tissue, which could be eaten, the scaffolding material should be edible, low cost, and its components must be readily available. To achieve a product that's comparable to

conventional meat, cells also could be co-cultured and differentiated into a 3-D scaffolding structure. The scaffolding must allow nutrient media to profuse the structure, such that all cells continue to receive the nutrient media.

Mechanical differentiation factors are important to consider as well. Exercising the cells in some fashion may be required in order to impart the appropriate texture and protein content for the eventual food products. Industrial scale maturation bioreactor systems have not yet been developed and will require perfusion capability and mechanical differentiation capability. These bioreactors will have to be able to feed the cells, exercise the cells, remove waste products, and maintain pH and other critical factors to maintain a healthy and quality product with real-time quality control systems. For scalability, development, and implementation of this set of bioreactors is critical.

Another option is the creation of tissue type products with multiple cell types such as muscle, fat, and connective tissue cells through 3-D printing of the cells into a tissue-like biological material. Next, we move to the harvest phase. The biological material, whether it be clumps of cells tissues or tissue-like materials, will be harvested. Once the material is harvested and is no longer supported by its life-sustaining culture media, the cells will soon become non-viable. Following harvest, the material then enters the traditional food manufacturing, packaging, and labeling processes. This concludes my presentation. It's been a pleasure to share this material with you and I look forward to the rest of the meeting today and tomorrow. [Applause]

Selena Kremer,
USDA FSIS Moderator

Thank you, Leah. Can we have our next few speakers come forward. So, we're going to go ahead and start with Session One. If you're following along in the agenda, it's the Current Regulatory Safety Frameworks for Foods and Products of Cell Culture Technology. Our first speaker this morning is Dr. Phil Bronstein. He's an Executive Associate of Regulatory Operations in the Office of Field Operations at FSIS.

Phil Bronstein,
USDA FSIS OFO

Hello, everybody. As Selena said, my name is Phil Bronstein. I work for FSIS in the Office of Field Operations. I'm a microbiologist by training, and today I'll be talking to you a lot about what the current regulatory framework is for FSIS and what FSIS does on a day-to-day basis.

First of all, who are we? We are a public health agency in the USDA, responsible for ensuring that all meat, poultry, and processed egg products are safe, wholesome, and properly labeled for U.S. consumers.

We have several different acts that give us our authorities. The three acts that I want to focus on today are: The Federal Meat Inspection Act, which was passed in 1906, the Poultry Products Inspection Act, which was passed in 1957, and the Egg Products Inspection Act, which was passed in 1970. These are the three major acts that give us all the authorities to regulate products at FSIS-regulated establishments.

What do we actually do? For meat, poultry, and egg products we provided inspection of domestic manufacturing. We also conduct multiple laboratory analyses, both chemical and microbiological, and pathology for all the products that we produce. We carry out in-commerce surveillance through 150,000 commerce facilities. We conduct outbreak investigations and manage product recalls - if something has gone wrong. We also determine equivalency of foreign food safety systems and reinspect all products at the point-of-entry that come into the United States.

Overall, we have about 9,600 employees and around 7,000 of those are out in the field. There're about 6,400 establishments throughout the United States, in the Pacific Islands andPuerto Rico. We have inspectors that are in each one of these domestic establishments. We also have 133 import inspection houses that are on the borders of the of our country where all product that is exported to the United States - that is meat, poultry, and processed egg products - goes through these I-houses to get reinspection. As I said before, we also have 150,000 in-commerce facilities nationwide. I'll focus on those very quickly.

We actually have a whole office - the Office of Investigation, Enforcement and Audit – and we have about 150 employees in this office. In addition, to responding to outbreaks, natural disasters, and intentional contamination events, they carry our authorities to everywhere FSIS products are stored, transported, and available for in-commerce, along with FDA and the states, to make sure that after the product leaves FSIS-regulated establishments, that it continues to be safe, wholesome, and properly labeled.

For the rest of the talk I'm going to go ahead and talk mostly about the FSIS-regulated establishment and what we do there. At our regulated establishments, we have continuous inspection at slaughter and this is what most people think of when they think of a food safety inspection service at USDA, is our carcass-by-carcass inspection of all animals that are slaughtered in the United States, whether they are livestock or poultry. But we also do inspection once per shift in every establishment that process meat, poultry, and we have continuous inspection for egg products. Once again, we have a hundred percent reinspection for imported products.

What does that inspection actually look like in terms of numbers? Well, for antemortem inspection, the animals that are outside of our slaughter facilities before they enter, we inspect about 9.6 billion head of livestock and poultry a year and we're mostly looking for animal health and humane handling at this point. We want to make sure that all the animals that are going to be destined for the American table are healthy and wholesome and suitable for food products. At postmortem, so after the animals have been slaughtered and they're inside the facility at slaughter inspection, we do about a million food safety related tasks a year.

It's a hundred percent carcass-by-carcass inspection in livestock and poultry. So, what are those food safety tasks? We'll talk more about this in detail later but,they're slaughter HACCP -HACCP stands for Hazard Analysis and Critical Control Point - livestock zero tolerance verification, poultry zero tolerance verification, good commercial manufacturing practices, and for our new poultry inspection systems we're also doing our zero tolerance food safety verification checks. Who are these people that are doing all of this inspection?

There is about 7,000 people in FSIS that we have nationwide performing inspections. The first group I'll talk about are the food inspectors, which there are about 2,400. These are the folks that are actually what we consider online at slaughter facilities. They're the ones that are checking carcass-by-carcass. They're our first line of defense. They also are involved in looking at product handling, general sanitation of the facilities, and doing the antemortem and postmortem inspection. We also have about 3,800 Consumer Safety Inspectors and these folks have a little bit more advanced training. They go in both slaughter facilities and processing facilities and they are verifying establishment programs having to do with Sanitation Performance Standards, Sanitation Standard Operating Procedures, which for short is SSOPs, and Hazard Analysis and Critical Control Point plans, which I will go into more in detail. On top of that, we also have approximately 750 Public Health Veterinarians throughout the nation and these folks mostly focus on disposition of animals, but they also do analyses of the facilities and equipment. We use their scientific training to not only look at the facilities and the equipment, but also to communicate with the establishment personnel.

Finally, we have an Enforcement, Investigation and Analysis Officers (EIAO). We have about a 130 of these throughout the field. These are our folks that are the most highly trained for food safety and in the field and they go from establishment to establishment and look at their comprehensive food safety programs; making sure that they're working

as intended, making sure that there's no process deviations, making sure that overall the food safety system of every establishment is working as intended. They do this both on a routine and for cause, if we have any potential issues. In those cases, we will have an EIAO go out to an establishment and perform a food safety assessment. Then they also go to do other consumer protection activities, and very recently we've also been highlighting their outreach. They go into the establishments without an enforcement hat on and try to explain FSIS tenets of food safety and making sure that the establishments understand what FSIS expectations are and how they can comply with those. So, just to reiterate, we coordinate not only inspection activities, but all of these people I just talked about in the field are also doing enforcement activities. If they do see a problem, if they do have an issue with the establishment they talk to the establishment. They can start an enforcement action to correct anything that is happening that is wrong out there in the field. Overall, they ensure that the products that FSIS regulates are safe, wholesome, and properly labeled. I wanted to make that point here because I won't be talking about labeling in my talk today, but you will have two talks tomorrow about FSIS labeling requirements.

The EIAOs and others perform in-depth evaluations and analyses of the establishments HACCP systems and sanitation. Perhaps one of the most important other parts that they're doing is they're actually collecting data. Our food safety system is far from static. We're always looking for ways to improve. We're always looking for additional data so that we can modify and improve our inspection practices and our regulatory framework. We use our in-field inspectors to gather data, which they input into the Public Health Information System, which is a centralized database for FSIS. We use that data not only to look for trends in industry but to identify potential issues in establishments and throughout the nation, and also, we use the data to develop new policies and regulations.

What are the steps in becoming an FSIS-regulated establishment? The first thing you have to do is get a grant of inspection. There are several things that you have to do before you can get a grant of inspection. One of the first things required is you have to have demonstrate that you have Sanitation Performance Standards. We want to make sure that the environment that you're going to be producing FSIS-regulated products is going to make sure that the product does not become adulterated. We focus on conditions that may result in the adulteration of the products, such as making sure that they have a reliable source of potable water and make sure that that water is not contaminated, have an acceptable sewage system so that all the waste that's being produced at these establishments is carried away and doesn't result in

in incidental contamination. Looking at their sanitary operations, we want our plants to be clean and sanitary. To do that they will be using a lot of chemicals, they need to demonstrate not only that they know how to clean the environment, but also that these chemicals are safe for their employees and our employees. Also, the establishment must have minimum: four walls, a roof, sufficient light, and receptacles for identified inedible and edible products. Because, the last thing we want someone to do is combine the two of those.

The next thing that they must demonstrate, is that they have Sanitation Standard Operating Procedures or SSOPs. Before the plant starts operations, they need to make sure that these are written. We want to see the plan. They have to have a plan that has written procedures that that outline what's going to be performed daily - before and after operations. To make sure that we keep their establishments clean and sanitary, we also want to see them to see that they have identified procedures to verify the sanitation on the food contact surface, equipment, and any utensils that may come in contact with the food. Also, specify the frequency and identify the personnel that are responsible.

Once the establishment has started and - I'll jump around a little bit but - what our people are doing is verifying that the SSOPs are being performed by the establishment. They're going to be conducting pre-operational procedures for SSOPs. Our folks will be around looking before production starts at the beginning of the day. If they see any sanitation problems or any deviations from the establishments written procedures, they can stop production until corrective actions are taken. They're going to make sure that the procedures that the establishment laid out are done at the proper frequency and are implemented properly, and if there are any issues, they're going to make sure that the establishments are taking the appropriate corrective actions to make sure that it doesn't happen again, and to ensure a safe and wholesome product. The last part of the of our food safety system for FSIS is the HACCP plan, the Hazard Analysis and Critical Control Point plan.

These requirements are laid out in 9 CFR 417 and you must have several components. One is a hazard analysis, one is the plan itself, and then the other requirement in 9 CFR 417 is that these records must be written and available to inspection personnel upon request. This is really important because you can't be everywhere in an establishment at all times. We want to make sure they have proper records so that we can check and see their records, as well as what they've been doing in all the in all the areas we can't be. Then, perhaps the most important part of all this, the HACCP system must be validated. It's great to have a system in theory; we want to see how it how it actually works out in

practice at the specific establishment.

So, what are the seven designing principles of FSIS HACCP plans? The first one is to conduct a hazard analysis. This can be biological, chemical, or physical hazards, so it may include pathogens or other bacteria that are associated with the products. It could be chemical residues from hormones or pesticides. We need to understand how the establishment, if the establishment thinks that there is a hazard reasonably likely to occur, and also physical hazards. There are many times when there are physical hazards, either through the process itself or pieces of metal or plastic can be introduced, we need to have the establishment consider all of those things and tell us where they think the hazards are reasonably likely to occur. For every hazard that they have found that is reasonably likely to occur, they need to determine how they're going to mitigate that hazard. Where are their critical control points, and at those critical control points, what are the actual critical limits that they need to meet, to make sure at that control point they are effectively managing that hazard? After that, we also want to see monitoring procedures.

It doesn't do any good to set a limit and never check to see if you're hitting that limit. We need to see how often and how you are going to be monitoring your critical limits. What happens if there is a deviation? If your spray cabinet stops working, or your x-ray machine goes down, or you do get a deviation in the process, what are you going to do to that product that is subject to that deviation, and how are you going to implement something new to make sure it doesn't happen again?

Finally, for the first of the seven, is the establishment of record-keeping and documentation procedures which is key to the HACCP principle and our inspection system. The very last one is to establish a verification procedure. We give our establishments 90 days to validate their HACCP plans once they start operating. The idea is that, we have a wonderful HACCP system, which has technical and scientific support for every critical control point and critical limit that we've set, and we need to make sure that the establishment can actually achieve that on a day-to-day basis when they're operating. What we ask the establishments to do is run for 90 days, collect data, look at their production data - which can include their HACCP documents, their critical decision-making documents for the CCP's, their critical operational parameter logs in the initial equipment setup, calibration documents, and any sampling results for their product or the process of interest. What we expect them to do is to put that together and demonstrate to FSIS that they can execute their HACCP system as designed and written in their written documents. FSIS personnel also will verify that those procedures and validation is appropriate. We haven't done this just for products, such

as meat and poultry, we also have recently implemented and applied the same FSIS regulations to Siluriformes establishments, or as we say in the United States typically, catfish.

For our Siluriformes, we've fully implemented this about a year ago. After an 18-month transition from FDA to FSIS, we have taken jurisdiction over all domestic establishments that produce catfish, or Siluriformes, and importing countries - countries that export to us - Siluriformes products, such as basa, tra, and swai into the United States. We've integrated about 110 domestic establishments, and at this point we still have three countries that export Siluriformes into the United States. Building on that point, we actually have in addition to those three countries there are 36 other countries that export about 4.1 billion pounds of product into the United States a year that is regulated by FSIS, and as I said previously, FSIS conducts a hundred percent inspection of all of that product at the point-of-entry.

There are many points-of-entry into the United States. Over 300 that CBP has identified and all of that product needs to be funneled into 133 I-houses, our inspection import houses, that FSIS has personnel at. We do 100% reinspection of all the product that comes in that includes looking at their certificate, the health certificate for that product, looking at the condition of container, and other frequency we will actually do laboratory testing to look for speciation, chemical residues, microbiological hazards, or any other thing. This is an important part of our equivalence process.

What is our equivalence process? FSIS has a relatively unique equivalence process. It has three different steps to it, and FSIS equivalence is a country-to-country equivalence process. What we're doing, what we ask countries that want to export products to the United States to do is to demonstrate that they have a food safety system that offers equivalent level of protection to the U.S. consumer that FSIS' food safety system offers for meat, poultry, and processed egg products. The first step of this is a document review. We ask the Central Competent Authority in the foreign government to send us all their regulations, training documents, guidance documents, all the written pieces of information that we can review, that show that they have a food safety system that is robust as FSIS'.

If after looking at these documents, we determine that that on paper they look equivalent, then we will send out on-site audits to the foreign countries and look at their food safety system in practice. Once again, it's great to have something on a piece of paper, we really want to see it in action, so we're going to go out there to the establishments, we go to their lab, we'll go to the foreign countries' labs, we'll go to there the

Central Competent Authority's government offices, we will do a records review, we will walk around with their inspectors, and we'll see if they are actually implementing their food safety system the way they told us they implement their food safety systems through the document review for products that are being exported to the United States, not necessarily all the products, but definitely the ones that are being exported to the United States. If the on-site audit gives us confidence that they are performing as they have written, and they have an equivalent level of protection for the products that are being exported to the U.S., then we will grant them equivalency, but the process doesn't end there. Just like we do in our establishments, we actually are going to be verifying - continually verifying that establishments and foreign countries are meeting the marks that they have laid out. We do, as I said before, the port-of-entry re-inspection for all the product that comes down as a final step and a final check in the equivalence process. In addition to that, we also do export certification. We have about 15 billion pounds of meat, poultry, and processed egg products that are shipped out of the United States to the rest of the world, and we actually provide health certificates for all of that product, to ensure anyone who is receiving that product throughout the world, that it is safe, wholesome, and properly labeled and up to FSIS standards.

We have a lot of a lot of folks, as I said before, think of FSIS at a slaughter facility and actually a majority of our work is not at slaughter facilities. We have around 6,400 establishments, 4,300 of them are processing only, meaning that they are taking the products that are derived from the carcasses and then further processing them. Of these, about 1,200 of them are dual jurisdiction with FDA. We already work very closely with FDA in the inspection space. These further processors are actually very complex food processing systems, which include canning, irradiation, high pressure processing, fermenting, enzyme-based processing, and advanced meat recovery. As a matter of fact, the technology in these establishments is always evolving at a very high pace. I've seen establishments that have lasers that graph out the size of the piece of meat and then air saws or water saws that will cut the designated size and shape of those products as they pass through a completely automated line. It's very impressive and FSIS has had to develop special processes to keep up with these process innovations.

In our Office of Policy and Program Development, we have a whole new technology review process, so we actually take a multidisciplinary approach with teams of microbiologists, toxicologists, chemists, biologists, meat scientists, etc. and we have a team here at FSIS that looks at every new submission. So, if an establishment wants to use a new machine, a new process, or a new intervention to control a hazard, they first must submit a package to FSIS. We take that package, if it's a

chemical or has other processes it usually goes through FDA prior and then FDA will pass the information on to us. If it's a chemical that is generally regarded as safe, then we're looking for suitability in that case. But in any case, we look at all the submissions from our industry, we make sure that it is going to be a safe and effective for our personnel, their personnel, and the consumer, any of their processes we do a technical review, and if it meets our standards for suitability and an establishment will produce a no objection letter, which means that it can now implement, with specific parameters, any of these new technologies into a processing establishment. Once again, that becomes part of their HACCP plan. We expect if it's going to be a large deviation from what's normally done, that they're going to have new critical control points and critical limits, and that they're going to need to look at and that we will verify.

I've outlined overall our very robust inspection and enforcement process, but mistakes do happen. We are always looking in our regulated establishments and in-commerce for any things that may have gone wrong. If we do identify a problem, we'll initiate an investigation, and if we do find that product that may have been adulterated has entered into commerce, we will take action. The first thing we do if we decided the product's adulterated is we ask the firm to do voluntary recall the product. If the firm does refuse to do that, we can move to cease and detain in-commerce to make sure that no adulterated product is available for human consumption out there. We're always investigating, as you can see from this slide, there's about 572 recalls of approximately 133 million pounds over the last five years or so that FSIS has recalled. A majority these are from undeclared allergens and this is actually a direct result of our inspection force going in there looking at records, production records, ingredient lists, sanitation records, a lot of times what actually happens is there's not great sanitation between products that are being produced with an allergen followed by production of products that are declared allergen free. We are constantly looking and making sure that all the product that comes out of our establishments are safe and wholesome.

In closing, I just wanted to let you know, that we are a science-based, data-driven organization and we're always looking for ways to improve and integrate new technologies, and looking for ways to ensure that the over 127 billion pounds of meat, poultry, and processed egg products that pass through the FSIS-regulated system are safe, wholesome, and properly labeled -- not only for the United States consumer, but the consumers of U.S. products throughout the world. Thank you.

Selena Kremer,
USDA FSIS Moderator

Thank you, Phil. I'm going to go ahead and introduce our next three

speakers. They're from the FDA's Center for Food Safety and Applied Nutrition. Dr. William Jones, he's the Acting Director of the Office of Food Safety, Dr. Jeremiah Fasano, Consumer Safety Officer in the Division of Biotechnology and GRAS Notice Review in the Office of Food Additive Safety, and Mr. Douglas Stern, Deputy Director for Regulatory Affairs. Dr. Jones.

William Jones,
FDA Office of Food Safety

Thank you, Dr. Kremer. Good morning. I'm going to spend a few minutes introducing the overall regulatory framework for food safety at FDA and providing a brief overview of some significant aspects of the Food Safety Modernization Act.

First, let's define our terms. Food is defined as anything used for food or drink as well as anything that is a component of something used for food or drink; chewing gum, which gets its own list entry is also included in that definition. You'll notice that the food and drink can be consumed by humans or by animals. Today we're going to be focusing on human consumption. The Federal Food Drug and Cosmetic Act sets out requirements for the safety of food. There are a number of conditions that could make a food unsafe or adulterated, and therefore, unlawful.

First and foremost, if food contains a poisonous or deleterious substance, which could be harmful, that food is adulterated. The Act differentiates between poisonous and deleterious substances that are added to food and those that happen to be present in food. For those that happen to be present, which are not uncommon in food, the requirement is that the level be low enough that it wouldn't ordinarily be harmful. Plants are a good example of this. Many plants naturally make toxic substances which protect them from being attacked by insects, mold, or other pests. At some level, those substances would be harmful to humans. However, in agricultural crop varieties while the substances may still be present and detectable, their concentrations are far too low to raise any food safety concerns.

Two other key conditions relate to food additives and insanitary conditions. First, if you add an unsafe food additive to food, you would adulterate that food and render it unsafe. We'll talk more about food additives later, but essentially this means anything you add to food must either be approved by FDA as safe for that use or must meet certain criteria that exempt it from the FDA approval requirements.

Finally, if a food is being made, packaged, or stored under conditions that would lead to contamination, such as microbial contamination, or would otherwise lead to that food becoming harmful for consumption

in some way, then the food is adulterated, unsafe, and unlawful. There are other adulteration provisions, but this gives a sense of the overall framework. The recent Food Safety Modernization Act increases FDA's focus on preventing food safety problems, rather than reacting to them. The law also provides FDA with new enforcement authorities that are designed to reinforce compliance with prevention-based and risk-based safety standards. In addition, the law gives FDA important new tools to hold imported foods to the same standards as domestic foods.

One key component of FSMA focuses on hazard analysis and risk-based controls. As section 118 of the Act says, this is about preventive controls, which are the cornerstone of the modernized approach under FSMA. The effective controls of this type are informed by hazard analysis of each facility's manufacturing processes and matched to the risks identified during that analysis. Each facility is required to develop a food safety plan incorporating these elements. The implementation regulation is found in title 21 part 117 of the Code of Federal Regulations, which also updates the Current Good Manufacturing Practices or CGMPs. This requires a written food safety plan with several required elements.

First, there's the hazard analysis, which should include known or reasonably foreseeable hazards of all types, including biological, chemical, and physical hazards. Second, appropriate preventive controls of various types should address hazards identified during the analysis. Based on the level of risk associated with each of them, the plan should also include steps to oversee and manage the controls including how to monitor them, correct any issues that arise, and verify the effectiveness of the corrections. Records must also be kept, and for manufacturers and processors, the plan must also address the facility's supply chain if relevant hazards are identified there during the hazard analysis. Finally, the plan also needs to include recall procedures that could be used effectively in the event a recall should ever become necessary.

Finally, I'd like to identify a few questions that are a good starting place when considering a new food production process for implementation in a manufacturing facility. First, what hazards are identified during the analysis phase of developing the food safety plan? Second, what preventive controls are defined by the plan? Do they cover all hazards associated with applicable risk, and are they sufficient to control the identified risks? Also, what substances are being used in production? Are all substances safe and lawful for their intended use? This is just a brief and quite broad overview of FDA's regulatory framework for food safety. As you can see, there there's a lot to think about, but these basic questions may be a good place to start. Thank you and I will now turn the podium over to Jeremiah Fasano. [Applause]

Jeremiah Fasano,
FDA Office of Food Additive Safety

Thank you. So, now I'd like to spend a little time talking about food ingredients. It's sort of inescapable when you're considering food safety. Next slide please. So, the definition of food ingredients is actually fairly broad. If you look at this as any substance, the intended use of which results into becoming a component of food, reasonably expected to become a component of food, or otherwise affecting the properties of food. It's a very expansive, inclusive definition. You'll see in the last part of the slide, there's even things that come into contact during packaging, processing, handling those are all technically included in the food ingredient definition.

So, it's true that many of these things may not have much practical impact on the properties of the food, but as a starting point for analysis, it's always worth considering the expansiveness of this definition. You've already heard from Bill about the standard of safety for substances that are constituents of food and at levels not ordinarily injurious. The standard of safety for substances that you deliberately add to food is reasonable certainty of no harm in the minds of competent scientists that the intended use is safe. That is a not an absolute safety definition. It is a definition based on reasonable certainty by qualified scientists.

How does that actually get put into practice? Identity and exposure are a critical factor in considering this both exposure to the substance itself as well as to metabolites that might be produced after consumption, came out of exposure to this and related substances in the diet. Relevant properties of the substance are also very important. We have a lot of tools now that can actually allow us to infer information about the properties of the substance before we even begin to do studies, whether it's from quantitative structure activity relationships, other kinds of read-across tools, various kinds of pharmacokinetic modeling information we have about interactions with ligands, especially those that are in the body. That's all very important information in figuring out what is the appropriate data in order to reach reasonable certainty of no harm, and this is going to depend a great deal on both the intended use of the substance and on the properties of the substance. In terms of how this works out in practice at CFSAN, there's three broad categories of substances that we think about and from a regulatory perspective.

First, there's food and color additives, so these are substances, which require approval by FDA, before you can use them in food and it's done

by a rule making process and all the rules are published in the *Federal Register*. Another kind of substance that we would consider a food additive but that is exempt from this requirement, it's authorized in a different way through a notification process, these are food contact substances, or substances from packaging or other materials, that might migrate into food. We have an inventory of those that we maintain. Companies can notify us, and we assess those as well.

Then finally, there's GRAS ingredient uses. This is another exemption from the food additive approval requirement, and the way that you get this exemption is to demonstrate that not only is there evidence showing that your intended use is safe, and its appropriate data, that evidence also has to be publicly available and you have to show that there is an expert consensus that the data shows the safety of the intended use. In that case, you don't need authorization from FDA because you've essentially already shown that the scientific community is on board with the view that that intended use of that substance is safe. But, in all cases, although there's a lot of variation in the kinds of data that you end up needing, depending on the properties of the substance and the intended use, this quantity and quality of data is the same regardless of which of these regulatory boxes you're in, it's just sort of the context in which it's presented that can differ.

Another thing to think about when you're thinking about ingredient safety, is changes in the manufacturing process. It's often easy to focus on the process for producing a food or food ingredient, but in terms of the lens we look at for ingredient safety assessment, we're really thinking about the properties of the food and the process is important to the extent that it affects those properties. That's what's really going to matter for the safety assessment. It's important to understand the potential impact on the properties that are relevant for safety. This is also another important point, that when you change a production process, you can change many properties of the food. The first part of the analysis is to identify those differences, but the next part is to think about which ones are actually going to be relevant for safety assessment, and then if you have identified changes, what information is needed to sort of rebuild the safety case depending on those change properties.

Next, I'm going to put this in more concrete terms and talk about a few examples from past experience. These are for various kinds of ingredients that are produced to biological production platforms. These are sort of an interesting variety of methods of manufacture. For these there's often a lot of variability in the process and so I thought it might be interesting to hear a little bit about how we had dealt with some of these. The three broad classes of substances are substances produced

by cultured cells, the cultured cells themselves, and then also new plant variety is produced by modern biotechnology. Substances produced by cultured cells have a fairly long history as food ingredients.

The canonical original example is the discovery that fungi actually secrete enzymes into the culture medium and you can recover those and use them for various purposes, including in food technology. This has all been later expanded to recovery of many other kinds of substances that were secreted from cells and culture, but enzymes are the starting one. We also have looked at a number of oils produced by cultured algal cells. They recover the oil that is produced by the cells, whether by processing of the cells, or in some cases, secretion. Then finally, this is a technique that's very common in the therapeutic space and industrial settings, but it's also common in food production as well, is the use of cultured cells as a production platform for transgenic proteins.

You can design your protein of interest, you can put it in a production platform, such as a microbrew yeast, and then recover that protein for use as a food ingredient. These are all examples of substances we've looked at produced by cultured cells. In general, you know you're looking to make sure that there's no unwanted metabolites that are produced by the production platform, and also that there's no microbial contamination of any kind. In addition to looking at cultured cells as a production platform, we've also looked at the cells themselves as direct ingredients, and we've looked at a variety of different kinds of cell types, including bacterial, algal, and fungal cells. The bacterial cells, I mean yogurt is the most obvious example of this, but there are many other instances in which people have generated bacterial cells and culture and then use them as direct ingredients in food. We've seen a number of those through our GRAS notification program. We've also seen some algal cells grown up in culture - in sort of suspension culture in a tank, and then harvested and used as a direct food ingredient. Then finally, fungal cells. Yeast is, again, the most obvious example, but we've also seen other kinds of fungi grown up in culture and then collected and used as a protein source, and in these cases the selection of the cell is an important consideration. You want to make sure you have the appropriate cell that will grow well, that it won't produce any metabolites of concern, and again of course, microbial contamination is an issue.

Then finally, this is a slightly different case, but it's an interesting illustration of thinking about using biological processes as a production platform for food. We've been looking at plants produced through modern biotechnology, new varieties, for over 20 years, and it's raised a number of interesting challenges that I feel like we've been successfully

able to address. The underlying technologies used to generate these new plant varieties have evolved over time. New technologies have been introduced, but the lens that we use to look at this is essentially to ask what substances are being added to the food, what changes in the properties of the food itself have resulted, and to what extent are those changes material for safety or nutritional concerns. Using that sort of framework to think about this, we've been able to deal with new plant varieties from a wide variety of underlying techniques for developing each variety. This has served us pretty well over that time, and you know some of the things that we encounter, which perhaps we'll return to a little bit later, are the questions of what are some of the fundamental characteristics of food from a plant? What can you expect in terms of key nutrients and other compositional properties? And, if you have introduced something new, does that raise any concerns from a regulatory perspective as a food ingredient?

In general, these are complex systems, and it is reasonable to ask to what extent when you're using these as ways of producing food, “how consistent can you be?, “how much control can you have over the process?” Our observation has been, there are often questions to ask when you're looking at a new production process, but it is possible to adequately characterize the food product with respect to key properties that would matter for safety or other material concerns, and to consistently produce these products in a way that all issues can be addressed before market entry.

I'll just close by reiterating something from our 2014 guidance on new manufacturing processes for ingredients, and just say that again, it's easy to have your focus drawn closely to a new production technology and often it is very interesting, and there's a lot of interesting issues to consider, but fundamentally it really comes back to the properties of the substance. Any predictable impacts on the properties of the substance that may come from the production process, and again, when you change those properties what relevance do they have for safety or other material concerns? Thank you. So, with that, I'll turn it over to our Deputy Director for Regulatory Affairs, Douglas Stern. [Applause]

Douglas Stern, FDA

Good morning. My name is Douglas Stern, and I'm going to speak a little bit about FDA's approaches related to this these areas that have been addressed and how we seek to do our job. FDA has a number of different responsibilities we'll get to in a minute, but we try to focus always on prevention as our goal, oriented by our mission, that is to prevent food safety hazards and other hazards before they arise, and we have various ways of doing that. There's a focus on inspection, which I'm going to get to. Inspection and compliance, which we do, and

we have certain actions that are outputs that are very visible. Those include some traditional enforcement actions, which include seizing product enjoining firms, that is ordering firms to follow a certain protocol or do certain things, prosecution, which is my first calling, and also there's other actions the agency takes that may be administrative, that may stop a company from doing particular actions.

Those are things that people focus on, but I think it's I'd like to step back a little bit and talk about our overall responsibilities and how they fit within FDA. FDA has huge responsibilities, we have more than 88,000 FDA registered domestic food facilities, more than 200,000 foreign foods facilities, that's the vast majority of the food supply is something that falls within FDA's responsibilities. We also have responsibilities, as Dr. Gottlieb mentioned, for all medical products, including all drugs, medical devices, and biologics -- all of which have a dizzying array of products, many of which are constantly innovating, especially today. We're really on the cusp of an environment where things are changing incredibly quickly, and a lot of that is being driven by technology, personalized medicine, and so we're seeing a lot of change in all those areas. We're starting to see more change in the food area as well. This is one example of that. We also have a very large import program. FDA has more than 40 million different product lines entering the country that it’s responsible for.

The question is, how do we do that? It's a very challenging mission, and what we do is we really focus on a systemic approach that is risk-based and founded in science. It's very important to think about these things. We believe systemically and focus on where the risk is. We believe in a lot of the traditional measures, which I came back to earlier, they are measures that check that system. Inspections and testing check that system, and our inspections and testing are risk-based, meaning that we adjust them up or down based on the risk, and as Dr. Jones and Dr. Fasano mentioned, there's particular ways in which we sort of flag that risk based on how we analyze what the product is and what the issues may be. We have different inspection frequencies within surveillance. We also will direct inspections where there's more of an issue, for whatever reason, and the depth may vary based on that as well, and our product sampling also is adjusted by risk, which we do both import and domestic. This systems-based approach is really embodied within the preventive controls rule, which would be the rule that would be applicable here, and this is similar to a lot of the thinking that's gone on broadly within quality thinking over a long period of time.

Preventive controls focus on a number of things. You have to have a sanitation control program that avoids cross contamination, that assures that you're sanitizing and cleaning your equipment, that you

have an appropriate environmental monitoring program - where warranted, and that you have an allergen control program that cleans the sanitizes equipment, avoids cross contact, has controls for labeling, you have to control your process - in terms of temperature controls, pH, and formulation, and we also have a lot of emphasis, and this is true for as Dr. Fasano mentioned, for ingredient control. A lot of products that we regulate have ingredients that go through multiple steps, so it's important to have supplier approval, receipt of incoming raw materials, and to verify. This is key - to verify - that whatever is coming into the plant had the same level of control that you would expect within the plan itself. We want to make sure that there is an appropriate safety approach to ingredients, as well as what's done at the finished product step, and all that should be in your food safety plan, which Dr. Jones mentioned. Part of that is to have a system to assure you've analyzed your hazards and you have a system and that under our approach you also should have procedures that are in line with a Good Manufacturing Practice, that's that acronym GMP, and these are modernized to make them flexible. I'm going to come back in a little bit to that.

I want to mention just a little bit about this systems-based approach, and what does it mean, and why did we get here. Inspections and testing are really good things to have. They're very appropriate. They check the system and we rely upon them and we believe in relying upon them. There’re also some limits to them. One is, depending on the hazard we have to make sure that we are looking at the right thing. There’re tests for a particular thing, and if you're doing an inspection, you may be focused on a particular thing. It's important that, within whatever approach that you have, it's focused at the right step. It's also important to try to fix and prevent. This goes back to the principle of prevention. To prevent issues before they arise, and that's why it's important to have an appropriate hazard analysis design a system that checks, executes, monitors, and remediates issues throughout. We really want to put a focus on that. These inspections and testing really are ways to check that. They also can be imperfect. Contamination is not uniform, so sometimes contamination is in one place and it's not in another. Sometimes there's a practice that is problematic. It's in one place, but it's not in another. Sometimes when we look, we can miss, and that is one of the reasons that we want to try to make sure that we put more resources where there's a greater risk, and that there's an analysis that advises us, in terms of that checking, as to where it goes. In terms of that generally, sometimes that's talking about building quality in. You may have heard that concept or continuous improvement. The idea is that we want to encourage companies to self-monitor, and then we check and oversee what they're doing. Within the medical approach, something that is usually referred to as a quality system, we have had some experience with that, and it poses some special issues related to

product innovation. As products change - and sometimes they change very frequently in certain areas - it poses certain challenges. Does the firm really understand what the risks are? Does whatever component that it's checking, whether that be a quality control unit within a facility or whether that be in outside agencies, such as ourselves or anyone else, do they understand what the issues are and can focus on it?

Sometimes if something is new, the risk can be underappreciated or over-appreciated. We've seen some products where there are things that emerge over time that we see as issues that are not fully understood initially. That's one of the reasons that we think it's important to sort of focus on that design approach and having a scientific understanding about what the plan is, and then have a plan to monitor that and remediate that, and that was mentioned to some degree in Dr. Fasano's comments. We do want to try to have an approach that accounts for that and also, we also want to be able to allow for changes in process, as if things are in an area where they're innovating quickly. There are ways that can be adjusted so that the product manufacturing may be more efficient or may be made even safer. If there are rules that stand in the way we have to be cognizant of that possibility and to try to use our authority tomake sure that we are doing things in a way that makes them safer, and as efficient as possible.

Our approach is to try to construct a system-based on oversight. If we have the plan, you can look at that plan we also want to look at your procedures and look at those procedures in line with what current Good Manufacturing Practice is, as well as outside indicators. Outside indicators may be, do we know if something is happening outside of that facility that might inform where we think a risk might be. That might be based on science, it might be based on outside sampling results, it might be based on something else, but we try to do that so that when we go into a facility and we are looking at that we can determine, "is this plan functioning in the way that it's intended to?" Then, our approach is adjusted, as I mentioned, by risk in terms of, how deep that look is going to be, how frequent. We have different levels of frequency depending on the issue, and then also by specialty. We have certain product experts in our field inspection that would come into a particular facility, depending on what the issue is.

FDA has a large laboratory capacity. We have 13 field laboratories in the United States and Puerto Rico, 8 of those focus on food issues, human and animal food, all of those are ISO certified. Among the types of testing we do, our detection of foodborne pathogens, veterinary drugs, pesticide, nutritional composition, and environmental contamination, including heavy metals. We also have facilities that work on method

development and other issues that are trying to improve our laboratory capacity and understanding in order to do the appropriate types of testing.

We have a wide import portfolio. We have a general principle that food from abroad must be as safe as domestic food under the Foreign Supplier Verification Program. Importers are responsible for ensuring that their foreign suppliers have adequate preventative controls in place. It's also true for ingredients under the preventative controls rule. FDA does thousands of foreign inspections, so we do have a considerable foreign inspection program, while at the same time we rely on coordination with other regulatory bodies. We have certain powers within FSMA that are important, in terms of mandating certification for high-risk foods. We have an expedited review system that we are building for certain importers that meet certain standards and have third-party audits, that have been accredited by FDA, and we can deny entry if access for inspection is denied. We do have 100% electronic verification. Part of our system is to check all the different products coming in have met all of the requirements they should require, given their type, and also it has triggers or flags within our system whether they are an apparent risk, so we are going to look wherever there's cause to believe or, in many cases, to suspect that there might be an issue. We have a risk-based approach there as well. Those are the approaches that we do for trying to make sure that there's a surveillance approach and that surveillance approach, and those outward actions, that I mentioned, are key back to our overall goal of prevention, that's our core goal. Our mission is to make sure that we do the best for the American people, to make sure that all food is safe. With that, I'm finished. Thank you.

Selena Kremer,
USDA FSIS Moderator

Thank you, Mr. Stern, and I'd also like to thank all of our speakers this morning. It's been great hearing from everyone and I hope you've already started to glean a lot of important information. We're going to go ahead and we're going to take a break right now. We're going to meet again in here at 10:20 sharp and get started. There are restrooms in Wing 4 and Wing 5, and make sure you have your passes with you, so you can move freely about those wings. You also can find the USDA cafeteria in Wing 3, but please note that food and drink are not allowed here in the Jefferson Auditorium. So, let's meet again at 10:20.

Selena Kremer,
USDA FSIS Moderator

Let's go ahead and get started with our next session. If everyone could please take their seats. Thanks for coming back. We're going to go ahead and get started with Session 2. We're going to talk about

potential hazards for cell culture technology products derived from livestock and poultry. Our first speaker today is Dr. Emilio Esteban, Chief Scientist in the Office of Public Health Science here at FSIS. Emilio.

Dr. Emilio Esteban,
USDA FSIS Chief Scientist

. Thank you for coming this morning. I'm just going to spend a few minutes giving you a big picture of what we do in the way of hazards and how we identify them and how we deal with them. If you walk away with anything today, I would like for you to walk away with the five concepts of how we deal with hazards in FSIS.

First point, and you heard this before from Phil Bronstein, we have continuous on-site inspection. There may be 6,000 establishments, but we are there every single day. The food is not produced unless there's a presence from FSIS in that place. We have continuous inspection, point one to remember. Point two, everything we do in the agency with drafting policy, taking enforcement action, monitoring something, everything we do is always science-based and the objective is to protect public health. There're three labs, and I am going to elaborate on what those three labs do in the next few slides. I'm moving on to the third bullet which is "Flexible."

We may be addressing a series of hazards, but we have the flexibility and the throughput in our labs to adjust depending of the hazards that are identified, and we do those things both in the micro, in the chemistry world, and physical things. As hazards occur in the environment where they defy something different, something new, we can adjust on the fly and keep going. The fourth point, everything we do is with full transparency, and by that, I mean, if we're going to use a new method, we publish it online 30 days before we start using it so you know what we're going to test for and how we're going to test for it, in case you want to do something ahead of time. That works also on the other side. When we collect the data, that is also be made public as soon as possible. So, it's transparency on the inputs and on the outputs. The last point is that we have ongoing monitoring programs, both for measuring trends in the environment, as well as for outbreak response or for emergency situations. These five bullets: continuous inspection, science lead decision-making, flexible, full transparency, and ongoing monitoring. Those five things, keep in mind, when you're working with hazards in FSIS.

How will we prevent illness? We have these four modules, if you will. The first one is, we perform inspection at every plant nationwide, and this includes, as you heard this morning, import and domestic product. The second module is, the second box to the left, we maximize interests and comply with food safety policies by looking at the labeling.

Everything has to be properly labeled and documented before we actually let it go into commerce.

The next one, we feel this is a team effort. Achieving food safety in public health is a team effort. We have a significant outreach effort through public health education of consumers, so that would cover not only those who are producing, it also considers who is consuming it. Finally, we collaborate with internal and external stakeholders. We're not going to do this alone. Our process is based on trust, but we verify. We work with industry, work with consumer groups, we cover the whole gamut from the farm to the fork, and from the people that produce the food to the people that consume the food. As I said before, we have on-site inspection every single day.

Our three laboratories - and we have one in Athens, Georgia, one in St. Louis, Missouri, one in Albany, California - we receive about 100,000 samples in those three labs. About 90,000 of those are microbiology, the other 10,000 are for residue chemistry. We actually do everything in real-time. When you get into one of our labs in the morning, and in the afternoon, you get a FedEx truck, and the whole FedEx truck is boxes of our samples coming in. Everything is barcode labeled. All three labs are ISO 17025 accredited. So, everything is it based on high-throughput lab.

We monitor current and emerging foodborne trends and we advise leadership on matters that have to do with science, so they can draft proper policies. These are the locations of the labs. The one thing I wanted to highlight from this slide is the last bullet, which is, when we have an isolate coming into one of our labs, it could be an isolate or it could be a sample. If it's a sample, we isolate something from that sample. We take it all the way to the end. We characterize that organism to its fullest, and I will go into details as to what this means in the next few slides. We have six groups of potential targets that we look at: microbiological, chemical, physical, emergent issues, things that come up in the environment, allergies, and identity. We have the capability and the capacity in our labs to test for these six groups of potential hazards.

For micro, like I said before, we tested about 80,000 samples last year. This year we have 89,000 samples that came in for microbiological work. We have three types of plants: large, small, and very small. On average, large plants sample once a week, the small plants sample every other week, and the very small plants sample at least four times a year or when they are in production. The point about that is, that we actually collect samples at every plant, and this is a key concept, we do samples to verify that the plant’s HACCP is under control. Our samples are verification that the HACCP system is operational. So, there are

verification samples, when we get an isolate from a sample that comes to one of our labs, we do the screening. We screen for all the pathogens that we're looking for. If we get any pathogen out of those samples, we do serotype, anti-microbial resistance, whole genome sequencing, pulse field gel electrophoresis. Everything is done in real-time and everything is publicly available through FOIA, except for the whole-genome-sequencing, which goes directly into NCBI at a public database. Like I said before, it is real-time and it's full transparency. On those 89,000 samples, last year in 2017, and 2018 was about the same, we got about close to 150,000 different tests samples. When it comes to the lab, we don't only test it for one target, we tested for multiple targets. For example, ground beef can be tested for multiple things *Salmonella, E. coli,* STEC (Shiga toxin-producing *E. coli*), for example, we look at these four major pathogens *E. coli* O157 and the other top six STEC, *Campylobacter, Salmonella,* and *Listeria monocytogenes,* and of course, we cover raw and cooked beef, pork, poultry, egg, and Siluriformes, which is catfish.

This slide is dedicated to just *Listeria,* because for the study, we consider this one of the environmental contaminants that may be relevant when you look at cellular agriculture. For *Listeria*, we have sampling programs that include not only sampling the product for contamination, but it includes surface sampling and environmental sampling at those establishments. We have ongoing programs that right now that we have historical data, going back for at least 8 years, we know if we ever have one of the *Listeria* isolates in that plant, we can trace it back up to 8 years, if it's still present in that plant. For harborage purposes, I think that it is going to be really relevant when we look at going forward to this type of production that we're discussing here today, where there may be environmental contamination.

This is the only slide that I have that has actual data. It's just to show you that in the graph to your left, the orange one, you see a slightly downward trend for comminuted chicken - ground chicken - on the left, both for *Campylobacter* and for *Salmonella* there's been a slowdownward trend. The one on the right, the same thing but for beef and beef trim for *Salmonella.* One point that is not present, but I would like to highlight is this, as we go through the years 2014, 2015, 2016 and you can see that that downward trend, consider the fact that not only is it trend going down, but the fact is that we're getting better at finding these organisms. Even though we get better at finding them, it's still going down. Which is a good thing for industry and for us to know. It is better protective of public health. We have lower contamination rates, even though we're looking at it with more detail.

The second group of hazards we're looking at is chemical hazards, and

for those, FSIS does not set standards. We enforce the standards that are set by FDA for veterinary drugs. Every sample that comes into the lab, again we have a scheduled sampling program for 6,000 - 7,000 samples, gets tested for up to 200 different compounds, 90 of which come from a single method that's called the multi-residue method. It tests for antibiotics, antifungal, anthelminthic, synthetic drugs, beta-agonists, and inflammatory and tranquilizer drugs. A single sample could be tested for all those targets at the same time. We have 6,000 of those and everything is done in real-time. We don't store them or accumulate them. When they come in, the test starts that same day. Our labs operate seven days a week.

When it comes to pesticides, again we don't set the standards we just enforce the standards and the tolerance that are set by EPA, and again for this one we have a single method that in this case, it detects about 108 pesticides. The current version is going to be detecting a lot more than that, and the pesticides can include everything from the classical persistent organic pollutants, like DDT, to the ones that are more commonly used today, like chlorpyrifos. The beauty of both methods that I described, the MRM and this PST method, this pesticidemethod, is that they're very flexible. We can add or pull compounds every year as needed, and we have a very tight ongoing collaboration with FDA and EPA. We meet once a year and discuss what compounds are relevant that we should be monitoring for the following year. Again, flexibility and transparency, two of the features that we have in the system. We work with our partners to decide what are the things that are really relevant for the environment and for the substrate we are testing, and then test only for those things.

When it comes to pathology our inspectors at every plant do antemortem and postmortem inspection of the animals. I've classified these potential pathology issues as both food safety conditions and non-food safety conditions. The animal itself, the whole carcass, will be condemned if it's unfit to be presented for slaughter. Simply, we do not let it in slaughter and condemn the whole carcass. On occasion, for some type of illnesses based on pathology results, we can only condemn parts of it, some of the meat, if it's not a food safety issue, and parts of it can be passed for consumption if they're not condemned. The other thing that we can find in pathology is foreign objects. You know, I could tell you stories about the things that we find sometimes in food that is weird. Mostly, it is little pieces of plastic or metal that passed through. But our pathology team is really good at finding all those foreign objects, and again, our sampling is for verification purposes. It’s another strong component that we have.

In addition to those three major groups, we have a whole testing

program that has to do with the quality and the wholesomeness of the food, and this is includes speciation, which has been very useful for Siluriformes, to make sure that if they say they are selling catfish, they are in fact catfish. It is also very useful, for example, for when somebody's claiming that you have a pork sausage and you want to make sure that it is actually pork and not pork blended with chicken or something else. We have a set of systems and methods that allows for speciation differentiation to assure people that the label claim is correct. In addition to that, we have some components, nutritional components, that we look for which include the water content, the protein, sodium, fat, and most recently we've developed a method that was transferred to us by FDA to address the top eight allergens. We will probably start using this in the near future.

Just three quick bullet points here on special focus that could be addressed with the cellular agriculture we're looking at today. Cell culture method usually use antibiotics and growth modulators, so we probably have to flex our systems to address those things. Some contaminants, such as mycoplasma, which we don't look for, we may have to adjust to create methods to look for those things and some undifferentiated cell lines could resemble cancer and could disease in immune compromised people. As we move forward with cellular agriculture, what I'm trying to say here is, that we will adjust to whatever hazards are identified.

Finally, I just want to close with this one slide by saying that nobody can do this alone, and in my 20-whatever many years career here, I've noticed we work very good with federal partners, with states, with tribal authorities, with all the stakeholders. We have meetings here with the stakeholders pretty much every month, and we don't do this in a vacuum. We work with CDC, FDA, Department of Defense, whoever is appropriate that we need to build with, we work with. It's a team effort. In order to accomplish our mission, we cannot try to do it by ourselves and we're much stronger by doing it with everybody else. So, with that, I'll close. [Applause]

Selena Kremer,
USDA FSIS Moderator

Thank you. I'd like to welcome again, Dr. Jeremiah Fasano to talk to us about the overview of potential cell culture technology hazards, including summary of hazards discussed at the FDA Science Board meeting yesterday. Dr. Fasano.

Jeremiah Fasano,
FDA Office of Food Additive Safety

Thank you. So, Dr. Esteban has just walked you through some of the

hazards associated with traditional meat and poultry production, for which FSIS has decades of experience in thinking about how to manage these risks and control them appropriately. I'm going to talk to you a little bit today about something that we all know a lot less about, which is the potential hazards associated with this new method of food production, and also summarize some things that we heard yesterday at the FDA Science Board Meeting, which might be of interest.

The Science Advisory Board is an is an interesting body. It contains folks with expertise in a broad variety of areas that are relevant to FDA's mission. From nutritionists and surgeons, to pharmacologists and epidemiologists, there's a lot of different kinds of expertise and I want to take a moment to just express my appreciation on behalf of everybody who was involved yesterday for the board's interest and engagement with this topic. We heard a lot of interesting stuff from them, that I'll cover in a minute. In thinking about potential hazards associated with this production process, we tried to cast a very broad net. We developed six questions, in consultation with USDA, that were meant to be useful as starting points for analysis for anybody thinking about cell cultured food from any source. So, any species going through this process. What are some things that might be useful to consider as a sort of points of analysis or departure?

First, I'm going to walk you through those questions that we shared with the board, and then I'm going to cover a few key themes, that after some reflection last night, seemed to me, to emerge from that discussion. There’re certainly many things that the board covered, and I'm not going to mention all of them today.

The first group of questions we presented to the board are really about adventitious agents. We were interested both in the potential for contamination in the seed materials and the raw materials going into the culture process, whether it's the animal cells themselves or other materials that go into the culture medium. As you know, right now, many of those are derived from animal sources like fetal calf serum. Those as potential sources of contamination, and then we are also interested in the potential for contamination during the culture process. As in the earlier talk where you saw some of the mechanics of how this process works, we expect there to be potentially multiple passages from one culture vessel to another. There could be contamination, at the start of the culture process or during one of those passages and so we're interested in hearing from the board their thoughts on the significance of those risks and what may be sort of appropriate ways to frame those risks.

The next group of two questions is really about substances that are

added during the culturing process. First, there's the culture medium. All these materials and signaling molecules the cells need to grow and then differentiate into appropriate cell types. Those are all things that need to be added, and then in addition to that, you also need structural elements from many of these cells in order for them to sort of remain viable and differentiate properly, and so, that's something else that's introduced both potentially into the culture medium, but then also possibly into the biological material that's harvested, particularly if you have complex structures, you're going to need some kind of scaffolding material. We're interested in the board's thoughts on what safety assessment considerations you might need for those materials.

Then the final group of two questions was about cellular properties, and there's two aspects to this. We certainly know from our experience in culturing other kinds of cells, that if cells are stressed or if the culture process is not optimal, they can produce undesirable secondary metabolites or other substances that you don't really want in the food. Certainly, there are methods to control that, but we're interested in the board's perspective on whether that was a concern for animal cell culture, and if so, what kinds of cells might there be or what kind of substances might they be.

Finally, we were interested in other cellular properties. These cells, they're obviously being used to generate a food, what are the nutritional characteristics of food we might expect from that? How would they compare to traditionally produced food products? Are there any other properties, and non-nutritional ones, that might be material are worth considering?

Those were the six questions that we put to the board, and they had a very broad and far ranging discussion. As I said, I think we didn't get a lot of answers from this discussion, but honestly, I don't think that we were expecting to. These products really aren't on the market yet. There's not a lot of specific experience with implementation. There's not a lot of concrete data that we had to offer the board and so this was really more in the nature of sort of a theoretical analysis or a preliminary analysis of the kinds of things that might be worth considering. I feel that we did come away with a lot of interesting avenues to pursue, and I'm just going to cover a few broad themes now.

The four that really jumped out to me were challenges of scale, the appropriate reference or comparators for risk assessment for these products, the role of exposure assessment in thinking about safety considerations for these products, and the challenges of designing effective preventive controls for this production process. I'll cover each of those in a little more detail.

I think the single word that we heard more than any other yesterday was “scale.” People were very focused on the challenges of bringing this technology from the bench top, to clinical settings, to industrial settings, where you are looking at potentially multiple orders of magnitude in terms of scale for the production process. While there's a lot of experience with managing biologic production process in the therapeutic side, production scale is going to be a lot bigger than that. It’s going to have to be for these things to be a meaningful part of the food supply. There may need to be some learning-by-doing. You may need to actually start ramping the stuff up at scale to learn some of the things you need to learn, and you know, you may need some new technologies to manage things at scale. Challenges or technical issues may emerge that are not present on a benchtop, or a a bench side reactor, that are going to be a problem when you get up to industrial scales, and because there is going to probably be some learning-by-doing, there may be need for strategic use of post market surveillance, in order to understand, as this learning is going on, that we’re properly capturing that and integrating that back into the assessment process. That's scale as a theme, and again, it was a very prominent one.

Another one, which I think was a key theme that jumped out at me was, what are the appropriate comparators for assessment of risk safety, other properties of these food products. There are many that you could potentially choose in a lot of different areas, and selection of the appropriate one is really going to be essential for informing a safety assessment process. There’re a number of areas to think about here. One is the risks of microbial or viral contamination. Potential references or comparators could be traditional meat, poultry, and seafood products, and thinking about how those risks compare. Cultured cells in clinical applications, we heard a little bit about contamination events that occur there. They're very rare, but they are obviously of significance when they do occur. Is that an appropriate comparator? What can we learn from that? What's useful and not useful? Then, also broadly distributed food pathogens that are present in a wide variety of food products. Things like *Listeria.* To what extent is that useful, as sort of a touchstone for comparison or thinking about microbial risk assessment in these products? That's one area.

Another one is nutritional characteristics. You could think of a couple of different ways and a couple of different perspectives were discussed here as well. If you’re sort of looking at a target food that you’re trying to match, that is one sort of analytical framework for thinking about the nutritional properties of a food. There could be certain kind of essential characteristic properties of a food that any cell cultured food might be expected to have, and in order to be appropriate for that food category.

You could also think of it as a design nutritional property without reference to a particular food. Those are all potential points of reference when you're thinking about nutrition, and that was another area that the board discussed. With respect to the safety of media and structural components. There was a number of potential references considered there as well. The point was brought up that many of these substances are things to which we have already had exposure. A number of the structural materials that were discussed were common biological materials, like cellulose, a structural material in plants, collagen, which is a structural material in animals, chitin, things like that, that we're already exposed to through food consumption. For a lot of the media components, I mean if you're thinking about this essentially you're trying to recapitulate the environment of the interior of an animal, so many animal products that we already eat you have some history of exposure to many substances are going to be similar to those in culture medium, whether it is derived from an animal, or as it's likely to be the case in commercial production of these foods, from an animal-free medium.

Finally, there was this idea about considering the components, whether they be in the media or in the structural elements in isolation, as opposed to in the context of an actual oral exposure. I think I'll just remind you at this point of something I brought up a little bit earlier. When we think about safety assessment for food ingredients, we're always thinking about an intended use. We don't consider the substance in a vacuum, but we think instead about what the intended use is, what is the estimated exposure. That all informs the safety assessment. That was something that kind of was brought up here as well.

The final area is thinking about risk assessment, with respect to cell properties. What, again, are essential touchstones? Thinking about cultured cells that are used in therapeutic applications, where there you get exposure via a non-oral route, whether it's systemic or parenteral exposure versus oral exposure of the cooked cells. Is that a good way to think about it? Can you think about the characteristics of cell exposure from traditionally produced meat, poultry, and seafood? Those are all potential points of reference when you're thinking about the properties of these cells. I'm almost done, I promise.

Two more themes, I'll quickly cover. The first one was just exposure as a theme. Thinking about, on the one hand, the exposure to a biologic or therapeutic product, versus the exposure to things that are in food, where people eat multiple times a day. Consumption is enormously broad, and so, even rare food safety events have a large significance and really the emphasis on the importance of making sure that those

events are as rare as possible, given how widely we consume food. There was this idea of exposure when you're considering an acute contamination process, microbial one versus chronic exposure to the ingredients that are used in making these foods, which led into a discussion of how the food ingredient safety assessment process addresses these kinds of issues of chronic exposure, which is something that we routinely consider.

Finally, another theme, in terms of exposure, was the importance of using that as an opening step in thinking about food safety assessment for substance. Again, the consumption doesn't occur in a vacuum. You have tools to actually think about what kind of exposure people are actually getting, and then do your safety analysis from there.

Then, the final theme was just the challenge of designing effective preventive controls, given how new this area is. There was discussion about our understanding of microbial contamination in therapeutic context, and what hazards are reasonably foreseeable based on that experience. Some discussion about the value and effectiveness of testing at different points during the production process. You've already heard here, from multiple speakers, about what testing is useful for and what other things need to be in place to make that effective.

Then, different kinds of contamination failures in clinical experience. It appears that many of the contamination failures that you see in clinical experience is, because the culture medium is so effective at growing microorganisms, the cultures fail before you can even complete the production process. So, there's visible contamination failures versus silent contamination failures, and the essential importance of making sure that your system is capable of catching particularly the second kind.

The final thing that came up in this idea of preventive controls and effective risk management programs was the idea that there is a lot of existing guidance out there and best practices from the biologics world when thinking about cell culture, and it might be useful to take that as a point of departure, and then as we gather more information, gradually modify or adopt practices based on the actual risks that were gaining insight into from our experience.

That's just a quick overview of some of the stuff that was covered. Again, I'd like to express my appreciation to the board. They spent five hours listening to presentations from us, from the public, and really grappling with these questions and it was extremely interesting and I think useful exercise. Thank you. [Applause]

Selena Kremer,
USDA FSIS Moderator

Thank you, Dr. Fasano. I just wanted to take a moment to introduce myself and Kari Barrett to you. My name is Selena Kremer. I'm the Team Lead in Congressional and Public Affairs at FSIS. Kari Barrett, she is the Advisor for Strategic Communications and Public Engagement in the Office of Foods and Veterinary Medicine, and we're your moderators today. So, Kari is going to go ahead and take over this next session for open public comments on potential hazards, and if we could have our ushers come forward. Thank you.

Kari Barrett,
FDA OFVM

All right, well thank you, Selena. We've come to the point in our agenda where we're really turning the mics over to you, essentially.. What we've done with this agenda is we have built in and designed into the format multiple opportunities for the audience to provide comments on different subject areas. We're starting now with the session that's focused on potential hazards. I believe the questions are behind me. What our hope is, is that you'll consider the session to be somewhat like a breakout session, or an open mic, where you can come up to either microphone and offer some of your comment, perspective, or line of inquiry, or thought on this topic. It's to benefit everybody in the room, as well as the agencies. There is a transcript of this meeting, so we'll be looking carefully at everyone's comments, but hopefully all of you will also be submitting public comment. This may be an opportunity to hear some new ideas and offer food for thought.

With that, the process is, if you would like to make a comment - and I want to pause on that because there are, the term comment comes up quite a bit in the agenda. This is really meant to be a pretty open opportunity. You don't have to have a script. You can come up and just make a remark. You don't have to speak for three minutes, but that is the maximum time that we have per speaker, so that we can hear a lot of perspectives. But if you would like, if you have come today with prepared statement that you were going to offer later in the formal public comment, and you want to use this time to talk about the potential hazards, you can do that. If you want to elaborate a little bit more in this area, where you may not have time to do that this afternoon, please feel free to do that. It's really an opportunity to share some good thinking and I want to encourage everybody to participate in this process.

We do have folks up front who can help direct you to the microphone. So please, let's go ahead and begin. If there's anyone who would like to offer some comment, you're welcome to come up, and we just ask that

you come to the microphone, give your name and affiliation. Come on down.

Come on up. Again, if you'll say your name and organization.

Thomas Gremellion,
Consumer Federation of America

Hi. My name is Thomas Gremellion and I'm the Director of the Food Policy Institute at Consumer Federation of America. I think these are great questions -- I want to thank FDA and USDA for having this meeting. I briefly wanted to remark that asking these questions now seems like a very good idea to both help protect consumers from dangers that might be associated with these products, but hopefully to move the food inspection system to a more risk-based approach. That is something we heard a lot this morning, and as I was thinking about these questions when the agenda came out. We work a lot with FSIS and trying to improve meat and poultry inspection for consumers, and microbial contamination seems to be the big factor there. You know, I've got some statistics. CDC estimates that meat and poultry cause 22% of foodborne illness and 29% of the deaths from foodborne illness, and the sources of that microbial contamination can fall into two categories. In a way, you can probably categorize it different ways, but things that infect the animals on the farm and in transport, and things that infect the meat in the slaughterhouse and the factories.

I wanted to underscore that a risk-based system really should be doing more on the farm. I know that's a little bit far field of what we're talking about today, but we could really be protecting a lot more consumers, going to the farm, making sure there's not *Salmonella* in the feed or getting transmitted from the breeders. With cultured meat, it seems like the hazards may be very different, and I think it's still very ambiguous what the big threats are going to be. I think a pre-market approval process is going to be very important inform the inspection system, and later, we'll talk more about that and I'll have a lot more to say about the GRAS system, and some of what's been said today, and that's for now, I think that's it.

Kari Barrett,
FDA OFVM

Great. Well, thanks for starting us off. Additional comments, perspectives? Again, if you will just say your name and organization.

Sarah Sorscher,
CSPI

I got to say, I'm surprised there's not more of a line in this room. It's a packed house. My name is Sarah Sorscher. I'm from the Center for Science in the Public Interest, we're also a consumer group, and I got to

say, I think one of the reasons there might not be so many comments is, that it's been a very wonderful and thorough set of presentations. Talking about the risks, in particular, I appreciated that the agencies are considering compounds that we may have traditionally in the food supply, when they're considered for a new use, like this one, you have to look at that safety assessment again. You have to look at exposure. You have to look at whether the conditions change the safety. I appreciated that.

I'd say that the thing I wanted to add was, it's really maybe, not so much a risk of this product, but a potential benefit, which is that Thomas nicely pointed out with traditional meat, we don't have a zero-tolerance standard for pathogens, and that product can be sold with contamination with *Salmonella* and other foodborne illness. This product, these could be sold cooked, ready-to-eat, they could be sold raw, and I think we should consider that consumers may have a different understanding of these products. In part because of the potential that they have, and they're already being touted as clean meat, as pathogen free, and that could mean that they end up being consumed raw more frequently than traditional meat. People are always pretty grossed out when I introduced this idea, but we do have meat that's consumer we have steak tartare, we have sushi, and you know consumers may decide to use these products in novel ways or not keep them separated when they're preparing salads, and so it's really important that the product live up to that expectation and have a zero tolerance standard, which ever regulatory structure is put in place for it.

Kari Barrett,
FDA OFVM

Great. Thank you, Sarah. Some more comments, perspective? I think our earlier speakers did do a very good job and laying a lot of this out. You may have some additional comments to add to that.

Thank you, and again, if you'll say your name and organization.

Barbara Kowalczyk,
Ohio State University

Barbara Kowalczyk, the Ohio State University. I think I wanted to just add to the aspects of the safety of these products that should be considered. I think, as was discussed and presented earlier, a lot of the microbiological pathogens that are found traditionally in meat and poultry products are likely to be found in these products, because of the way they're grown, but when it comes to traditional, and I don't know the answer to this, so this is something that the agencies need to consider, in traditional meat and poultry products in intact cuts of meat the pathogens sit on the surface and so it's well recognized that an intact cut of meat needs to be handled differently than a non-intact cut of meat. So in producing these products which should they be? Would

they be considered an intact or non-intact, and how do we communicate that?

To follow upon Sarah's point, how do we communicate that risk to consumers? Because non-intact cuts of meat … pieces of meat and poultry products need to be cooked thoroughly in order to fully kill all pathogens. Whereas, intact meat and poultry products they can be cooked because most pathogens sit on the surface. That's an aspect that I haven't heard come up yet, but I think should be considered.

Kari Barrett,
FDA OFVM

Great, thank you. Another comment?

Thanks, and if you'll say your name and organization.

Shiraz Ziya,
Loughborough
University

Hi. My name is Shiraz Ziya, from the UK, Loughborough University, and so I've got interests in cell therapy and represent the International Society for cell therapy. There's two topics I think will be covered perhaps later which I'm quite interested by hearing about. One is raw materials, that's obviously a huge factor in traditional cell therapeutics, where the suppliers aren't really aware of the GMP regulations and some of the products that were produced perhaps cell therapy locations weren't particularly adhering to those regulations or qualifications, so some issues around know FPS and the […] qualification.

The second thing is around facilities, so where would these products be produced, and again, that's been quite an interesting thing I've looked at during my Ph.D., which is been around how those facilities were built within hospitals produce cell therapy. How would they be produced, if produced for the food application, whether it be where would they be produced and also what talent will be required to actually produce these materials? What training will they need, and sort of the capacity required for them?

Kari Barrett,
FDA OFVM

Great, thank you. Thanks for coming up. Some more perspectives? Yes, thank you, and if you have, again if this was something you're going to speak to in your prepared remarks and you want to go ahead and cover that ground and, in this session, and shorten your remarks for later, you're welcome to have that kind of an approach as well.

Rosemary Versteegen,
International Serum Industry
Association

I am Rosemary Versteegen and I'm with the International Serum Industry Association. I'd just like to pick up on a couple of things that have been said. I think there's a tremendous amount that we can learn in this area from the biotherapeutics world. I think there are major advances that have been made in terms of control in terms of management of systems in that area. Cell therapy is very new and is still happening very much on the research side, and I think it will obviously develop and is developing into a more mature science, but there's an awful lot that's out there already to learn. So, I would strongly encourage that continuation of discussion.

Kari Barrett,
FDA OFVM

Thank you. Additional comments? If you'll repeat your name and organization.

Leah Stitz,
FDA CFSAN

Leah Stitz, Center for Food Safety and Applied Nutrition in FDA. One comment that I meant to make in my presentation today but failed to do so, which I was just reminded of by someone else's comment, is that these processes, these phases as I discuss them this morning, could all be endpoints.so The procurement and qualification of cells could be an endpoint and then that product be sold to someone else. The process can go all the way through by one manufacturer or it could be done in segments. One of the key areas for hazards that needs to be considered is the transportation of these end products from a supplier to the buyer. Thank you.

Kari Barrett,
FDA OFVM

Great. Thanks, Leah, for coming up. Okay, I'm going to offer, I'm going to make it another deal with you. Since not everybody's warmed up yet. If you are offering public comment later this afternoon at the end of the day, when you may not have as much energy, and you'd like to take some time now to give that public formal comment to read your statement, if you're in the first categories –1A or 1B. If you'd like to take this time to go ahead and do that, you are welcome to come up. The mics remain completely open for anyone else to make a comment, as well.

Danni Beer,
U.S. Cattlemen's Association

I'm Danni Beer with the US Cattlemen's Association. I have a question about the end product or by-product. Is there anything at the end of this process with these products that we end up with and who regulates that?

Kari Barrett,
FDA OFVM

Thank you, and on those kinds of questions. This is an open public comment process, and so we hope that folks will provide us with their thoughts on that very important question when they submit their written comments to the docket.

Isha Datar,
New Harvest

I am giving a comment later, but this is not that comment. My name is Isha. I'm with New Harvest, which is a non-profit organization that has been funding research in this space since 2004. I think the hazards that are the same between traditional meat products and those from cell culture technology are, to me it's quite obvious, that they're questions of contamination. Whether viral, bacterial, or fungal, but we already have quite a bit of expertise when it comes to understanding contamination and controlling for it.

I think something that's missing from this conversation are the hazards of traditional meat production that are externalized and actually don't come from the product directly, and those are things like viral epidemics and antibiotic resistance, which do not generally come into the discussion of regulation, but I think should be factored into understanding how important it is to advance these new technologies.

I think one of the reasons why there are so few comments is because of something that came up in the science board meeting yesterday, which is that there are pockets of expertise related to this field right now, so there are people coming from cell-based therapies, people coming from large-scale production of cells for biomedical biologic purposes, and then there are people from the meat, poultry, and meat science world, and we have not seen a lot of crossover between those two worlds so far, and I think that's absolutely necessary to best move these conversations forward. Thank you.

Kari Barrett,
FDA OFVM

Thank you so much for your comment.

Rhonda Miller,
Texas A&M

I'm Dr. Rhonda Miller. I'm a professor at Texas A&M University and I represent the American Meat Science Association. I'm going to use some of this time to make my later comments shorter.

I think as meat scientists, we know that the chemical, physical, and microbial hazards associated with production of cultured animal tissues likely will differ due to the differences in the production system, and I

want to commend the speakers for doing a very good job. I really liked the discussion from the FDA meeting from yesterday. I think we're all aware that there are differences in the production systems and that there's the potential for the cross contamination during production and anybody that has worked with cell tissue culture know that even in a very sterile environment the cross contamination issues can be a real problem, be very problematic, and as we upscale this technology, I think there's a lot of things that we still don't know about how to control some of those.

I appreciate the comment from my colleague that at harvest, muscle from healthy animals are basically free of bacteria, and it is through cross contamination on the exterior surface of the meat that we obtain mainly microbial hazards. Also, we can get physical and chemical hazards, but as we know, most of those are microbial and the potential for cross-contamination in cell cultured tissue, especially we're growing that at in layers of cells most likely provide opportunities for the interior of the cell not to be sterile, and that was one of the things that I think is a huge question on a lot of meat scientists minds, that we use interventions to control critical control points and to reduce hazards and meat production systems, but will those interventions that are conventionally used be the same? Will we be able to utilize that technology? What interventions do we need to develop, and as we know, there's not a lot of meat available? This is all evolving, we know that and we're willing to work on that. Thank you.

Kari Barrett,
FDA OFVM

Great. Thank you very much. Again, if you'll say your name and affiliation.

Mike Selden,
Finless Foods

Sure. My name is Mike Selden, Co-founder and CEO of Finless Foods. I'm also hoping to make my comments later a little bit shorter. I'm going to try and talk on some topics that others are a bit less likely to bring up. Finless Foods is a company that's developing sustainable seafood using animal cell culture technology. We call this cell-based fish. We take a sample of cells from a real fish and grow them out in order to create healthy and sustainable seafood without the presence of substances such as mercury and plastic, which I believe ties into the topic that we're on. Large doses of mercury have the potential to impair the development and functioning of the brain and nervous system. Based on current evidence, carnivorous fish at the top of the food chain have the highest mercury levels because mercury is bioaccumulated. This means that it can rise up the food chain and it becomes concentrated at the top. Because of this, the FDA and EPA have advised that many large

fish species be consumed in limited quantities by at-risk groups, such as women of childbearing age.

With our technology, we have the potential to remove mercury as a concern entirely, since mercury travels through a pathway that doesn't play a part in our means of production. The effects of plastic found in wild caught fish on the human physiology is less well studied, but we believe it is still a cause for concern. Studies that have been done on how plastic consumed by fish can affect their physiology have been conducted with some pointing to signs of liver toxicity and pathology, reduced feeding and shoaling behavior, and altered metabolisms. Our process has no ties to the ocean other than the tiny starter culture, and so the recent studies indicating that there will be more plastic than fish by weight in the ocean by 2050 aren't of concern to people's health through the fish they eat, if they are eating fish produced using animal cell culture technology.

Current wild-caught fish productions tied to nature make for a less than stable supply chain. Time and time again, it has been shown that a sizable chunk of the fish that we eat in America is mislabeled. This is often because of supply chain instability. Using the process we are developing we hope to have a much higher level of certainty of how much fish can be produced, providing increased stability, and making the mislabeling of fish a thing of the past.

Something that we feel very strongly about, in the main thrust of what I'm trying to get at here, is that we must in some way or form, potentially with qualifiers, use the correct terminology and label these cell-based fish that we produce as fish - tuna as tuna, salmon as salmon, etc. An estimated seven million Americans are allergic to seafood, which is about 2.3% of the population. If one is allergic to animal-based seafood, that person has a high probability, I'd say almost a 100% certainty, of being allergic to the seafood produced using our technology, so labeling it in any other way has a large potential of creating a public health hazard for these millions of people. I hope this perspective proves itself informative and look forward to continuing the conversation with all of you in forums open and beyond that. Thank you very much.

Kari Barrett,
FDA OFVM

Great. Thanks for coming up. They're folks who have built some commentary about the hazards and their formal comments you may want to provide that perspective at this time. If you'll say your name an organization.

Alex Shirazi,

SVCMS LLC

Thank you. My name is Alex Shirazi. I'm with SVCMS. We host events and facilitate investment in the cell-based technology space. One question I had, or one thing that I was thinking in response to what Mike from Finless Foods said, was that cell culture technology allows us to have a more control over the process, which is better for contamination, from consumer perspective, but one concern that I have as a consumer, is that if we are consuming large amounts of meat or the product from one source or one cell line is, are there any hazards with that?

Kari Barrett,
FDA OFVM

Thanks for raising that up. Again, something to submit comments on as well. Yes, another speaker.

Larissa Rudenko,
Mass.
Institute for Technology

Hi. My name is Larissa Rudenko. I'm a visiting scholar at the Massachusetts Institute of Technology, where I'm looking at emerging technologies and their governance. One of the things I think that we've learned from many emerging technologies used for either medicine or food, is that some of the hazard and risk questions that come on early in the technologies are generally applicable across the technology, as opposed to specific processes. Although, there is specificity of hazard and risk to a particular process, and I know that yesterday Ms. Datar talked a little bit about funding for some of these basic research questions, and I would like to just simply raise the issue of whether or not either FDA or USDA is thinking of providing a grant or funding program for the regulatory science that goes into the across-the-board hazard or risk kinds of characterizations that would apply to this technology. Thank you.

Kari Barrett,
FDA OFVM

Thank you. Another speaker?

Paul Shapiro,
Author

Hello. My name is Paul Shapiro, author of the book *Clean Meat*, and I want to echo the sentiments of the previous speaker, because we know that the governments of Japan and Israel are investing in this type of research and helping the startups in this space, because they want to be providing the protein of the future. I think it's incumbent on USDA, perhaps through Agricultural Research Service, or maybe through other avenues who also see about fostering some of this innovation here in the United States, so that we in the U.S. can be a leader not a follower, when it comes to the cellular agriculture field. And to the point that Mr. Selden made earlier, from Finless Foods, I do think that it's important to

emphasize that we do call this what it is, because as he noted, people with allergies to various meats will also be allergic to this, and it brings to mind a little bit of the ice shipping industry of old.

You think about how 150 years ago, we had huge blocks of ice being harvested out of lakes and shipped all over the world, and when you enter the advent of industrial refrigeration, you all of a sudden had a much more efficient way to produce ice, just by cooling the water down right in front of you, and the ice barons were livid over this technological innovation, railing against what they called artificial ice, saying it might not be safe, that the ammonia in the coolant might leak out and harm you. Fast forward to today and virtually all of us have artificial ice makers in our homes; we call them freezers and we don't think there's anything unnatural about them at all, and we call it ice even though it is not made by nature. It's made by a human invention, a very sophisticated technology that we call refrigeration. We don't think there's anything unnatural and we call it just ice because that's exactly what it is. I think similarly with cellular agriculture, we have a chance now to produce what for millennia was only produced in nature, and now we can produce, through a very efficient and safe way of growing meat from animal cells ourselves.

I personally have eaten this kind of meat about half a dozen times now. I felt great after doing it. I still feel great today and I think that it should be one of the points of discussion, as this very admirable public meeting goes by, which I'm very grateful to both USDA and FDA for holding, that the naming of this product is something that we ought to consider, because we see that debate happening elsewhere, whether it's in plant-based milks and cheeses and other types of debates that FDA is considering right now as we speak, and so why not get that discussion started as well on cellular agriculture produced meats. Thank you.

Kari Barrett,
FDA OFVM

Great. Thank you for your comments and we will be talking tomorrow quite a bit about labeling and claims with these products. If you'll say your name and organization.

Jack Bobo,
Intreckson

Sure. My name is Jack Bobo. I'm with Intreckson and I want to pick up a little bit on what Paul just said about what's going on globally and the opportunity for the United States to be a leader, but I also think that it requires countries to come together and determine what the appropriate comparator is for this, and that could be work done through OECD or some other body, and the question I think is not necessarily obvious, because is the comparator this exact breed of animal from which the cells are taken, or is it the comparator all of beef

for a beef product, and so I think deciding how that's going to work, and I think there are some examples of how maize and other products are used in the OEC database to determine the comparator for genetically engineered crops and other things.

Just finally, on the point of naming, I think that it's a really important point. I also think though that, how the information is communicated to the public is separate from the question of whether or not it's meat, because some consumers may be interested in knowing about this, if there are differences, whether those are benefits or risks, I think that needs to be communicated so that the public is aware of it. Now that could be done through government engagement or it could be something that industry itself comes together to figure out, but I think that both what it's called, but also how you communicate the fact that it may be produced in a different way is also important. Thanks.

Kari Barrett,
FDA OFVM

Yes, thank you for coming up. More comments perspectives around potential hazards? I'll also open it up more broadly, if there is someone again who is giving a formal public comment this afternoon and you're in a category 1A, 1B, 1C, or 1D and you want to go ahead and offer that comment, you are welcome to do that at this time as well. I can up that ante, and anyone who is giving a formal public comment today, who was scheduled to be given at the end of the day, and would like to give it now, we would really welcome you to do that. Just please let us know if that is your intention, and again, if you'll say your name and organization.

Elan Abrell,
Good Food Institute

Hello. Elan Abrell from the Good Food Institute. This was going to be our public comment later for the afternoon. I'll go ahead and give it now. The Good Food Institute is a non-profit thinktank with 50 staff members across science and technology, innovation, corporate engagement, and policy. We're grateful to the USDA and FDA for engaging stakeholders in robust and open dialogue about cultured meat, sometimes called clean meat or cell-based meat. We appreciate your commitment to enabling innovation and technological advances in the food sector and ensuring the safety of the resulting food products.

The United States has a robust regulatory regime that is more than capable of ensuring that cultured meat is safe and truthfully labeled. The regulatory path to market must assure consumer safety and confidence without imposing unnecessary or duplicative regulatory barriers to producers. As the National Academy of Sciences has recommended, there should be a single point of entry into the regulatory framework for the products of biotechnology to streamline the approval process for products like cultured meat.

It is abundantly clear that the FDA has the pre-market authority and expertise to be that point of entry. A position echoed by the vast majority of companies and organizations that submitted written comments to the FDA's docket regarding foods produced using animal cell culture technology, irrespective of any other positions they held on cultured meat. The FDA currently evaluates microbial, algal, and fungal cells generated by large scale culture that are used as food ingredients, as well as ingredients in meat and poultry, and it also manages safety issues associated with cell culture technologies in therapeutic settings.

As Dr. David Welch, GFI's Director of Science and Technology, and other speakers explained to the FDA Science Board yesterday, the potential hazards associated with the production of foods using animal cell culture technology are not significantly different than those associated with the other forms of food production and processing that the FDA already regulates, and as was discussed yesterday, there are well-established controls to effectively mitigate against these hazards. Once pre-market safety has been established, inspection and labeling requirements should ensure a truly fair and even playing field for all meat, poultry, and seafood producers. In particular, if you exercise regulatory authority over cultured meat and poultry products. It should apply basic principles of fairness equally to cultured and conventional meat producers. Cultured meat is expected to be identical to conventionally produced meat in its basic nature composition and all other essential characteristics and producers should be able to use meat and poultry related terms on their labels. Any additional labeling requirements, including statements of identity, information about production methods, and species origins of meat, should apply equally to both conventional and cultured meat products, to ensure consumer confidence and to avoid prevent prejudicial requirements that could disadvantaged producers.

As Secretary Perdue astutely observed to reporters earlier this month, quote, "We don't want this new technology to feel like they've got to go offshore outside the United States to get a fair regulatory protocol." end quote. GFI agrees wholeheartedly. Some foreign governments have already begun investing in cultured meat companies as a means of addressing food security, food safety, antibiotic resistance, and climate change. The U.S. is currently home to some of the leading cultured meat companies and the U.S. can and should play a leading role in bringing clean meat to the global market in a way that is safe efficient and fair. That's why it's critically important to guarantee all producers are playing on a level playing field. We're very grateful for this opportunity to comment on the regulation of this extremely promising new technology, and we look forward to continuing this dialogue. Thank you.

Kari Barrett,
FDA OFVM

Thank you so much for your comment, and again, if you are giving what you would give us for your formal comment later today, just note that.

Lou Cooperhouse,
Blu Nalu

I was scheduled to speak in 1A this afternoon. Hi everybody. My name is Lou Cooperhouse and I'm Co-founder, President, and CEO of Blu Nalu, a San Diego based company that is a pioneer in the emerging field of cell-based seafood, which we call cellular aquaculture. During my 35-year career in the food industry, I've led teams of food safety, R&D, regulatory policy, and operations personnel at a number of food companies under FDA and USDA inspection. I'm also certified as a trainer in HACCP and preventive controls for human foods, have been educated in both food science and microbiology.

As a result, I am very familiar with the regulatory processes and inspection requirements for both the FDA and USDA. While these two agencies operate quite differently, both are quite consistent with their risk-based methodology for assuring safety to our nation's food supply via HACCP. The principles of HACCP originated over fifty years ago and have been enhanced several times since then, resulting in continued improvements to the food safety in our nation, a dramatic reduction in illnesses and deaths as a result. HACCP principles are mandated by USDA for facilities that produce meat and poultry and similarly mandated by FDA for facilities that produce seafood products.

HACCP methodology has recently evolved as a result of FSMA regulations and now HARPC, a system of hazard analysis and risk-based preventive controls is in place. HARPC includes elastic assessment of any food safety hazard may occur in our food supply including biological, physical, chemical, hazards that we all know about, and those that may be naturally occurring or unintentionally or intentionally introduced into a food product.

These categories of potential hazards that exist in cell-based meat, poultry, and seafood are entirely consistent with those that exists in many other food industries, including meat and poultry products that are conventionally produced, and these existing HACCP and HARPC methodologies are absolutely appropriate for cell-based products. Our cell-based food companies will produce large stainless tanks with agitation and process controls to provide proper growing conditions in an environment that is free of environmental contaminants. In fact, this process is far more sanitary than what occurred from the harvesting of animals which today originate in the ocean, seas, farms, fields, and slaughterhouses.

The FDA and USDA already have the tools and expertise in hand to effectively regulate products produced using cellular agriculture and aquaculture, and these are consistent with all other products that they regulate, but also be quite consistent and logical for FDA to continue to serve as a sole agency with regulatory authority for cell-based seafood products. This discussion today is extraordinarily significant as cellular agriculture and aquaculture companies have the potential to transform the food supply of our planet.

As Secretary Perdue said this morning, the USDA and the FDA are all about feeding the world. The timing is critical, as our planet is facing a crisis. Due to climate change and a host of environmental factors, our supply for seafood cannot keep up with global demand. We are unable to feed the world in the decades ahead.

In addition, consumers are increasingly concerned about the health effects of what they eat. Seafood products may contain mercury, toxins, and other poisons, pathogens, viruses, and parasites, microparticles of plastics, and a variety of other environmental contaminants. Consumers are also very concerned about animal welfare and the way in which fish is raised and how they are killed for human consumption.

Yes, we all need to change our ways and restore our planet. We also need to create another solution and to do so quickly. A production of cell-based seafoods meats and poultry is that solution. This is an enormous opportunity for all of us to work together. Thank you very much for inviting stakeholder comments as you consider the best path forward.

Kari Barrett,
FDA OFVM

Thank you for your comment.

Mark Dopp,
North American Meat Industry

Good morning. My name is Mark Dopp. I'm with the North American Meat Institute and I have some remarks to make. Because you invited us up to talk about other topics, I'll feel free to do that if that's all right. First, let me say that the Meat Institute appreciates the opportunity and the willingness of both the FDA and the USDA to host this public meeting.

In my view, this issue isn't really that complex, so let me be clear, it's incredibly important that USDA and FDA work collaboratively to ensure the safety of these products, but primary jurisdiction regarding the regulation of cell-based meat products rests with USDA. I'm an attorney. I could bore you with the details, citing the statutory authority

supporting that conclusion, but I'm not going to do that today because I've got limited time. Not only does the law say that, but it's a conclusion also based on common sense, and it's a conclusion that benefits not only traditional meat processors, but also cell-based meat processors, and most importantly consumers.

The meeting agenda, as we've seen, asks a series of questions and we will, at the Meat Institute, we will respond to all those questions in our written comments in detail, but I have some additional questions that I think need to be asked and I think they need to be answered in a public fashion. The inspection system FSIS administers is more rigorous than the one administered by FDA, this is undeniable. Administration officials have said as much to me, but I'm baffled, frankly, baffled why those who advocate that FDA should have primary jurisdiction over cell-based meat products want to deny the companies that manufacture those products the benefits of FSIS inspection, and yes, I'm talking about the benefits. For example, why deny a cell-based company an opportunity to have their products bear the mark of inspection. A mark that matters very much to consumers. Likewise, why deny cell-based companies the benefits of explicit preemption protection provided in the meat poultry statutes. That preemption protection protects companies from arguably ill-considered state requirements that are out there that cover not only labeling, but how a plant operates, its packaging, its facility design, amongst a variety of other considerations. That same preemption provision is not found in the Food Drug and Cosmetic Act, and why are we going to deny cell-based companies the benefits associated with prior label approval, I know we'll talk about labeling tomorrow, but prior label approval is important. That approval effectively precludes the frivolous plaintiffs' bar litigation lawsuits that we see running rampant through our legal system.

The process can be cumbersome, and we complain about that sometimes; that's the downside, but it also benefits consumers and it benefits the regulated industry, because it helps ensure that product is accurately labeled and is not represented to be something that it is not. FDA, in contrast, has no such a label assistance or label approval program. Show and tell time. I bought these products, just a couple days ago, on the internet. One says original sausage beer brats the other one says artisan sausage andouille. They both represent themselves to be sausage and our standards of identity that FSIS has for both products. Guess what? There's no meat in either one of them. I'm going to ask, by the way, that these be admitted into the administrative record.

Kari Barrett,
FDA OFVM

Thank you. We are almost out of time here.

Mark Dopp,
North American Meat Industry

Finally, at a recent Good Food Institute conference, Dr. Marc Post, Co-founder and Co-Chief Science Officer at Mosa Meat, said consumers top concern with so-called quote unquote “clean meat” is food safety, and for that reason, the industry should embrace regulation. So why do those who oppose FSIS inspection wish to deny consumers the confidence that comes from knowing cell-based meat products, a product category in its infancy, are subject to daily inspection rather than inspection once every three to five years. I look forward to the answers to my questions. Thank you.

Kari Barrett,
FDA OFVM

Thank you for your comments. If you’ll say your name and organization.

Bruce Stewart Brown,
Perdue Farms

Hi. Bruce Stewart Brown, I’m a veterinarian with Perdue Farms, responsible for food safety, quality, and live operations. As I hear the part about hazards, I'm wondering, how big can the batch be and how many things cross over from one batch to the other, and in the end, I wonder how big a recall would be on a cell culture-based product.

To me, from what I hear and how it sounds, it could be huge. It could be really big; I would think. My only comment would be, we do this process, you might not know it, that every company that has a meat product typically does a huge amount of mock recalls in a given year, where they take product and suggest that “what if this part of it came under question? How big would the recall be associated with products that might be implicated?” and you have a number for everything, and you judge yourself on how fast you could do it and the implication to the marketplace. At the at the very least it would be fantastically interesting and perhaps important to do mock recalls on a cell culture-based product.

Kari Barrett,
FDA OFVM

Okay. Thank you for raising that up.

Dan Kovich,
Pork Producers Council

Good morning. I am Dan Kovich, Staff Veterinarian and Director of Science and Technology with the National Pork Producers Council. I will go ahead and give my comments I was going to make this afternoon now, as they are focused primarily on one particular hazard that we as America's pork producers feel is not receiving due attention. That is, the source material for the cells you would like to produce these products.

As mentioned this morning, currently any animal presented for

slaughter in the United States is subject to antemortem inspection by the Food Safety and Inspection Service. This is very important, to ensure that the animals are fit for human consumption. It is also a core component of our general animal health surveillance system in the United States. We've also heard this morning that the cell lines utilized to produce culture products have their origin, either from a biopsy from a live animal or from cells that were harvested at slaughter. We believe it's essential that the same mechanisms that are currently in place for live animals be utilized to ensure that the animals that serve as the source of these products are both fit for human consumption and do not suffer from another animal disease malady. I think this is particularly important if we look at situations in terms of cell cultures, particularly if they're moving internationally, that we take into consideration animal health risks, things that may not be a food safety risk, and therefore, subject to a food safety procedure but may again have a valid animal health risk.

Now currently, the USDA is the only agency that has the expertise both to do antemortem inspection of animals and serve as source materials and to ensure that any product moving either interstate or internationally does not pose an animal health threat to this country. Therefore, we feel that it's absolutely essential that the USDA have the primary role in ensuring the safety of these products, both in terms of food produced, but as well as a general component of our agricultural system. Thank you.

Kari Barrett,
FDA OFVM

Thank you for your comments. Other comments, perspectives?

Ashley Peterson,
National Chicken Council

These are some of my comments for this afternoon. My name is Ashley Peterson and I'm the Senior Vice-President of Scientific and Regulatory Affairs with the National Chicken Council. Let me start by thanking both agencies for hosting this critically important and timely public meeting.

Regardless of your views on the regulatory oversight of cell culture and meat products, I think we can all agree that it is important that all food products, whether derived from plants or animals, are safe, wholesome, and properly labeled. Taken with the efficiency of traditionally derived meat and poultry production, the recent growth of cell cultured meat products is evident that the U.S. food production companies are, as Secretary Sonny Perdue stated, continuing to feed people efficiently and effectively. As these new technologies are being explored it is critical that they receive fair and proper regulatory oversight to ensure that consumers maintain the same level of confidence in the safety and

labeling of these products, as they have since 1906 under the Federal Meat Inspection Act and for traditionally derived red meat products, and since 1957 under the Poultry Products Inspection Act for traditionally derived poultry products. To that end, the National Chicken Council believes that the following principles are essential for ensuring that cell cultured meat products are safe and properly labeled.

The USDA, FSIS should regulate the labeling and safety of these products. It is not appropriate to refer to these products using terms such as clean meat, nor should these products be named or described in a way that disparages conventional animal proteins. These products should be named or labeled in a manner that clearly discloses the process by which they were made.

Finally, claims that these products are superior to conventional animal proteins should be prohibited, unless these claims can be substantiated by scientific evidence. To reiterate, NCC believes that it is essential to ensure customer confidence and all meat and poultry products, whether traditionally derived or cell culture. NCC believes that both of these products should receive the same regulatory oversight, a framework that will rely on FSIS' expertise, but may also draw on FDA's experiences as well.

FSIS has the statutory authority, relevant experience, and robust regulatory framework to perform continuous oversight of daily production practices. Additionally, FSIS has detailed process to oversee the labeling of such products in a manner that clearly discloses the process by which they were made and otherwise ensure that they are labeled in a manner that is not false or misleading.

Likewise, FDA may have additional expertise to fill a role in regulating these products. FDA has long ensured that ingredients used in meat and poultry products are safe for use in food through FDA's authority over food additives. Additionally, FDA has experience with similar food production technologies, such as microbial, algal, and fungal cells generated by large-scale culture and used in direct food ingredients. This may lend itself for FDA to address the technical safety of the cell culturing technology used to create such products and determine whether these results, whether the results of these technologies are or are not approved food additives.

We look forward to working with both agencies moving forward, as the regulatory framework for these products is developed. Thank you.

Kari Barrett,
FDA OFVM

Thank you for your comments. Do we have others who want to give

some perspective or your comments?

Alex Shirazi,
SVCMS

I was originally going to make these statements in section 1D, but I'll make them now. My name is Alex Shirazi, I'm with SVCMS. We host events and facilitate investment in the food science space. Regarding labeling as a precursor to tomorrow's agenda, and for the sake of efficiency, I think it's important that we make sure that the naming does not deter consumers from these products and what these products may be. Really call it what you want but don't stunt the growth of this technology and the many benefits that will come to both people and industry.

As a consumer I have great faith and great trust in the American food system, thanks to the USDA, FDA, and the state authorities. Advancements in cell ag technology can really improve the food system, but I think it's important that moving forward in the industry we work with the USDA, we work with the FDA, we work with organizations like NCBA and North American Meat Institute, and also the companies in industry, and when agencies like USDA and FDA get involved I think that's a good thing and I think when parties in the traditional meat industry can get involved, that's a great thing.

Kari Barrett,
FDA OFVM

Great, thank you for your comments. Other comments? Okay. I think, looking at the time it's 11:45, I think we could go ahead and break for lunch and please be back in the room at 1:15. I'll turn it over to Selena. Thank you.

Selena Kremer,
USDA FSIS Moderator

Just a reminder for folks, to take your personal belongings with you when you head to the cafeteria. The cafeteria can be found in Wing 3. If you have any questions, please stop at the registration desk; our staff is happy to help. Thank you. We'll see you back here at 1:05. Thank you.