

Food Produced Using Animal Cell Culture Technology (07/12/2018)

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U.S. FOOD & DRUG ADMINISTRATION
OFFICE OF FOODS AND VETERINARY MEDICINE
CENTER FOR FOOD SAFETY & APPLIED NUTRITION

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Foods Produced Using Animal Cell Culture Technology
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P R O C E E D I N G S

WELCOME & HOUSEKEEPING/LOGISTICS

MS. BARRETT: Good morning, folks. We are hopeful that everybody can take a seat and we'll get started with today's public meeting.

So if you are in the back standing or in an aisle, if you can go ahead and take a seat, please, that would be great. I'll just give one more minute here. I'm going to do a little sound check. Can you all hear me in the back? Just kind of nod yeah. Okay. Good.

All right. Well, we'll go ahead and begin, and I just want to welcome everybody to today's FDA public meeting on foods produced using animal cell culture technology.

My name is Kari Barrett and I'm going to be moderating most of today's meeting. I work at FDA in our Office of Foods and Veterinary Medicine on our strategic communications and public engagement team and I do spend a lot of time working with our stakeholders on engagement.

I do see -- I'm looking around the room. I do

see a number of familiar faces. But I also see a lot of new faces. And I know that this issue is bringing in some new stakeholders. So I really want to welcome all of you in the room and also on our large webcast audience today. I know we have quite a few people who are listening via webcast.

Today, we're going to be focused on sharing scientific and safety information around the foods produced using the animal cell culture technology. I just want to walk you through briefly what the day will bring.

We're going to start with some remarks from our FDA leadership on this topic. We'll continue with a few presentations from our subject matter experts. We'll then hear an overview of the technology. And then, we'll round out the morning with a panel of external perspectives on this topic.

In the afternoon, we'll be listening to the public comments that folks have registered to offer. So there really is a theme here today of information gathering. That is the stage that we're in. We're looking to gather information again on the safety

considerations, on the science with this technology.

All of the information from today, all of our presentations will be captured in a transcript that will be posted on the FDA website and we'll also be posting the PowerPoint presentations that you'll see. And that may take a day or two as we have to make sure that they're compliant with the appropriate posting criteria.

We also want to recognize that there are a lot of aspects to this issue of animal cell culture technology. But again, I really want to say in advance that we appreciate your time today to consider the scientific and safety considerations.

Before we jump into the program, there's always housekeeping. So I'm going to try to go through it quickly. But there are a number of things I want to just draw your attention to.

All of you should have a folder that you received at registration. In the folder, there's the agenda. Also importantly, there's the biographies for all of the speakers today. So typically I'm just going to say the name and title because you have that

background information.

You're also going to find in that packet a one-pager on how to comment on this issue. The docket is open until I believe September 25th. So please look at that. For our Web audience, you should also have access to similar materials through the FDA website and this meeting webpage.

And do note too that we have a number of folks from the media here today. And I just want to be sure that you've had the opportunity to check in with our media staff. I'm looking at Jen Dooren, who's down here, and Megan, I see Megan at the top. They both have blue ribbons on. So please, if you haven't checked in with them, do so.

We also have, for the folks who are offering public comment today, Juanita Yates -- I'm looking for Juanita. She is right here in the back of the room. If you can just check in with her maybe during a break or lunch so she knows you're present and we know who we do have for that lineup this afternoon.

Lunch today, we recommend the Wiley Café, which is at the front of the building. You do have to

leave the building. So if you have lunch there, just be sure you have your nametag coming in. That'll help you with security.

For the restrooms, they're in the hallway as you came in to the registration desk. There's also a conference room directly across from those restrooms that is open and available if anybody needs to gather and meet somebody today. The room is 1A002.

I do want to remind folks that you are not to bring food and drink into the auditorium. We just really appreciate you paying attention to that.

We have exits at the back of the room. Phones, everybody always needs that reminder. Please turn off your first phone, your second phone and anything else that you have that might ring or make noise.

Unfortunately there is not Wi-Fi support in this auditorium. I know some people have asked about that. But we do not have that here.

I also want to comment on the temperature. It's sort of warm as we're starting out. It may get cold. We'll try to keep it regulated. But it is

challenging in this room. So just in advance, I want you to know we're aware and we'll do the best we can.

If you have any general questions or comments throughout the day, again, Juanita Yates is your go-to person or anybody at the registration desk.

So with that, I do want to now officially start off our program with our speakers who are offering opening remarks. So Dr. Gottlieb and Dr. Mayne, if you'll come up?

We are very pleased to have with us today Dr. Scott Gottlieb, who is the commissioner of FDA. And we also have Dr. Susan Mayne, who is our director for the Center for Food Safety and Applied Nutrition, or as we call it, CFSAN, also at FDA. And so, with that, Dr. Gottlieb, I'm going to hand the podium to you. Thank you.

OPENING REMARKS

DR. GOTTLIEB: Thanks a lot and thanks for having me here today and thanks for joining us as well. Good morning to everyone. I want to take a moment up front to just thank our colleagues from USDA who are joining us today. I think many of them are joining by

WebEx, and also thank my colleagues from FDA who helped to put together today's important conversation.

Today is the start of a dialogue about two significant and complementary objectives. First, our efforts to keep the food supply safe and also helping enable technological advances in the food sector that could improve productivity and expand choices that consumers have.

Since coming back to the agency more than a year ago, I've been focused with a lot of my time on our efforts to advance safety innovation in America's food supply.

And we're hard at work here at the agency ensuring that FDA is taking steps to modernize our food safety activities into a prevention-oriented framework and we're embracing the latest advances in technology for the detection of these food safety concerns.

I'll give you one example. We're expanding our use of genomic tools to detect and track when outbreaks of human illness are related to food sources. And we're taking new and comprehensive looks at our existing food safety and labeling regulations to ensure

that they're promoting innovation while at the same time protecting consumers.

Keeping up with modern food production is a big job and it's a mission that we're deeply committed to here at the FDA. Agriculture, in my view, is one of the 20th century's modern miracles. How we produce and sell, consume food today is very different from even a couple of decades ago.

Advances in production techniques, food processing and packaging have given consumers a multitude of new options. The innovation in American agricultural production dwarfs the technological progress we've seen in almost any other sector over any comparable period of time.

And this innovation is also tailored to meet consumer demands. We see this every time we walk into the supermarket. America enjoys the safest food supply and more consumer options than perhaps any other nation.

It's the goal of promoting innovation and meeting consumer demand that brings us here today to discuss cell-cultured foods and doing these things in a

way that ensures that consumers are kept safe and fully informed about the food options that they have.

While FDA has been well-versed in the use of cell-cultured technologies in medical applications for some time now, we now find ourselves with the need to look at these technologies in the context of food production.

That owes to the continued ingenuity of the food and agricultural industries that are adopting these tools and the recognition of new marketing opportunities by entrepreneurs.

This technology is gaining interest among a number of food campiness. It's gaining some early adoption by some long established and household names in the food industry.

It's also drawing interest from a number of new startup firms. Efforts in the private sector to develop different food products using cell-cultured technology are now fully underway and food products that are derived from these new techniques are likely to reach the retail shelves in the near future.

Given these events, it's critical that our

scientific and regulatory bodies think carefully about the frameworks needed to ensure the safe production of these products.

Adjusting to new technologies is not new for us at FDA and not new for food regulators. There are numerous examples of other emerging technologies in which FDA played a role in helping advance novel practices.

FDA is constantly evaluating new areas of food innovation and establishing guidelines on how new technology can safely advance. Industry sponsors look to us for important guidance when it comes to our nation's food supply, including the pathway for bringing forward safe, emerging food innovations.

Equally important, consumers look to us as well for reliable information that can help inform their food choices. And just as we've done with other advances in food technology, the FDA is going to help advance these evaluations as well when it comes to cultured foods.

Our past experience with novel food technologies and our extensive background in cell-

cultured technologies in the medical products space will help inform our approach to evaluating the safety of these cell-based food products.

This meeting gives us an important opportunity to share our initial thinking on the science, our initial regulatory tools and how they may apply to this novel area of technology. And most importantly, this meeting gives us the opportunity to hear from the public and those of you who are joining us here today.

The FDA is committed to working with stakeholders to foster innovation while ensuring the safety of our food supply. In fact, the success of the foods program has been built on a dialog with industry, with consumers and with other government partners.

These partnerships have guided how we use our authorities. It's guided the development of our programs to ensure food safety of new products, new ingredients, new methods of manufacturing and how these things are developed.

And we're looking forward to a robust dialog on the complex and evolving technological considerations that need to inform our thinking in this

new space.

Some of the questions that we're seeking your input on are questions like what are the opportunities here and what are the challenges.

What considerations specific to animal cell culture technology would be appropriate to include in the evaluation of food produced in this way and what variations in manufacturing method would be relevant to safety considerations with this technology.

And finally, what kinds of substances would be used in the manufacture of foods and what are the safety considerations with respect to these? We also want to know if there are any potential hazards from these products that are different from those associated with traditional food production.

These are all important questions where your feedback will be helpful to us and important to moving forward. Our intent is to work closely with our partners and to engage in public discussions on these involving technologies to ensure that we understand and consider all of the factors.

This meeting today marks a very important

beginning to these conversations. And based on the turnout for today's meeting in person and by video where we have many people joining us, there's clearly a lot of interest in this emerging area of technology.

So I want to thank you all for taking the time to be here today. I hope you find the discussion to be useful and timely. These products are evolving very quickly, and we need to be prepared here at the FDA.

We need to be in a position to answer the many important questions that are going to come up and to help this field move forward in a way that's safe and effective for consumers. Thanks again.

(Applause.)

DR. MAYNE: So, thank you. I know we're getting a few people seated. We'll just get the last group seated here.

So it's my pleasure to welcome you here to the Center for Food Safety and Applied Nutrition, for those of you who are here in the audience. And for those of you who are attending via the webcast, we welcome your participation.

I want to start by echoing what Dr. Gottlieb

said about FDA's commitment to supporting innovation while assuring safety.

In fact, I've learned in my three-and-a-half years here as the director of FDA's Center for Food Safety and Applied Nutrition how committed my colleagues, from researchers to leadership, are to advancing food technology.

It's an area to which I am also personally committed. For example, I have prioritized attending future food tech conferences in 2017 and 2018 to help prepare the center for the technological advances that we know are in the early stages of development but will soon coming to us here at the FDA.

Animal cell culture technology is one of those advances. We have been in contact with companies on this issue for several years to determine what data and other information we will need to evaluate the safety of these products.

We have been engaging with experts in FDA's Center for Biologics Evaluation and Research, also known as CBER, to gain insight into technical issues and other considerations based on their extensive

experience in therapeutic applications of cultured cells.

We are planning a fall meeting of FDA's science board on this subject, facilitated by FDA's Office of the Chief Scientist. The board advises Commissioner Gottlieb and other FDA leaders on complex science and technical issues central to our mission to protect and promote public health.

And we have been attending public presentations outside of FDA on this subject, including conferences such as the Future Food Tech Conference.

Today, we want to facilitate an open and transparent dialog focused on the food safety questions involving these products as we anticipate that they will be coming into the U.S. market in the near future.

These are still early days. But make no mistake that FDA has been preparing for this for quite some time. We will always look at these advances through the lens of food safety.

It's our mission to protect and promote public health and we are onboard with supporting innovative products. But they must be safe products. And if we

want consumers to have confidence in the safety of these foods, conversations like the ones we are having today are critical.

Having food technology innovators engage with food safety experts and regulatory authorities is essential to building that consumer confidence.

Consumers care deeply about ensuring both safety and accurate labeling surrounding their foods and these are both roles that FDA has been charged with carrying out for the products that we regulate. In fact, we regulate about 80 percent of the food supply.

This is not our first rodeo, so to speak, in this area. We have multiple authorities and programs that can support efforts to bring products with new ingredients to the market.

For example, FDA has evaluated a variety of foods produced by cell culture, including microbial products such as probiotics, algal products such as spirulina and fungal products or the mycoprotein products as well.

We issued a guidance document in 2014 on how to assess the effects of significant changes in the

manufacturing process, on the safety and regulatory status of food ingredients and food contact substances including color additives. This includes the use of nanotechnology. We have both premarket and post-market programs for evaluating the safety of substances used in the production and manufacture of foods.

So we're ready to face the challenges and to support the promise of this and other emerging food technologies. We will take the necessary steps to update or clarify science-based policies to advance innovation, promoting risk-based regulatory approaches and increasing regulatory predictability.

We are early in the process. But we are looking forward to learning from you so that we can be better prepared to support innovation. Thank you.

(Applause.)

MS. BARRETT: All right. Well, thank you. And we will now bring up our FDA subject matter experts. If we can have Bill Jones and Jeremiah Fasano come up?

At this point, what we'd like to cover is the regulatory framework for food safety here at FDA, as

well as FDA's historical experience with food safety evaluation and some of the future considerations that are ahead of us.

Our speakers are William, or Bill, Jones, who is our acting director for our Office of Food Safety here at CFSAN. And we also have Jeremiah Fasano, who is our consumer safety officer in our Division of Biotechnology and GRAS Notice Review, Office of Food Additive Safety, CFSAN, FDA. These titles sometimes are quite long.

But welcome both of you. And we're going to start with Bill, who will have some slides. So Bill, I'll have you come up to the podium and then Jeremiah will follow. Thank you.

REGULATORY FRAMEWORK FOR FOOD SAFETY AT FDA

DR. JONES: Good morning. I'm going to spend a few minutes discussing the overall regulatory framework for food safety here at FDA. This will include a brief overview of some significant authorities under the Food Safety Modernization Act.

Thank you. That's the slide we're looking for. So 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 that is used for food or drink. Chewing gum, which gets its own list entry, is also included in the definition.

You'll notice that the food or drink can be consumed by humans or animals. Today, we're going to be focusing on human consumption.

On the next slide, we'll address the Federal Food, Drug and Cosmetic Act setting out requirements for the safety of foods. There are a number of conditions that would make a food unsafe or adulterated and therefore unlawful.

First and foremost, if food contains a poisonous or deleterious substance which would be harmful, that food is adulterated.

The act differentiates between poisonous and deleterious substances that are added to a food and those that happen to be present in a food.

For those that happen to be present, 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, fungi and other pests.

At some level, those substances could be harmful. In wild plant species, that's a concern. But in agricultural crops, while these substances are sometimes detectable, levels are far too low to raise any food safety concerns.

Next, two other key conditions relate to food additives and insanitary conditions. First, if you add an unsafe food additive to food, you 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 could lead to contamination such as microbial contamination or could otherwise lead to that food becoming harmful for consumption in some way, then the food is adulterated, unsafe, unlawful. There are other adulteration

provisions. But that gives you a sense of the overall framework.

Now, 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 -- the next slide, please -- focuses on hazard analysis and risk-based -- we'll go to one more slide ahead, please -- one key component -- thank you -- of FSMA focuses on hazard analysis and risk-based controls.

As section 118 of the act says, this is about preventive controls which are a cornerstone of their modernized approach under FSMA.

Effective controls of this type are informed by a hazard analysis of each facility's manufacturing processes and matched to the risks identified during

that analysis.

Each food facility is required to develop a food safety plan incorporating these elements. The implementing regulation is found in Title XXI, 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 one of them.

The plan should also include steps to oversee and manage the controls, include how to monitor them, correct any issues that arise and verify the effectiveness of the corrections.

Records must 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.

Next, as I've mentioned, FDA also now has a number of additional regulatory tools as a result of FSMA. In addition to the mandatory food safety plans, we have regulatory tools related to inspection and compliance, as well as enforcement.

There are mandated risk-adjusted inspection frequencies for both domestic and foreign facilities. There's a mandatory record access, which means we can ask to see both a facility's food safety plans and their records of implementation and monitoring.

We have the authority to require a recall. We can suspend the registration of a facility if needed.

Importers can be held accountable for ensuring that their foreign suppliers have adequate preventive controls in place and we can deny entry of foods from a foreign facility if FDA is denied access to that facility.

We don't relish using the enforcement tools.

We favor compliance. But these are tools that can help us achieve that.

Finally, I'd like to identify a few questions that are a good starting place when considering a new food production process for implementation into 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 of the hazards associated with appreciable 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 has just been a brief and quite broad overview of FDA's regulatory framework for food safety. As you can see, there's a lot to think about. But these basic questions may be a good starting place. So, thank you. And I'd now like to turn the podium over to Jeremiah Fasano.

(Applause.)

FDA'S HISTORICAL EXPERIENCE WITH FOOD SAFETY EVALUATION
AND FUTURE CONSIDERATIONS

MR. FASANO: Thanks, Bill. So if we could have the -- excellent. So my name's Jeremiah Fasano and I'm going to talk to you a little bit today about some of our experiences in the past with evaluating food safety in a particular context.

And I'm going to be using primarily here a food ingredient-focused lens and we'll go through a few particular experiences that may potentially be useful as sort of background information and context in thinking about the subject of today's meeting.

Next slide. So first, let's talk a little bit about what a food ingredient actually is. I've drawn here from the definition for a food additive.

I'm using the term ingredient just to indicate that I'm talking not only about substances that require FDA approval for use, but also the substances that would fit within the scope, but, for one reason or another, are exempt from those requirements for FDA approval.

So you can see that a food ingredient is something that is a component of food, may reasonably be expected to become so or may otherwise affect the characteristics of the food. This is a pretty broad definition and it includes also any substance intended for producing, manufacturing, packing, preparing, treating food. So the scope is pretty broad here.

Now, it's true that in many cases materials that come into contact with the food are going to result in extremely modest exposures, if any, from the substances in that contact material which can simplify the safety assessment process.

But as sort of a first principle or starting point, the scope of potential substances we would look at in evaluating the safety of a food or food ingredient are fairly expansive.

Next slide. So you already heard a little bit from Bill about the safety standard for substances that are present in a food.

The safety standard for substances that are added to a food is a little bit different. And that standard essentially is reasonable certainty in the

minds of competent scientists that the substance -- there's reasonable certainty of no harm for the intended use of the substance. Right. So reasonable certainty of no harm.

What goes into that? There's a number of factors. The first one is the identity of the substance and its anticipated exposure, including both exposure to the substance itself as well as any breakdown products or metabolites that might occur during use, cumulative exposure to this and similar substances, appropriate safety factors and then appropriate data and information. We'll talk more about that in a minute.

But I just want to note here that the appropriate data and information can vary a great deal, depending on the properties of the substance and the intended use from the resulting exposure.

Next slide.

MS. BARRETT: Jeremiah -- [off mic].

MR. FASANO: Oh, excellent. A little more autonomy here. Okay. So how does this work out in practice? The quality and quantity of the evidence

that's required for a safety assessment is always going to be the same. But there are a number of channels through which you can reach that status of lawful for the intended use, which all ingredients are required to have.

The first one that I'm going to talk about is food and color additives. And I haven't mentioned color additives before.

So let me just briefly say here they are substances that are intended to impart color used in food as well as in biologics, drugs, medical devices. They're held to similar safety standards as for food additives.

So the way that these can become lawful is by approval by FDA. You submit a petition to the agency with the identity of the substance, intended use, supporting material and data and information on safety.

If FDA approves that, the FDA will write a regulation which goes in the Code of Federal Regulations approving that use. So that is one way that you can have substances that are lawful for use in food for some defined use.

Now, as I mentioned before, things that come into contact with food are also food additives. And for food contact materials and food contact substances from those materials, those can be dealt with through a food additive regulation framework. And certainly we have regulations on those kinds of substances.

But the act also provides for a notification process which is manufacturer-specific. And in this case, a notification can be submitted to the agency describing the identity of a substance made by a particular manufacturer along with the sort of exposure scenario and the limitations on use.

And if that notification becomes effective, then that is another way that a substance can be authorized for that use. And we maintain a public inventory of all of those notifications.

The final channel I'm going to talk about today is for substances which are exempt from the requirement for FDA approval prior to market entry.

And the reason for this, they have the same requirements for safety data for the quantity and quality of that data. But the difference in this case

is that all that data is public.

And instead of having convinced the agency's scientists that there is reasonable certainty of no harm, essentially that information, that public information has convinced the scientific community that there is reasonable certainty of no harm.

And under those circumstances, it's exempt from the requirement for FDA approval. And we call those generally recognized as safe ingredient uses.

And FDA does run a program through which you can notify the agency about a conclusion that you have made that your intended use of a substance meets the criteria for GRAS status.

The notification would include the identity, intended use, anticipated exposure and all the data and information that would support that conclusion of GRAS status. And we also maintain a public inventory of those notifications as well as our responses. So that's all available on the website.

Next, I'd like to talk a little bit about the considerations that actually go into a safety assessment. As I think everyone will agree, the

identity of the substance and its exposure are a critical starting point for this kind of safety assessment.

Different exposure scenarios can raise different kinds of safety questions and thus require different kinds of information to address them.

Another important point, something that's becoming increasingly important as useful, is the kinds of information that we can infer about the properties of the substance just from its structure alone.

Tools such as quantitative structure activity relationships, other kinds of functional grouping and read-across techniques, different kinds of pharmacokinetic modeling can give us a lot of information about the potential properties of a substance and its metabolic fate even before any studies are conducted.

So that kind of information can be extremely valuable in identifying the appropriate studies to be used in a safety assessment. And so, this idea of really, you know, matching the data needed to the properties and intended use of the substance is really

important.

We certainly have recommendations, guidelines for frameworks for thinking about food safety assessment and food ingredient safety assessment. But they always need to be sort of refined and matched to the actual properties of the substance and the intended use.

So FDA has been thinking for a fair bit about potential impacts of manufacturing changes on the properties of a substance and its impact on safety.

There are a number of different applications of this idea, one that I'm sure you're all familiar with is the idea that the size -- the sort of particle size of the substance can have a big impact on its properties, right.

So you could have the same chemical identity of a substance and yet the properties could change a great deal depending on the actual size of the particles of the substance in the food.

And with increasingly greater control over the manufacturing process, fine grain control over that particle size has become increasingly routine.

And so, the guidance that we issued in 2014 essentially just walks through some of the things you should be thinking about if you introduce a significant manufacturing change.

In some cases, it may not matter at all. But in some cases, it may have a meaningful effect on the properties of the food. And if it does, some of those changes in the properties may actually matter for safety. And so, considering those two steps is very important.

We recommend that after you do that assessment, that you consult with the agency about your conclusions and see whether any additional regulatory steps would need to be taken.

As it happens, this illustrates two key themes of FDA's ingredient safety assessment process. The first is just that, as I mentioned before, while we have some general guidelines and recommendations, such as in our red book guidance, every safety assessment is always case by case.

It's dependent on the properties of the substance, the data and information available, the

intended conditions of use. All of these things go into any individual ingredient safety assessment. And the other point is consultation.

So we recommend consultation early and often. We welcome anybody who is thinking about developing a new technology, a new substance for use, a new manufacturing process to come in and talk to us.

And we feel this kind of consultation process really benefits not only industry but the agency and the public. We find that that's been extremely valuable.

So as I've already alluded to a number of times, it really is the properties of the substance that the safety evaluation is focused on and not really the process.

But that said, the process can often have a significant impact on the properties of the substance or on other safety considerations that you might need to take into account when you're doing your assessment.

For example, if you're extracting a chemical from a plant versus synthesizing it in a lab, even if the primary product of the process is chemically

identical, you might have different safety considerations because of your manufacturing process. You might have different secondary constituents to be concerned about. You might have different process controls or specifications.

So those are all legitimate things to think about in doing your safety assessment of the product. And because the information that you might need will change depending on aspects of the process that affect the properties of the substance.

So given a particular manufacturing process, you may need additional or different information in order to reach a conclusion of reasonable certainty of no harm for your ingredient safety assessment.

Next I'm going to talk about a few historical examples of broad classes of substances that could provide some useful context. And none of these are exactly parallel to the topic of today's meeting.

But they all could potentially provide some valuable insights into the general way that we think about new manufacturing processes.

And the three that I'm going to talk about are

substances that are produced by cultured cells, cultured cells actually consumed directly as food ingredients and new plant varieties produced by modern biotechnology.

So first let's talk about substances produced by cultured cells. In this scenario, essentially you're using the cell as a small manufacturing plant that is producing a substance of interest which you then collect and use as a food ingredient.

We've had a fair bit of experience with these, starting with sort of taking advantage of a natural phenomenon, which is that fungi, when they grow in soil or some other local environment, they need to get nutrition from their surroundings.

And one way they do that is to make enzymes to break down their surroundings and put them out into their environment. And then, that creates nutrients that the fungi can absorb. And it occurred to -- and it turns out that many of these enzymes actually have useful food technology applications.

So it occurred to folks that they could culture these fungi in some sort of bioreactor or a

growth medium, let the fungi push the enzymes out into the medium and then collect them and use them for food technology applications as well as a number of other industrial applications.

So that is an early and still used example of using cultured cells in order to generate a substance that then becomes a food ingredient.

Another one that has become fairly widespread in recent years is the use of algae in culture to produce oils. In particular, some algae produce omega-3 fatty acids, which are the subject of significant consumer interest.

And for that reason, there was an impetus for industry to develop a culture process by which you could culture algae at large scale in bioreactors.

They would produce a lot of the omega-3 fatty acids and then you could harvest that for use as a food ingredient. And in fact, many products on the market today contain these algal omega-3 oils.

So that's another example of where cell cultures are being used to produce an ingredient.

And then finally, now one of the most common

ways to produce a protein if you want to use it for research, for clinical applications, for food technology applications is to take the gene that codes for that protein, put it in a cell -- typically a bacterium or a yeast -- and then have the cell make that protein of interest, which you can then collect.

This started out as a fairly esoteric research tool. But now, it's extremely common both in therapeutic and in food applications. And we have seen a number of substances produced through this method in microbes that are used then as direct food ingredients.

So all these substances we would evaluate through traditional food ingredient safety assessment processes. And our experience has been it has not been an issue. Considerations specific to these manufacturing processes, the primary two really are unintended metabolites that could be produced by the cells.

So that's always a consideration to take into account what other substances are the cell making or are any of them of concern and also occasionally materials that are introduced into the growth medium.

For example, if you're using a material from an allergenic source, that potentially could be a concern. And so, those kinds of issues have arisen during evaluation.

But we have been able -- our experience has been we've been able to address them by specifying the kinds of cells used, understanding potential metabolites that might be produced, appropriate process controls and specifications.

Next I'd like to talk a little bit about cultured cells themselves used as direct food ingredients. So there are some extremely mundane examples of this. And one I'm sure you're all familiar with is yogurt, right, to which bacteria are added.

They have an effect on the properties of the dairy products to which they're added and then we consume them, often live.

And in fact, we have seen both live bacterial cultures and heat-killed bacterial cultures used as direct food ingredients. They've come through our food ingredient safety assessment program.

We've also, as Dr. Mayne mentioned earlier,

seen some algal cells grown in culture used as direct food ingredients. And then finally we've seen fungal cells. The most common one is one that many people don't necessarily think of as a fungus.

But yeast is a single-celled fungus. And in addition to its baking applications, we've also seen a number of food ingredient packages where the yeast is being used for some other purpose.

So that's an example of growing cells up in culture and using them as a direct ingredient. In addition to that, mycoprotein, which is a fairly widespread alternative protein source, is in fact a fungus grown in culture and then harvested for use as food.

So we have seen that as well through our food ingredient safety assessment program. And again, we evaluated -- have evaluated these successfully using traditional food ingredient assessment techniques.

In terms of specific manufacturing considerations, they're really similar to the ones that I mentioned for using cells to produce ingredients. You're interested in potential undesired metabolites

that you might need to be concerned about and also substances added to the medium.

And again, our experience has been that by understanding the sort of properties of any particular cell type, you can predict what metabolites might be a potential concern and manage them through appropriate process controls and specifications.

And then finally, I'll talk a little bit about new plant varieties produced using modern biotechnology. It's a bit of a mouthful but it sort of captures the breadth of the concept.

In this case, we're looking at agricultural crops where new varieties are produced and what kinds of safety considerations might be necessary to ensure that they are as safe as food is required to be.

We've had decades of experience at this point with evaluating foods from these kinds of crops. Early on in that process, we actually issued a policy document. The flowchart here is drawn from that, which identifies some of the key considerations that are involved.

What kind of substances are you adding to the

crop? What's the source of those substances? What kinds of methods are you using to introduce it and do they have any impact on the properties of the food?

These are all sort of fairly broad and sort of practical considerations about what the consequences are for food safety.

And that sort of framework for thinking about those consequences has proved to be flexible and adaptable and robust over the evolution of the technologies that we've seen over the years.

I mean, a variety of different strategies have been used to generate these new plant varieties. As we pointed out in that policy document, these same considerations would apply to more traditional methods of developing new plant varieties. You're always interested in the properties of the food, what changes you might have made, what consequences it might have for safety.

And so, this is sort of another example of dealing with a variety of production processes for food where focusing on those key questions and what are the consequences for safety and what kinds of variation are

going to actually have an impact for safety have been very helpful.

So just to draw some general observations for that little historical excursion, I think it's fair to say that biological production systems are fairly complex.

And it's reasonable to ask questions about sort of the consistency of the production process, adequate characterization of products from that process and appropriate control of variation during the production process.

But as I said, we actually have a great deal of experience with a wide variety of biological production systems, some of them quite complex.

And our experience has been that it is possible to adequately characterize those substances that come out of the process with respect to safety, to understand what the potential variations are that are relevant for safety and to appropriately control them.

And these questions in the ingredient assessment processes that we've done have been successfully addressed prior to market entry.

So I'm going to close by reiterating a few themes from that 2014 guidance that I mentioned earlier. Ultimately it is the properties of the substance that is going to be used as food or a food ingredient that matters.

But it's worth thinking about the potential impact of the process on those properties. In some cases, multiple different processes will result in an identical product.

In other ones such as some of these complex biological production systems that we've been talking about, the variations in the process can have a significant effect on the identity and properties of the substance that comes out of it.

It's also worth considering what potential constituents or contaminants you might introduce or if there are hazards that are specific to a particular production process that you need to take into account in your safety assessment.

That said, it's always important to remember that not every property of a food is important for safety. And so, it's important to apply a critical eye

to those changes in the properties of a substance and ask what is the consequence for safety going to be.

And that general framework is one that we discuss in the 2014 guidance and that we -- is typically how we think about impacts of manufacturing changes.

So with that, I'll conclude my presentation. Thank you for your attention. I hope you've found that this has been useful and help provide some context that may be helpful in providing comments both today and to the docket. Thank you.

(Applause.)

MS. BARRETT: All right. So we are a little ahead of schedule. What I would like to suggest, and it's always a bit dangerous when you get off your routine agenda, but what I'd like to suggest is that we go ahead and break now, that we take a half-hour break, that we come back at 10 of and I think we can use some of that extra time for both our next speaker and our panel, since it's quite large.

So with that, we'll go ahead and break. And again, if we could be back in the room at 9:50, we'll

start at that time. Thank you.

(Whereupon, the foregoing went off the record at 9:21 a.m., and went back on the record at 9:52 a.m.)

MS. BARRETT: All right. As we're gathering, if Rhonda Miller or Peter Licari are here, if you could just come down and be seated close to the stage for the panel.

Again, Rhonda and Peter, if you're in the room, that would be really helpful. And again, if folks can take seats? Again, if Peter Licari, if you're in the room, if you can just come down to be near the stage, that would be super helpful.

All right. Okay. Well, welcome back. And again, I'm Kari Barrett. At this point in our agenda, we're going to start to hear from some folks outside of FDA regarding this technology.

We're going to start with an outside expert who will give an overview of the technology. And then, following that, we'll have a panel of a number of folks offering different perspectives on the technology.

So we'll start with our external expert on the

animal cell culture technology. We have Dr. Paul Mozdziak. He's a professor at the Prestage Department of Poultry Science at North Carolina State University. And he is right here with us. So Paul, I'm going to turn the podium over to you. Thank you.

OVERVIEW OF ANIMAL-DERIVED CELL CULTURE TECHNOLOGY

DR. MOZDZIAK: Thank you. So what I'm going to talk about today is I'm going to try to give a broad overview of animal-derived cell culture technology.

UNIDENTIFIED SPEAKER: Can you use the mic?

DR. MOZDZIAK: Oh, sorry. Better? Thank you. So what I'm going to try to do today is I'm going to try to give a broad overview of animal cell culture technology and then I'm going to try to talk about failure points.

So each of my slides has some type of a take-home message. And really, where I want to start is to start by talking a little bit about the history of cell culture. There are no great mysteries when it comes to cell culture. This technology has been around for a very long time.

If we go back to 1865, Rowe (ph) first

isolated cells arguably. Carrel developed aseptic techniques somewhere between 1912 up until the 1940s.

And it's really continued today in the 2000s with the development of disposable bioreactors and applications of engineering technology for scale-up and cell culture. So that's just an overview as to what the technology is and what the history is.

Oh, there we go. Now, the next point that I want to make in terms of landmarks in terms of the development of the cell culture is that the things that really propelled cell culture technology forward were during the 1940s and 1950s, the development of antibiotics and really two things developed the push cell culture forward.

It was first the development of clean air, filtered air for aseptic technique. This is a biological safety cabinet. This is a laminar flow hood.

And secondly, the development of cheap, disposable plasticware. There's a great deal of interest in using disposable plasticware obviously. And when it comes to bioreactor culture, there is a

great interest in using disposables because if you use disposables, there's much less chance of a product failure with a disposable bioreactor than a clean in place bioreactor. And then, the last picture on the slide is just showing the development of cryopreserved cell lines.

So these are the things that really pushed cell culture forward. Now, the issue is when it comes to using animal cells in food products is that the present state of the art is that animal cell culture technology is well-established.

It is well-known and it is frequently done. In general, in terms of the process, we know where the failure points are. We know how to monitor process.

The issue with food is we don't know what the products are going to be. You know, one potential platform could be just cells. It could be cellular muscle protein.

It could be cells with plant material. You may grow cells on microcarriers. I'm not really going to talk much about microcarriers. But I just wanted it at one place in the talk because it is something that's

going to have to be thought about from a regulatory standpoint. And the so-called Holy Grail is going to be an actual piece of biomanufactured muscle.

So what this is showing here is a pellet of cells. And this is a picture from Mark Post just showing a piece of muscle in the cell culture dish. This is where the technology is today.

So, you know, what kind of products might we see. You know, there's a whole range of things that can come about that maybe none of us have even thought of yet. But where things are today, we could have a product made with a cell pellet like this formed into a protein bar like this.

Now, the issue with the upstream technology is that from vaccine manufacturing, all of the guidance is well-established. FDA guidance was published in 2010 and we're not working in a vacuum. You know, today we can make cell pellets with selected cell lines, serum-free media and there are master cell banks around.

Now, the issue is, is with biomanufactured muscle, there's significant technological challenges along with regulatory challenges that need to be

considered.

Now, before I talk about that, I just want to give a couple of slides on the biology so I can set the framework for what the challenges are for just growing cells versus just growing biomanufactured muscle.

So if we're going to scale up cells into a pellet, you're going to grow a cell that looks like something like this.

Compared to bacteria, they're huge. Compared to muscle fibers, they're small. It's a very simple system, a single nucleus, some lysosomes, some endoplasmic reticulum, some protein.

When you start talking about muscle or a muscle cell, they are multinucleate cells. They range anywhere in length from one to 40 millimeters, anywhere in diameter from 10 to 100 microns. So they're a log factor bigger.

So that growing those cells in culture at scale has some significant technological challenges. And again, if you're going to make muscle, you're also going to have to have adipose tissue in there and you're also going to have vasculature.

So to illustrate the structure of muscle and to show what the challenge is in terms of making the filet or the T-bone steak in vitro, I just have one picture just to show what a muscle looks like.

You have a layer of connective tissue that surrounds the muscle cells. And then, you have groups of muscle fibers in the muscle surrounded by connective tissue.

And then you have the individual muscle fibers. It's very dense. The muscle fibers are multinucleate. They are very large. They have myofibrillar protein, which allows contraction.

It's a very complicated system. It's a very dense system. And in terms of making a biomanufactured steak like this, there are a lot of technological challenges that need to be overcome.

Now, in terms of capturing and making that muscle, I just want to talk briefly about the biology that you have to capture to make a muscle in vitro.

Within the muscle back here, there's a small resident population of stem cells called satellite cells, myoblasts, whatever you wish to call them.

There is a population of these uninucleate cells that are capable of proliferating. They're capable of rebuilding muscle. A muscle can be injured multiple times and the muscle will rebuild itself due to this resident population of cells.

In order to biomanufacture a muscle, what you need to do is to capture this muscle, recapitulate this sequence of myogenesis to get the cells to proliferate as uninucleate cells. They align and fuse into myotubes.

Once the cell fuses into a myotube, it is no longer able to differentiate. It is no longer able to grow or proliferate.

So this is a terminal process. The technical challenge is how do you get the cells like so to proliferate at scale, to get them to align and to develop into a myofiber and then to mature into a muscle fiber and then actually to produce muscle.

So the take-home message is what you would like to do with these cells is theoretically to grow them up in some type of a suspension process. And then, what you would want to do here is to get them to

differentiate.

Now, the challenge to myogenesis is, in an ideal production platform, you have the single nucleate cells here frozen down. And then, you go through a series of transfers into an increasing amount of media.

Each place in the transfer is a place for contamination to get in, bacterial, microbial, viral contamination.

And then, you wish to go to a bioreactor and then ideally you would seed it on some type of a scaffold that looks something like this. That's a scaffold of a heart because there's a lot of interest in using this technology to biomanufacture organs.

So, your thing died. Okay. Back. No problem. Okay. So that's the process. So the general procedure to isolate cells, you know, where did the cells come from. You have to isolate the cells, establish cell lines potentially and then the question is, is are you going to have an immortalized cell line.

And once you have the immortalized cell line, you know, what kind of media are you going to use. Is it going to be classical media containing serum or is

it going to be serum-free? So this is the general process of isolating and propagating a cell line.

Now, what I want to talk about next is the concept of immortalization. On the first slide that you couldn't see, there's the theory of the Hayflick limit. Theoretically most animal cells have the ability to divide 52 times in culture before they reach the end of their replicative lifespan.

So what happens if somebody is working with a finite cell line is they put the cells in the culture and they propagate them for about three months. And then, what happens is the cells magically stop dying or they become transformed into a continuous cell line.

Transformation is a relatively rare event. And again, this is a very historical procedure. The first cell lines that were developed were developed without any concept of the biology. They were just able to grow cells without any understanding.

So there are naturally selected cell lines that you'll see on the next slide. There are naturally occurring cell lines, such as stem cells. If you take a stem cell out and you cultivate it under the right

conditions, a stem cell will grow continually. And so, there is no modification to those cells. It is only propagating them.

Now, there's also the concept and the ability to do genetic modifications to immortalize a cell line, to change the characteristics of a cell line. In each type of -- each type of cell lines are important things to consider from a regulatory standpoint.

So cell line development is well-established. The cell lines that are probably most popular in muscle biology is the C2C12 cell line from myosin L6 from rats. They were isolated in the '70s. And again, this is just a laundry list of all of the cell lines that are frequently used in research. Everybody has heard of HeLa cells. They date to 1952.

Cell line development, selecting cell lines just by simply growing them and waiting for the cells to go through the transformation process has been used since the 1950s and it's been successful. Ancient technology.

Stem cells. Stem cells are not genetically modified. That technology in the mouse has been around

since the 1980s. And again, there's nothing magic about it. It's just cultivating -- just isolating and cultivating the cells and the only real challenge to stem cell culture is keeping the cells in an undifferentiated state.

Now, I'm just going to talk -- mention very quickly two types of genetic modifications that might be used to develop cell lines. Induced pluripotent stem cells are very popular. It's a very popular technology that's come on in the last 10 years.

You know, the issue is, is you take an adult cell. You take a cell line. You transfect in DNA to change the characteristics of a cell. So this is one technology that might be used in cell line development in biomanufactured food.

The other type of technology that could be used in immortalization and altering the characteristics of cell line is CRISPR. Everybody has heard about CRISPR, the genome editing technique.

The issue with CRISPR where there's a lot of chatter out in the regulatory world is actually a good issue in that theoretically CRISPR does not change the

footprint of the DNA. You can go at very precise locations in the genome and very efficiently edit or change the genome using the CRISPR technology.

It's extensively used in genetically modified animals and it is probably the most hottest technology in animal cell culture and science in general right now. So those are two important issues to think about.

Now, to go back to reality rather than what could happen, I want to talk a little bit about stem cells and specifically avian embryonic stem cells essentially for one reason.

You can have a product using avian embryonic stem cells today because, as I'll talk about, the cells are already being used in the pharmaceutical industry. They're already being used to make influenza vaccines. So there's a great deal of experience in growing these cells to scale.

You know, what is -- what is an embryonic stem cell? An embryonic stem cell is a cell that's isolated for the most part from the inner cell mass of the blastoderm. You take the cells and put them in the culture dish and cultivate them and keep them in an

undifferentiated state.

In this micrograph, what you can see is the stem cells here, these other cells are STO cells which are an inactivated cell line that's used as a feeder layer. You know, again, it's just something to consider about what are the other things that are going to go into if somebody's going to use these cell lines.

And again, it's very established technology. Dr. Petit had a nice paper in 2004 and the patent literature in the U.S. goes back to 1994. I cited the one in 1997 because I think it was a little bit stronger patent.

Now, I've taken this slide from Vivalis to essentially illustrate what the process is. What Valneva did, they used a duck for their vaccine manufacturing.

Here they got an egg, which is arguably sterile, took out the embryonic stem cells in a sterile environment, put them into culture, cultivated them and then what they did next was to adapt them to suspension. They are genetically stable. They are in suspension. Nothing really magical has been done to

these cells other than to cultivate them.

And so, you know, the point here, on this slide, is, again, the process. When the cells were isolated, they took the cells and they simply put them in these things called shake flasks and grew them under agitation. And then, they scaled them up to bioreactors. And then, they used them in vaccine manufacturing. So again, nothing's been done to modify these cells.

Serum-free media was developed for the cells. Serum-free media contains buffers, amino acids, vitamins, recombinant growth factors. I'll talk a little bit more about media when I talk about primary cell culture.

You know, the other concept that needs to be considered is the concept of a cell bank. In most biomanufacturing situations, what is done is that you take a mother culture. You make a master cell bank from 10 to 200 vials. You qualify it. You make sure it's not contaminated with bacteria.

You check the safety of the master cell bank and then you take one vial from that master cell bank

and use that to seed your cultures. And then, that's done in a routine process. And the types of quality control testing that's usually done on a master cell bank are things like viruses, bacteria, yeasts, mycoplasma and I'll talk a little bit about cell line authentication as well.

So this again is just showing the overall process, that what's done in biomanufacturing today with avian embryonic stem cells is they have a qualified master cell bank.

They take the working cell bank and then they scale it up from increasingly larger flasks with increasing amounts of media. They often go through a disposable bioreactor.

Then, they may use a clean in-place bioreactor for the final step. Each transfer -- each media transfer is a place for the cultures to get contaminated. And those are the things to think about.

So embryonic stem cells, the regulatory framework exists. Serum-free media exists. You know, what I want to talk about next is other potential production platforms, the technological issues with

them and hopefully I can bring out some of the issues that are important to consider from a regulatory standpoint.

So as I mentioned, if somebody's going to make a product, there's a whole series of places people can get cells from to make a product. Stem cells, iPSCs and also directly from the muscle.

And again, I'm going to talk about this because it's the most obvious place to get cells for biomanufactured muscle.

And, you know, the first issue is if you're going to get cells, they have to come from somewhere. In general, for most meat-eating species, there is not a lot of cell lines around that are immortalized. And what you have to do is go to the animal. You can get a biopsy. You can kill the animal.

But the first potential failure point is at harvest because that's when it's going to be open to the environment. That's when you're going in with scissors to cut pieces of muscle out. It is when the things are likely to be the most exposed.

Then after you get the muscle, I showed you

all the myofibrillar protein. I showed you all of the satellite cells. Okay. You have to digest away all of that myofibrillar protein to liberate the cells.

So in general, most individuals are going to treat the muscle with some type of an enzyme. I mean, there are other alternatives, to just let the cells crawl off.

But, you know, in general, somebody's going to treat with an enzyme. The enzyme can be recombinant. The enzyme could also be classically derived. So that needs to be thought about. Again, this is all very routine cell culture.

Now, once the cells are out, what you need to do next -- and then, the other thing I forgot to mention is the collection fluid.

When you collect muscle, you generally do not collect muscle in complete media. You generally collect the muscle in some type of a basal media that just contains buffer salts that maintain physiological pH and osmotic pressure.

Now, basal media, basal media is media that was empirically derived. It's defined. Now, in most

cell culture processes, most individuals first cultivate cells and cell lines in classical media. Classical media contains animal serum. And then, they migrate towards serum-free culture.

And the issue with classical media is that it's generally made of three components: basal media, which is defined.

Basal medias were all empirically derived. They contain physiological pH buffers. They maintain physiological osmotic pressure. And they also contain vitamins, amino acids, lipids and all sorts of good stuff that you can look up.

Okay. And the issue -- the next issue is, is that they were empirically derived by somebody. So they have the name Dulbecco's, Tom's, Eagle's.

Now, for the most part, most buffering systems in cell culture tend to be bicarbonate base because that's the pH buffering system in the body. It's not a hundred percent for cell culture media. Other buffers such as HEPES are used.

But something needs to be done to maintain the pH of your cultures. And so, in most -- if you're

going to use a bicarbonate buffer, you have to add carbon dioxide gas to maintain the pH in the process.

Now, with the basal media, serum is generally added to the basal media because basal media was shown basically in the '50s and the '60s to not have enough nutrients for cells to grow.

The issue with basal media is we don't know what's in it. We know there's growth factors and, you know, in the space, I don't really know how much commercial interest there is in using serum-based media because, from a production standpoint, there's a lot of lot-to-lot variation.

There's the potential for viral contamination. There's the potential for microbial contamination, specifically mycoplasma. So serum has all of these downsides. It's just been historically used because it makes the cells grow really well.

The other thing in classical media is antibiotics. Penicillin and streptomycin is frequently used. Gentamycin is also frequently used. Or alternatively, I've become less a fan of antibiotics in many of my cultures as I've gone along in my career.

But there's a lot of individuals. There's a lot of good reasons to not use antibiotics as well.

So what's serum-free media? Serum-free media basically somebody went and took all of the components of classical media and replaced it with recombinantly derived growth factors, you know, proteins like albumin transfer and the issue with serum-free is that, again, it's defined. You know exactly what's in it.

Now, when you scale up, I just want to make the next point about muscle. The reality is, is if you get the muscle cells out and grow the muscles up as these uninucleate cells, you're going to have to seed them onto something. You're going to have to get them to differentiate.

You know, one production process may be to use these roller bottles and just have sheets of muscle that you trypsinize off. Another production process would be again to grow the cells like this, differentiate them into myotubes and mature them onto myofibers using scaffolds like that.

The issue is, is to get the cells to attach, you have to coat the plasticware in general with

something. You don't necessarily have to. But some individuals will definitely do it. You might want to use collagen, fibronectin, laminin, other extracellular matrix components. What we use in the lab frequently is gelatin.

Okay. So, you know, with scaffolds, there's been a lot of interest in using plant materials as scaffolds. There's a lot of interest in hydrogels. Hydrogels can be made from commonly edible materials like alginate, agarose, fibrin, collagen, you know, both plant and animal-derived. And simply you take these materials, hydrate it and then you can form it into a scaffold that looks something like this.

You know, the issue is, is once you have the scaffold, you have to put the cells on the scaffold and then you have to direct the cells to actually form muscle.

Now, contamination, where's contamination come from? You know, if you have a closed vessel and you have a sterile environment, in general things are not going to get contaminated. You know, in bioreactors, where most of the contamination comes from is a failure

in the cleaning process.

And in cell culture, most contamination comes down to personnel. Somebody did something wrong somewhere and it tends to be very difficult to trace. So whenever you transfer fluid, whenever the fluid is open, there's a chance for contamination to happen.

Well, what is contamination? Contamination is anything in your cell culture that you don't want to be there. You know, the issue is, is that bacteria, yeast, molds have a cell cycle time on the order of 20 minutes.

Animal cells at best have a cell cycle time of 14 to 16 hours so that if you get bacteria, yeast or molds into the process, they quickly overgrow the culture and people lose a lot of money.

Mycoplasma is a small, slow-growing prokaryote and it's something that's routinely tested for in most processes. And again, that one is significantly more difficult to detect because classically the way it was detected was when your cultures magically stopped being happy and stopped working.

So, you know, if you're going to work with

validated cell banks, all of this is very easy to control and very easy to monitor with post-production testing.

You know, if you're going to be working with finite cell lines each time in the process, there's a lot more to worry about when it comes to these type of contaminants. And again, in a food product, is it okay to include *E. coli*? You know, again, that's not for me to decide or for me to judge.

The other things that are -- you know, the other things to think about is there are chemical contaminants that could happen during the process. But they are uncommon.

And again, what this slide is showing is from a publication that I read where they assayed 451 cell lines coming into a cell bank. You know, 10 percent of them came in from other researchers with mycoplasma. People weren't sending stuff out with viral -- or not viral, but with bacterial or fungal contamination because mycoplasma is a lot harder to detect.

Now, probably one of my most important messages in this seminar is the message of cell line

authentication. Cell line authentication has been a huge problem in cell culture. It continues to be a problem in cell culture today. And what I mean by cell line authentication is if you have one cell line and it's contaminated with another cell line.

This has been a big issue with HeLa cells, which were really the first important cell that was ever isolated from a person. They grow so well that they will outstrip other cells in a culture. They will withstand just about any type of abuse.

There have been various surveys done over the years that HeLa has contaminated a significant amount of the cultures at ATCC. They screen for it very well. And again, this has been a big problem in animal cell culture. You know, what's usually done right now is short tandem repeat PCR analysis.

You know, the next issue is next-gen sequencing is coming down to such a low level that that's one technology that could be considered as well. But again, there are still reports of cross-contamination saying that they're about 25 to 30 percent of the cell lines in the published literature

that are contaminated with something other than as reported in the literature. And NIH has started writing strict guidelines about cell line authentication for its grantees within the past few years as well. So I think that's an important point to consider as we go through this.

And again, I'm almost done. And I just want to mention the other thing to not forget about is downstream. Okay. You know, what I do when I get up in the morning is I'm thinking about upstream. I'm thinking about cells. I'm thinking about the cells that are growing.

You know, the next issue is once you get the cells out, how are they going to be treated in the downstream. How are you going to ensure the final integrity of the product?

And again, you know, the things to think about and the questions to ask, you know, what -- how are going to going to harvest? Are you going to use enzymes? What kind of enzymes?

Now, post-harvest, I put this slide in for the normal postnatal pH decline after an animal is killed

to remind everyone that when an animal is killed, you know, your pH is about seven to 7.2. And then, the pH rapidly -- well, relatively rapidly declines and then bottoms out somewhere arguably around 5.8.

You know, the issue is, is that this postmortem pH decline has caused or can cause all sorts of meat quality defects. What happens if there's some issue and the material comes out tougher than anticipated?

Are you going to allow enzyme in the products? Are you going to allow tenderization? And again, one thing I don't want people to forget about is that in the post-harvest, there is opportunity to contaminate all the way through packaging.

So my final thoughts. What are my final thoughts? My final thoughts are cell culture is established technology. Everything I've talked to you about today is very well-established technology. We know how to isolate cell lines. We know how to grow cell lines. Cell lines are used to produce pharmaceuticals.

The question is, is what are the cell lines

that are going to be used as production platforms.

What is going to be allowable? What's not going to be allowable as food intersects with the biomanufacturing realm?

And the point of this little cartoon is cell line authentication. You know, the joke is everything was going fine until they discovered their HeLa line expressed Y-chromosome markers. Okay. HeLa tumor was derived from the reproductive track of a woman. So there's going to be no Y-chromosomes.

You know, this happens frequently in the world that I work in, in laboratories. You know, cell lines getting cross-contamination, things growing in cell culture that shouldn't be growing in cell culture. You know, I'd go on to say it never happens in my lab. But it happens.

Okay. So I think I'm on time. Thank you.

(Applause.)

MS. BARRETT: All right. We're going to do a little bit of a set change. So bear with us for just a moment. We're going to bring up our panel of external stakeholders who are going to be offering perspective.

So let us just get everybody up here and then we'll begin again.

This session is going to be moderated by Leah Stitz. And I do just want to briefly introduce Leah. She is a public affairs specialist in our Food and Cosmetic Information Center, in our Information Center Branch, Division of Education, Outreach and Information, Office of Analytics and Outreach, CFSAN, FDA.

I hope everybody tracked that. But I'm glad you have it in your agenda. So with that, Leah, if you'll come up, and we'll also ask the panelists to come on up to the table. And we'll get everybody situated. Okay. We're just about there. Thank you for your patience on that.

STAKEHOLDERS PERSPECTIVE PANEL

MS. STITZ: Thank you everyone for your patience while we've been getting our panel seated. As Kari said, I'm Leah Stitz. I work as a public affairs specialist in the Food and Cosmetic Information Center here at CFSAN.

I would like to start our panel by introducing

Isha Datar. Isha is the CEO/director of New Harvest, a nonprofit focused on funding academic research in cellular agriculture. Isha?

MS. DATAR: Thank you, Leah. Thank you to the U.S. FDA for convening the milestone meeting. Fourteen years ago, in 2004, New Harvest, a 501(c)(4) organization, was founded to advance meat produced through animal cell culture rather than through animal husbandry.

Why did New Harvest set forth with this unique goal? Today, conventional farming practices in industrial societies have optimized animal agriculture for productivity. In general, breeding and husbandry conditions have evolved to maximize the amount of food per animal.

Despite achieving this, animal agriculture remains prone to uncontrollable factors such as climate, bio-epidemics and extreme weather events. When outbreaks like the 2014 avian flu demand the cull of 50 million chickens and turkeys and when storms like Goliath in Texas kill 40,000 head of cattle overnight, livelihoods, food security and safety are put at risk.

As a means to diversify our food production processes and build resilience into our food system, I believe we should take a portfolio approach to how animal proteins are made. To me, this includes farming cells for food.

So who am I and how did I get here? My background is cell biology. I have a master of biotechnology and I previously worked in policy and public affairs in the pharmaceutical industry. I learned about in vitro meat from my poultry science professor in a meat and meat processing graduate-level course.

The idea of growing meat from cells seemed to me like the obvious next step for food technology. But what was less obvious was how exactly this technology would exit the laboratory and come to change the world.

I dedicated my career to this work because I believe this transformative technology was inevitable and I wanted to be there to ensure that it entered society in the most responsible way possible.

To do this, my work at New Harvest focuses on advancing public research to adequately equip all

stakeholders as this technology moves from concept to commercialization.

New Harvest's goals are threefold: one, to create a scientific community that specializes in the production of foods from cell cultures; two, to develop foundational research that asks and answers fundamental questions related to this technology and its applications including safety and sustainability; and three, to inform and engage policymakers and the public at large about the opportunities and challenges of this technology.

New Harvest addresses these goals by funding and coordinating multi-institutional, interdisciplinary research. Our funding comes from philanthropy. And in turn, we fund science and academia. As science funders, we've created mechanisms to encourage real-time collaboration and communication amongst our research network.

This coordination work is not trivial. This research spans many disciplines including tissue engineering, cell biology, biochemistry, chemical engineering, meat science and food science.

Bringing these fields together is important if we are to establish a common understanding of the products, processes and practices relevant for the production of foods from animal cell culture technology.

The foundation of this technology has its basis in regenerative medicine, which is the growth of tissues and organs for human patients. This medical application is a set of goals and constraints that are quite distinct from the goals and constraints presented by the food application.

Although these kind of two tracks share some common features, they have different research priorities driven by their intended uses. For instance, the tracks will vary in terms of the species and types of cells used, the cost and edibility of the substances and materials used, the cost and scales of production and safety.

Clearly, tissues grown for medical purposes compared to tissues grown for food will be measured with different yardsticks. The food track is quite new and underfunded compared to the medical track.

This slide from the *Journal of Tissue Engineering* shows a very basic schematic for how a cell-cultured meat could be cultivated.

The four main elements are cells from a particular tissue from a particular species of animal; scaffolds, which are the materials that aid in tissue development; media, a feed for the cells comprised of macro and micronutrients that contribute to cell proliferation and differentiation; and a bioreactor, the machinery that houses cell growth.

And after collecting the cell culture from this bioreactor, I expect there to be some activities loosely categorized as food processing before we arrive at a food product.

I would group the considerations around evaluating the safety of this technology by each of these elements.

For instance, just pulling out cultured media, what are the components of the growth media? What is the sterility of the growth media? What is the variability of the growth media? Does it contain active ingredients? Does it contain toxins, viruses or

antibiotics? How is the media manufactured? How is it stored? What is its shelf life? Does it remain in the end product?

I would also look at the substances involved in the manufacturing method as they fall into these four categories.

Remembering that a lot of this science comes from the medical research context, it would be expected that the go-to, off-the-shelf materials in animal cell culture technology research today come from the biopharmaceutical world.

But as we create and foster the food context of animal cell culture, I can see many familiar, low-cost, food-grade materials coming down the innovation pipeline and being potentially suitable for this technology.

I expect that because this food technology is so process-oriented rather than organism-oriented, that there could be quite a range of manufacturing methods for foods produced via cell culture. These methods look radically different from animal husbandry but look quite familiar in the context of other approved cell

culture products.

Understandably, if there's a range in manufacturing methods, I can imagine there would be a range of food products, food ingredients -- sorry, food ingredients and culinary experiences coming via animal cell culture.

When we think of a cell-based cell-cultured meat, we tend to think of the meat that we know and love just made in a completely different way.

But we have to remember that this technology is a toolbox, not an outcome. And in creating a new toolbox for producing foods, we can open up a whole suite of products that we can't fathom today.

I often cite fermentation as a toolbox in the same way animal cell culture technology could be. Before we had the tools of fermentation, we had milk and we could not have imagined that we wanted that milk to be hard, stinky and solid or smooth and spreadable. We couldn't have envisioned the hundreds of cheeses and yogurts that result from adding live cell cultures to milk.

Similarly, if we begin to produce foods from

animal cell culture technology, yes, we can produce foods in formats that are very familiar to us.

But there is also this enormous innovative potential that we should be aware of and open to because the technology may guide us down some very exciting paths where mouth-feel, appearance, nutrition and flavor become tunable.

The foods from this technology that I suspect will come to market soonest are probably going to be quite familiar and probably fall into existing categories fairly easily. But in setting a pathway forward for these products, we should consider creating capacity for different iterations down the road.

When I began this work over five years ago, I was one of less than a handful of individuals committed full-time to the development of foods from cell cultures. Today, there are at least 100 full-time individuals in this space supported exclusively by philanthropy or venture capital.

I hope this meeting leads to some collaborations and opportunities to work with government and industry. Thanks to the FDA for putting

together this important event. This field is growing and it's an opportune time to convene stakeholders and create a clear path forward to safely introduce foods produced through this technology. Please consider New Harvest as a helpful resource and a keen collaborator in this process. Thank you.

(Applause.)

MS. STITZ: Our next panelist is Eric Schulze, from Memphis Meats. Eric?

DR. SCHULZE: It is a pleasure to be back at FDA. Let me say that. So Memphis Meats appreciates the opportunity to provide our perspective on regulatory issues pertaining to our products and the steps we're taking to assure safety in our production process.

As a member of the food production community, we believe that collaboration and open dialog between regulators and industry is critical in both ensuring a safe and reliable food system and fostering innovation to feed the world's growing population.

Our remarks today aim to support both of these goals.

Memphis Meats produces meat, poultry and seafood products in a manner that enhances consumer choice and promotes increased efficiency and sustainability. The critical difference between our products and conventional products is the process by which ours are produced.

We produce meat, poultry and seafood from cells that we source from healthy animals, then grow in cell culture within a controlled production environment.

Our finished product is produced ex vivo, meaning outside of the animal in a way that is safe and scalable without the need to maintain large herds of livestock and without having to slaughter these animals.

We produce only the edible tissues for consumers to enjoy eating and we avoid rearing and slaughtering animals to use only a portion of their bodies as meat.

While a number of terms are being used to describe meat, poultry or seafood products developed in cell culture, including clean meat or cultured meat,

for the sake of brevity and the purposes of this meeting, we will use the term cell-based meat. We believe this term to be clear, factual and inclusive.

We are at a remarkable time in food and agriculture innovation. We now have the most reliable and safest system of food production in the history of our planet. This system largely supports 7 billion people and is a far cry from the practices of our ancestors who subsisted on what they were able to hunt and gather.

This progress is not without its challenges or limits. In 30 years, the world's population will exceed 9 billion people and the vast majority of those people will reside in urban areas. To feed this larger and more urbanized population, food production must increase, but in a much more efficient and sustainable way with a much smaller footprint.

If we are to meet these and other challenges, we must innovate. And this pursuit of innovation must occur not only in industry but also within government. Appropriate regulation allows for innovation while ensuring safety through sound, risk-based policies.

Over the past several decades, a host of innovative food products have been introduced into the market. FDA has consistently approached these products under a risk- and product-based paradigm. We believe that the existing framework can be readily applied to cell-based meat.

Before discussing the application of this framework to cell-based meat, I'd like to briefly describe our products and the key components of our production process to help build a better understanding of our technology.

While we're still refining our production process and have not begun marketing our products, our research and development to date has demonstrated that cell-based technology can be used to produce meat and poultry products that are safe to eat and otherwise comparable to conventionally produced products.

The finished product is meat, real, familiar, delicious meat like the kind consumers eat right now. Our products are not plant-based. Instead, they are comprised of muscle and other tissues derived from cows, chickens and other animals. In short, our beef

is beef and our chicken is chicken.

Up to this point, there has been no way to produce meat other than by animal husbandry. This has meant that producers have had to raise and then slaughter animals to obtain the animal tissue that we consume as meat. With the advent of cell-based meat, we can now grow meat directly.

Methods and concerns we use are based upon those that have been used for many years in existing regulated industries. We cultivate directly from animal cells within a controlled production environment. The growth and maturation system is referred to as a cell culture system.

The overall production process, which includes the system of knowledge, production equipment and the workflows it employs, including the cell culture system, is referred to as a bioprocess.

The entire bioprocess cycle takes less than a month in our facility and can occur more or less continuously from a single stock of cells. Production largely occurs in four steps: first, cell procurement and characterization; second, cell expansion; third,

tissue formation and maturation; and finally, harvest. Thereafter, we use established food manufacturing methods to produce the tissues into familiar meat food products for handling and consumption.

Let's briefly walk through each of these steps. First, we source high quality cells from target tissues of animal deemed to be healthy at the time of biopsy to prevent carryover of pathogens that may pose a safety risk for consumers. Currently, for our current cell procurement, the health of these animals is assessed via USDA anterior postmortem inspection.

We then aseptically transfer the cells to a cell culture system which is designed to maintain clean environmental conditions and support proliferation and maturation into a harvestable product.

We feed the cells a mixture of nutrients found widely in consumed foods which allows them to proliferate and they cryopreserve them in banks so we have a consistent uniform supply that can be used in the future.

The cell banks are characterized to ensure they are free from adventitious agents and microbial

contamination and produce the intended cell types with consistency. Next, these cells are expanded and matured into meat tissues.

To grow large quantities of edible meat tissues, we need to allow the cells to proliferate by many orders of magnitude and then form them into tissue.

Once we've expanded these initial cells, we then direct their maturation into meat tissues that have nutritional, compositional and organoleptic characteristics that are within our specifications.

Our bioprocess technicians cultivate the cells in an aseptic tissue culture system which helps prevent the introduction of contaminants.

The cells are fed a nutrient medium that provides water, amino acids, vitamins, sugars, lipids, trace minerals and specific naturally occurring protein factors that the cells need to thrive known as feed or cell culture medium. These nutrients enable the cells to expand exponentially in our culture system and are the same nutrients needed to grow meat in animals.

After cell expansion, our bioprocess

technicians further direct the cells to mature into meat tissues by tuning environmental cues.

For example, we grow meat tissues in a vessel called a cultivator which is based on modern bioreactor design, but implemented specifically for our production needs. This cultivator allows us to control the nutrient feed supply, as well as temperature, pH and oxygen levels that lead to efficient tissue formation.

The cultivator system is continuously operated and monitored to ensure safe and reliable production. And at the point of harvest, the culture system is drained -- the culture medium is drained from the tissues.

The tissues are then harvested by aseptic removal from that cultivator. They are rinsed to remove residual medium, weighed, sampled and analyzed in accordance with our standards placed in place previously. Products that meet our standards are placed in food-grade storage containers or cold-stored for further downstream processing or analysis.

That describes our production process at a very high level. In undertaking this process, we take

into account FDA's approach to safety under the agency's longstanding risk- and policy-based framework.

Under this framework, the safety of foods produced by new technologies is assessed by what changes, if any, have been made to the finished product and its more conventionally produced counterpart with respect to safety and functionality.

In other words, and as explained by FDA, the assessment considers the characteristics of the finished product and the safety of its intended uses as compared to the food's conventional counterpart rather than categorically judging all products produced by the new technology as intrinsically harmful.

We believe that this approach provides a high level of premarket oversight, is consistent with longstanding precedent and is appropriate for assessing the safety and quality of cell-based meat.

We have designed our production process to conform with FDA's approach, including identifying and managing potential differences between our products and existing meat products.

Toward this end, we review every aspect of our

production process to identify what potential risks may be introduced and then we manage and process and implement controls to reduce or eliminate the risks.

For example, production risks could include the introductions of impurities or toxicants during the cell procurement and tissue formation process or the enrichment of certain adventitious agents in cell culture. Each of these hazards is well-understood and we are designing our production process to mitigate these risks.

We also understand that the identity of finished products is critical for establishing safety on a consistent basis. While we continue to refine our process, we have considered a range of data elements for affirming identity, consistent with current standards and analytical methods.

For example, we are developing molecular and compositional assessments to evaluate nutritional characteristics of our finished products, as well as performance attributes related to taste and texture.

We believe that identity is important not only for safety considerations, but also within the context

of product labeling. And while labeling is not the primary topic here today, we believe that cell-based meat, like other foods developed through innovative technologies, should be subject to a labeling regime that is based on scientific evidence and longstanding policy.

So in conclusion, we thank FDA again for inviting us to participate in this panel and convening this public meeting on cell-based meat and a potential pathway forward. We also wish to thank the greater public for their interest and continued support.

We view the U.S. regulatory system as a beacon for safety and innovation for a better future and look forward to continued collaboration and dialog on these important issues. Thank you.

(Applause.)

MS. STITZ: Thank you, Eric. I forgot to mention that you are indeed the vice president of product and regulation at Memphis Meats. So our next panelist will be Peter Licari. He is the chief technology officer for JUST. Thank you, Peter.

MR. LICARI: Thank you for inviting me to

speak on behalf of JUST, a food technology company on a mission to build a food system where everyone eats well.

Back at our headquarters, members of our R&D team, who hold 29 advanced degrees across 14 scientific disciplines, are working hard to address some of the biggest challenges facing the global food supply.

Leveraging a one-of-a-kind platform and expertise from a Michelin star team of chefs, we're combining ingredient discoveries with decades of culinary expertise to create delicious, accessible, healthier and more sustainable products to feed the world.

In just a few short years, JUST introduced millions of consumers to plant-based condiments, cookies and, most recently, egg analogs through major retailers throughout the country and partnerships with restaurants, schools, sports stadiums, hospital systems and more.

Nearly two years ago, we started working on expanding our R&D efforts to solve the challenges of creating real meat made from cells instead of

livestock. Our methodology of discovery is similar whether we're finding a plant to replace dairy and ice cream or a plant to feed cells for safe, sustainable meat.

With plants providing nutrients for animal cells to grow, we believe that we can produce meat that is infinitely more efficient than conventional approaches with a fraction of the greenhouse gas emissions and water use.

I thought it would be valuable to outline my experience as it relates to biotechnology and regulatory. I have been working with animal or microbial cell cultivation for 30 years.

I was in the drug industry for 20 years, working primarily on the development of new technologies. I have been involved in putting many CMC sections together, working with both CDER and CBER. I'm fortunate to be on the development teams of two commercially available drugs produced through cell culture.

Approximately 11 years ago, I transferred to the food industry. I have been involved in five GRAS

submissions that received "no questions" letters, some of which were discussed today around algae.

I provide my background because I feel that the United States, specifically the FDA, has both a robust food regulatory system and the expertise that is capable of ensuring the safety of our meat products.

I wanted to address some of the questions specifically. The first question was what considerations specific to this technology would be appropriate to include in evaluation of food produced. Although the FDA has yet to see a clean meat dossier, I believe they have seen all of the key manufacturing steps we are likely to use in producing meat.

You have seen these in your evaluation of drugs and biological compounds for therapeutic applications and are well-versed in evaluating their safety in that context. We believe elements of the existing framework can be easily applied to cell-based products for use as food.

As you've heard, a basic process begins with the establishment of a master and working cell bank. These are the starting points of any well-controlled

process in animal cell culture. At the start of each manufacturing process, each batch, a vial of the working cell bank, is thawed and grown in flasks.

The growing cells are then amplified over multiple stages. The final stage is growth in a bioreactor, which is simply a large tank that provides the proper conditions for the growth of the cells.

After growing the cells, they are washed to remove residual media components and then concentrated. From there, they may be used in a formulated food product. Anchorage-dependent cells may be grown on a matrix like microcarriers. Again, this is technology that the FDA has seen and evaluated for safety.

From our perspective, the following should be considered. Thorough characterization of the cell banks, the GMP manufacturing process and process controls, disclosure of media components and methods of preparation, consistency of the manufacturing process and final product release assays and the results.

We believe clean meat will be similar to meat we consume today in all important aspects except that it is produced in an aseptic environment. Thus, the

risk of contamination will be significantly reduced.

To effectively culture animal cells, the manufacturer has to invest in a high degree of cleanliness and sterility to assure the culture is not contaminated. This level of control also provides an assurance of the quality of the food produced.

A clean meat facility will be similar to what the FDA sees every day in both biologics and food processing plants. It will not look like a slaughterhouse but much more like a clean, fermentation-based food processing plant.

The second question posed was what kinds of variations and manufacturing methods are relevant to safety for foods produced with this technology. The primary and most significant variation that the FDA will observe is the cell type being used in a given food product.

Cells utilized can be from different species and different tissue types such as muscle, adipose or fibroblast. And multiple cell types will be used in food products.

Cell line testing for contaminants and

adventitious agents is well-documented. It's well-documented in the biologics area and can be readily applied here in the context of a food product.

Since cultured cells are to be consumed as food, process controls will be present to mitigate any potential exposure to pathogens or microbial contamination.

It is also important to ensure safe levels of ancillary materials from cell culture media are removed. Post-harvest solutions, same thing. And potentially scaffold materials that are being used. Beyond this, existing regulations for food products should be applicable and sufficient.

The third question, what kinds of substances would be used in the manufacture of foods produced using this technology.

It is anticipated that serum-free growth conditions will be most cost-effective for the manufacture of clean meat. And therefore alternative, non-animal protein sources are being used. These are being used as supplies of proteins, peptides and amino acids.

However, it should be noted that this strategy has been employed for decades. Adequate characterization and qualification of these materials should be done as it is for the biologics field.

For clean meat products, requiring or utilizing cell differentiation processes, other components may be utilized. Residual concentrations of these materials should be quantified.

The fourth question, are the potential hazards associated with production of foods using this technology different from those associated with traditional food processing.

We do not believe the potential hazards associated with producing foods using animal cell culture technology will be different from those associated with traditional food processing. In fact, we believe clean meat products will be inherently safer than traditionally produced meat due to the well-controlled environment in which the cells are produced.

Antibiotic use prevalent on farms today will not be used in a well-controlled cell cultivation process. Without the use of antibiotics, our approach

will not add to the growing problem of resistant organisms.

Cells for clean meat products are cultivated in bioreactors, similar to the way yeast is grown in fermenters.

Traditional food production has seen the use of such processes for decades, most notably for the production of beer, wine and amino acids. We are producing meat in an analogous manner. The primary difference is the starting material, the cells. They're animal cells.

Potential hazards and control measures are readily identified by combining the existing experience of multiple groups at the FDA. At JUST, we have developed an experienced team from both the biologics and food industry to assure a safe, nutritious food product.

When one thinks about our food supply, the source and type of food has changed over the course of human history and will continue to do so.

Today, there is an opportunity for the United States to be a leader in the development and

commercialization of these new technologies. The FDA has the expertise to balance support for innovation with regulatory involvement so regulators, industry and consumers can have full confidence in these products when they do hit the market.

We are ready to move forward now and hope you can provide us the necessary direction. Thank you.

(Applause.)

MS. STITZ: Our next panelist is Rhonda Miller, past president of the American Meat Science Association and professor and research fellow at Texas A&M. I should remember that. My husband's a graduate. Thank you, Rhonda.

DR. MILLER: Thank you very much, Leah, and thank you very much to FDA for inviting me to be on this panel.

I'm going to take a little different approach. I am here representing the American Meat Science Association and its over 1,200 scientific members from academia, government and industry. And these are not my personal opinions. Dr. Dustin Boler will also be providing some comments during the open comment period

representing AMSA.

I'm going to first just give some general comments and then answer each of the questions, as appropriate. I'd also like to thank Paul for setting me up so well for my comments. You led that in very nicely because I'm a meat scientist and that's what I represent.

So this is a little bit different take. This is going to be more on the post-processing or post-production side.

Using tissue culture technology to provide an animal tissue food product or cultured tissue, as I'll refer to it, is a very interesting and emerging technology that could provide avenues for alternative protein sources for human consumption.

However, knowledge about the specific processes and the resulting product is known. And most of my comments will talk about the resulting product.

As you will hear from Dr. Boler, meat scientists do not have enough information about cultured tissue to determine whether it should be called meat or how it should be regulated.

At the most recent meeting of the American Meat Science Association, which is called the Reciprocal Meat Conference -- it was only two weeks ago -- two sessions were formed around cultured tissue.

Dr. Eric Schulze was actually one of our speakers on that panel and he addressed our membership to talk about the concurrent -- about the cultured tissue production processes and products. Many members of our organization interacted with Dr. Schulze and requested cultured tissue samples for meat science research.

Please note that samples of cultured tissue have not been available for evaluation of the safety, composition, nutritional bioavailability, functionality and sensory properties to understand how it compares to meat from conventional animal production.

With the interaction of our members, Dr. Schulze and other similar companies -- Isha, for example, also reached out to many of our members -- it is anticipated that this may soon change. And so, very importantly, I'd like to leave you with this message. AMSA strongly supports and encourages this research and

this characterization.

Concerning eh four questions, I'll briefly answer each of those, as Peter did. What considerations specific to animal cell culture technology would be appropriate to include in evaluation of food produced by this method of manufacture?

From a food safety standpoint, chemical, physical and microbial hazards associated with production phase of cultured tissue likely will differ due to differences in production practices between meat from conventional animal production and cultured tissue.

I think you've heard that from a number of the speakers prior to me and certainly that's more their expertise. These potential hazards need to be carefully investigated.

Meat and muscle biology scientists who conduct cell culture research, and we heard from one of the eminent ones today, understand the potential for microbial, chemical and physical cross-contamination in tissue culture systems.

And the cartoon was great. I haven't quite seen them at that level. But I have colleagues who certainly look very distressed on certain days when their cells die.

These hazards within the cultured tissue production system need to be controlled with proper regulatory oversight. While FDA regulates biomedical and food products of biotechnology, cultured tissue for human consumption has many unknowns.

The effects of temperature and time, pH, water activity, nutrient availability, gaseous environment and chemical content need to be understood and controlled.

There are many attributes when comparing cultured tissue to meat produced from conventional animal production that are not known. Some of these may be issues or they may not. We just have not had an opportunity to investigate them.

Let me just list a few. Is color chemistry the same in cultured tissue and meat from conventional animal production? Is color shelf life the same? How does cultured tissue react in different packaging

environments? We have anaerobic and aerobic environments and we have combinations. Are they the same? What is the shelf life and ultimate pH of cultured tissue? Does pH vary within a product and from different production lots? And Paul brought that up. I work more on the fresh meat side.

And from a researcher, I can tell you that those are -- those are not minor issues within animal production systems.

Is the amino acid content, nutrient bioavailability, micronutrients and, very importantly, as you talk about using this in further processed products, is the protein functionality the same and does that carry through when the product is either unprocessed, processed, cooked, cured, smoked, dried, fermented or other things.

Do spoilage -- and this is a very important question -- do spoilage and pathogenic microorganisms grow and proliferate at the same rate in cultured tissue versus meat from conventional animal production. And that conversion issue is tied to that. Is water usage and antibiotic usage comparable?

Question two, what kinds of variation in manufacturing methods would be relevant to safety for foods produced by animal cell culture technology. An unknown for meat scientists is how the conversion of muscle to meat occurs in cultured tissue produced for commercial production.

Conversion of muscle to meat is a critical step in meat from conventional animal production that not only affects meat quality, but meat shelf life and safety.

It is well-documented that in conventional animal production, meat from healthy animals are free of bacteria upon presentation to harvest. While the harvesting process may result in cross-contamination of microbial microorganisms on the outside of the muscle, the interior is relatively sterile.

It's important that this is also the case with cultured tissue. It is not yet clear how cultured tissue would be handled when removed from the culture system. It also will go through some form of conversion from muscle to meat as the living tissue is removed from its life-supporting environment.

And as I have done research on this, it looks like there may be some variation in how that's done. And not that one way is better than the other, but knowledge of that and the subsequent product is very important.

During this conversion of muscle to meat and in post-conversation processes or processing, the potential for introduction of hazards are similar to those from meat from conventional produced animals.

Also cultured tissue has been presented as a potential component of a food product such as chicken nugget or a cooked meatball. Issues associated with these products as currently produced and assume to be the same as when cultured tissue is used.

But we haven't had a chance to test that. This strongly supports that cultured tissue needs to be subjected to the same hazard analysis and critical control point regulations, food labeling oversight and food security as meat produced from conventional animal production.

Third question, what kinds of substances would be used in the manufacture of foods produced from

animal cell culture technology. I think you've heard from the people who are in the field about that.

So the comment from the American Meat Science Association is that regulation should be the same and of the same rigor as for meat produced from conventionally raised animals. Safety oversight through HACCP inspection, food security and labeling regulation should be the same.

Substances used in production of cultured tissue would need to be GRAS, as we've heard over and over, just as they are with conventional meat. And then, there are all the issues I've already previously talked about.

Question four, are the potential hazards associated with production of foods using animal cell culture technology different from those associated with traditional food production and processing.

The only difference from traditional food production and processing that we know of would be in the valuation of hazards and critical control points that are uniquely associated with the muscle cell growth in culture. And I think our previous speakers

have all addressed that.

It's been stated that scaffolding material is food-grade. And I know Eric talked to us about calcium and sodium alginate as examples. Scaffolding materials would need to be monitored for purity and lack of hazards. Additionally, remaining scaffolding in the product may be a concern.

There may be unique opportunities for introduction of hazards during the cell proliferation phase of production. It should be assured that the subsequent cell cultured tissue is free of microbial organisms and free of hazards after completion of conversion from muscle to meat, as previously stated.

In other words, we should start with the same type of product when we start looking at it as meat and going through the process of providing a food for consumers. Additionally, cultured tissue should be held at safe, refrigerated temperatures or frozen after considered food.

So in conclusion, regardless of whether cultured tissue products meets the definition of meat, AMSA strongly contends that the regulation, safety

system and labeling regulations provide the same level of safety and oversight as for meat produced from conventional animal production.

From a consumer standpoint, both the labeling and safety assurance systems need to have the same rigor, regulation and oversight as for conventional production of meat, especially in a competing marketplace where these two products would be competing as they may provide -- if they're not labeled the same, consumers may have a difficult time really understanding the label differences.

And there are some articles and some references I have if anybody is interested in them. Because we need to provide full disclosure and transparency to consumers.

It would be misleading and confusing when purchasing cultured tissue and conventionally produced meat if labeling requirements were not the same.

AMSA strongly supports the production and marketing of safe, healthy and accurately labeled meat for human consumption, as required by our current regulations. Additionally, continued research by meat

scientists characterizing cultured tissues for human consumption is needed and our meat scientists are very much engaged and willing to do this and excited about the technology. Thank you for the opportunity to comment.

(Applause.)

MS. STITZ: Thank you, Rhonda. Our next panelist is Michael Selden, CEO and founder of Finless Foods.

MR. SELDEN: Thanks so much, Leah. I'm from Boston, so I speak kind of fast. This is going to be an attempt to slow down. Bear with me.

Good morning, all. Thank you so much for inviting us here in order to have this conversation. It's an honor to be selected and an honor that our industry is finally hitting a larger stage and being considered by the major players in the world as a technology that can make an important change in our food system.

As Leah has said, my name is Michael Selden. I am the CEO and cofounder of Finless Foods, the first company developing sustainable seafood using animal

cell culture technology.

What we do is we take a small 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 or plastic.

We are essentially working to create an environment that imitates the process of growing muscle inside of a fish, outside of a fish.

This means that everything, right down to the materials we use, are attempting to closely mimic the inside of a fish so that these cells do what they are naturally inclined to do, which is to divide and grow.

We believe that people want real fish meat, not an imitation. And so, we aim to provide that by simply changing the production process rather than the end-product itself.

We also aspire to create a food system that can create healthy fish meat efficiently on land, rendering the long transportation time from the water to people's plates obsolete.

We hope that through this process, we can reduce food waste, spoilage and deliver a fresher and

more delicious food supply.

At Finless Foods, we are excited by the possibility of this discussion with Food and Drug Administration, as we're eager to ensure that there is a transparent, thorough and evidence-based regulatory process in place in order to ensure food safety and confidence in the foods we hope to bring to market.

We do firmly believe in the safety of the food that we are creating, since we're the ones working with it on a day-to-day basis. That said, at the end of the day, if we want to change the food supply, we do need the confidence and trust of the people who will be doing the eating.

We believe that working with FDA is the best way to engender that trust and confidence. There's a lot of talk about high-tech companies in some industry sectors flouting regulations and throwing their products on the market, choosing to beg forgiveness rather than ask permission.

But we feel that this is the wrong approach. We are not a scooter rental company. We can't just throw -- we can't just throw our food on the market and

assume that people will trust us.

Food is considerably more personal than that. We need to first show people what we are working on and how safe it is in order to gain their trust using evidence and to get them to believe in what we're making in the way that we do as people who have intimate knowledge of the science.

Isha, Eric, Peter and Rhonda have done a wonderful job at describing the general differences of this technology with regards to safety. But I'd like to dive into the potential -- I can't avoid the puns -- into the potential of this technology to improve safety and quality in seafood specifically, since that's what we do.

Several of the questions FDA has posed for this meeting address whether new cell-based manufacturing processes pose issues relevant to food safety and to FDA safety assessment.

For several reasons, we believe that cell-based manufacture of seafood offers the potential of delivering a safer, more predictable manufacturing process. Although some of the needed methods are still

being developed, we can point to several potential safety differences when compared to traditional methods of meat production.

One of the main potential differences, at least as it pertains to what we are making at Finless Foods, is that we have no reason to believe that any of our seafood will contain the mercury and plastic levels present in wild caught fish.

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 bio-accumulated, meaning it can rise up the food chain and become concentrated at the top.

Because of this, FDA has advised that many large fish species be consumed in limited quantities by at-risk groups such as women of child-bearing age. With our technology, we have the ability to bring these mercury levels down and have the potential to remove mercury as a concern entirely.

The effect of plastic found in wild caught

fish on human physiology is less well-studied. But we believe it is still a cause for concern. Studies 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.

In the end, more work does need to be done to ascertain direct effects of consumer plastic on human physiology. But we believe that consuming less of it is an idea that the American people might get behind as a better safe than sorry measure.

Our process has no tie to the ocean. 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 rather than by wild catch or mariculture, which is aquaculture done in the ocean itself.

Current wild caught fish productions tied to nature make for a less than stable supply chain. Time and time again, this 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 processes we are developing, we hope to have a much higher level of certainty of how much fish can be produced, providing stability and making the mislabeling of fish a thing of the past.

In conclusion, we believe that there are many variations in manufacturing methods specific to fish produced using animal cell culture that are relevant for food safety protocols. This does lend itself to a difference in potential hazards, many of which I have outlined in the past few minutes.

I hope this session proves itself informative and look forward to continuing the conversation with all of you. Thank you very much.

(Applause.)

MS. STITZ: Our last panelist for this morning is Gregory Jaffe. He is the director of the Project on Biotechnology at the Center for Science in the Public Interest. Greg?

MR. JAFFE: Good morning, and I want to thank FDA for inviting me to participate on this panel today.

I'm here representing the Center for Science in the Public Interest.

CSPI is a food and nutrition consumer organization located here in Washington, D.C. We've been around for more than 47 years now, educating consumers about food and nutrition and the relationship between the food they eat and their diet and their health and advocating on behalf of consumers to try to ensure that we have good, nutritious food that's safe out there for consumers.

We don't take any grants from the federal government and we don't take any funding from industry. And that's been important to us because we do lobby the government all the time and we try to put pressure on industry. And so, we don't want to have any potential conflict of interest there. So I wanted to set that out at the beginning.

I wanted to make three points here today about the topic of this public hearing. The first point I wanted to preface with a lead-in from my work with genetically engineered crops. And I was glad that Jeremiah brought up in his talk today as one of his

three examples biotech crops and some of the safety assessment work that FDA has done on that.

And it also was important that Jeremiah brought up the issues of how FDA does regulate food ingredients. He mentioned the food additive process there where they do an approval and a rulemaking.

For genetically engineered crops, however, those aren't -- those don't go through as food additives.

They are considered GRAS and FDA has established a voluntary consultation process where manufacturers can provide information to FDA and FDA can look at that. But in the end, FDA doesn't give its own opinion about the safety of those crops.

So where does that leave consumers? Consumers therefore are left to have to rely on the safety determination of the developer, whether that's Monsanto or DuPont or somebody else.

One of the positions that I've advocated at CSPI in the biotechnology project is that FDA should have a mandatory premarket approval process for those genetically engineered crops. That process shouldn't

necessarily be the food additive process, but a unique process tailored to the potential risks of those genetically engineered crops. That process would ensure safety and in that review FDA would give its opinion about the safety of those foods.

So why do I bring this up? Well, I think there's been a growing international consensus about the safety of those crops that are grown and the food made from those crops that consumers are eating today.

But many surveys of American consumers find that many consumers don't believe that those crops are safe to eat.

So this has led to a proliferation of non-GMO products in the marketplace, companies that are avoiding GM ingredients and even a mandatory disclosure law that now FDA -- that USDA is now implementing.

If FDA had been in the lead approving these products and ensuring their safety for the public, maybe the marketplace would be different, would be a different place.

So how does this relate to cultured meat? I think -- it is because I don't think anyone wants to

see the same thing happened with cultured meat, where the products are safe but consumers don't think that they're safe or don't believe the developers' determination that those are safe.

So the federal government, with its independence, needs to be the one that reviews this cultured meat technology and the products and affirmatively determine safety before those products reach the marketplace.

As I said, FDA has the food additive process at its disposal to approve those new foods. We would support FDA if it used that authority for cultured meats.

However, we also understand that there are problems with the food additive process. And when you try to look at that for cultured meat, you know, much of the data and testing currently required for food additives may not be relevant for cultured meat. So it may or may not be the best fit.

In our mind, the best way forward would actually be for Congress to give FDA authority to address all these different new food technologies --

these new technologies in food with broad authority to ensure the safety of new technologies, FDA could determine the potential risks of a particular technology and the products made from that technology and then fashion the appropriate and proportionate regulatory process that would ensure safety.

Then, they could do this for the cultured meat industry. It could be done for the whole technology. It could be done for specific product lines or even for specific products.

The critical point however is before cultured meat is in the supermarket or restaurants, FDA needs to affirmatively ensure those products are safe and FDA's opinion, I think is going to be critical to consumer acceptance of this technology.

My second point involves some of the questions being asked by FDA for this public hearing about what safety concerns might arise from the production process for cultured meat.

What are some of the areas of production where we think FDA needs to focus their attention when reviewing cultured meat? First and foremost would be

to ensure that the cell lines are and remain microbial contaminant-free. That I think is a critical thing.

Secondly, to ensure that the cell medium doesn't contain any compounds that are problematic and that the final product doesn't have any of those compounds in amounts that are different than humans have consumed in traditional meat.

So for example, if ferric nitrate might be used in the cell culture medium, that compound is not found in the FDA database of substances added to food.

So is that -- the question is, is that compound in the final product. Is the level of that compound different from what would be found in conventionally produced meat? Is there any safety issue associated with that?

So I gave that as one example that may or may not be used in the production process, but to point out that you've got to look at this, the specific thing in the medium.

There also may be hormones used in that medium. And if so, we want to make sure there's no issues for hormone exposure in the final product. Of

course we want to make sure that there are no new compounds in the final product that could be allergenic in any way.

And again, ensuring that the compounds being used in the process of producing this are chemically identical to ones currently found in meat products, if they're found in meat at the end, that they are identically chemically.

And also in particular there's been mentioning about scaffolding that would be used to bring the product together.

One would want to ensure the food safety of that scaffolding depending on the material being used as well as ensuring that there's no allergenicity issues that arise from that scaffolding, especially if that is going to be part of the final product that consumers would be eating.

And then, I want to talk about my final point, and that revolves around the issue of clean meat. So whether the cultured meat product is officially labeled clean meat or not, the cultured meat industry to date is currently calling their product clean meat.

The message to consumers is that the product does not involve slaughter and is free of microbial contamination.

Now, if this is actually true about the microbial contamination, that could be a real food safety benefit to consumers since current meat production does result in microbial contaminants in the product that consumers purchase.

However, that clean meat claim needs to be independently verified by the federal government. Procedures must be put in place to ensure that all products are in fact free of microbial contaminants and remain free of microbial contaminant up to the time they are consumed by consumers.

Consumers may treat clean meat, because they hear about it, different from conventional meat because of that marketing such as they may try to eat it raw or they may not refrigerate it.

So federal regulators need to both validate the claim and then also make sure that the conditions are use -- or what are the conditions of use that might be required so that microbial contamination doesn't

occur before consumption by the consumer.

Clean meat may also refer to the product being better for the environment. As an organization representing the interest of the consumers, we would also want the federal government to independently verify that claim, although we don't know that that doesn't have a food safety component necessarily about it that might be involved with FDA.

Finally, I would also like to point out that FDA appreciates -- that CSPI appreciates FDA calling this meeting now and determining the way forward before products are about to enter the marketplace.

When FDA reviewed somatic cell cloning of food animals, it asked the industry to carry out a voluntary moratorium and not allow milk or meat from cloned animals and their offspring to enter the food supply while it determine d if there was a safety issue.

That process took several years. FDA eventually said that there was no issue. But consumers should not have to rely on the goodwill of industry while FDA plays catch-up on a new technology about to enter the food supply.

FDA should develop its oversight before the industry matures so that products are not entering the marketplace before FDA has been able to determine if they are regulated and whether they are safe.

Consumers expect that from the U.S. government, from FDA.

And so, we're glad that we're having this hearing today before those products are at the doorstep so we don't have to rely on -- the consumers don't need to rely on voluntary moratoriums or do other things that products are in the marketplace until those safety determinations have been made. Thank you very much.

(Applause.)

MS. STITZ: Thank you very much. I appreciate all of our panelists, Isha Datar, Eric Schulze, Peter Licari, Rhonda Miller, Mike Selden and Greg Jaffe. If we could all please give them a round of applause?

(Applause.)

MS. STITZ: Thank you very much. We are in the good fortunate of having a little extra time to have a slightly longer lunch break. You are all excused for lunch, if you would please return to the

auditorium no later than 1 p.m.

(Whereupon, the foregoing went off the record at 1:00 p.m., and went back on the record at 1:01 p.m.)

MS. BARRETT: I just wanted to mention I am aware that there is still a line getting through security. So we are going to give folks, you know, a couple additional minutes. I appreciate you being prompt. But let's give them just a couple of minutes and then we'll get started.

Let's go ahead and get started. Just checking, everybody warm enough? Okay. That was a bad joke. Welcome back. And I'm hopeful that maybe the temperature will cool down a little. I do realize it's quite warm and not as comfortable as we would like.

But with that, again, I'm Kari Barrett. And thank you for again being back here promptly. We will begin our afternoon session, which is really focused on hearing public comment from folks who have signed up to offer that.

What we'd like to do is a couple of things before we begin that process. One is I'd like to

introduce our FDA panel and what their role is. We have our FDA panel of experts.

And really what the role is, is that as we begin this process, Jeremiah will walk us through again the questions that we posed in the Federal Register notice, the ones that we are eager to hear from you on. We will also post the questions on a slide. But he'll just give you a little context to those questions.

When he sits down, I'll begin the public comment process, which I'll speak to more as we begin that. But really, the FDA panel, they're here to listen to you. There is an -- you know, they always have the opportunity, if there was something they just needed clarification on, so that they understand a point.

They may ask a question. But typically, there's not a lot of questioning. So I really just wanted to emphasize that. I know not everybody is used to giving public comment. And it's certainly something in the back of your mind. I don't expect that you'll get a lot of questions. But again, if there is a need to just ask a clarifying question, there is that

opportunity.

So with that, let me introduce our FDA panel. Again, we have Jeremiah Fasano. He is our consumer safety officer, Division of Biotechnology and GRAS Notice Review in the Office of Food Additive Safety, CFSAN, FDA. William Jones, or Bill, acting director, Office of Food Safety at CFSAN.

Leah Stitz, public affairs specialist, Food and Cosmetic Information Center, Information Center Branch, Division of Education, Outreach and Education in our Office of Analytics and Outreach at CFSAN.

And Andrew Yeung, who is our chief, Egg and Meat products Branch, Division of Dairy, Egg and Meat Products, Office of Food Safety, CFSAN, FDA.

So they are the folks here today who will be listening to the public comment who are actively working on these issues in the agency. And so, again, I do want to welcome Jeremiah back to the podium to give a little background and an overview of the questions that we have posed for the public comment session.

OVERVIEW OF FDA QUESTIONS

MR. FASANO: Great. Thank you, Kari. So we've already heard I think very nice sort of set of passes through these questions from many of our panel members, which I think has been very helpful in sort of illuminating some of the different perspectives and the information.

I'm just going to go through them one more time and share sort of some of our thinking as we develop those questions and that will provide hopefully helpful context for the public comments that we'll be hearing in just a few minutes.

Let's find out which one of these works. Not that one. All right. Excellent. So the first question, is technology specific considerations.

And really, this is about trying to understand what particular properties of substances made by this manufacturer we should be considering that are relevant to the process, so what things that are particular that maybe if you got a similar food in a different way, you wouldn't be thinking about, but in this case, you might need to. What sort of issues might arise? So that's really the first -- the first question.

The next one, and this is sort of -- if I could have the next slide, please -- this really sort of gets a little more deeply into some of the questions about variations in process.

So if you have an overall process that produces particular types of products, what variations in that process are going to be meaningful from a safety perspective. And this is important for two reasons.

The first one is that we expect, and as I think a number of folks on the panel alluded to, that different firms are going to have different kinds of production processes, right.

So those processes will vary from firm to firm. And understanding the implications of those variations for properties that might be relevant to safety is going to be important.

But in addition, we also expect, because this is a developing technology, that each individual firm will also be sort of evolving of finding, diversifying their processes over time.

And so, understanding the impact of those

changes on properties that might be relevant for safety assessment also seems something that potentially could be important.

So that's sort of the underlying thought process here for this question. You have these variations in manufacturing process. Which one should we really -- should people be focusing on when they're thinking about implications for safety?

Next slide. This next one is also something that we've heard touched on a few times already today. But it's not as simple as just having these cells and having them multiply and then taking them and making food out of them.

There's a lot of other sort of supportive material that needs to be in place in order for this process to happen successfully. There's the basic nutrients that are involved.

But there's also a lot of other sort of proteins, growth factors, cytokines, other kinds of cell signaling substances that are going to be important for keeping these cells happy, for allowing them to multiply and then ultimately allowing them to

differentiate.

And as we've also heard, often when the cells are differentiating, they may need some sort of mechanical attachment or some sort of structure to grow on. And so, that sort of extracellular material or scaffolding is another kind of substance that we expect is going to be involved in this process.

And so, for these kinds of substances, you know, we have wanted to pose some questions about, you know, what classes of substances are going to be involved. You know, what aspects of those will be important for safety?

I think we also had heard some discussion about, you know, sort of washing out of culture material or out of culture media.

And so, that's, you know, another thing to be thinking about is to what extent are these substances that are used in culture going to be present in the food at the completion of the process. So that's another thing to potentially consider in terms of factors that may be relevant.

Next slide. And then, finally, just thinking

about the potential hazards that might be involved in the process and the appropriate controls. So, you know, one way to think about this perhaps is from a comparative perspective.

So we already, you know, broadly as sort of a foods community have a lot of experience with manufacturing processes that produce similar kinds of protein-rich foods for which you have particular concerns, you know, sort of appropriate controls and handling processes to make sure they remain safe up to the point where they reach the consumer.

And then, we also have a fair amount of experience, as we discussed earlier today, with manufacturing processes that are similar to what the topic of this meeting, different kinds of cell culture processes.

And so, using those two as comparators, what kinds of issues might you need to be concerned about that are particular to this manufacturing technology, both sort of with reference to those two comparators and sort of things that might be different from either of those. So that's sort of the underlying thought

process for that fourth question.

And so, with that, that's the sort of end of my presentation. I just wanted to briefly take you through those again.

I think I can say on behalf of the panel that we're looking forward to hearing from our commenters today.

And I also want to remind folks that even whether you're commenting today or whether you're not, everyone has an opportunity to submit information to the docket, which will be open for several months. And we strongly encourage you to provide comments there as well. Thank you.

MS. BARRETT: All right. Thank you so much, Jeremiah. All right. I do want to just go over our process for the public comment session.

I want to first thank everyone who has signed up. I want to thank you in advance for your public comment and for the time that you've taken to put your thoughts together and to offer them here today in person.

I know this is not a really friendly space in

terms of getting around the auditorium. We have one microphone for giving public comment. What I'm going to do is I'm going to go down the list in the order that I have here. I'll call out your name.

And if you can come to the microphone and then speak, if you know that you are sort of near in the queue to that person, if you can just be in a position where you can sort of easily get to the microphone, that would be greatly appreciated.

And again, I know this is not an easy setting to navigate necessarily in that regard. The folks who have signed up, we do have quite a few. So we do ask that you stay to your four minutes for remarks. That is what guidance we have given.

If at four minutes you haven't finished your remarks, I will ask you to wrap up. I hope you understand that we do need to be respectful of everyone's time. And there is certainly the opportunity, if you've not had a chance to complete your comments, again to submit the full set of comments to the docket. So I'd just ask everyone to be mindful and respectful of the four-minute time allocation.

I also would ask too when you come to the microphone to speak into it. I'm going to say your name and call you to the microphone. But if you will repeat your name clearly and your organization, that's for the transcriber and that's very much appreciated.

And again, I mentioned the role for the FDA panel, that there is the opportunity to ask a clarifying question based on the remarks that you have given. So with that, we will begin the process. And our first presenter is Michael Hansen, Consumers Union. Michael?

PUBLIC COMMENTS

DR. HANSEN: (Off mic) -- oh, sorry. Without a doubt, there are potential food safety problems associated with the production of foods using animal cell culture technology.

This technology involves taking cells from a food animal and getting those cells to grow and differentiate in a suitable growth medium that contains vitamins, lipids, amino acids and growth hormone/factors, often including fetal calf serum.

The vats in which the lab meat is cultured can

become contaminated with disease-causing bacteria, viruses, fungi and mycoplasma. It is appropriate for the federal government to assure the safety of such foods prior to their marketing.

We can see arguments for either FDA or USDA taking that responsibility. We are concerned however by elements of FDA's initial explanation as to why it believes it can take on this issue under existing programs.

While FDA has broad responsibility for food safety, there are some serious gaps in its safety net which lab-grown meat could well fall through.

FDA, for example, states it, quote, "administers safety assessment programs for a broad array of food ingredients and foods derived from genetically engineered plants," end quote.

But for GE plants, this is a voluntary safety consultation, not the same as a mandatory safety assessment. To assure consumers of safety, assessments for lab-grown meat should be mandatory.

FDA also states it, quote, "has issued guidance on how to assess the effects of significant

manufacturing process changes on the safety of a food ingredient," end quote. But FDA guidances are also voluntary, not mandatory.

FDA further states it, quote, "has a variety of pre- and post-market programs for evaluating the safety of substances used in the manufacture of foods including, for example, food additives and color additive regulations," end quote.

We are particularly concerned about the use of the food additive process for these food ingredients since there is a huge loophole in the form of generally recognized as safe notification process.

FDA, in a Federal Register notice issued in August 2016, made explicit that under the GRAS notification process, that a company wishing to introduce a new substance into a food can itself determine if it is safe. It need only assemble a small panel of scientists of its own choosing to review the substance's safety. The company need not even notify FDA of their review.

Lab meat industry representatives reportedly have already suggested they may take advantage of this

loophole, including in an April 2, 2018 article in *Food Navigator*.

This piece reported industry as saying that, quote, "Technically as cultured meat is a whole food and not a food additive, no premarket approval would be required, although this would be product-dependent," end quote.

The article continued, quote, "However, given the novelty of the process and the scrutiny pioneers will face, companies in the space are working closely with the FDA as they approach commercialization and may put together GRAS determinations, predicted one industry source," end quote.

Finally, there is the issue of the name to give foods derived from cultured animal cells. It is important that the name informs consumers that the food is different from conventional meat and gives consumers some idea of how it was produced.

Consumer Reports conducted a nationally representative phone survey last month of more than 1,000 people. The survey found that the vast majority of Americans think that food produced from cultured

animal cells should be differentiated in some way on the label.

Forty-nine percent said it should be labeled as, quote, "meat, but accompanied by an explanation about how it was produced," end quote, while another 40 percent said it should be labeled as, quote, "something other than meat," end quote. Only 5 percent thought it should be labeled as, quote, "meat, without any further explanation," end quote.

In addition, when given a list of seven terms and asked to choose which would constitute accurate labels, the most commonly chosen terms were, quote, "lab-grown meat", 35 percent; artificial or synthetic meat, 34 percent.

The least commonly chosen terms were cultured meat, 11 percent; clean meat, 9 percent; and in vitro meat, 8 percent.

In sum, Consumers Union appreciates the opportunity to comment. Cultured meat products should be required to go through a premarket safety assessment and the GRAS process is clearly inadequate to assure safety.

We also urge that these type of products be named in a manner consumers will readily understand such as, quote, "lab-grown meat" or, quote, "synthetic meat."

Thank you again for this opportunity to comment. And we will submit detailed written comments to the docket that deal with a number of these issues.

MS. BARRETT: Great. Thank you. Thank you very much. We'll now go to Paul McCright, Biotrack Diagnostics. And Paul, I understand you are in for Gerard. Okay. Welcome.

DR. MCCRIGHT: Good afternoon, and thank you for the invitation and possibility to elaborate a little bit on one of the most critical aspects of tissue culture. By the way, I am Paul McCright.

MS. BARRETT: Thank you.

DR. MCCRIGHT: I am the executive vice president of Biotrack Diagnostics, from Dallas, Texas. My comments will relate primarily to question number two regarding manufacturing processes and to question number four regarding the control measures because we will be talking about quality assurance.

One of the major problems is the potential for contaminating cell cultures by all kinds of microorganisms. And I represent a technology which was developed in Europe, the Netherlands, as a matter of fact, that's now being introduced to the U.S. market.

We feel there's an extremely good match between animal cell culture technologies developed over here and the monitoring technology developed on the other side of the Atlantic Ocean.

Now, Professor Mozdziak this morning made very clear that current practice in tissue culture requires a multistage approach from a small volume cell culture in one flask at the lab bench to a full-blown tissue culture in a bioreactor system takes several so-called passages, which is re-inoculation of a grown culture into a larger volume of sterile medium.

Each such passage in essence is a critical contamination point as defined by the HACCP guidelines. It is therefore of imminent importance to be completely sure that all procedures applied and media used are completely sterile. Also, the working environment has to be totally hygienic. Ideally an inline system for

continuous monitoring of microbial contamination should be operational at all times in order to avoid gross production loss and then potential health hazards for the public.

Now, this is a point where the microbiological paradigm kicks in and becomes an inhibiting factor. It should be realized that classical control systems for microbiological contamination still heavily rely on analytical principles devised by Louis Pasteur a good 120 years ago.

Classical microbiological techniques for the assessment of microbial contamination are, for the most part, still culture-based and have time-to-results typically of 24 to 48 hours. This time-to-result is obviously completely inadequate to allow for rational sterility control of the tissue culturing process.

In the case of mycoplasma, things get even nastier because these organisms are very difficult to culture using classical microbiology. We at -- excuse me, we at Biotrack Diagnostics have developed a fully autonomous micro laboratory solution capable of identifying and enumerating microbiological

contaminants of cell cultures, media and supplements necessary for cell culturing as they occur or develop.

This system, we believe, will be of great importance in preventing potential contamination of tissue culture processes as it can continuously monitor the process on the occurrence or growth of unwanted microbial components.

The reason for this may be clear from the characteristics of our system. Our micro laboratory solution functions culture-independent and therefore realizes time-to-results within minutes, not hours, as a lower detection limit of one organism per 100 milliliters of the sample is validated using international standards and has been certified in Europe.

It uses DNA probes as diagnostics principle and it has validated probes for over 30 species of contaminants that are already available. Our DNA probes typically show a specificity of greater than 99 percent.

We therefore believe that our micro laboratory solution will be a great support for the further

development and monitoring of animal cell culture technology and processes by providing inline biomonitoring of the tissue culture process, the possibility for rational and adequate process control, significant reduction of product loss and significant increase in product safety.

I just want you to know that there is a rapid, accurate, cost-effective microbial testing unit available. Thank you very much.

MS. BARRETT: Great. Thank you for your comments. Our next speaker, Jessica Almy. Welcome. And again, if you'll repeat your name and organization?

MS. ALMY: Thank you. I'm Jessica Almy. I'm the director of policy at The Good Food Institute.

MS. BARRETT: I'm wondering if I'm hearing you as well -- okay. There we go.

MS. ALMY: The Good Food Institute is a nonprofit think tank. We have 50 staff members across science and technology, innovation, corporate engagement and policy. And we've been heartened by the response we've seen to clean meat innovation from the scientific community, from entrepreneurs, from

corporations including meat companies, some of whom are present here today, and policymakers.

We are grateful to the FDA for engaging stakeholders in a robust and open dialog about clean meat. We appreciate FDA's commitment to enabling innovation and technological advances in the food sector and ensuring the safety of the resulting food products.

We are very heartened to see that the FDA is engaged in thinking through how clean meat can come to market under the existing regulatory framework. Really appreciated the comments of the FDA members who spoke earlier today in walking through some of the possible parallels.

The United States has a robust regulatory regime that is more than capable of ensuring that clean meat is safe and truthfully labeled. The regulatory path to market should ensure consumer safety and confidence without being onerous to producers.

As Peter Licari, from JUST, explained on the panel this morning, clean meat is similar to conventionally produced meat in its basic nature and

composition except that it's produced in a sterile environment which reduces the risk of microbial contamination.

Thus, we call this sector clean meat.

Individual producers may ultimately label their products using different terms.

Last year, the National Academies produced a report on the products of biotechnology. Written and researched by more than a dozen top scientists and peer-reviewed by an additional 17, the report recommended a single point of entry into the regulatory framework for the products of biotechnology to streamline the approval process for products like clean meat.

We've been thinking about the regulatory framework and talking with stakeholders about how clean meat ought to be regulated for years now. Our best thinking is that FDA is well-situated to regulate and be that primary point of entry for this industry. As was evident from the remarks of Commissioner Gottlieb, FDA has the expertise to regulate clean meat.

Clean meat facilities resemble the food

production facilities under FDA's oversight much more than those that FDA regulates under the Federal Meat Inspection Act or the Poultry Products Inspection Act.

As Jeremiah, you said in your remarks, the FDA currently evaluates microbial, algal and fungal cells generated by largescale culture that are used as food ingredients. And the industry also manages safety issues associated with cell culture technologies in therapeutic settings. This gives you expertise to regulate this space.

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.

As the commissioner pointed out in his statement that accompanied the announcement of this meeting, FDA has regulatory authority over all seafood other than catfish, meaning that FDA will be the agency responsible for overseeing the inspection and labeling of clean meat fish.

FDA oversight of the inspection and labeling

of clean beef, pork, chicken and duck will ensure that the same rules apply to all the producers. And that's critically important, that everybody is playing on a level playing field.

We are confident that this industry is committed to cooperation and transparency, which is evidenced by the involvement of Memphis Meats, JUST, Finless Foods, BlueNalu and Higher Steaks in this meeting today.

And we're very grateful for this opportunity to be talking to you about this technology and the great promise that it holds for consumers in the United States. We look forward to continuing the dialog.

MS. BARRETT: Thank you. Thank you for your remarks. Okay. Our next speaker is Maggie Nutter, U.S. Cattlemen's Association. Maggie? And again, if you'll say your name and organization?

MS. NUTTER: Hello, and thank you for the opportunity to speak. I'm Maggie Nutter, a fourth-generation rancher from northern Montana and currently mentoring the fifth and sixth generation in ranching. That's my son and grandsons.

I serve as director of the United States Cattlemen's Association, which is a producer-oriented organization committed to people whose daily lives revolve around the needs of the cattle and the marketing of these cattle.

The United States Cattlemen's Association has always been a strong advocate for truthful and transparent labeling. We believe that the term meat pertains exclusively to a protein food product that was harvested from the flesh of an animal in a traditional manner. Cultured cell protein would not be included in this definition.

As a rancher, the term beef is very important to me. Every time a cow is sold or changes ownership, a mandatory dollar is collected and placed in the beef checkoff fund. When you hear, "Beef, it's what's for dinner," you are hearing the marketing that millions of checkoff dollars have paid for.

When other products use the term meat or beef, they're taking advantage of the years of hard work the beef producers checkoff has put in building beef's reputation. They're hijacking our branding for benefit

of their own marketing.

As ranchers, we don't want anything that isn't beef or meat to be labeled as such. There are multiple USDA research and promotion programs which market everything from beef to popcorn and cotton to watermelon.

If the cultured cell industry wants to somehow benefit from checkoff programs, they need to create their own checkoff program and not ride on the coattails of beef and the goodwill that our products enjoy with the consumer.

Consumers are hungry for facts about their food. They want to know where it comes from, how it was grown, what's in it. They are concerned about safety, nutrition and how the production of their food impacts the environment.

Research shows that ranchers are constantly improving the production and efficiency of beef cattle through improving genetics, handling, seeding and veterinary care of the cattle. We are raising more tonnage of beef on less acres and less resources than ever before.

The meat industry has come a long way since Upton Sinclair's book, *The Jungle*. Temple Grandin's latest project, called Glass Walls, gives consumers a clear and transparent view into the industry's processes and facilities.

In short, consumers know exactly what they're getting when they buy beef or meat in the grocery store.

While we can read statements from the cultured cell protein companies and advocates stating that their products will reduce environmental impacts, be clean and safe, the United States Cattlemen's Association believes that research backing such claims needs to be made readily available and any health and nutrition claims be substantiated.

Also any labeling for these products should clearly differentiate it from the traditional beef or meat.

The FDA asked what hazards may be associated with cell-cultured food production. While the culturing of animal or human cells may be common for medical use, culturing animal cells for food is new.

There may be consequences that will not be recognized until actual product is on the grocery store shelf and being consumed.

We are glad to learn more today about these proposed products, how they're manufactured and the U.S. Cattlemen's Association would like to thank the FDA for bringing all these stakeholders to the table for this discussion. Thank you.

MS. BARRETT: Thank you. Thank you for your remarks. Our next speaker is Tiffany Lee, North American Meat Institute.

DR. LEE: Good afternoon. Thank you for the opportunity to provide these remarks today. I am Dr. Tiffany Lee. I am director of regulatory and scientific affairs and staff veterinarian for the North American Meat Institute.

Although the Meat Institute appreciates the Food and Drug Administration's hosting of this public meeting I'm both surprised and disappointed that no one from the United States Department of Agriculture is on any of today's panels. This meeting should have been held jointly by USDA and FDA.

Let me be clear about the Meat Institute's position. Primary jurisdiction over the regulation of cell-cultured meat products rests with the United States Department of Agriculture.

The Meat Institute supports innovation and welcomes new ways to bring the nutrition meat offers to consumers.

This support however does not alter the fact that just as with all meat and poultry products, there should be a comprehensive system regulating cell-cultured meat and poultry products to ensure they are wholesome and safe for consumption and are labeled and marketed in a manner that ensures a level playing field in the marketplace.

USDA is uniquely equipped to accomplish this task. Inspectors are onsite daily and USDA approves all product labels to ensure products are what they claim to be and prevent consumers from being misled.

The elephant in the room is that companies producing cell-cultured products want to market those products as meat. Everyone in the room has seen the term clean meat in the media. You've heard it used

here today.

If these companies wish their products to be marketed as meat and if one can find USDA's definition of that term at 9 CFR 301.2, then the production of these items should be regulated by the agency Congress chose when it enacted the Federal Meat Inspection Act. That agency is USDA. I appreciate this opportunity and I thank you.

MS. BARRETT: Great. Thank you. Thank you for your remarks. Our next speaker is Dustin Boler, American Meat Science Association. Again, if you'll repeat your name and organization? Thank you.

DR. BOLER: Hello. My name is Dustin Boler and I am here representing the American Meat Science Association.

The American Meat Science Association is a nonprofit scientific organization that includes over 1,200 national and international meat and food scientists from academia, industry and government. This organization generates and disseminates information about meat science to make scientifically-based recommendations for producers, consumers and

regulatory agencies.

As of today, research is ongoing to culture animal tissue from cells in a liquid medium with the goal of ultimately producing meat without harvesting animals.

The American Meat Science Association has published a meat science lexicon which is a guide to nomenclature associated with meat.

According to this lexicon, to be considered meat, cultured animal tissues must result in a product that is comparable in composition, functionality and sensory characteristics to meat naturally derived from animals.

To the knowledge of the American Meat Science Association, there is no publicly available information or actual product available for independent scientific evaluation to determine if food produced from cultured animal tissues are similar to meat obtain naturally from animals in terms of composition and functionality.

In time, the technology required to produce cultured animal tissue for food may advance to the point of producing products in sufficient quantity for

scientific evaluation. At that time, a reevaluation of the composition and properties of cultured animal tissue should occur to determine if it should be called meat.

Because cultured animal tissues have not been fully characterized, the American Meat Science Association has determined there is not enough scientific information available to conclude that cultured animal tissue should be called meat.

Appropriate categorization should be determined when these food products become available for rigorous independent scientific evaluation. Until that time, it is premature to assign a government agency to regulatory oversight of food production from cultured animal tissues. Thank you.

MS. BARRETT: Great. Thank you for your remarks. Our next speaker is Stuart Pape. And again, if you'll say your name and organization? Thank you.

MR. PAPE: Thank you, Kari. I'm Stuart Pape, shareholder and chair of the food and drug practice at the law firm of Polsinelli. I want to first thank FDA for convening this meeting. I think it's critically

important that regulators and other policymakers get timely input from stakeholders so that policymakers can develop sensible policy in a timely fashion.

As I think we've heard earlier today, the development of these products is continuing apace. And if there becomes a mismatch between product development and the existence of regulatory pathways, that will produce a circumstance that none of us will want to have to deal with.

I think FDA is uniquely situated to deal with these products based on its long history of experience dealing with a variety of food production and other FDA-regulated products as well as having the requisite experience.

Balancing the need for regulation here to ensure consumer confidence without materially impeding innovation is not going to be easy. There are lots of competing considerations. I don't think there's an existing regulatory pathway that is really suitable for these products. But I think there are lots of parts of existing pathways that FDA should pick up to fashion an appropriate approach.

It seems to me the regulation here should focus on the process. Is the process that is used well-designed, well-controlled and well-conducted? And then secondly, is the end product appropriately categorized? Is it what it's supposed to be and not something else?

So how might FDA fashion a regulatory approach here? Well, I think the agency should consider using concepts that exist with the processing authority used in food regulation so that you'd get a higher degree of process control than you might otherwise have in a normal food production process.

Coupled with a notification process that maybe results in a more affirmative FDA conclusion than the agency gives with the GRAS notice, which is we don't have any reason to object to the conclusion you reached.

I think Greg Jaffe made a useful point this morning that that less affirmative conclusion by FDA gives rise to some of the consumer uncertainty that plagues some GRAS substances.

I think without going to rulemaking, which

would be completely incompatible here with balancing innovation and regulation, I think FDA could nudge that conclusion up a little bit to a point where consumers could properly have more confidence in this.

I think submitted dossiers by companies should be publicly available because if it's not a transparent system, there's no reason why consumers should have confidence.

And finally, I'd encourage FDA to continue to develop that regulatory framework so that companies can continue their product development with assurance that the regulators will be ready when they're ready. Thank you.

MS. BARRETT: Great. Okay. Thank you very much for your remarks. Our next speaker is Sophie Moscovici-Troyka. You're going to correct me in a moment, I know.

MS. MOSCOVICI-TROYKA: That was close.

MS. BARRETT: I know. You're a student, and I understand with Princeton University.

MS. MOSCOVICI-TROYKA: Yes.

MS. BARRETT: So, welcome.

MS. MOSCOVICI-TROYKA: Hello. First off, thank you to everyone at the FDA for convening this meeting and soliciting public feedback on foods produced from animal cell culture. My name is Sophia Moscovici-Troyka. It's a little complicated. And I am a rising senior at Princeton University studying public policy.

I have been following the emergence of cultured meat for over three years now and am writing my thesis on it.

I first of all want to express my excitement that the FDA is preemptively engaging with this innovation and evaluating how the existing regulatory framework may apply to provide a safe and efficient path to market.

The implications of removing animal slaughter from the productions of animal foods are profound. This technology holds the potential to reduce the suffering of food animals, minimize risk from animal-borne disease outbreaks, mitigate animal agriculture's impact on climate, air and water pollution and land use change and improve food security in the face of an

increasing global population.

However, the societal implications are not the standard for oversight. I want to echo previous sentiments that the FDA must hold this technology to a high standard of safety to maintain consumer trust in their evaluations.

Cultured meat also raises technical and philosophical questions over the definition of meat. Given that cultured meat tissues are chemically equivalent to conventional meat tissues, it satisfies technical criteria.

Practically speaking, meat and dairy terms are already regularly used for non-animal food products such as veggie burgers or even peanut butter because consumers need a basis for comparison that is already used in common language.

In this case, cultured meat is not even a plant-based imitation. So to label it other than meat would mislead and confuse consumers.

However, in the spirit of transparency set forth by the industry, cultured meat should inform and educate consumers about the production process. The

promise of this technology for advancing public interest calls for continued engaged dynamic interaction from the government. And I am glad to see that the FDA is taking the lead.

Thank you for your time and thank you to the FDA for organizing this public meeting.

MS. BARRETT: Thank you for your remarks. Okay. Beth, I see you coming. Beth Briczinski, from National Milk Producers Federation.

DR. BRICZINSKI: Good afternoon. My name is Beth Briczinski and I am a dairy food scientist at the National Milk Producers Federation. NMPF represents the nation's dairy farmers on issues of public policy.

The focus of today's meeting is the use of animal cell culture technologies to manufacture meat, poultry and seafood products to resemble their traditional agricultural counterparts.

Now, this matters to our members because these rapidly evolving technologies also impact dairy foods, specifically, the use of genetically modified yeast to produce proteins that share chemical identity with milk proteins.

Just as laboratories can now make meat, they will soon be able to manufacture milk protein-based compounds for use in foods as ingredients, all without dairy animals.

When it comes to products manufactured from cell culture technology, FDA has asserted its legal jurisdiction over such products and touted its extensive expertise and scientific experience. FDA has also acknowledged that issues such as labeling and naming are relevant.

While National Milk agrees that these are important, we would argue that another important issue also needs to be considered. And that is FDA's willingness and ability to enforce its existing regulatory authority in this area.

The U.S. dairy industry is very familiar with manmade products attempting to mimic traditional milk and dairy foods.

For decades, manufacturers have been making fake milk and other imitation dairy foods and inappropriate using the names of products that have clear FDA standards of identity on their labels. You

are very familiar with the products I'm talking about. As examples, soy milk, almond milk, soy cheese and rice yogurt.

What began as a very clever marketing tactic has led to the rampant abuse of standardized dairy terms, all while FDA has looked the other way.

Most importantly, it has resulted in misleading consumers over the nutritional composition of these products in comparison to traditional milk and its contributions to a healthy diet.

Over the last 20 years, the dairy community has made repeated requests to FDA to take enforcement action on these misbranded products. Each time, FDA has brushed off our request by claiming the issue is not an agency priority.

As a result, we now have an "anything goes" attitude in the marketplace. If the development of a regulatory framework continues to linger and enforcement is as lax for synthetic meat as it currently is for imitation dairy products, we will see abuse by product manufacturers. We will see further consumer confusion and a lack of fairness in the

marketplace.

So today, I'd like to conclude with a plea to the agency. America's dairy farmers again call for a commitment from FDA to enforce existing standards of identity and labeling regulations for dairy products. It's well beyond time to resolve this problem.

I'd like to thank you for the opportunity to share our comments. We will also be filing written. Thank you.

MS. BARRETT: Thank you for your comments. Our next speaker is Vincent Sewalt, DuPont Industrial Biosciences.

DR. SEWALT: All right. I'm taking the microphone in my hand because I'm too tall to talk down into it. I'd like to thank FDA for the opportunity to make a few comments. I'll speak specifically to most of the requested issues.

My name is Vince Sewalt. I'm with DuPont Industrial Biosciences, which is a division of DuPont that has been involved for over 30 years in the development and commercialization of microbial products, including enzymes and small molecules for use

in food, for use in animal feed and other industrial applications.

I mention animal feed here. In fact, I am an animal scientist and animal nutritionist by training. So I have learned everything there is to learn about how animal protein is raised in agriculture. I'm also a biotechnologist in practice.

So at DuPont, we do think of ourselves as thought leaders in safety in a number of different applications, including food safety as well.

It's very encouraging to see that FDA is reaching out to practitioners of this new technology, as well as other experts to learn about the technology and to incorporate many of those learnings into its thinking of how it's going to oversee products from animal cell technology.

With regard to some of the questions, so are the potential hazards associated with animal cell culture, are they any different from products produced with other food production methods. And I will draw some parallels specifically with microbial products here.

So I think that the general food safety considerations such as the need for GMPs, identification of microbial hazards and other contaminants and so on and a documented plan to control them apply equally to animal cell culture as it does to traditional methods.

The parallels that the agency can draw between products produced with animal cell culture technology and products produced with well-established microbial fermentation -- also known as microbial cell factories -- are pretty clear.

Including the use of well-established safety evaluation decision trees such as the one in use by the enzyme industry. Granted, it would need some adaptation of course to fit the need for animal cell culture evaluation.

So for each type of cell culture, one can distinguish the following five determinants of food safety. One, the identity and, if it exists, the history of safe use of the final product. This may include substantial equivalence considerations as well.

Two, the identity and, if it exists, the

history of safe use of the cell lines, whether these are animal cells or microbial cells. Of course, with regard to animal cell lines, whether they are finite or immortalized, whether they are genetically modified, whether it's by CRISPR or other means needs to be taken into account.

Number three, the inputs into the manufacturing process need to be assessed as well as their safety. With these inputs are meant items like scaffolds, items like growth factors as well as the cells themselves.

Also needs to be considered the impact of the various manufacturing steps and changes or variation thereof as they impact product purity and/or level of potential contaminants.

Number four, the safety data for the finished product, whether that finished product is an ingredient or whether it is actually a final food.

And finally, the exposure assessment, right, of that ingredient or total consumption of that final food and margin of safety, if that is even feasible to determine.

So what specific animal cell culture considerations would be appropriate to include? Some specific considerations are needed for the inputs into cell culture and muscle tissue differentiation.

As these inputs are likely produced by biological means, they need to be well-characterized and their variability needs to be understood as well.

And in fact, evaluation of these inputs could look at each of the five points that I just referred to as well.

MS. BARRETT: Okay. We will need you to --

DR. SEWALT: To wrap up?

MS. BARRETT: -- to wrap up, yes. Thank you.

DR. SEWALT: Okay. Then finally, what kinds of variations in manufacturing methods would be relevant.

Again, analysis to the microbial fermentation techniques, I would say whether or not these techniques involve solid states or submerged cell culture and the resulting products from these two types of culture, their ability to wash out and remove any potential metabolites or other substances of concern. That type

of difference will be important.

And finally, another one is the potential use of closed loops in cell culture, as has been proposed, and of course the potential of metabolites to accumulate in these closed loops.

MS. BARRETT: Great. Thank you. Thank you for your comments. Our next speaker is Erica Meier.

MS. MEIER: Hi. Thank you. My name is Erica Meier, and I am the executive director of Compassion Over Killing, a national farm animal protection organization.

We represent hundreds of thousands of consumers who are extremely concerned about the welfare of billions of animals used for food every year.

And our mission is squarely focused on the negative consequences both for people and animals of our current system of animal agriculture, which is ethically, economically and environmentally unsustainable and externalizes heavy costs to be borne by all of us.

I want to thank the FDA for holding this public hearing and letting us share our comments

regarding foods produced using animal cell culture technology, commonly referred to as clean meat.

Compassion Over Killing conducts undercover investigations to give consumers a glimpse of what happens to animals on industrial factory farms and inside slaughterhouses.

In the past year, one of our investigators worked inside a Tyson Foods chicken supplier in Virginia. We found birds who spent their short lives crammed by the thousands into large windowless sheds.

We saw workers violently kicking, slamming and throwing live birds, chickens who were run over and crushed to death by forklifts as employees worked to round up the birds for slaughter.

On top of these awful conditions, many birds suffered from painful leg injuries and other deformities because they had been bred to rapidly grow abnormally large in order to yield the most meat as quickly as possible. Upon arrival to the slaughter plant, these animals face a gruesome death.

In 2015, Compassion Over Killing went inside a North Carolina chick slaughterhouse where our

investigator documented birds being violently thrown around the facility and workers forcefully slamming birds into shackles, workers punching, shoving and pushing birds who were hanging upside-down in shackles.

This is the plight of 9 billion chickens every year in the United States. I want to repeat that figure. Nine billion living, breathing, suffering animals. These are not isolated incidents of cruelty. Investigation after investigation shows similar mistreatment of animals across farms and slaughterhouses nationwide.

In 2015, as another example, we went inside a pig slaughterhouse in Minnesota. This specific facility is participating in the USDA's high speed slaughter reduced government inspection pilot program that the agency wishes to expand nationwide.

We documented pigs being beaten, shocked, dragged and improperly stunned. Sick and injured pigs endured particularly egregious abuse because they couldn't walk to the kill floor.

We need a real alternative to this suffering. We need an alternative to cruel and inhumane conditions

forced upon billions of animals. We need an alternative to artificial insemination, to overcrowding, to genetic manipulation, to long transport and slaughter.

We need an alternative to abuse endured by animals who feel fear and pain and we need an alternative to foodborne illness and the proliferation of antibiotic-resistant bacteria.

The last thing we should be doing is putting unnecessary burdens on the development of new technologies and new businesses that may provide these alternatives.

Whatever hurdles stand between where we are now and a future that can provide a safe, more sustainable and ethical alternative to the meat industry as it is now should be aided rather than hindered by FDA.

I know that FDA is also interested in comments regarding the labeling of clean meat. This new product is made from real animal cells and to label this product as anything other than what it is, meat, would be insincere.

I'd like to urge the FDA not to subject this nascent industry to unnecessary regulation. Clean meat offers real possible, positive possibilities to eliminate the needless suffering of animals and to provide an abundance of safe food. Thank you for your consideration.

MS. BARRETT: Thank you for your remarks. I'm not sure if Memphis Meats was speaking again. That might have been a carryover. Okay. I'm just going to check that. Kate Krueger, New Harvest?

DR. KRUEGER: Hello. My name is Dr. Kate Krueger and I am research director at New Harvest. New Harvest is a 501(c)(3) institute funding multi-institutional research in foods process using animal cell culture technology. We term this convergent research cellular agriculture.

Before joining New Harvest, I spent time in academia and biotech, earning my PhD from Yale in cell biology and working at Perfect Day Foods, a startup that uses yeast cell culture technologies to make milk proteins. Contributing to Perfect Day's milk protein patent.

As research director at New Harvest, I lead New Harvest's technical arm and the more I get to know the field, the more I realize how small it is and how few people are currently doing research in this space. Cellular agriculture is an interdisciplinary field, the convergence of engineering, biology and chemistry.

And like many burgeoning inter-disciplines, it needs support to fully realize its potential. That's where New Harvest comes in. New Harvest is an organization that provides the resources and convenes the experts necessary to support this young field.

To this end, New Harvest, one, develops foundational understanding in cellular agriculture; two, trains the next generation of cellular agriculture experts; and three, engages the public in opportunities and challenges in the cellular agriculture space.

Addressing regulation in this technology is an important part in that process. It is likely that this technology won't lead to one product so much as an entire product category.

Animal cellular technology as a method of manufacture will be different from traditional meat

manufacture. So questions about the machinery and the substances used for production and edible materials involved are highly relevant.

There may be added considerations for a full range of products that have characteristics not yet available to the meat sector. These products could include nutraceuticals, meat products produced with additional bioavailable micronutrients.

They could involve variation between products. So additional assessment of nutritional composition may be required. This technology may involve hybrid foods such as muscle cells grown on top of plant tissue. In this theoretical case, percentage of muscle cell content may need to be assessed.

Some products may contain beneficial components such as non-digestible carbohydrates that manufacturers may wish to label and declare as dietary fiber on nutrition labels, for example.

In addition to nutritional differences, variation in manufacturing methods might affect the materials that make up the machinery of this technology. The ingredients in the edible parts of the

food produced. Production is much more likely to be sterile for cultured products and it may be subject to different considerations for transportation temperature, shelf life and storage.

Manufacture for this technology is different. Thus, the hazards will be different from those present in the traditional meat manufacture.

Unlike traditional meat manufacture, increased product sterility means that microbial threats may be reduced relative to those of uncooked meat. It is possible that the temperature required to safely cook such products may be different.

Some of the substances used in the manufacture of foods produced using this technology are closer to those used in modern biotech than in the traditional meat industry.

Substances such as amino acids are familiar to the bodybuilding community and have been incorporated into food products for years. Others may be more novel. Thus, the considerations in place for such fields as biotech and supplement production may be more appropriate in evaluating the safety of the

manufacture.

Thank you for holding this meeting today. It's wonderful that organizations such as the FDA are joining the conversation about animal cell culture technologies. There is much to discuss. New Harvest looks forward to further conversations on this matter.

MS. BARRETT: Thank you. Our next speaker is Benjamina Bollag.

MS. BOLLAG: Hi. Good afternoon. I'm Benjamina Bollag, cofounder and CEO of Higher Steaks, a clean meat company. We are extremely grateful and enthusiastic that the FDA is engaging with stakeholders and we would like to thank you for hosting this meeting today.

While our technology allows for different species, we are starting with pork. As a chemical engineer, safety has always been at the center of my focus. We believe that the key to a safe clean meat product lies within the synergy between science and engineering.

As a clean meat company based in Europe, we are committed to connecting with both the United States

and European regulatory bodies to ensure that our products meet and exceed global safety standards, enabling us to responsibly serve our customers.

We are using induced pluripotent stem cells to create muscle tissue and have identified a number of areas specific to animal cell culture that we feel should be considered when developing regulatory guidelines.

When developing clean meat using these technologies, cells are guided to become muscle through either the use of differentiation factors, small molecules or genetic engineering techniques.

We feel that it is important to demonstrate that the end product produced through these methods is free from differentiation factors or small molecules.

We also think it is important to demonstrate that the molecular makeup of the meat created is identical or superior to that of traditional meat.

At Higher Steaks, we are striving to ensure that our protocols and process are as simple as process, safe by design and use as few chemicals as possible, which is why it's so important that we're

here today.

By simply refining our protocols, it will be easier to evaluate the safety of our components. It is also important to consider the methods for achieving induced pluripotent stem cells. There are now advanced methods that are much safer and do not integrate within the cell genome.

Clean meat offers the opportunity to efficiently create meat without the use of antibiotics. However, plant design must be carefully considered to achieve this.

To remove antibiotics and ensure safety of meat produced through cell culture, a closed system where no microbial growth is possible, that limits human interaction within the system is important.

Additionally, plant design must allow for sterilization as well as constant and regular in-process sampling of cultures to ensure no microbial growth is possible.

We look forward to continuing engagement with the regulatory bodies, food scientists, engineers and the wider scientific community to ensure that our

products are safe for our consumers, allowing us to deliver sustainable, animal-free meat globally.

Higher Steaks will be happy to discuss this further with the FDA and its scientists after this meeting. Thank you.

MS. BARRETT: Thank you. Our next speaker is Lou Cooperhouse.

MR. COOPERHOUSE: Thank you. It's Cooperhouse.

MS. BARRETT: Oh, Cooperhouse. Thank you.

MR. COOPERHOUSE: Good afternoon. My name is Lou Cooperhouse and I am cofounder, president and CEO of BlueNalu, a company that is a pioneer in the emerging field of clean or cultured seafood, which we call cellular aquaculture.

I am familiar with both FDA and USDA regulatory guidelines as I have served at senior leadership positions for a variety of food companies over the past 35 years and also consulted extensively on best practices in food safety technology and marketing strategies, most recently as the founder and executive director of the Rutgers University Food

Innovation Center.

And I later served on the board of a number of trade associations over the years. I'm also certified in HACCP and in preventive controls for human food. I have educational degrees in food science and microbiology.

BlueNalu's mission is to provide outstanding seafood products that are safe, trusted and delicious, that are healthy for our consumers and support the health and sustainability of our ocean and our planet.

We are currently in our R&D phase, isolating living cells from fish tissue and seeding them into culture media for proliferation.

Once this protocol has been optimized, we will organize and assemble these cells in a fresh and frozen, value-added seafood products. These will ultimately be distributed to food service and retail markets throughout the U.S. and throughout the world.

It's my strong belief that the FDA has robust guidance documentation already in place that supports the manufacture of seafood products, as well as meat and poultry products, that utilize cell culture

technology.

These existing food safety systems are based on the guidelines of the Food Safety Modernization Act and the principles of HACCP and are accepted by government agencies, trade associations and the food industry around the world.

These same HACCP guidelines utilized today have been utilized over the past few decades for food products derived from live animals are absolutely relevant to products that we manufacture via cell culture technology as well.

With HACCP, it's the responsibility of a food processor to identify any biological, chemical and physical hazard -- excuse me -- that could be introduced into a consumer product.

The safety of our food supply is dependent on properly identifying these hazards and then properly identifying the critical control points, or CCPs, that will prevent or eliminate these hazards from occurring or show that they have reduced to an acceptable level.

Furthermore, all companies complying with HACCP must adopt prerequisite programs, including

sanitation SOPs, personal hygiene and GMPs, written detailed specifications for all ingredients and procedures.

It's my recommendation today that the FDA develop a model HACCP program that could be utilized by companies manufacturing products via cell culture technology and require our companies to utilize HACCP in our processes, no different than is currently the case for seafood, meat and poultry products produced via live animals. HACCP transfers from FDA into USDA, as we know.

At BlueNalu, we already have a HACCP team in place and our team would be pleased to collaborate and cooperate with the FDA towards the development of this model HACCP program and its associated guidance documents.

This discussion today is extraordinarily significant. Cellular agriculture and aquaculture companies have the potential to transform the food supply of our planet. This is an enormous opportunity for all of us to work together.

As a result of our collective efforts,

consumers will be able to enjoy seafood that is free from mercury, pollutants, micro plastics, pathogens and other environmental toxins and contaminants and meat and poultry products that will result in a dramatic reduction in greenhouse gas emissions.

In all cases, consumers can enjoy these satisfying products with the knowledge that no animals were harmed in the process.

In addition to all of these benefits that I have mentioned and due to the sanitary nature of clean meat processing, I also feel very confident that the broad adoption of this technology will result in a substantial reduction in the number of foodborne illnesses our nation and our world experience every year.

Thank you very much for your support of this exciting and critically needed innovation to our nation's food supply.

MS. BARRETT: Great. Thank you for your comments. I'm going to check. Is JUST -- will JUST be speaking again? Okay. Again, some of these are carryover. All right. Danielle Beck, National

Cattlemen's Beef Association? (Sneeze.) Bless you.

Take your time. As I said, it's a hard room to navigate. So, and if you'll again state your name and organization, thank you.

MS. BECK: Good afternoon. I'm Danielle Beck, and I'm director of government affairs for the National Cattlemen's Beef Association.

NCBA is the nation's oldest and largest trade association for U.S. cattle producers. Producer directed, our top priority is to produce the safest, most nutritious and affordable beef products in the world.

On behalf of NCBA and our nation's beef producers, thank you for the opportunity to participate in today's meeting and share our perspectives regarding the proper model for regulatory oversight of meat food products derived from animal cell culture technology.

While NCBA applauds the pointed questions FDA has posed regarding risks, hazards and manufacturing methods of lab-grown meat food products, we believe that the more pertinent question that must first be answered is that of jurisdiction.

NCBA respects the expertise of the FDA. However, the appropriate agency to ask the questions under discussion today is the agency that will ultimately have jurisdiction over lab-grown meat food products.

While there may be some ongoing debate internally among FDA and USDA, NCBA believes that the law governing oversight of meat food products is clear and that any fair reading of the law places lab-grown products within the primary jurisdiction of USDA's Food Safety Inspection Service.

Meat food products derived from animal cell culture fall within the statutory and regulatory definitions laid forth under the Federal Meat Inspection Act.

For example, under the law, the definition of a meat food product has two fundamental characteristics that products derived from animal cell culture fall within that legal definition.

First, meat food products are any article capable of use as human food. And second, they must be derived either wholly or in part from any meat or other

portion of the carcass. Cultured meat products are derived from livestock species and the tissue necessary for production is part of the carcass of that animal.

Further, as stated today in a previous panel, cultured meat products are specifically designed to be comparable to conventional meat food products.

The only difference between cultured and traditional meat food products allegedly is the process by which the animal parts are grown and harvested.

Current FSIS oversight stipulates that meat and meat food products undergo contiguous inspection and that plants evaluate hazards and incorporate interventions at critical points to effectively control these hazards.

NCBA recognizes that the risks and hazards may differ depending upon the method of production. Yet the concept of hazard analysis and critical control points contained in USDA regulation of meat and meat food products would reasonably account for these differences.

From a food safety standpoint, it is critically important that all meat food products,

regardless of the method of production, are subject to the same set of stringent physical, biological and chemical standards, that establishments are subject to the same rules governing sanitation standard operating procedures and that all establishments are subject to continuous inspection.

These critical food safety oversight objectives can only be accomplished if USDA complies with the law and asserts jurisdiction over cultured meat food products.

It is important to note that there is a significant precedent which supports USDA jurisdiction, including several of FDA's previous decisions on agricultural technology.

For example, when presented with the issue of cloned livestock, FDA determined that cloning should be thought as an extension of the assisted reproductive technologies and opted not to claim any role in oversight.

In conclusion, the current manner of raising and slaughtering livestock is one method of production, but not a mandatory criterion in determining whether or

not a product meets the definitions laid forth under FMIA.

Interpreting these definitions not to include cultured meat food products based on production method when the end product is structurally and functionally similar could contravene longstanding USDA and U.S. policy and precedent and it would be a disservice to producers of all food products and consumers alike. Thank you.

MS. BARRETT: Thank you for your remarks. Our next speaker is Amanda Starbuck, Food & Water Watch.

MS. STARBUCK: Good afternoon. My name is Amanda Starbuck and I'm a researcher and policy analyst at Food & Water Watch, a national nonprofit advocacy organization.

We believe that the federal government's current regulatory framework is insufficient for overseeing the novel technologies and risks associated with using animal cell culture or other biotechnology processes to make alternative animal products.

We urge federal agencies, including FDA, to update their existing frameworks for regulating

biotechnology before allowing new products to be rushed to market.

This includes embracing the cautionary principle to ensure that all new products and ingredients are proven safe before they reach consumers and that consumers are fully aware how these foods were produced and what they contain.

The federal government's approach to regulating engineered food relies on outdated regulatory tools that predate the first wave of genetically engineered products.

As a result, products have come to market without being sufficiently evaluated for safety and without continued monitoring of health and environmental impacts.

FDA, for example, has granted GRAS status to the vast majority of genetically engineered products that have come to market despite the fact that these are novel ingredients created through new technologies that have no substantially equivalent ingredients in commerce.

Providing GRAS status to these products

ignores the unique risks of the technologies used to create them. FDA encountered this challenge when Impossible Foods disclosed its use of soy leghemoglobin, or SLH, in its Impossible Burger.

Documents submitted to FDA demonstrated how the production of SLH resulted in the creation of 46 additional unexpected proteins, none of which had safety assessments submitted for them.

This could potentially have serious ramifications to public health in terms of toxic and allergic reactions. Thankfully, FDA determined that Impossible Foods did not establish the safety of SLH.

But such an example demonstrates the weaknesses of a process that relies on industry-submitted studies for safety assessments.

Instead of allowing companies to essentially self-regulate, FDA should conduct its own risk assessments of each and every novel ingredient and product created using animal cell culture technology and genetic engineering techniques. And FDA should continue to monitor these products once they've come to market to screen for possible adverse health effects.

As such, GRAS status should not be given to these novel ingredients created through emerging technologies.

Instead, food products created through animal cell culture technologies might be better regulated under processes for food additives and potentially even new animal drugs which would initiate a more rigorous regulatory process.

This process should also incorporate reviews from other federal agencies, including EPA, which should investigate the risks of environmental contamination that may occur from the production and use of these new technologies.

Finally, FDA needs to regulate the claims that companies are making about these products. This include statements such as purely from plants when using yeast and other non-plant inputs and sustainable when synthetic biology relies heavily on feedstocks like corn and natural gas.

We urge FDA and other federal agencies to first update their existing frameworks for addressing biotechnology before assessing alternative animal

products made with emerging technologies. Independent risk assessments, transparency and engagement with the public at every step are all essential components of a rigorous regulatory framework. Thank you for the opportunity to comment today.

MS. BARRETT: Thank you. I'm going to also check, Finless Foods, did you want -- no? Okay. That's what I thought. Well, what I'd like to do is really give a round of applause for all of our commenters.

(Applause.)

MS. BARRETT: We really appreciate the thoughtfulness and the array of views. So we are now going to move into our wrap-up session. And I'm going to invite Dr. Susan Mayne back to the podium. Thank you.

WRAP-UP

DR. MAYNE: All right. So in the final wrap-up session, we're providing an opportunity for some of our panelists, if they wanted to react to anything we heard today before we close the meeting. So I'm just going to open it up to the panelists who have been

listening to all of the points of view, all of the issues that have been raised here today. And I'll open it up for dialog, questions, comments from our panelists.

DR. JONES: I'd be happy to make just a couple of fairly general comments. Many of you have highlighted the new wide variety of different parameters that are involved here in developing this new technology.

So it's clear that there's still a great deal of information to be gathered and I'm glad that we're involved in that process now. Many of you thanked us. So I want to just reiterate what others have said, to say thank you all for bringing your comments here and contributing to this process.

It's an ongoing process. And along those lines, again reiterating what others have already said, remember the docket. They're not out in some cyberspace netherworld.

A lot of people I've talked to believe that they're wasting their time if they sent comments into docket. And I just want everyone to know that they

are read. They're fully considered and they're extremely important to us, whether they're from a not-for-profit, a private entity or a private citizen.

So please take advantage of the opportunity to inform us even further through the dockets process.

MR. FASANO: I just want to echo what Bill said about really appreciating the participation in the process today and also in terms of contributions to the dockets, those are not only read by us.

But they can be read by anybody. Those are public, right? And so, there's an enormous amount of value in contributing detailed comments to the docket, not only for us, but for all other people involved in this conversation.

All of the different stakeholders will be able to see and read your comments. And so, we think that's really extremely valuable. And everyone will be able to benefit from that information.

I want to just say I'm heartened to hear that so many folks are thinking about what some of the critical control points might be and appropriate controls.

It sounds like some people are already thinking about sort of practical implications and where some of those issues might be and also hearing Dr. Mozdziak talk about some of the ways in which that already has been handled in a more laboratory or clinical setting.

And finally, I just want to note that we have heard a lot today, it struck me, about sort of identity and characterization of these products. What do we know about them? What could we know about them if we wanted to and how much do we need to know and for what purpose?

There's a number of different reasons that people are interested in identity and characterization of these products for a number of different purposes. And I think we've heard a lot to think about on that front today. Thank you.

MS. STITZ: This is Leah Stitz. I want to point out to you that you have in your folders instructions on how to submit the comments to the docket. The docket is number FDA-2018-N-2155. We really do want to receive everyone's comments and they

will all be fully considered. And the instructions are one page. It's really easy. So please do it. Thank you so much.

DR. YEUNG: I, just like the rest of the panel, I just want to extend my thanks to all those that have commented.

And I think there's a lot of good information being presented today and if there is any additional information that you can provide, I mean, we are very interested to hear from you in terms of the technology, in terms of the hazards and things that you have already mentioned. So again, provide your comments to the docket. Thank you.

DR. MAYNE: All right. So with that, we're going to begin the conclusions. And I just want to thank everyone on behalf of the FDA for participating in our meeting today about foods produced using animal cell culture technology.

We've heard several different viewpoints today and we really appreciate the time you have all taken to attend and provide input into this topic. And we look forward to additional input. I also want to reiterate

my comments -- the comments from the panel. The docket is open until September 25th. So we encourage you to submit comments into that docket. And you have the instructions in your handout, in the packet how to do so.

And as I mentioned this morning, we are also planning a fall meeting of FDA's science board to continue information on this subject, facilitated by FDA's Office of the Chief Scientist.

The board advises Commissioner Gottlieb and other FDA leaders on complex science and technical issues that are central to our mission to protect and promote public health.

Today has been a really wonderful opportunity to learn more about animal cell culture technology and to hear input from a variety of stakeholders in response to the questions that we pose in relation to evaluating the safety of these products so that consumers are protected.

We are committed to working through complex questions with our federal partners, as well as other stakeholders, to help new food technologies safely

advance. Our primary goal is to continue to help ensure the safety of the nation's food supply, regardless of how it's produced.

So thank you all for your contributions to this meeting today, and we're going to adjourn. Thank you so much.

(Applause.)

(Whereupon, at 2:22 p.m., the meeting was concluded.)

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I, NATALIA THOMAS, the officer before whom the

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July 24, 2018

DATE



Benjamin Graham