UNITED STATES DEPARTMENT OF AGRICULTURE

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USE OF WHOLE GENOME SEQUENCE (WGS) ANALYSIS
TO IMPROVE FOOD SAFETY AND PUBLIC HEALTH

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8:00 a.m.

U.S. Department of Agriculture
South Building, Jefferson Auditorium
14th & Independence Avenue, S.W.
Washington, D.C.

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M E E T I N G

(8:16 a.m.)

MS. HRETZ: Good morning, guys. I'm going to go ahead and do a little bit of housekeeping before we go into the introductions for the first panel.

So my first housekeeping is, if you guys have luggage, we have space along the back wall. We also have space under a table in the atrium, and we will have staff out there all day today, so it will not be unattended. So if you guys had to check out and bring your luggage, feel free to store it in either place or ask any of our folks in the atrium. They can assist you.

And then, of course, I want to invite everybody -- I know that we're limited with our setup, and so I invite all of you to sit close together, and to move forward, and to act like you like each other, so that you have a better view, and so that perhaps it's a little bit better. If you happen to be just, you see it perfectly from back there, then you're awesome.

And then one more housekeeping announcement, and it's not really housekeeping, but for you guys, at lunch time -- and we'll try to remind you at lunch time -- today, across the street, in the parking lot of the Whitten building, which is the building that's connected to this building by the little bridges, and by a tunnel, in the parking lot -- and you can see it when you walk out of these -- you know, out of Wing 5, you can see it across the street, is the last USDA Farmer's Market of the season.

So it's a pretty cool market anyway, but they're doing a lot of extra special fall pumpkin stuff, and some pumpkin soup sampling and lessons, and there's also some different food vendors that set up to make things while you wait.

So if that's something you're interested at lunch time, it's a really cool experience. And since you have an hour and a half, you have plenty of time to go around and enjoy all the local vendors. So that'll be a pretty cool opportunity. And it's the last one.

So, with that, I want to welcome you guys to the second day of the WGS public meeting. Thank you for all being here. Thank you for taking your time to be with us. This is really going to help us as we go forward, to have gone through all these perspectives, to have this dialogue, and to inform, you know, our decisions, going forward.

Today we're going to hear perspectives from the international and national partners and stakeholders. WGS is obviously being employed in many countries and international organizations, including the Global Microbial Identifier (GMI), the World Health Organization, the International Standards Organization, which most of you know as ISO. And everyone is attempting to develop international consensus in this growing field.

We've asked representatives from GMI and two major trade partners, Canada and Mexico, to be here today to provide their perspectives on the use of WGS in public health.

The speakers are Jorgen Schlundt from GMI, Cathy Carrillo from the Canadian Food Inspection

Agency, and Brenda Martinez, who will be speaking for Mexico's National Service for Health Safety and Agrifood Quality, or SENASICA.

And again today, to keep up with our ambitious schedule, we will be alerting presenters with our handy-dandy colored sheets of paper, with 10 minutes, 5-minute warning, a 1-minute morning, and then a little card to tell you when your time is up. And that's just to keep us on schedule because we've crammed so many wonderful speakers into our day.

And then please hold your questions for the end of the presentation, after these three speakers. As we've done yesterday, we'll have a panel, quick Q&A afterward. And then we'll take questions from both in the room and from online.

So the last warning is, of course, if you're on the phone listening, please mute your phone, as we're ready to begin. And with that, I'm going to turn it over to Dr. Jorgen Schlundt.

DR. SCHLUNDT: Good morning, everyone. It's really, really early. I'm flying in from Singapore, but originally, I'm from Europe, and in

Europe we don't start this early. You know, we are -- I mean, generally we are really lazy in Europe, compared to the U.S.

So sometimes it's good to come to the U.S. and then see how things are done, in some areas.

(Laughter.)

DR. SCHLUNDT: So I'm going to talk about this breakthrough that I believe that we are seeing just now, which I think is the biggest thing that has happened in microbiology for more than a hundred years. And I'm not really joking.

So next.

Yeah. There's going to be a lot of that, so I'll rely on you to move on, I guess. So --

But here are some of the things that happened in the good old days. That was when Europe was leading in science. Now, no more. Well, maybe they are, in some areas, but certainly not in all.

And if you click next one --

I think this is the big thing, and actually the biggest thing since Pasteur, and since Pasteur and Koch started to make pure cultures of

microorganisms. Basically we are identifying microorganisms the same way that Pasteur did in -- from 1872 or '76 or something like that.

So nothing really big has happened since then. I know that we also had some serotyping and things like that, but nothing really big has happened since then. We're still using biochemical testing to identify microorganisms. We've really been slow in microbiology compared to many other areas of science.

But now, next-generation sequencing will take us to the next level, in my opinion, especially if we get our act together. And my point is that we are not really getting our act together at the moment.

So next. Yeah, next. One more.

So these are three statements, and you can just put them up like that, that came out of a meeting.

One more, yeah. And one more.

We're saying that we now have the possibility to share these DNA data across the Internet in almost real time. And this gives us

fantastic new opportunities.

And this is a statement from what we now call the first GMI meeting. GMI was not really formed at that time, but that was the first international meeting when we got people together from all over the world, and everybody agreed that this is something that could be done. So that was in 2011.

Next, please.

This is a statement from a smart Mexican guy who worked in Mexico, was Minister of Health in Mexico, was Assistant Director General in WHO, and now Dean, Harvard School of -- I've heard that he's moved on. Maybe he's in Singapore. I don't know. All the good people always end up in Singapore. Or maybe the old worn-out people end up in Singapore. It's more like that.

So the advantages that we would see in relation to this, I think I'm listing four. And you can just put them up like that.

So we will be able to diagnose, identify, characterize microorganisms in a totally new way.

Outbreak investigation, we talked about that several times yesterday.

Prevention and surveillance, we have a totally new opportunity in relation to that also at the global level. And then research in general, these are the four that I'm listing.

Next.

So we should not only think in these areas, because there are a number of other areas where we are also clearly gaining some new momentum by actually using this technology. And the clinical area, I'll get back to that a little bit later on, because the detection possibility that we will have is again, totally new.

Metagenomics, we already now have global projects where sewage is analyzed in a small, unimportant country in north of Europe from 80, more than 80 major cities of the world. And in there, you can then find basically everything by metagenomic testing.

Imagine what that would mean for global surveillance if it was put into a real global system.

It's a really fantastic opportunity. Basically, you just scoop up two liters of sewage from wherever you live, you freeze it to minus 80 and you send it to Copenhagen. I mean, you could also send it somewhere else, but that's where they're testing it.

And then they do metagenomic testing and then they put out the results, I hope. I'm not quite sure because Denmark is now trying to keep data, you know, to themselves. I don't -- I mean, I don't know. You don't know anything like that, do you? Keeping data to themselves? No. No, no. That would really be stupid. But, of course, we know Denmark is sometimes stupid.

(Laughter.)

DR. SCHLUNDT: Linking human and animal pathogens is also really a big thing. Outbreaks, talked about that. Source attribution was already mentioned yesterday, and I'll -- I'm going to also have an example here.

Next, please.

And then, we don't talk so much about this economical issue, at least not in Europe. I know

that sometimes in the U.S. there are some estimations, and basically, they are very, very crude estimations. But just look at this one.

We're talking antimicrobial resistance, which most likely, if we don't do anything, will increase tenfold, at least tenfold at the global level by 2050, when we believe than 10 million people will die every year in the world from antimicrobial resistant microorganisms.

Just imagine the cost there. This is the cost at this time, so 0.1% of the GDP in the U.S. So 10 times that is, I think 1% of the GDP. And this is only AMR.

So we're talking about a huge, huge cost, and of course, a lot of dead people. I mean, 10 million per year in the world is more than cancer. It's more than cancer. Cancer is 7 million in the world per year.

This is according to WHO. We have to believe the data from WHO.

Next, please.

So we're getting into a system where we

have a totally new way of forensics. You all know that. We talked about that yesterday. We can use it for all the different types of microorganisms that we have. We can use the data immediately, almost immediately, if we want to.

It's routine in the U.S. Again, I would say the U.S. is ahead of the rest of the world in relation to that. And you can do traceback investigations in totally new ways, something we couldn't do before.

Next please.

So then people say, but why is that so fantastic? So we've had genomic testing for a long time. So PFGE -- especially CDC will say that, but that's also because it's a fantastic move forward that, again, came out of the U.S. with PFGE. It was fantastic.

But that's PFGE. We're just cutting the genome into 20 small pieces. And then we compare the size of these pieces. It's really not the same thing.

So, next please.

Of course, you know that this is whole genome sequencing.

And next again.

So I would say that if we compare two isolates with PFGE, it's like comparing two books by comparing the length of the chapters. So if the length of the chapters in the books are the same, we say the books are the same, which is, of course, totally stupid. Maybe not stupid, but it's not so smart.

And it would be smarter to actually compare all the letters, and that is what we're doing with next-generation sequencing. And this is why also PulseNet is moving towards next-generation sequencing.

Now, they only take small steps in PulseNet, so they only moved to MLST instead of going the full Monty. But that's a long discussion, and we also need to have that at an international level. At some stage, we need to find out why would we not share the full whole genome sequence whenever we are doing whole genome sequencing.

Next please.

But that discussion has to be done also at the national level, I think.

So this is why we want to do this in relation to outbreak.

So next.

So you will see that when we used PFGE, this is basically when we could actually document where the outbreak would come from in relation to the food, so we are clearly after the outbreak curve. So we are basically really not helping.

Next, please.

So the -- I mean, the source of contamination only identified out of -- after the outbreak. We have many, many examples like that.

Next, please. So next.

So if we move here, which we could do with next-generation sequencing, we would be finding the link before the outbreak. Now, would that be a good thing?

I hear clear silence in the room. Oh, there's somebody nodding. Fantastic. Thank you.

Maybe falling asleep, I don't know. But -- of course that would be a good thing.

And really, you know, when I hear somebody, and that can be from many different angles of whatever we're doing here, from industry or governments and like I say, is that not -- isn't that really a good thing? Do we really want to do that?

Yes, we want to do that. That is why we are doing food safety testing. That is why we want to be able to find the links before things are happening. Industry should love this. Forward-looking industry is loving it already. So we just need to convince the backward-looking industry that this is the way forward.

And I believe, you know, at some stage this is come -- I mean, 20 years, this is definitely going to be totally pervasive. Everybody is going to do this. So the longer it takes before you actually move onto the train, the worse for your company, in my opinion. But we can discuss that.

Next, please. Yeah. So next.

So that's just what I said.

Next again. Yeah.

So yesterday we saw something about this, *Listeria* cluster metrics, this has been explained. I don't need to explain that again. Clearly, we -- if we had a global database and if we had industry add their data into the global database -- oh, that's totally not possible. Of course it is.

If we had that, we would actually be finding outbreaks even earlier than what the U.S. is doing now. You have an excellent -- that's what we've seen now. So clearly, it's documented in the U.S. now that you can find the outbreaks much earlier, and therefore the outbreaks become smaller.

Is that a good thing? Of course it's a good thing. You're saving human lives. That's what we're supposed to do. Is it a good thing for industry? Of course it's a good thing. The earlier you stop the outbreak, the more likely it is that the company will survive. And we have many examples in U.S. and in Europe and elsewhere, that companies can go down on things like this.

So, again, I would say that even from an

economical point of view, even from an industrial, food industry, economical point of view, it makes sense, apart from that it also saves some lives, which I think should also count just a little bit.

Next, please.

So -- but we're talking about outbreaks, but I also mentioned that I think that it also concerns other areas. And I think we need to accept this thing that most food safety systems operate in the same way across the world.

I know that some countries want to go to the rest of the world and tell them how to do. You know which countries I'm talking about. I'm, of course, talking about Denmark and Sweden and things like that.

But we also know that mistakes -- no matter how we try to do things in our national setting, mistakes will keep on coming in across the borders. And it does not help to test things at the border.

I'm sorry to say that, especially here in USDA, and also too, USFDA, I think when we look at it in a scientific way, it's really not efficient to

test at the border unless you test everything, which of course you would never do.

So if you have issues in food with relatively low prevalence, we know -- and we know that from plenty of scientific data, that it doesn't make sense to test at the border.

It sounds very well to the politicians. We have a problem; let's test some more. It's really good if we test some more. No, it's not. We need to find a way to work together across the world, in order to be able to prevent outbreaks by doing good things also in our food safety system. Thank you.

Next.

So this example, source attribution, in my opinion, before whole genome sequencing, we could only do that for *Salmonella*. If we start employing whole genome sequencing in a smart way, we most likely will be able to do that for all microorganisms.

Next.

So this, the link here is that you link the *Salmonella* serotype to the serotypes that you have in

the different types of food, or from tourism or whatever, and in that way, you're able to say, what's the percentage of this *Salmonella* problem that comes from chicken or from eggs or so on? And we have used that.

Next, please.

And this is just telling you how we are using the serotypes. And because we have more than 2,500 different serotypes of *Salmonella*, we can do this. And then we can also subtype them further. So it makes it even better. But because we don't really have a same system for other microorganisms, it's not so easy.

Next, please.

So this was used since, I mean, late 80s in Denmark. And so you have the line up here, the incidence per 100,000 humans. And you will see that it started with a top that came from broilers. And they could document that through looking at the serotypes and doing the source attribution.

So they started doing something, and you can see, up to '91 or something like that, the line

was dropping, so number of people getting sick from *Salmonella* dropping. Then it started to increase again.

Of course, politicians would tell the regulatory agency, what the -- yeah, they curse in Denmark sometimes, but I don't need to say that in English, of course. You made us waste all this money and now we have an even bigger problem than before. What are you doing?

But then they could actually document, no, this is not from poultry; this is from pork. So let's do something in the pig production. They did that. Then there was another problem. Then it was in eggs. They documented that. They did that. Now, they have actually taken out *Salmonella* from eggs in Denmark. *Salmonella* in eggs has been eradicated in Denmark.

Just for USDA or anybody else who wants to listen, if you can do something in Denmark, you can do it everywhere, because Danes are not very smart.

Then we have a second -- just to prove that, we have the last top there, and they never

found out where that come from. They just -- I mean, Danes are not that smart. But the -- actually, they ended up on a good side. You could argue that maybe you don't need to do anything. The *Salmonella* would drop anyway.

Okay. I will not argue that, because I don't think it is correct. But actually, they used source attribution to do something sensible, and I think that something like that can also be used for other microorganisms if we introduce whole genome sequencing.

Next, please.

So this is the global idea. So if we take a patient or a food, we do DNA sequencing of the microorganisms, we put it to the cloud, we get -- we have all DNA sequences in the cloud. We will get an answer back in 2 minutes, which will tell us what the microorganisms is and whether it's resistant to which and what.

We can then treat the patient or the food. I know we don't treat the food, but still. The data can also be used for surveillance if everybody was

using that system, because we would upload that to the cloud again.

I think there's one more arrow. Yeah.

So this is basically idea. If we did that, if we agreed to do that, we would really be helping each other with a machine that can tell us what the microorganism is, how we can treat the microorganism, and with a real-time surveillance system that would be global.

So you would immediately know whether something is moving in Hong Kong or Singapore. Not in Singapore, of course, never in Singapore. There's never a problem in Singapore; which is clearly not correct because we have problems in all countries of the world. Yeah. Of course we have.

But the thing is, this is a fantastic opportunity. Then countries say, no, no, no. But is that a good thing? Should everybody know if something is happening in Hong Kong, or in Singapore, or in Denmark? Is that a good thing?

And probably some politicians would say no, it's really not a good thing. We want to keep it to

ourselves.

Are they going to keep it to themselves? Of course they are not. The biggest issues with big outbreaks here have been when somebody is trying to hide something. We've had that in a number of cases in Europe.

The government of Belgium went down because of a food safety scandal, not because of the scandal but because they tried to hide it.

The EU Commission was changed. The Commission of the EU was changed because of a food safety event, not because of the event but because they tried to hide it.

Every time we try to hide anything, we are doing even worse. And then, by the way, we are also doing worse to the people who will die from the food-borne contamination that we are trying to hide, if it's spreading.

And even in the agreements that we have under the WHO, the World Health Organization, the International Health Regulation clearly says -- and everybody, all countries have signed that -- that if

you have an event with -- a public health event with an international potential to spread, you have to inform WHO, who then has to inform everybody else.

So all countries agree that they have to inform. So there's really no way that you can keep it secret, not even Canada. And Canada knows that, because of SARS. And Canada, of course, didn't like that WHO told everybody that SARS was in Canada. But, of course, WHO had to do that. Of course they had to.

And I would argue with any Canadian, including up to the Prime Minister, it doesn't make sense to try to keep something secret. It does not work, not in today's society anyway. It will get out.

Next, please.

So GMI consist of the platform, community network. You can just go into the web page, and then you can become a member. There's no fee or anything like that. There's no money involved in that. We have four work groups. I'll just make -- mention them, just later.

Next, please.

So these are the four, political challenges.

Next one.

Repository storage of sequence and metadata, analytical approaches, and ring trials, quality assurance.

So just to let you know that on the working group -- so we have a meeting every year. GMI 10, the 10th meeting was in Mexico, May this year. Next one is going to be in Geneva in the week of 14 May 2018, just before the World Health Assembly.

I just want to point out, also, that Working Group 4 is running these ring trials, or proficiency testing for, I think, 60 or 70 labs now. So we are actually already -- we already have a system where we are trying to combine the capacity in different countries in relation to the labs.

Next, please. Next, please.

So this is just the home page that you can go into if you want to become a member of Global Microbial Identifier.

Next, please.

So these are the meetings that we have had since 2011. So we just called them all GMI, even if they might not have been called GMI in the beginning. But the Number 10 down there in Mexico and then 11 in Geneva.

Next, please. Next.

So we know that -- that's what I said before, that really all data will get out at some stage. And the worst situation for a government or a company is if it looks like they tried to keep the data hidden. You should never try to do that.

And then, of course, there's so much to gain from everyone, for everyone, in relation to sharing the data, and I think that should also be realized, or at least discussed. Thank you.

Next.

So we don't even -- I mean, so we are also saying that this is -- clearly, this will go on in the rich countries. It is already in the U.S. It is, to some degree, in some European countries.

We have this capacity that if you were in a

poor developing country and starting to create your system, why not create it using whole genome sequencing from the start, because it means that you can use the same lab for everything. Because whatever you want to identify, whether it's a virus or any microorganism, other microorganism -- some people don't like to call viruses microorganisms, but I will still do.

So whatever -- you use the same machine because GNA and RNA is the same, almost the same. And the -- you can detect it and characterize it in the machine, whatever. And again, it's a One Health opportunity. I think that was clearly also mentioned yesterday.

Next, please.

So we were only able to do something in Denmark because that, we got researchers, regulators and food industry to work together. If this triangle had not worked, it would not have worked in Denmark.

In the beginning, of course, the food industry would say, no, no, no, it's totally impossible to do something about *Salmonella* in

chicken; cannot be done. Chicken, if we want to take them out of these big flocks, it'll -- chicken will double in price. I think somebody even said triple in price.

Now, we know that it's -- I mean, it's maybe 1 to 2% increase in price. It's nothing. It's absolutely nothing. But you have to convince industry in order to get it done.

The other thing is, industry might be smart in some areas, and in relation to some of these things, because if you really want to have efficient solutions you need to know something on the ground, and researchers don't necessarily know what's going on, on the ground.

Regulators might not even know, too. Of course, they will here in the U.S., but in some other countries, they might not know the realities on the ground, but industry will know that. So you have a lot of information from industry that you need to move on into the system. And that was why it was successful, I believe, in Denmark.

Next, please.

So these are the major, three major obstacles. I would say, researchers' pride, what does that mean? So it means that if I am doing whole genome sequencing of a number of strains, I want it to get into nature. So I won't put it in the open database until in 7 months' time. I mean, I'm not even kidding you. This is happening. This is happening.

Next, industry's reluctance, I've talked about that. I think forward-looking industry is trying to embrace this already, but we have lots of other industry also.

Country's sovereign right, I mentioned also that countries think that they are doing good things for their constituents or whatever by hiding data. They are not. They are really not.

Next, please.

So we have these GMI, I would say, achievements, the -- we have WHO, FAO, and also OIE involved in our Steering Committee, but we really need to get the discussion into the international level, into the intergovernmental discussion. And

that is why we are trying to suggest to countries that this should be discussed in WHO and FAO and OIE. And hopefully some countries will listen.

Next, please.

So just a few slides from Europe, just so that you don't think we are totally in the Dark Ages. There is something happening in Europe. They set aside money in the Horizon 2020, which is the 5-year -- 7-year funding program for research in Europe, called COMPARE. And you can see what it means up there.

We got money into that program by saying, U.S. is already doing it. That's the worst thing you can say to the EU Commission; U.S. is already doing that. Then immediately they will put money into the SHARE.

Okay. So -- but they are doing lots of good things, and actually, along the lines of also discussion of what we are doing in GMI.

Next, please.

So they want to set it up like that. They are talking about harmonized standards, analytical

workflows. And, of course, we need to have these discussions about how we join forces to do this in the best way, also across the Atlantic, and basically, I would say, across the globe.

Next, please.

And they have all these different ways of involving stakeholders. And they're doing all these things the European way. You know, it's always very convoluted in Europe. You have to talk to everyone, and you have to include social scientists, and so it's probably very good.

Next, please.

This is just to show you that this is all the major institutes in, across Europe that are actually participating in COMPARE.

Next, please.

Yeah. And this is just an advertisement for Technical University of Denmark because they have this WHO Collaborating Center, and they are putting out a number of methods, or an easy way of actually using your data by sharing openly the different finder -- PlasmidFinder, ResFinder, and all these

other different programs.

And they are really easy to use, and this is how it should move forward, in my opinion, at the international level. We need to have discussions across the different countries and the different agencies and the different entities that are working on this, NCBI, DTU, other -- FDA, so on.

We need to get all these people together, and that is actually what is also happening in GMI. But we need some intergovernmental discussion to move it to the next level.

It's not enough that we have 250 or 300 scientists, or semi-scientists discussing it and agreeing that this is a good idea. We need country representatives to sit down and actually, probably at minister level, and agree that this is a really good suggestion.

Next, please.

So we're starting that by sending out a letter to the world. And we are doing that within a couple of weeks, I hope. We had a problem finding the address for the world. I mean, it's like, we

have to find all these ministries of health. And it's not as easy as you might think. We can't just get them from WHO because they don't want everybody to just send out spam emails. I don't know why.

But we will find it. We did it in Wikipedia. Wikipedia is so much more helpful than WHO in relation to this.

Okay. Next, please.

I'm not talking about Wikileaks. I'm talking about Wikipedia.

So this is what we are saying in the letter, basically is what I am -- I've been saying here, that really, if we have this technology, we should actually try to do something like this, and it would help us in a number of different ways, and then just also, relating it to the rise of antimicrobial resistance, because that's something that some of the governments or many of the governments is now making action plans to do.

Now, if they're making action plans just now, why not include whole genome sequencing and how we can share the data across the world for that?

Next, please.

Yeah. This is just what I've told you about GMI 11, so let's just go through that. So we link it up to the World Health Assembly, and hopefully maybe next year, 2019, they can then put it on the agenda and have that intergovernmental discussion.

Next, please.

This is just an example, so that you would not think that I'm just talking about something I don't know anything about in practice. Actually, I don't really know anything about it in practice, but theoretically, we are doing something also in our region.

Next, please.

We are actually suggesting to countries around that region to send isolates to us. And then we do the sequencing at the university, and then we look at the results together with the countries. That is a way of showing to some of these countries, this is how easy it could be done. Maybe you should buy a sequencer.

So I think you should go ahead like that. I think U.S. should go ahead like that. I know that you have been, with some countries. I think European countries should go ahead like that. That is a really easy way to start discussing, having that discussion with other countries.

Next, please.

Yeah. So this is just the last, I'm happy to say. Okay. Going out with a bang here. So I don't know if -- I'm sure that you know this quote, but I've modified it a little bit.

"We choose to create this system in this decade, not because it's easy, but because it's hard, because that challenge is one that we are willing to accept, because that challenge will bring so much benefit to global health and global food science and safety, and global food industry." I forgot to put them there.

Thank you.

(Applause.)

MS. HRETZ: Thank you. That was a -- it was not only a great way to set the stage for today,

but I think it was the lively talk that we needed this early in the morning, because as you say, we start a little early.

So, with that, I'd like to welcome Dr. Cathy Carrillo from Canada. And she's going to give us the perspectives and priorities from one of our major trade partners.

DR. CARRILLO: Good morning, everyone. I hope you can see me behind this podium.

I am a -- I just wanted to start off by saying I'm a lab person at the Canadian Food Inspection Agency. I don't make decisions. I was brought in about -- 4 years ago, actually, I started.

And I was hired through a food safety modernization initiative. And we were just trying to look at -- the CFIA was interested in how whole genome sequencing could contribute to their food-testing programs. So I've been working on that for about 4 years now.

Next slide.

So I'm going to talk to you today, and to start giving you a little bit of an idea of what the

Canadian Food Inspection Agency does in Canada. I think our system is a little bit different than in the U.S. And then I'm going to talk about how we've implemented foodborne pathogen sequencing in our organization.

And I thought it would be a good idea to give you an idea of what value we see in it by presenting a few targeted case studies. And then I'm going to end by talking a little bit about the interpretation of whole genome sequence data, that SNP data interpretation.

And this is really only a very small part of the sequencing work we're doing at the CFIA, but I thought, for this meeting, this would be the most appropriate.

Next slide, please.

So the Canadian Food Inspection Agency, we do food testing, but we also do testing for animal health and plant health. So food is part of it. And we also do things like feed analysis as well. And the goal of this testing is to verify compliance to standards and regulations that are set by other

organizations, by Health Canada, for example.

Next slide.

For food microbiology, we have six testing labs that are distributed throughout the country. So we are doing thousands of samples of food testing samples every year. And this occurs across the country.

And what I want to say about this is that we don't get very many positives, you know. We can do tens of thousands of samples, and we're getting about 250 isolates from this program every year. And that's because we're not testing things like --

Well, next slide. Sorry.

We're not testing things like raw meats. That's not done through our organization. So we're generally testing foods that we would expect to be microbiologically safe, or absent -- not having foodborne pathogens.

So we have programs in meats, fish, dairy, egg products, fresh produce, manufactured foods. And we also test food processing environments.

We do, every year, a targeted survey. So

we'll take a food commodity and look for -- try to get an idea of prevalence in a specific food commodity. But even there, you know, if we've got a 0.1% prevalence rate, you have to test thousands of samples to get two or three isolates.

And I think that's one of the big problems with linking foods to clinical cases. It's going to be very hard to get your food and environmental numbers up.

We respond to consumer complaints, and we're also involved in cases of outbreak investigation, and resolving -- testing foods in an outbreak investigation, looking for scope of the contamination, and we're involved in the hazard mitigation response to the outbreak.

We're also members of PulseNet Canada. So as of this year, we're sharing all *Listeria* sequence data with PulseNet. And we haven't -- they haven't moved to *Salmonella* yet, but it's -- we're starting with the whole genome sequencing in that program.

Next slide.

So this is really currently the way things

are happening in the lab. So, of course, we get isolates from the food testing programs. And we're -- for the whole genome sequencing, we're only talking about the step where we characterize the small number of isolates that we get every year.

Right now, in Canada, we have to -- you know, we could do the biochemical identification of an isolate when it comes in, but the isolates actually -- you see that some of the labs are distributed throughout the country. The isolates have to be sent to a lab in Ottawa for PFGE testing, and for serotyping it goes to another lab in another part of the country.

So even just shipping costs for these isolates costs a lot of money for the organization. So -- yeah. We wanted to look at how whole genome sequencing could replace some of these things.

And so for the past 3 years, we've been sequencing everything that comes in to the CFIA. And we're doing this in parallel with the, you know, the testing methods that are in place, which I think our labs find difficult, as you've heard before.

So we've got bioinformatic pipelines in place, so everything that comes in through a sequencer goes through the same bioinformatic pipeline, which works with all organisms. And we do a report of analysis on anything that comes in.

One of the interesting things about this, doing this in parallel with the traditional phenotype methods is that we are seeing cases where the phenotypes are wrong. We had a couple of cases of *Salmonella* serotyping where we asked the lab to go back and redo the serotype because the whole genome sequence gave a pretty definitive answer. And it was actually the serotype that was wrong.

And that's really interesting, that we're getting better results from the sequenced data than the traditional methods. And that's going to help us make the arguments to stop doing these older approaches.

The other thing I wanted to say was, you know, when we are involved in an outbreak investigation, I've been -- we -- I've been called for data before we even received the strains.

They're asking me for data. So they're -- they want the data yesterday from an outbreak investigation. So we've been really looking at ways of generating the data faster from our machines.

Now, we're pulling information right off the machine during the sequencing run. And we can do a *Salmonella* serotyping, for example, based on whole genome sequence, within 24 hours of having a colony on a plate. So it can be pretty fast, and you can get the whole genome sequence data very fast, if that's important.

Next.

So we send -- this is what we send to our clients. We have a Report of Genomic Analysis, and that sort of summarizes all of, you know, virulence factors, sequence types, MLST, rMLST, and if there's any matches to our database.

So now we have a database of everything that's been collected since 2009. Then we will have some sort of tree of that, to show how closely related they are to historical isolate.

Next.

And so we're trying to answer three questions: What is it? Is it dangerous? Have we seen it before? And, of course, you get a definitive identification with a whole genome sequence. It's, you know, you can really tell what species it is.

In terms of, is it dangerous, as I think we've heard the past couple of days, that's a pretty hard question to answer. We need a lot more information to understand how virulence factors play into human infectivity.

But the question, have we seen it before, is a lot harder than you would think to answer. And that's the idea of matching strains to historical isolates.

Next.

So one of the things that, when we started this, we were asked that, you know, is whole genome sequence data too high in resolution? People didn't want to use it because it was too much information. They didn't know what -- how to interpret it.

And I would say that you can look at it at any level. The nice thing about it is you can look

at it at any level of resolution. And you know those CSI shows where they zoom into a license plate and they can read the letters? You can't actually do that if you don't have those pixels in there.

It's the same thing with -- well, whole genome sequence gives you the opportunity to zoom in as much as you want and get every, you know, piece of information out of that strain.

So if my question in that resolution diagram is, are the -- is the font black, I could tell that from the R. I don't need very much resolution for that. But if I want to know what font it is, I need to look, you know, at a few letters and get higher resolution images.

Next.

And so we can do that with whole genome sequencing by looking at, as you've heard, MLST, which is based on seven genes. Our MLST --

Next, sorry.

Which gives you 53 genes that you can look at. And this is a lovely typing scheme, because it's useful for all bacterial organisms. Or you can go to

Core Genome, which gives you more information.

Next. Just the next two.

And this, you know, has been really -- you can go to the nucleotide levels. So you can say, are there any nucleotides different between two different strains?

Next.

So as you've seen in the past couple of days, PFGE does not give you, always give you very reliable information. This is a case of -- there's a bunch of samples taken from the same factory. And there's three different PFGE patterns.

Next.

And you can see, there's -- but there's only 2 to 11 nucleotides different among these isolates. So based on PFGE, you would expect that there'd be more differences among the strains than there actually are. So it's not a very informative technique for these isolates.

Next.

We had a situation where we had this very unusual *Listeria* PFGE pattern come in off of a cooked

chicken product. And at the same time, from another lab, the same very unusual PFGE pattern came in from a liquid egg product. And so people were asking, you know, is there a link between these two food types.

Next.

And there -- by whole genome sequencing, we were able to show that there was 274 nucleotides that were different between these isolates. And so that really put a stop to the need to do any investigation in that case. So now we have a really clear answer; strains are not related, and we don't need to do anything further with these samples.

Next.

And that happens a lot at -- we're asked -- because we have our data in our organization, we're not doing a very good job of sharing yet, except *Listeria* is now going in to the PulseNet system. But we're asked all the time to, you know, provide all the sequence data we have for a certain PFGE pattern when there's a cluster of clinical samples that are being investigated.

And I don't think we have one case where we

have found anything in our database that matches the cluster of clinical isolates that -- you know.

And so this is a case of *Listeria* pattern LMACI.0015. And we looked at everything we had for 7 years back, and the closest match was 39 to 49 SNPs apart from the clinical isolate. So we could show that -- you know, we could exclude all these foods right off the bat, which is fairly useful, still.

Next slide.

But once you do the epidemiological investigation and you get more information from the patients, then the -- you know, once you narrow down the food, and in this case, it was chocolate milk, then it fits right within the cluster of clinical cases.

So here we have 0 to 6 nucleotides difference from the chocolate milk strains compared to the clinical cases.

Next slide.

This is another case, and this is looking at persistent -- when we compare strains to our historical samples, if we do see a match, like a 0-

nucleotide match, that's pretty strong evidence that it's the same thing.

This was *Salmonella* Gaminara in a sprouted flax seed product. And you can see at the top, there's one at 750 nucleotides away. That was a *Salmonella* Gaminara from sprouted chia. That was completely unrelated. There's a lot of nucleotides difference. But it was taken in the same time period.

So we isolated a bunch of *Salmonella* Gaminara in Year 1. And then one year later, we got *Salmonella* Gaminara from the same food product, and there was a question of whether it's related. And it was 0 nucleotides apart, so definitely related.

And we were able to figure out that this *Salmonella* was in the seeds that were used to be -- that were being sprouted, but we were not able to isolate any *Salmonella* from the seeds, so we couldn't -- there wasn't enough in there to actually isolate any. But when it was sprouted again, the same *Salmonella* came up, and there was 0 nucleotides difference from it.

So that provided some very valuable information for the food safety investigators.

Next. Next slide. Okay.

This is another situation that we see, though. This is *Salmonella* Typhimurium in shell stock. And over -- we keep isolating *Salmonella* Typhimurium from shell stock from the same location, and this is over a 4-year period. And it's always the same Typhimurium, but now they're 0 to 72 nucleotides apart.

And you see that they don't -- it's not -- they're not clustering based on year. They're just all over the place. They're very different. If you saw this in a -- you know, it would be hard to find a cluster of clinical cases associated with this because you can't -- it's got quite a large amount of variability.

Next slide.

So whole genome sequencing can be very useful, in our experience. We've found some really useful information based on doing the whole genome sequencing in parallel with our other methods. But

it's complicated.

And interpretation of SNP data can be hard, because it depends on how the contamination came in, and rate of evolution of the strain, as I'll go into right now.

Next slide.

So we wanted to sort of look at that question about rate of evolution of strains and how that might impact, you know, SNP identification.

So we did a field study where we inoculated lettuce with three -- well, we used four different serotypes of *E. coli*, and inoculated each lettuce head with a million *E. coli*. And then we tried to recover them in -- you know, right away, at Week 1, Week 2, Week 3.

And we did this 2 years in a row and tried to get three isolates -- isolates from three heads of lettuce for each serotype, which worked really well at time zero when you inoculate, and you recover right away. But again, after that, it got really, really hard.

We got no -- in 2 years in a row, we got

none of the O157 back from the lettuce after Week 1, but we got it in Week 2 and 3. So we're not sure why this happens. Obviously, we need to do far more samples for this type of analysis.

Next slide.

But we sequenced all the isolates that we did get, and what was interesting was we saw no nucleotide differences for the O157 over the period of time of the study, no nucleotide differences for the O103.

We had an O26 in there, but we weren't able to recover it at all, so that was dropped from the study. But for the O111, we saw a lot of nucleotide variation.

Next.

And we -- that -- we saw that variation at time zero of, you know, when we inoculated and then we recovered it right away. So every strain we collected had a median of 5 nucleotide difference from the inoculating strain.

We see a little bit of a peak in Week 1. We don't know what that is about, but -- and then

we -- you know, in general, we're seeing about 5 per strain.

Next slide.

And if you looked at that on a tree, these strains would look really different, you know, they wouldn't have that -- with this particular strain, you wouldn't have that close 0 to 6 cluster that you would expect. And so that's -- you know, this is a rate of evolution that's higher than what most strains are.

And we heard a little bit about rate of evolution yesterday, but there's some evidence that stress might lead to, strains to go into a hypermutator state. And that might be something that could happen in a food production environment. So it's something that we really have to think about when we're -- and learn more about when we're studying -- you know, when we're having to interpret these trees.

If you look at the orange box here, you can see the -- this is the same culture that's been sequenced multiple times, so it's not coming -- the

SNPs are not coming in through a sequencing problem. But it's really a true biological difference. And these were verified by Sanger sequencing.

Next slide.

So whole genome sequencing is a valuable source of information, and it can be useful in food safety investigation. And in terms of -- it gives really good answers.

You know, we know that we are -- we can distinguish the new train from a control, which is a question we get asked a lot in a recall. And we can also show that that strain has never been in that lab before.

But you cannot really, right now, interpret the whole genome sequence data in the absence of epidemiological information, and I don't think we'll be doing that anytime soon. But it can be very useful in targeting your epidemiological investigations.

Next.

And I'm just going to leave you with this. This is a picture my 7-year-old brought home. And my

friends were a little horrified by it. They thought it was a devil with horns sticking out of it. But this came at Christmas. I don't know if you can see, it's actually Rudolph, so context is everything.

(Laughter.)

DR. CARRILLO: Next slide.

So I just wanted to acknowledge the -- my team, research and development team at CFIA, who is heavily involved in all of this work. We are really lucky. We now have three bioinformaticians instead of just one. So we feel like we might get somewhere soon. We have to spend a lot of time arguing with IT over what we need to do this work.

And the work on the SNP analysis was done by Austin Markell and Dominic Lambert.

Thank you.

(Applause.)

MS. HRETZ: Thank you. I think that was -- that was also a great look at some of the same concerns that we have throughout different governments and throughout different public health programs, because we're facing the very same things.

So I think you bring a good case for working together.

And with that, I would like to introduce one more trade partner. So we have Dr. Brenda Martinez here from -- she's going to speak on behalf of SENASICA. And I really want to send our appreciation, because we threw her in last minute, in the deep end, because we had some travel issues with our original speakers from Mexico.

So thank you so much, and I'll give it over to Brenda.

DR. MARTINEZ: Thank you very much.

Good morning. My name is Brenda Martinez. I am Agricultural Advisor at the Agriculture Office of the Embassy of Mexico.

On behalf of SENASICA and SAGARPA, I would like to thank the organizers for letting us share Mexico's experience with whole genome sequencing.

Next.

For those of you not familiar with SENASICA, SENASICA is a decentralized agency within Mexico's Secretariat of Agriculture, Livestock, Rural

Development, Fisheries and Food, responsible for animal and plant health, as well as sanitary regulation of primary production of processing of agriculture, aquaculture and fisheries foods.

It also regulates and promotes the application and certification of risk management systems in order to facilitate domestic and international trade of agricultural products.

Next.

Within the commitment of keeping Mexico at the forefront of technology, and increase the level of trust regarding food safety, SENASICA implemented, in 2013, the whole genome sequencing for *Salmonella* characterization isolated from fresh and minimally processed products.

Back in 2013, only 14 samples were sequenced, but the use of new technologies with increased analytical capacity has allowed exponential increase in sequenced samples. As you can see, by 2016, 976 samples were sequenced, and during the first 10 months of 2017, that number has surpassed a thousand.

In addition, SENASICA has also implemented different pipelines for that -- and interpretation.

Produce, as well as animal product samples are used to conduct WGS. The samples are provided not only by SENASICA, but also by the Secretariat of Health, Federal Commission for Protection of Sanitary Risk, better known as COFEPRIS, and by academic institutions with whom SENASICA has collaborative projects.

The WGS general workflow begins with the reception of either the sample or the isolate by SENASICA's Pathogen Detection Laboratory. If a sample is received, the laboratory technician proceeds to isolate the pathogen. If the isolate is received, the technician will condition the isolate as needed.

Once ready, the isolate is received by the Sequencing and Bioinformatics Unit, which will proceed to extract the DNA and conduct the sequencing and the bioinformatic analysis. Once everything is complete, a report is produced and updated to SENASICA's genomic database.

This is -- sorry. Since 2013, SENASICA has sequenced over 2,000 samples. As you can see in the chart, most of the samples have been taken by COFEPRIS, as part of the *Salmonella* project.

Next.

Currently, there are 1,872 isolates in SENASICA's genomic database, which includes food isolates from fresh and minimally processed produce and animal products, as well as environmental and clinical isolates. Over 80% of those isolates are *Salmonella*.

As mentioned before, back in 2015, SENASICA and COFEPRIS developed a joint *Salmonella* project whose objective is to generate and manage and analyze genomic data to detect and characterize the field of geographic distribution of *Salmonella* strains isolated in Mexico.

This project is a crucial analytical tool needed to better understand the effects and prevention of foodborne illnesses, as well as AMR gene detection. The isolation is performed by the National Public Health Laboratory Network, which

includes laboratories in all 32 Mexican states.

The *Salmonella* project currently has 1,375 sequenced isolates. Most of the samples come from the state of Michoacan, well known for its agricultural production. Most isolates come from processed animal products.

As you can see in the pie chart, 58 different isolates have been identified. The top five include *Salmonella* Typhimurium, *Salmonella* Anatum, *Salmonella* Agona, *Salmonella* Derby, and *Salmonella* Infantis.

The pipelines implemented by SENASICA allow them to determine AMR gene present in the sequenced pathogens, which helps SENASICA to collaborate in the national plan on AMR, and strengthen the health and surveillance system to prevent and manage AMR in Mexico.

It has also allowed Mexico to cooperate with international partners to strengthen the evidence base and develop new responses to this global threat.

The Sequencing and Bioinformatics Unit has

also conducted WGS on isolates provided by the National Center for Diagnostics in Animal Health, who leads the national plan on AMR, and the National Center for Animal Health Assessment Services, that provide isolates from the *Salmonella* monitoring program for raw meat in federal inspection type establishments, also known as TIF.

SENASICA has 25 sequenced isolates to date, and has identified 9 different serotypes of *Salmonella*.

As previously mentioned, SENASICA has developed different collaboration projects with academic institutions that benefit both parties. For example, the National Autonomous University of Mexico, the largest public university in Latin America, has provided meat isolates and amplicons for neurovirological research.

The National Polytechnic Institute has provided *Aeromonas* isolates as well as *Salmonella* isolates.

The Autonomous University of Sinaloa has provided environmental isolates from agricultural

water.

These joint projects provide students with great field work experience and training, using the latest technologies, which has proven very useful and may lead to careers at SENASICA or other laboratories in Mexico.

With a commitment to maintain the highest standards of cooperation and data sharing to ensure and improve food safety in Mexico and around the world, SENASICA belongs and collaborates with networks that have implemented on, or are in the process of implementing WGS.

Mexico is an active member of PulseNet Latin America and the Caribbean. In November 2015, during the 12th Annual PulseNet Latin America and Caribbean meeting, PulseNet Mexico was formed by SENASICA, the Institute of Epidemiological Diagnosis and Reference, or INDRE, and COFEPRIS.

Furthermore, 3 weeks ago, during the Third GenomeTrakr International Conference held close by, SENASICA expressed its interest in becoming part of the GenomeTrakr Consortium.

With the use of WGS, SENASICA assumes and maintains leadership at the national level as the reference laboratory in WGS, establishes and operates the National WGS Network that includes federal public agencies, increases collaboration with academic institutions to develop specific lines of research to meet the needs of agricultural and the agrifood sector, incorporates Mexico into global networks that use WGS to promote and ensure food safety, and strengthen the monitoring and surveillance of the -- of national -- of animal products through the use of WGS in the national programs of federal inspection type establishments, which allow the -- which allow it to have a genomic type map of the identified pathogens.

Mexico is one of the largest agricultural and agrifood producers in the world, and a top exporter of fruits and vegetables. For that reason, ensuring food safety and quality are strategic tools needed to increase the competitiveness of Mexico's agriculture and agrifood products.

SENASICA continues to develop new

strategies and partnerships that will allow Mexico to better respond to food safety challenges. SENASICA's working with U.S. government agencies as well as stakeholders from industry, trade, agriculture and academia, to enhance food safety.

Finally, SENASICA collaborates on a wide range of partnerships and has established formal arrangement with U.S. counterparts designed to improve information sharing on emerging food safety threats, and to work closely together when addressing product safety issues that may impact consumers on both sides of the border.

This is a picture of the team at the -- the highly specialized men and women who work at the Pathogen Detection Laboratory in the Sequencing Bioinformatics Unit in Mexico City.

Thank you very much for your attention.

(Applause.)

MS. HRETZ: Wonderful. And that's going to bring us to a short Q&A for this module. So if I could have all three of my speakers.

I know. I know. We're going to keep you

up here Brenda.

If I could have all three of my speakers, we're going to set you up at this table and take a few questions in the room and online.

Have we lost Jorgen? Okay. We'll --

And to our speakers, you know, as we answer questions, if you don't mind, when -- we'll bring up microphones for you guys. But as you answer, if you don't mind reminding the audience of your name. That way our listeners on the phone know who's answering. Although I'm pretty sure they'll know if it's Jorgen.

Okay. And we'll start. It looks like we maybe have one question in the room. You want to start us off?

DR. BRADEN: Hi. Chris Braden from CDC. One person, two questions, if I'm permitted.

First is to the -- for SENASICA. In your presentation, I didn't see any incorporation of WGS, of isolates from clinical cases. So what is the status of conducting whole genome sequencing in Mexico of pathogens from clinical cases, and how is that integrated into your environmental and food

databases?

DR. MARTINEZ: I'm going to have to defer that, because I'm actually not an expert. I had to come in for my colleagues in Mexico City. So I can definitely pass along your question, and we'll definitely get back to you via email, if we can.

DR. BRADEN: Okay. All right, thank you. And one other question.

So this has to do with the issue of diagnosing clinical cases in humans. The background is that in this last year in the United States we have demonstrated that culture-independent diagnostic testing of people has actually now influenced our surveillance for pathogens in the United States, to the extent that it's -- our trend data is actually unreliable, given -- just relying on our historical case definitions based upon culture.

I would like to know if other partners are seeing the same issue. And one of the industry partners that I think is important has not been really addressed here, and that is the diagnostic manufacturing industry.

As we look forward, and probably culture-independent diagnostic testing is the future of diagnostic testing in animals and humans, we need to determine what is the platform for testing and what is the data that we're all going to need, and will those diagnostic tests of the future provide the data for public health?

So what is the interaction -- Jorgen, maybe you can address this, kind of more on the global scale, the interaction to address this issue having to do with direct-from-sample, culture-independent diagnostic testing as it relates to the manufacture of diagnostic tests?

DR. SCHLUNDT: I would always want to speak. Whenever somebody asks me a question, I will speak for the next five minutes.

But this is clearly a major issue and has also been discussed internationally in GMI, but should be discussed in a broader sense, also, I think.

So first thing is, if we go to moving away from actually having isolates, we also have this

issue that if we find DNA, and we sequence it, and it fits with a *Salmonella enterica* type, do we know that this is actually a live microorganism, or was it just DNA from a dead microorganism? Because if you are in industry and you're looking into your products, it's really important that it was alive, because if it was killed, it doesn't mean anything.

So there needs to be discussion about how we start using also RNA testing, you know, to combine it so that we can actually have some sort of live/dead discussion linked to that DNA sequence that we will use in the future.

But I really -- but this is a technical issue that could be dealt with if we put some more funding, I guess, into some of that type of research. I know that that is going on in a number of different countries now. Again, I would suggest that we would need some sort of international interaction about that, because it's a really, really big issue.

And I don't know that we have that at the moment. Again, if there was an initiative, an intergovernmental initiative to actually do something

actively in this direction, this would be one of the areas that they would cover.

Maybe some -- just one more sentence, although maybe a long one. Maybe the things that we would suggest to do should be compared to something like say, Centre Européen Recherche Nucléaire, which is the big machine under the ground in Geneva where you smash atoms together.

This was put together by, I don't know, 45 countries, just after the Second World War because all countries -- maybe apart from the U.S., who had enough money on their own, but all the other countries would say, we don't have money to make a machine like that, but maybe if we got together with all these other rich countries, we could make a global machine or machine that we could use for purposes.

Now, of course, there's been spent hundreds and billions of dollars on CERN, and I think they found one small particle. And I think we are all very happy with that.

But we are suggesting making a major

machine that would actually make economies of countries better, that would actually save lives, that would actually do international surveillance, which is something countries have talked about for at least 20 years without moving, really, forward.

And I think, you know, if countries were discussing it in that way, there would be ways of actually creating the big machine, but it would be something the same level, or the same size as CERN. And CERN is, at the moment, 10,000 people working, 10,000 people working there in Geneva.

We could have the same thing in a global machine for something like this. And then we would move forward the agenda in a big way.

DR. BRADEN: So I'd just like to follow up on one thing and --

So I think it's important to actually talk to the diagnostic development, or the diagnostic manufacturing companies, because the diagnostic tests that they're going to produce for the future is probably going to be sequence-based. But the actual data that they use for those tests may be a very

small fraction of the data that's, may be produced.

How do we, and a public health community, actually get access to the types of data that we need for public health more so than just the diagnosis that is needed for patient care?

And so I think there is a partnership, the discussion with the diagnostic test manufacturing industry so that those tests are developed such that that data is available.

DR. CARRILLO: There's been some really good surveillance projects recently, where they're looking at the sewage projects. And I think that might resolve some of those issues if we -- I think you have to do the surveillance of clinical samples outside. Because the diagnostic tests are just going to be cheaper to do. And that's going to drive the movement of diagnostic tests to pathogen-free.

So I think we have to have another way of doing this in our countries. And I like the sewage projects because they get away from having to ask permission. And in Canada, we have a lot of rules around permission to sequence isolates from patients.

So it gets on around some of these issues.

DR. SCHLUNDT: Yeah. Just to let you know that they -- in some countries, they have asked permission to take the sewage, and were denied permission. So in Japan, for instance, they had to not send the 2 liters of sewage because Japan government denied them this, I think Japan and maybe one other country. I don't know.

MS. HRETZ: So I know we have one question -- we have two questions online, and then we'll go over here. So we're going to start with one online. We'll go back and forth.

(Pause.)

MS. HRETZ: So I think this first question is -- and I'm going to give Scott a microphone, so he can clarify -- is going to relate to, actually, the last 2 days of meetings, because this question is about do any of your organizations do random testing at retail? And if contamination is found, is that forwarded immediately for sequencing?

And so this is about retail surveillance, random retail surveillance for pathogens. So does

that -- okay.

So if you guys want to comment on systems. I know that this relates to NARMS retail in the United States but, you know, how does that relate to any of your systems?

DR. CARRILLO: Yeah. We're definitely taking samples from retail, random samples from retail so, at CFIA, and Health Canada does that as well. And if we do find a positive then, you know, it goes to a food safety investigation. And everything is sequenced now.

MS. HRETZ: Okay. And we have -- I'll go over here to the left, and then we'll go back online.

DR. STRACHAN: Okay. This is a question for Jorgen, and I -- and --

DR. SCHLUNDT: Can you speak up? Because some of -- or one of us up here is really old, you know, and not hearing so well.

DR. STRACHAN: Okay. Is that a bit better? I'm speaking more directly into microphone now, so that might help.

So I enjoyed your talk, and actually

enjoyed all three talks.

But the question I had was, I was really interested in your point about getting ahead of the outbreak curve. And what I could -- when thinking -- just thinking about it and sitting down, if you're trying to head out of the outbreak curve, in terms of human cases, you're only going to have sporadic cases.

And it's great with whole genome sequencing that we're able to actually connect some of these sporadic cases because they're actually outbreaks, but there's still a lot of them there.

And you mentioned about source attribution, which I think is very helpful. And I think that helps us actually get ahead of the outbreak curve because we can look at the sources of the sporadic cases and do, perhaps do something about that.

But the other thing you mentioned was, you mentioned about food safety management systems and what the food industry might do as well. But maybe, could you maybe elaborate a bit more on that? Because I didn't really find out what the point you

were making on that particular perspective.

DR. SCHLUNDT: So I didn't really get the last part.

DR. STRACHAN: So what you said was something about food safety management systems and how the food industry could help us get ahead of the outbreak curve. I think that's what you said in the talk, if I picked you up correctly.

I was just wondering if you could make it a bit -- express that a bit more clearly, what you were trying to say.

DR. SCHLUNDT: So in the big picture, in the future, somewhere into the future, we will have a big data -- I'm not in doubt about that. We're just suggesting we should start doing it now.

We will have a big database that will have all the isolates that everybody has at -- and at ever, and any time, in any type of food isolated, we will have that in the database.

That means that as soon as we get an outbreak, or we have one case -- because it could be only one case -- we would be able, in principle, to

link it to where it comes from, I mean, in principle. Yeah?

So the idea is that if we had these major databases, we would be able to find issues that we cannot find at the moment, and we would probably find that most of the sporadic cases that we say are sporadic are actually parts of small outbreaks or even large outbreaks that we could never find before. And I think there were even examples of that yesterday.

So in my opinion, that would change the whole way of food safety management, away from random testing, which is really not helping. I mean, we've tried that for 30 years and we haven't done anything to the global foodborne disease burden. Sorry to say, we have not.

We have wasted so much money. And I'm one of the guys who have wasted lots of money, so I'm also pointing at myself. We've wasted so much money without doing something about a problem.

In safety -- in traffic safety, they have scientifically looked at where the hot spots are, and

they have done something about it, and they have reduced the number of death in traffic, in X country, like Denmark, at least threefold over the last 10 years. What have we done in food safety? What have we done? Really, nothing.

DR. STRACHAN: Well, I think I could probably argue. I think that all the organizations have done some things, to defend them. I think the point you're making, that it's really important for industry when they isolate organisms, that they put forward those organisms so that they can be sequenced and put into databases, which will help with the comparisons in the future.

DR. SCHLUNDT: Yeah, yeah. But I'm saying we've done nothing because the disease burden has not gone down.

I know that in the EU, they have taken down the disease burden from *Salmonella* almost 50% over the last, I don't know, 10, 15 years. So there, they have done something.

In the U.S., there is also a reduction at some stage. I don't know if it's continuing or not.

But the idea of wasting all this money on all our scientists in relation to food safety is that we're doing something about the problems, yes? I think that's the idea, or else, why would society waste all this money on us anyway?

Now, we finally have the tool that could actually move forward this agenda in a big way. And then we are still bickering between different countries, between different systems, between different agencies.

We have all these problems. We are seeing a fantastic solution -- I heard all these presentations yesterday -- fantastic solution that can really bring things forward, and could actually reduce the real disease burden significantly. And that's what we're supposed to be here for.

And now we're having all these small discussions and we don't want to share the data and whatever. It's really, really depressing, when we are looking at this area where we could do so many good things.

MS. HRETZ: So, and I think basically -- I

mean, you guys are saying the same thing. You know, we have a huge burden, globally, to attack illness, and we've each been chipping away with it, you know, as we can.

But I think, you know, there's a potential, working together and with this technology and the great amount of information that it gets us, if we work together, the faster that we get it going, the faster we get these databases and cooperation going, we can take a, hopefully a big chunk, maybe something measurable, maybe something more significant, you know, globally, instead of these little pieces that we've been doing.

So certainly everybody's been chipping away, but we might be able to really ramp that up and accelerate the progress by using all of the tools at hand and actually adopting them faster, which there is always going to be some tape in between, but I think that's why we're all here. So --

DR. STRACHAN: Thank you.

MS. HRETZ: I'm going to take a question from online.

DR. UPDIKE: Yes. We have one more.

It's will the global database, GMI, include a surveillance program to sample very high-risk populations like food preparers, farm workers, veterinarians, etc.?

DR. SCHLUNDT: Could you say again?

DR. UPDIKE: Yes. Will the global database, GMI, include a surveillance program to sample very high-risk populations like food preparers, farm workers or veterinarians?

DR. SCHLUNDT: Well, the -- I mean, so we are presenting the idea from the GMI community, and we are suggesting that it needs to be discussed between governments. So when governments want to discuss something in international setting like in WHO or FAO, they -- usually, they have a background from expert meetings.

So we would suggest that we need to have a number of expert meetings, which would include discussions about these issues and the whole setup, because this is not an easy thing to do. I'm not suggesting that it can be done in a few months.

It'll take long time, and you need to have intergovernmental discussions of how you want to do that.

But these are clearly good ideas, and there are lots of other good ideas to be included in that.

MS. HRETZ: Okay. And I think we've got one more in the room.

Or Peter, are you going to --

DR. EVANS: Okay. So this question is primarily for Jorgen, but anybody can answer.

In your slides, you talked about the experience in Denmark where industry and the regulatory work together to use serotyping to identify the sources of *Salmonella*, salmonellosis, and target the right sectors.

And so I want to ask a more general question about, what were the critical factors that, you know, you can take from that, or maybe what's happening in Singapore, to encourage industry and regulators to work together to solve food safety problems?

DR. SCHLUNDT: I'm sure that there were

many things, but I'll mention two things. One, that in general, government is perceived to be a good thing in Denmark, which is not the case in all other countries. And I know, you know, if -- so if the farmer sees government come to his farm in Denmark, he's happy, because normally the government is helping him or her, which is not the case everywhere. So that's the first thing.

The second thing -- so in general, there was a positive sentiment from industry, food production industry. Of course, they will still complain. I mean, Danish farmers will complain about everything, the weather, also the government and things like that. They will still complain.

And they will say, cannot be done, will be very expensive. But in the end, they will agree, because they can see science and how it working.

The other thing I wanted to mention is, that in the Danish system, there is a lot of collaboration between the different producers. So all the way back from 1870-something, you have these collaborative system. It's not socialism.

But you have these -- I have to say that in the U.S.; it's not socialism. But it's the -- all the farmers are working together in one big collaborative system. So if they can do that, they can also speak and negotiate in one voice. And I think that meant a lot, because it meant that all the farmers would be doing the same thing.

It wouldn't be like, okay if we do it, what about the other ones? Are they supposed to do the same thing?

So I think these were two very important areas. But I think also, this -- the tradition of working together in these -- in this triangle is also a good -- it's a good thing, and it's something that you have to practice. I'm sure you're also doing it in the U.S.

MS. HRETZ: No, absolute -- that's a -- it was a good question, and also, definitely, we're going to see that later, because in our Stakeholder Perspective, we're going to have some of the perspectives from some of the groups of corporations and industry and consumer groups that actually helped

make this meeting happen.

So we definitely do have that sort of common voice coming through in the United States, and that's exactly why, again, we're here.

And so I'll go to this gentleman on the right.

DR. MUSSER: Steve Musser, FDA.

Could you -- two questions, really. Are you using data in the public databases to support your own work?

And the second question is, can you talk a little bit about obstacles for uploading and submitting genomic and metadata from food, environmental and clinical samples in your country, and ways that we might overcome those obstacles to improve the database?

DR. CARRILLO: Are you talk -- is that for me?

DR. MUSSER: Well, all three of you are from --

DR. CARRILLO: All three, okay.

Yeah. We have -- there has -- at our

organization, there's been a lot of -- they asked the lawyers, and the lawyers said no. And that was the biggest problem. And we tried to sit with them and see what exactly their problem was with the metadata upload.

And it's been really hard to even get a discussion going. But I think we're -- right now we just had our first access to information request for genomic data. And it's been a really big, hard thing for our organization to organize.

So that might be something that pushes things forward, the fact that, you know, the data is -- we're supposed to be an open data government. So if people want the data, we should have it in a public repository.

There's -- you know, I think with the metadata sheets that you have, we could -- the minimal data that's required should be okay. They don't want identifying information for companies or company addresses or anything like that, but that's not required right now. So I don't think it's anything there.

It's about having conversations with the right people who -- and being able to address their concerns in a -- sort of finding out exactly what the concerns are and being able to respond to them directly.

But I find it's always a game of telephone in government. So whoever has the objection, there's three levels that I have to go through before I can -- and it gets passed back and forth for a long time.

DR. SCHLUNDT: In the region around Singapore, we are trying -- with this small project, we are trying to start the discussion, because we will get whole genome sequencing of, I don't know, 500, 600, 700 strains from the region, maybe more. And then we will suggest to upload them into GenomeTrakr or something else, probably GenomeTrakr.

So then we will start the discussion in that way. And I don't know how it will go, but at least we will start the discussion in six different countries, whether that makes sense or not.

I know that there are a lot of countries

that will say, oh but this is very difficult; we can't do that. But the thing is, it seems like GenomeTrakr is working, even if -- even though you are actually putting the isolates up within, as I understand, few days. And I don't see anything falling apart in the U.S., at least not in this area.

So I'm pretty sure that it can be done. And again, the example from U.S., that you can actually do that without hurting industry or hurting someone else, or hurting other countries, would really be a very strong example to take to other countries and say, it can be done. But we just have to start doing it.

That's also why we're starting that small project there. It's just so that countries will start to get used to that this is the way of the future. And I'm really totally convinced that it's going to happen.

Of course, all the concerns of different stakeholders and, you know, they have to be addressed. Again, that's why we are saying we need to have intergovernmental discussion, not

conversation between people like us, because we are way too low. Maybe you are not too low, Steve, but the rest of us, we are way too low-level to discuss this.

This has to be ministerial level in countries. It really has to. And even in some countries, it might have to be prime ministerial level.

DR. MUSSER: Thank you.

MS. HRETZ: Do we have anything else online?

(No response.)

MS. HRETZ: Okay. Do we have anything else in the room for this panel?

(No response.)

MS. HRETZ: Okay. Well, that puts us a little bit ahead of schedule, which is never a bad thing because we've got a lot going on after this panel. And so we have a break until 10:30. So that's plenty of time to get coffee, get moving, and then we'll be right back here for our Stakeholder Perspectives.

(Off the record at 9:51 a.m.)

(On the record at 10:33 a.m.)

DR. SHAW: Hi, everyone. I think we're going to get started for our next session.

So for any of you who don't know, I'm Bill Shaw, and I'm from FSIS Office of Policy and Program Development, and I am the Director of the Risk Innovations and Management Staff.

While I do have the floor, I want to make a shameless thank you to my staff members who have -- you've been seeing for most of these past 2 days. A lot of people throughout FSIS have worked hard to put this on, but while I'm up here, I do want to thank especially Peter Evans and Stevie Hretz, who you probably have talked to at some point over the past 2 days.

And I want to thank you -- thank them for their work, and various other parts of my staff that have been doing logistics for the past 2 days. So thanks for bearing with my shameless thank you to them, because they've worked really hard.

And moving on to our actual session, so

this session is entitled Stakeholder Perspectives. And WGS has and will continue to affect the food industry and consumers of food, and that's all of us. And many concerns were expressed, which encouraged us to organize this public meeting.

And these next talks will talk about a lot of those perspectives throughout, with industry and consumers and other academia, and their impacts and their experiences with whole genome sequencing.

So the speakers for this session are Jennifer McEntire from the United Fresh Food Association, a fellow Blue Hen and graduate of University of Delaware, as myself; Angie Siemens from Cargill Protein Group; Mansour Samadpour from IEH Laboratory and Consulting Group; Alvin Lee, Institute for Food Safety and Health; and Vanessa Coffman for Center for a Livable Future.

We will be taking questions at the end of the presentations in a Q&A session like we've been doing for the past 2 days. We'll also -- if people online have a question, type that in and we will sort of filter them in during our question and answer

period.

And for no other needs, I'm going to hand it over to Jennifer.

DR. McENTIRE: Good morning, and thank you very much.

I first want to -- are we working? No.

I first want to give a real thank you to USDA-FSIS and -- for putting on this public meeting. I'm here to represent the breadth of the food and beverage industries and the perspective that we collectively share, although I am with the Fresh Produce Association. And I'll make a couple of comments specific to fresh produce.

In terms of who is food and beverage --

Are you able to advance the slide please? Thank you.

To provide a little bit of background, about, almost 2 years ago, several of the industry associations realized that we all had similar concerns and initiatives around *Listeria monocytogenes*, and began to coordinate our efforts, the American Frozen Food Institute kind of

spearheading that gathering, and many of the discussion led themselves to whole genome sequencing.

And we realized quickly that whole genome sequencing is not applied solely to *Lm*, and that maybe we needed to have another group, a more inclusive group on whole genome sequencing.

And so several of us, those indicated here, got together, and we have about a monthly conversation, not to really talk about our initiatives, because I think we're very early in the process, but to talk about some of our mutual concerns, and just share knowledge. And so I have shared this deck with others at these associations, and so I hope that my comments accurately reflect the discussions.

What industry heard, I would say, a few years ago, and the reason that we have this concern amongst our collective memberships, is that whole genome sequencing is the greatest thing ever, and we really don't need epi anymore. Epi, ah, off to the side. We have whole genome sequencing, and that is the silver bullet. We can now solve all cases of

illness, match them to facilities perfectly.

Perhaps it wasn't said exactly that way, but that's what industry heard. More recently, including at this meeting, we've heard a much more tempered, balanced perspective that a whole genome sequence match between a food and clinical isolate doesn't always mean, it doesn't necessarily mean that that particular food caused illness, and that epi and traceback are still critical components of the investigation.

Still, I think sometimes we continue to get mixed messages, and it's very difficult, when industry has heard the former assertion that whole genome sequencing is it, it's very difficult to undo that perspective. And we've seen action taken against the industry based on whole genome sequence finding.

So here's an extract from a warning letter that, comparing the whole genome strains found within a facility to the whole genome sequence database and looking back in time at other isolates taken out of that facility "shows that *Lm* has maintained its

presence in your facility since at least" the time that it was first isolated, and that this means that you are potentially preventing -- you're not capable of preventing the contamination of food, thus a warning letter.

And this is a very serious deal to the industry, obviously, to receive a warning letter. Nobody wants that. And it has prompted some questions around whether or not that assertion is valid, whether the finding of a specific pattern over time is always indicative of insanitary conditions.

On the FDA regulated side, I'm not sure that when the FD&C Act was written oh so many decades ago, that Congress had the foresight to envision whole genome sequencing and use that as a tool to make a claim of insanitary conditions.

We do know, and see the benefit of whole genome sequencing in outbreak investigation, and we know that it's resulted in recalls. Sometimes there is fantastic epi and traceback evidence that supports whole genome sequencing. Sometimes some of these things are a little bit more questionable.

It also makes us wonder about the definition of an outbreak. When we're able to look at nine illnesses over the course of, in one example with the frozen vegetables, nine illnesses over 2½ years that that's -- you know, does that still meet the definition of an outbreak as we've conventionally thought about outbreaks.

In the Wawona recall, associated with stone fruit, there were a couple, a couple of cases of illnesses, two, another two that were ruled out, that had -- seemed similar by PFGE but whole genome sequencing was able to rule them out.

So we see, obviously, the power of whole genome sequencing to link a food isolate or a facility isolate with just a couple of cases of illness.

Looking back again at the frozen food outbreak, there was this corn, and *Lm* was isolated from the frozen corn. It was closely related, genetically, to eight isolates from ill people. But the report goes on to say that subsequently, other facilities were swabbed. And in one, the Oregon

Potato Company, they also had isolates closely genetically related to eight of -- to these eight.

So what is the relationship between an individual food in an individual facility to illness versus looking more broadly and looking at the supply chain and the variety of inputs, factors, ingredients, shared fields, shared equipment, that may make the situation much complicated than perhaps we originally think, that one food out of one facility is absolutely always linked to cases of illness?

And so as our associations, various associations were discussing some of these concerns and seeing what was happening to our members, the way that this was impacting our members from a compliance standpoint, a regulatory standpoint, we developed a list of questions that we felt we wanted the agencies, FDA, FSIS, and CDC to address, collectively, in a public meeting.

So roughly a year ago, we put our list of questions together. We sent it to the agencies. And again, very much appreciate that FSIS has taken the

lead in putting this public meeting together.

So the questions that we asked in that original letter were, is there equivalency of methods between regulatory and public health agencies, SNPs versus MLST?

There has been some work done, some studies published, that show that typically, these different methods of interpreting the genome do result in similar conclusions, that the differences are perhaps a little more academic than based in -- and not a cause for concern.

Are there any plans to sunset PFGE? And very recently, FDA had a meeting on GenomeTrakr where we heard different things from different agencies and governments in different parts of the world about their plans to increase the use and the reliance on whole genome sequencing versus PFGE.

Is there, or will there be a compliance policy guide to govern the use of whole genome sequencing? Again, looking at it from the regulatory and compliance perspective, as we evolve in our understanding of the science, as we collect more

data, as we build the database, how does this tie in to actions that are taken against facilities?

And how is epi and traceback information used in conjunction with whole genome sequencing? So is it that first blurb, that whole genome sequencing is it? Or is it the latter blurb, that epi and traceback still play critical roles in an investigation?

We understand that, you know, sometimes there can be sample mix-up; sometimes there can be contamination within the database. And so we want to understand and make sure that if a claim is made against a facility, that it is based on good science, and sound and transparent policy.

Of particular concern, and -- what we often talk about is retrospective analysis. So once a pattern is in the database, whether it's clinical or from food, it seems like it would be there forever.

And so there is a potential and a strong fear that clinical isolates, and especially as the public health agencies go back into their freezers and begin sequencing older clinical isolates, putting

them in the database, that it will be a match to something present day.

And will that be a smoking gun, even if these are years apart in time? Again, it ties into our questions about the role of epidemiology and traceback.

We'd also like to understand the collaboration with other federal agencies, other types of programs -- I know the NARMS meeting immediately preceded this -- and internationally, so we heard about GMI and the need for those intergovernmental discussions about everybody's use of whole genome sequencing.

We'd also like to understand the flow of that sequence information. There are a couple of different databases out there. Again, at that GenomeTrakr meeting, there were some interesting comments made, interesting back-and-forth between CDC and FDA about the different databases and the confidence that the agencies had in those databases and the data in them.

Many of these questions -- again, these

were submitted about a year ago, and we have had many discussions. There have been many opportunities to discuss several of these questions. And I do want to recognize that.

So IFSH -- and Dr. Alvin Lee will be speaking later on this panel -- has coordinated a lot of these efforts, a lot of the discussions between the industry, academia and government. And there have been one-off meetings between different associations, different product types, with the relevant agencies.

And usually the topics have been around the science itself, methods, interpretation, the concerns around regulatory use, although I think we still -- although we've asked the questions and the dialogue has begun, it seems that the regulatory agencies are still working on putting those policies down on paper so that a standard is clear to the industry.

And then consistency and alignment between the public health and regulatory agencies, so I think the topics are, have been discussed, and fall into, usually, these three categories.

What I'd like to do now is give you an illustration of a situation that I was involved in with one of our members pertaining to whole genome sequencing and this claim of a potential resident strain. So it's small, but I'm happy to share my slides. I'll read you the pertinent information.

This was from a letter, not a warning letter, but just an individual letter to this facility, from FDA, from the district, that said that in the 2017 inspection, there were two environmental swabs that were positive for *Lm*. And it goes on to state where they came from.

And the Agency notes that in 2015, there were three locations that were also positive for *Lm*, and in 2013, that inspection revealed *Lm* in three locations. So we've got eight isolates altogether, over -- found over three times.

The bottom sentence -- so then there's a -- there was a bunch of stuff in between the two paragraphs, then a paragraph describing what whole genome sequencing is. And the bottom sentence concludes with, "WGS analysis finds that there are

resident strains of *Lm* within your facility."

So the member's kind of freaking out a little bit, says, what does this mean and what do I do? I said, well, finding an element in a facility is definitely not a good thing. We all understand that.

But I asked, of these eight isolates, where exactly were they? So we can see the two that were found most recently, but of those other six, where in the facility were they? And are all eight related by whole genome sequencing, or is it just a few of them? How many of them are related?

And the member said, I don't know. This is the whole letter. I'm sharing with you what I got. I said, well you need to find this out, so that you can really investigate and try to understand what's going on. This is a fresh produce operation, which has its own challenges in trying to understand if this is truly a resident or a repeat introduction of I guess what I'd call a resident in the field.

So I said, well if we can understand where in the facilities these positives were found, how

many of them were linked through whole genome sequencing, you know, then maybe we can try to further investigate this, but you need that information.

So the member asked FDA, and got an email back 3 weeks later. I mean, it took her a couple of day to ask, but the response came 3 weeks after this letter, that said, "As requested, I have attached the samples," and I saw some of them, and it was the PFGE patterns, "which have been analyzed and found to be positive for *Lm*. The WGS data will be provided at our meeting."

So FDA, in that original letter, had asked for a meeting to discuss this situation. So, "The WGS data will be provided at our meeting. It requires clearance and is being processed."

And I thought, that's, that seems kind of strange to me. So I said, well ask some more. Let me give you a real list of very specific questions for you to go ahead and ask.

So at Day 34, we got the response. "Late yesterday afternoon, I" -- the investigator --

"received the WGS report. The tree doesn't include the verbal analysis, which is really the most useful information." Yes. "Analyzing and interpreting these trees are delegated to our experts to avoid misinterpretation. CFSAN experts will further explain the analysis during the meeting."

So I later -- eventually the firm was provided with that tree. I was able to take a look at it. And while helpful in some regards, the samples were coded -- encoded, in a way that you couldn't tie it back to where in the facility these positives actually came from.

So it was really inadequate to provide actionable information to this facility to understand what might have happened, do their investigation and take their corrective actions.

The meeting occurred at 56 days. And I will, to FDA's credit, let you know -- I think it's fair to let you know, I have talked to Steve Musser about this, walked through this particular situation, and he agreed that yeah, this didn't quite happen right.

But I think that that's what prompts us to ask, what is the policy? What is the standard within the Agency itself when communicating information about whole genome sequencing and, you know, the claim that there's a resident strain to a facility?

So what are the things that we would like to see provided by the agency, or agencies, when reaching out to a company that may in fact have a resident strain?

On the science side, providing that actionable information, so where were these pathogen sample positives actually found? In what zones were they? What were the dates, the specific dates over time, tied to the location? Has any product tested positive?

In this case, only at that meeting did this facility find that the database did have product positive, not tied to their facility, but that there were additional positives within the database.

And it's very difficult to react on the spot to that information. It would have been much more helpful for the operation to know this before

walking into that meeting.

Can they see the full analytical packet, the full set of data that supports the information, in this case, in the letter? So really, what is the evidence?

And how similar are they? So while we may debate how many SNPs you need to be similar or different, still, I think it would be very helpful to know if there is 0 or if there is 20.

What was the method to determine these differences? What is the reference strain for determining relatedness? This is information that I think should be pro-offered. We shouldn't even have to request this information.

Importantly, of course, a facility would want to know, has any of these sequences been associated with human illness? And if so, are there any metadata? Can we begin to ascertain whether or not this illness may have been associated with product produced in this facility?

And again, I'll point out, and I think it's really worth emphasizing, that for products that

don't have a kill step, myself representing fresh produce, but other raw products, that a repeat transient is certainly possible.

I just -- I'm not sure that we've collected enough information, that we've done enough research to understand the prevalence of the strains in the environment, that we understand the evolution, as was mentioned before, to really differentiate between a true resident and a problem within that facility and sanitation within the facility, and a potential contamination of incoming ingredients, incoming raw materials that are constantly introduced.

I think it would be very fair to ask a facility, show me your environmental monitoring. I think that would help support or defend the facility against this claim of insanitary conditions.

So, again, looking at the total picture, not just the reliance on whole genome sequencing alone, but understanding what's happening in the facility, what is the relationship with a potential food product, has this equipment moved from one facility to another? And could it be the source,

even if it's a different food product? As the previous speaker said, it's complicated.

So here's just a visual kind of illustration, when we have in this case, an orchard, that maybe there is -- we know for *Lm*, we call it ubiquitous in the environment. So we know that there's some low-level out there. And how low it is, how often you find it, again, we don't have adequate research, the science to support that just yet.

But what is the diversity of isolates? What is the rate of evolution? There is discussion about hypermutators. Do we understand the organisms themselves enough to make a differentiation between a resident that's really a transient in a facility or a true resident?

We also want to see -- better understand the policy alignment, so working NARMS, the states, many of them are doing whole genome sequencing. Department of Homeland Security, other research projects, many groups are doing whole genome sequencing for different reasons. How do they communicate with each other and when do they

communicate with each other?

If a non-regulatory agency is -- finds a positive, do they communicate with the regulatory agency, and what's the process? What happens? What's the flow of information? And when does industry get looped into this?

So I've been asked by our members, should we be doing -- we as industry be doing whole genome sequencing? And the pros and cons, obviously the con is, your sequence goes into the database, and you may wind up being penalized for that.

So although you want to be doing the right thing, you want to be utilizing new technology, you don't want to have that progressive and proactive stance held against you.

We know, of course, it could be incredibly useful when a facility does have an issue, and they're looking -- now my recommendation to them is to not use whole genome sequencing right off the bat. But perhaps, further down the road in an investigation, it could be very helpful if you're finding repeat positives, to understand, are these

repeat positives potentially genetically related to each other?

And then I can, as a facility, look. And well, does it lead me down the path of a crack in a floor, or is this a traffic flow type of issue? So I think that the information could be quite useful, but there's a great deal of reluctance to have that information today. So in this case perhaps, maybe ignorance is bliss.

There's also concern that if a facility collects this information, does move forward with whole genome sequencing, must they share the sequence? Again, is ignorance bliss? Would you rather not do any testing to begin with?

If you testing and you get an isolate, would you rather not know the sequence? And so certainly we don't want to encourage that kind of behavior, but I think the regulatory environment today is such that these are very real risks that need to be considered.

Even services that offer to blind the data, that, you know, they will manage the data for you,

does that really reduce the risk? And I think we need a discussion with lawyers to understand where the lines are drawn here, and what -- who has access to what information, when, and under what circumstances.

I mentioned previously that it would be helpful for an industry to have metadata to understand if perhaps that positive was linked to them. On the other hand, they're probably pretty reluctant to share their own metadata because then you could look in a -- one could look in a database, depending on the access of information, and really pinpoint which facility was having issues, through the associated metadata.

There are some real opportunities, and needs, I think, to progress with whole genome sequencing and expand it much more fully. We know that this year and last year there's been a real uptick in cases of cyclosporiasis, associated with -- or not associated with foreign travel, so domestic cases.

And we don't have a way to differentiate

cyclospora from one another. Whole genome sequencing could really help us understand if these 600 or so cases are all the same, or if they're different.

We've also heard on *Listeria monocytogenes* that when you're really evaluating the genome, and if you can begin to understand virulence, that perhaps this would drive *Lm* risk assessments, recognizing that it's the more highly virulent *Lm* that are resulting in illness. And maybe not *Lm* or all *Salmonella* or even all STECs are the same.

So how can we use and really harness the information in the genome, understand how it relates to the phenotype, and understand how it relates to illness?

So, in summary, the industry recognizes that whole genome sequencing is here to stay, that it's not going away, that it is an incredibly powerful method, but wants to make sure that policy decisions, the decisions around compliance, are based on a full -- a relatively full and well understood dataset, that the limitations of those datasets are understood.

So our outstanding questions, I think, opportunities for discussion are around the role of whole genome sequencing in an outbreak investigation, how it relates to one-off sporadic cases of illness, the quantitative methods that was discussed before, live verse dead.

Do you have the opportunity to enumerate, to start to think about dose response? You can't do that when you have a culture independent method. The retrospective analysis, and then finally, what guides regulatory use, that's what industry wants to know. What are the rules of the road? And please be transparent in the use of whole genome sequencing.

So, with that, I know we'll save questions to the end, and I will pass it back over to Bill Shaw. Thank you very much.

(Applause.)

DR. SHAW: Thank you, Jennifer. I think those are things that we all need to be thinking about as we move forward.

And moving on to our next speaker, I'm going to ask Angie Siemens from Cargill to come on

up.

DR. SIEMENS: Good morning. My comments are going to be very similar to a follow-up with Jennifer, and I think they'll complement well.

My focus today is on the meat producers. And really, a differential, and you'll hear a little bit of this between how USDA has approached meat and poultry as a regulatory space and as opposed to FDA. And there's some historical perspectives, I think, that gets us in a different place today on that.

But the first part I want to talk about is talking about some stakeholder roles in how we move forward, because we've heard an awful lot in some spaces -- and we'll come back to that -- what's working in meat production, because I do think there are some models that are working in how FSIS is approaching the meat industry.

Concerns, although not perfect, right, so we still have some concerns. And then there was a question about what -- does whole genome sequencing have an application for meat production? Me, as a meat processor, what might I use in this space? So

I'll come back to that just a little bit in the end.

So first off, let's talk a little bit about the stakeholder roles. You heard a little bit, the speaker this morning talk about the triangle, right, between innovations and technologies. You know, there's a stakeholder in the industry, and love that space on how do we get to the innovation? What are those new technologies? How do we move forward in the food safety space?

Then we've got laws, regulation, compliance, right, and then application to safe food. There most of the time is a dialogue, right, that occurs between these, and back and forth. And a lot of folks refer to it as a two-way street.

I cannot just drop an innovation into our facilities and run with it. Lots of issues end up occurring associated with it, particularly when we don't understand the law and regulation and compliance portion of some of those innovations.

We've had to eliminate some interventions because they've not been approved internationally, right. And so there's a lot of dynamics that go on

between the stakeholders relative to how do we get to a food safety system that ultimately delivers that food safety product?

Now, I would like to say that it's not quite the two-way road, you know, exchange. I kind of look at it as a spiral, right, you know, in this spring with lots of tension, right, that ends up occurring. And I think we're in that tension space right now, particularly as we're trying to understand a new technology rolling in.

Do we really have all of the answers relative to the policy? Do we understand the compliance? And you heard that from Jennifer before. I think right now, that spring, pretty high tension right at the moment.

But we all have that goal of having a food safety system that ultimately delivers a safe product, and we've got to figure out how we adjust that tension and have that dialogue, moving forward.

So, with that, there's a couple of things that I do want to say, and how we relieve some of the attention in the meat space. First off, what is

working?

I really do believe that the more tempered approach that USDA has taken has come with 20 years of maybe some intensity and some tension. But they're using a tool within the current policies. And it's been, like I said, a 20-year piece in putting some of the policies together since the mega reg came out in 1995.

So what are those? The use and allowable use of prerequisites as part of our pathogen control policies, I think, has been a big piece, that has allowed us to have a little less tension in the meat space. What do I mean by that? Let's talk about *Listeria* control.

In the late 90s, we had some major issues in the industry relative to some outbreaks associated with meat and poultry. At that time, the industry, working with USDA, determined that the industry was allowed to go in and seek and destroy. And as long as they were continuing to do that, show their corrective actions, then they weren't penalized for finding *Listeria* in the environment.

I tell you what, listeriosis has dropped over the last 20 years related to meat and poultry items because USDA has allowed us to go in, look in the environment, take action, document it. They provide oversight, you know, with that. And we understand more about our supply chain.

We also understand that just because it's not in the -- or because it is in the environment, i.e. a drain, does not mean automatically that it's on a food contact surface. That is a huge piece that we have learned with the data that we have created.

And that has allowed us to have this conversation of hey, if I have a resident whole genome pattern, I can probably say yeah, I probably knew that, because we do find *Listeria* in the environment on a repetitive basis in someplace that's -- now repetitive can be every 6 months, a year. We will find it. But the action is to assure that if I find it in the environment, I do not get it on product contact.

And that is huge. Allowing us to do that prerequisite program as part of our food safety

program, to allow tools like whole genome sequence add a little more data, and allows us to continue to reduce the possibility that it ends up in product.

Same thing with STEC and in the *Salmonella* space. Non-O157 *E. coli*, right. Taking a look, and a watershed moment in 2002 when USDA declared that we could test product for *E. coli* O157, and a negative would be a negative, and a positive would be a positive, and allow us to continue that testing program, and subsequently do disposition on the positive product.

We would have not moved forward with control of *E. coli* O157 had we not been given that opportunity. And I can tell you today, we still have positives in raw meat. But we are allowed to work with that, continue with our control programs, go back to our sanitary dress, and have those programs in place to continue to work on not repeating the same failures we did on the last positive.

That's been huge in the meat space, and we've had great advancements because of that. And I think the learning curve that we've been on the last

20 years, the FDA with FSMA and those parts of the industry that's not had that 20 years are trying to put that in like 2 years. And I think it's going to take a little longer than that to make that happen.

Foodborne illness investigations. *E. coli* O157 has presented lots of opportunities for the Agency to work with the industry relative to how do we go through foodborne investigations.

USDA very early came out and said, even if we have whole genome sequencing information, epidemiology matters. And I tell you what, the industry applauded. I know I've been in lots of conversations -- let me temper that, maybe not lots, a few conversations, relative to investigations, and really asked, you know, I want to know that my product was available for sale, for consumption of the individual that was ill.

And I will take the right action. I want to make sure that I've taken the right product out of the system, not too much, not too little. And the epi is critical to that, you know, part of the discussion, even if I've got a whole genome sequence

match, you know.

And USDA's been very good. I know, the one piece that I will come back with is, the timing is horrible. Right. You get a PFGE; you start an investigation. You get it from three states. You kind of think you know what the lot may be, and the source.

And then, in swoops two different additional data points from a state that's 2 weeks behind on their analysis because their resources are different. And then oh, by the way, we get the whole genome sequence in about 5 days later.

We've got to figure out the coordination of how data during an investigation comes in, and when is the appropriate time to take some action. And there's a real tension today on public health alerts, on the timing related to when do you take action and not, because we are not on the same time frame across the public health and particularly state labs as they're pulling this data together.

And it really is difficult to make an informed good public health decision if you're in

those situations, going forward.

What are compliance? I really do think -- and we have the luxury of having -- I'll put that in quotes, inspectors in our facility every day. And so they are familiar with our programs. They're familiar with the corrective actions that we take in place.

There's been really established compliance associated with it. So that is a differential, really, between where the food industry is, and the meat industry is, and it's helped. And FSIS recognizes that, so we have a lot more history.

All right. So what are some of the concerns that we have? I really do think this discussion that we've had, including the NARMS discussion about international quality standards, you know, what is the quality of the data and what's the quality of the metadata that's going through?

With all of the international products that are coming in, do I really know if I've got some matches? You know, if it doesn't match anything in the USDA database, is that because we haven't reached

out and understand on a spice coming in, that it might be an issue in another country and being able to take a look at that?

How can we do a better job of assuring that we've got quality assurance where we need to, databases that talk to one another, so that we can understand the entire supply chain, not just the parts that are being focused on today?

Informatics, I don't know how many times we've gone through and asked some folks about informatics, and it depends on who does it, what it might tell you, particularly when you get into some of the STEC stuff and some of the *Salmonella* pieces there.

So we do have some concern about, what is that proficiency? How can I really have confidence that if you say it matches, it matches on that?

Inconsistent metadata, I mentioned that. What is a match? And that's been talked about numerous times. That where the epi, for me, really comes in.

And as Jennifer made a comment, too, all

right, if you said it's a match, tell me if it's 2, tell me if it's 20. Let's be transparent relative to what the definition is or the data that's presented.

Initiatives to close that gap, we mentioned the GMI. If it's not GMI, then what is it? Right. How can we move to kind of that global standard so that we can share?

I know there's some ISO development going on right now in terms of some of the procedures. I applaud that. That helps us in making sure that we have confidence if somebody presents it to us, that we can take action on good data, moving forward.

Agencies will approach the pathogens the same. A conscious decision was made by FDA and USDA to focus in on *Listeria*. And there's some real differences between a *Listeria*, you know, with a conserved core. They've showed that, you know, over 10 years, you can have the same strain occur in a facility. The supply chain varies, especially when you get in to the STEC and *Salmonella* world.

Listeria, while produce can bring it in, you know, STEC and the supply chain is totally

different. Most of that is entering a facility from the animal sector. And I buy from the same feed lots as my competitors do.

So we've really got to understand, what does that look like? What's the difference? How do you treat the actions associated with matches in each of these pathogen sectors, because I really do believe they vary?

Ubiquity in supply chain variation, I talked about that already a little bit. A lot of us have common live animal and raw match supplies. And I had the opportunity to take a look at the raw material supplies in a PFGE basis in the past.

And I can tell you that if I bring raw material in from the same facilities, I'll bring those patterns into both facilities. And it's a matter of how it occurs in the facility and go through, so I'm not sure a database is broad enough and expansive enough to make those one conclusion, if I found it in this facility, you're it.

Now, I've gotten those calls that say you are a plant of concern. I don't know how many of

you've had those. But they have been tempered on trying to understand, then, the supply. And I appreciate that from USDA on asking that. But I tell you what, we share supplies; we share raw materials.

Ground beef, particularly, is a formulated item. We have lots of sharing that goes on all the way through.

Do we have enough nonclinical samples? I really struggle a little bit on some of the connections and then, really, do we have that, particularly in the non-meat space, as we go forward?

I've heard a lot of discussions. There's some really cool stuff that's going to be able to, at some point, be able to lend us to some risk assessments. But if you take a look at the data today, in the database, you would point to papayas as being, you know, the number one issue.

But I really look at the database and -- give you an example. If I have a hundred -- you know, just say the database has a hundred strains in it. If you looked at the data that was presented, 10 of those could be the papaya, so your risk assessment

would say it counts for 10%.

But when you go back and look at the ten, those 10 were probably all generated through one crisis, one supply chain. So as doing a risk assessment, does that lend 10%? Or should it be pulled back and counted as one?

I think there's a time and space that we have to figure out within this database if we're going to move forward with it in risk assessment. So I'm really concerned in that space right now.

This is my favorite topic, and anybody at USDA that's talked to me knows this. 5000.2, most of you outside USDA will not know this. This was a directive that was given, and pretty much said that the inspector has the ability to look at any information that they deem that we are making a food safety decision off of. They deem.

And it has dampered the kind of work that's being done in our facilities. A lot of research folks, I've had researchers approach me about doing research studies, you know, help me understand how non-O157 comes down my slaughter line. All right.

That data, under 5000.2, has the ability to be shared with the Agency and goes to an inspector who does not have training in looking at research studies, doesn't always know if I'm looking at new interventions, what that implication is.

We have continued to have dialogue with the Agency and struggle on how can I use the new technologies when I don't know what they mean, and give me the ability to figure out what they mean before they go into a compliance realm, and really struggle with that piece of it.

I also struggle with the -- and Jennifer alluded to this as well, with those folks that move forward, those early adopters of technology that have more data, end up being penalized in some cases because they have more data.

And I don't know where we align that, moving forward, you know, in some cases, versus the folks that choose to do the regulatory minimum. You don't have the data to take action.

Application in the industry, you know, we've heard all of these kinds of things, you know,

on anywhere from whole genome sequencing to the partial genome sequencing. We've got TAS, AMR, GMO, there's all kinds of application in this new generation sequencing, you know, portfolio.

For me, as a producer, the one I'm most excited about is in this space. I do think there is a tremendous amount of things that we can understand about our population, you know, in our plant, right, as it relates to *Salmonella*, and how does *Salmonella* interact in a, in say, a turkey barn, right.

How do I know what is exclusive, inclusive, relative to *Salmonella*, and how does it grow in the barn? Or for shelf life; let's take a look at the micro-population I have there, and when does it shift? That is applicable data to me. I can do something with that type of data.

A single strain that repeats twice, I could have told you I had *Listeria* species in my plant. Right. Do I need to know that it's the same one? Yeah, in some occasional applications, it does. But I can get to that point on a generic.

So I don't think you're going to see the

industry in totality run out and do individual strain data. But I do think we're going to have some application in the metagenomic space.

So, with that, I talked about these, right, on just some opportunities and application, and a lot of great dialogue. I'm looking forward to the conversation or to the questions. Thank you.

(Applause.)

DR. SHAW: Thank you, Angie.

And then, so now our next presenter is Samadpour. Mansour is from IAH Laboratory and Consulting Group, and he's going to talk to us about the commercial laboratory perspective.

DR. SAMADPOUR: Thank you.

In our function as a lab resource to the industry, we are between the industry and the regulatory agencies. And in many, many instances where they are contacted about these type of issues, they come to someone like me or one of our colleagues in other laboratory groups.

And what we have seen is that a lot of excitement overblowing the role that this thing can

play, as good as it is, and then a lot of what I call irrational fears.

It brings the memories of PFGE. If that one was *Scary Movie 1*, next-generation sequencing is *Scary Movie 2*.

For those of you who were around when PFGE came along, we had like meetings like this on a regular basis, just trying to explain what that thing did and its applications.

So I can sum up some of the things that have already been mentioned, but one fear is epidemiology without epidemiology. Could we just have a connection through whole genome sequencing, next-generation sequencing and say that this processor is behind such and such outbreak?

These type of things don't happen. Epidemiology is the king. Without consumption history, linkage, no one is going to be able to come in and ask you to recall your product, or link it to an outbreak.

We had at least one instance where a mistaken linkage happened. That was an outbreak that

happened in Atlanta, Georgia. This was beginning days of PFGE. And that was a lesson that everyone learned and emphasized that you have to have the epidemiology backing you up. Otherwise, you know, just the fact that you had three PFG patterns, you know, making a connection doesn't mean much.

Enhanced ability to link a food processor to a small cluster, that is really true. Now, an outbreak is defined with just one case. A single case could be an outbreak. There is the ability to make that connection.

And the last one, linkage to historical cases. You know, a company could be linked to an outbreak that happened 6, 7, 8 years ago. And in personal injury cases, you have 3 years to file, but you just become aware that this outbreak happened, so that opens a lot of legal issues.

Foodborne epidemiology doesn't get a lot of resources, chronically underfunded. And the way it's structured, it relies on, people get sick, they go to their physicians. A portion of them will get tested. And as was mentioned by John yesterday, clinical labs

are no longer -- you know, they've started not doing culture confirmation.

And we don't resource our epidemiologists. You know that most states rely on receiving grants for foodborne investigations. So we have that.

As a result of that, we know for a fact that we have many, many clusters at any given time. Our colleagues from CDC would tell you, at any time there are tens of clusters all around the country. But there is the ability to link very few of those to a given food or a food processor and that is because of lack of resources.

There came next-generation sequencing, which has been seen as a hack, basically, to shortcut the system. And it has been very effective, as it was mentioned yesterday.

So as I said, this fear that a mere linkage is going to cause the Agency to link you to an outbreak is what I call irrational fear. It's not going to happen. Everyone realizes that a given food company can have a clone in this environment, but this clone can present from other places at the same

time.

This one is for real. There is now enough resolution to go to these databases, make an initial linkage. But once whole genome sequencing points to a possibility of a food processor, at that point, there has to be an epidemiological connection. Epidemiologists have to go and re-interview, and that would result in potential linkage.

And you have seen several reports where they say, of the group of nine cases, six of them -- once they did a -- so they start with a PFGE match. After that, they go to whole genome sequencing, eliminating some of those. After that then, you know, they will have to do another interview to establish the linkage.

The good news is that next-generation sequencing has far more sensitivity and precision than what PFGE gave us.

This has happened couple of times where larger windows of time were open and cases were identified. And again, there are some legal issues that are going to come into play.

This is what I call trademarking a clone. This PFGE pattern is such-and-such company's. I've heard it. You guys probably have heard that. This is not necessarily, you know, a good practice. We have seen, we have data to show that we see exactly the same clone and same whole genome sequence presenting from more than one company.

And this is just scratching the surface. So the more of this type of data becomes available, the more understanding we'll have of the movement of these clones in the environment and the way they're traveling in the food supply.

This is probably the issue that is a real issue, because the term "harborage" is being used quite loosely. So the trigger for asserting that there is harborage is when we see the same clone isolated from the same production facility, or food from that facility more than once.

So at that point, rightly so, flags are going to go up. But some of us look at harborage as, you have an infection point in the facility; you have a contaminated spot where this organism is growing,

and is allowed to now go and spread.

So the easy definition for harborage is where you no longer have a pest; you have a pet roaming around in the facility.

But we could see the same isolate repeatedly if you have a -- now, you have raw material coming in, which is constantly seeding your environment. Then you'll have a frequent transient that could be mistaken as a resident strain. Or you could have a contamination event where, you know, that through beginning of stage of sanitation they get these high-pressure hoses and spread everything all over the map.

So you could have your contamination in large area, happening once. And if you look at those as like land mines, during this environmental monitoring, we start working on these things, over time.

So these are -- these were there, but the resolution of the environmental monitoring is such that we are not going to capture them, you know, next week. We may find them over the next 2 years, 3

years.

For the epidemiologist, and people who do this type of work, it's really -- this is a very over-simplified diagram of movement of microbes through different stages of production. You have ranches, you have dairies, you have feed lots. You have people who go around and start buying animals and taking them to slaughter houses.

You know, they end up in -- same clone, same group of animals that have a resident strain can go to many slaughter houses. From there, they can go to many grinding operations. Things are going to get mixed. Products from four different countries are going to, you know, come in and play a role.

And then we see them in, presenting in production facilities and in patient populations. So, again, this is extremely over-simplified, but can show the complexity of the system.

Now, I'm just going to go briefly over some of the uses that can help us, you know, those of us who are working with the food industry.

Lab contamination, it happens. So it's

just one of those facts of life that when you have food labs receiving samples, and then they have positive controls, highly contaminated samples can potentially contaminate the environment and your positive control can also contaminate the environment.

This was a situation where the lab, lab's positive control ended up in the product. Some of these things have like millions of dollars of products at risk. And through whole genome sequencing, we showed that there was only one SNP difference between this, the food isolate and the lab positive.

This was really interesting. This was a lawsuit that dragged for years. And PFGE patterns were done for the isolates. Isolates no longer existed. And one of the sites for this lawsuit made a huge deal that serotyping wasn't done. And they were asking the court to dismiss.

So we managed to find the plugs that were used for PFGE, and did the whole genome sequencing, identified the serotypes through that.

Serotyping is just like -- we are routinely now using whole genome sequencing for serotyping and getting rid of the classical methods for that.

It's an amazing tool for shelf-life extensions, that is, and for cause of spoilage analysis. The situation where we had spoiled roast beef, and there's an indication here that you cannot spoil a spoiled product, so even when we enrich it, you know, the population doesn't change.

But we do this all the time. We do several different types of enrichment. And we do the metagenomics. And this is where you get the spoiled product compared to a non-spoiled product from the same batch.

And it's clear that, you know, the population difference is just tremendous. By just looking at this, you know that you have a clostridium problem.

In 2 days of metagenomics, you had -- we had identified 95,000 hits here, and 65,000 in the control. It takes a microbiologist a lifetime if you want to do that.

This is another situation. This was a veggie puree. And metagenomics on the bacterial site, no difference. Then you go on the yeast and mold site, bang. There's the tremendous difference. And this was identified. *Cryptococcus* was identified as a cause of spoilage.

We are doing a lot of work on antimicrobial resistance. We have several active projects. This was NDM-1, which we published the draft genome. Another cause of spoilage, in this case, the kind of stock.

Again, when you look at the control versus spoiled product, it just hits you right there. Just, all you need is a couple of days of metagenomics.

Once in a while we get bored and we do our own kind of a market survey on different things. This was on shrimp, imported shrimp. And so first we did the metagenomics, and these are the major components that were identified through metagenomics.

Then we looked at the minor components, and Vibrios. In that group, I'm not sure in the data here, and the imported shrimp, finding *Listeria*

monocytogenes was not surprising, *Salmonella*, okay. Who cares.

We had *E. coli* O157, a classical toxigenic. That was kind of surprising, but again, given the fact that, you know, they come from contaminated waters, you could have expected that.

And the *Vibrio*, we had *vulnificus* and *parahaemolyticus*. And then we had this bundle of joy, *Vibrio cholerae*. But that's a kind of a "oh shit" moment for lab owners, or people who operate labs. At that point, you have to notify a lot of people.

So while we were confirming this using the FDA methods, we used the next-generation sequencing, and we found that the *cholerae* toxin wasn't there. So when we gave a package to FDA and notified that we had found, technically, a *Vibrio cholerae*, you know, kind of, okay, it's not -- it doesn't have the *cholerae* toxin. So it's just a tremendous shortcut to what we used to do.

So far, we have been able to identify eight or nine new species of microbes. We have published

one. This is the second one that -- slide -- we are working on publishing this one. It's new species. This came from a spoiled pear.

And this was a situation where there was a, you know, spoilage, and they thought it was *Clostridium botulinum*. And when, you know, they did a recall, major recall, it came to us. Once we did the whole genome sequencing, we said okay now, it's not -- not only it's not *Clostridium botulinum*, we have never seen something like this before, and this was published.

Did I miss one? Okay. So, in summary, there are lots of concerns in epidemiology, the power of the method. There is increased chance of linking food companies to events, to public health events. This could be as few as one case, a person getting sick. Previously, we relied on larger numbers to be able to detect outbreaks. Epidemiology is all about numbers.

On the regulatory side, it truly allows regulators to micromanage your microbiology data and, you know, contact you and say well, you know, we are

get this -- repeatedly, you are seeing the same thing and you have a resident strain, stuff like that, which I think that requires a broader kind of a discussion on the subject of harborage and residency.

Has tremendous utilities in plant and animal genetics, in shelf life extension, and it is changing the way we do food microbiology. Most of the methodologies that we use today are going to be obsolete in 5 to 10 years because of this -- advances in next-generation sequencing.

Thank you.

(Applause.)

DR. SHAW: Thank you, Mansour.

And then our next speaker is Alvin Lee, from the Center for Processing -- and I want to make sure I say this right -- Processing and Innovation.

DR. LEE: All right, thank you.

Good -- I guess it's still good morning. So, again, thank you to USDA for the invitation to talk today. And I'm going to give you a little bit of the perspective from the government and academia and industry partnership side of it, in terms of what

IFSH, or the Institute of Food Safety and Health, is actually working on.

So I guess the Institute has been mentioned a couple of times. I thought I'd just have a slide or two here just to describe what the Institute is.

IFSH, or the Institute of Food Safety and Health, is an FDA Center of Excellence. It's one of four Center of Excellence within FDA itself.

So our charter here, our mission here is to cascade and work with industry on the research and the outcomes between academic and government, and be that conduit to industry, so basically trying to have this three-way private-public partnership.

We have, as one of the centers, and probably the only center with a division of FDA -- the Division of Food Processing Science and Technology is located there with the University -- and also, we try to work on projects that also have industry inputs. It's not all the time, but we try to encompass all three elements into our projects.

We are located in Chicago, and again, being associated with a university, we do have graduate

students, have the graduate students do work in our lab, and also in FDA labs as well. All staff move across FDA space and our space quite commonly, and we share a lot of facilities.

So with outbreaks, what we are seeing nowadays, if you look at the outbreaks over the last few years, you know, we've seen outbreaks from traditional sources of foods, you know, things like raw milk, raw soft cheeses, sprouts and eggs.

But over the last few years, we have seen also outbreaks that are also a lot more novel as well. You know, think about, at this time of the year, probably a couple of years ago, we had caramel dip apples was around. And then more recently, the ice cream outbreaks, these are quite novel foods and they have never been really classed as high-risk or foods that may be of concern

And they have all been tracked with whole genome sequencing, or next-generation sequencing if you like to call it that way.

This is one that I pulled from the CDC website, where the ice cream outbreak was tracked.

And you can see from the slide here where, you know, the distribution of where the cases were is actually over a very large space. And they can track this down to a particular factory or plant.

So if you look at Cluster 1 and Cluster 2, they all came from a very different plant itself. So I guess with industry here, is that they -- you know, and in terms of academia, we know what the power of whole genome sequencing or the technology can actually do.

So, with that, I think, from that outbreak where the ice cream was, the sharing of the data between FDA and CDC with the company here, I guess it helps to sort of stop a contaminated product from being produced and going into retail sale, but also allows them to recall the product.

And if you look at some of the recall notices, they have also very specific time frame as to when the recall of product actually happens as well. And also, at the same time, you know, if you look at ice cream, and it was never attributed to be, or recognized to be a hazard or something that is of

high risk foods.

But the outcome of the outbreak, based upon, you know, the tracking and all that, led to a novel food being implicated, but also it led to changes in the industry in terms of the companies' practice, in terms of sanitation, in terms of how monitoring is conducted, but also in terms of implementation of preventive controls.

So in light of the FSMA, or Food Safety Modernization Act, foodborne outbreaks, as I see it here, is -- the outbreaks are going to be more dispersed, is going to be more spread over time, is going to be spread, probably, over large distances.

You know, given that how food are being traded, food are being manufactured and transported across large distances, even through various countries as well, in future, potentially, those outbreaks are going to be much harder to track.

The outbreaks are then also probably associated with foods that we have probably not really accustomed to, in terms of looking at those products. So things like fresh produce, mainly

processed foods, you know, as a result of what consumer wants, food companies are producing foods that are a lot more minimally processed, so to speak. You know, preservatives are being taken out.

There's a call for salt and sugar reduction in foods. So this all leads to changes in terms of how food are being manufactured, and obviously, also changes in the ecology of the food itself.

We also see more of the imported foods. We also see foods that are previously not recognized as hazardous, but we are also seeing routes of contamination that has never been identified before.

So with what IFSH has been working on with an initial request from FDA was to explore the technology with industry, getting industry sort of accustomed to what is that technology, right, and then how is that technology used.

So we have quite a few of the CDC people, the FDA people and USDA at one of these three meetings as well. And we have already three face-to-face meeting where industry participated with government and academia in terms of looking at how

the information was used, what is that technology, getting their toes wet in terms of what those technology can be used for, or can potentially be used for.

So, with that, what happens was, it resulted in the formation of an Industry Advisory Committee that meets sort of quarterly, and also the Industry-Government Council as well, so as to tease out exactly what are the issues that faces industry, but also what the regulators want from the technology.

So some of the concerns here, I guess, industry issues and concerns, you know, I think we just opened up Pandora's Box here is, you know, what information and identifiers can be collected?

And what kind of identifiers will actually be put out on the databases, and what can be retracted; there was a lot of discussion about that one. How would the information be used by regulators?

So I think some of the concerns there with industry was well, the sequences are going to be

available, but how are they going to be used? Is there a model that they can follow on and actually look at how the information can be utilized?

There's also, I guess, some concerns within industry companies as well, is that if the sequences are out in the public domain, can another company use that sequences for benefit over their competitors? I think those are genuine concerns from the industry.

What are the implications in the absence of a culture? So we are talking about going away from culture-dependent methods, then, you know, what are the implications in future?

We know that we still have some ways to go in terms of trying to distinguish between live and dead, but what about pathogens, for example, with viruses that occur in very, very low levels? What is the sensitivity there?

At the same time, you know, if it's derived from -- do we know if it's derived from a dead versus a live? Right. So we -- a lot of these technologies that we are looking at right now, in terms of how foods are being processed, the technology does not

necessarily kill the bacteria.

It may hold the genomic materials. If you look at high-pressure processing, there are certain bacteria that will burst open during processing, but not all do. Okay. So, for example, like viruses don't really break open. They remain more or less intact. But they do not function as a live virus anymore.

So how would that technology be used in that way to differentiate between live and dead?

Can the company self-incriminate? So one of the things here was, when we spoke to industry here, was for them to donate isolates that can be used as a way of demonstrating how the technologies can be used. Right.

So the companies will ask, will say, well if I give you those strains, and you put them up on the database, would I be shooting myself in the foot here by saying we have an issue? Or if you -- if we sequence -- do a shotgun sequence from a swab that they have taken, for example.

So those are concerns over there, and also

the legal issues relating to the use of whole genome sequencing as well.

And then I think one of the things that came out quite strongly was, what was the benefit does industry get from whole genome sequencing? I think it's -- there's still some ways, in terms of educating industry, because I think they know the power of the technology, what it can do, what it cannot do, but how does it benefit them? Right.

So we have seen cases where whole genome sequencing or next-generation sequencing can be used to track and evaluate quality of a product, or ingredients that are coming in. But, you know, between government and industry, what kind of benefit does it flow back to the industry side?

Legal issues in donating sequences from plant-derived isolates, so again, I think this touch back on, you know, if a company donates samples for research purposes, and then they are being put up on the public space, then what are the legal implications from that donation.

So at the same time, as well, you know, we

have been also establishing our own capability on whole genome sequencing. So you see a dedicated lab has been established with two MiSeqs. And we will also work quite -- work collaboratively with Eric's group at CFSAN as well.

We noticed all the, that the uses here, and this was one that we sort of have spoken to industry about is, you know, that the power of the technology can be used to identify closely related isolates, and then used as a way of tracking sources of contamination.

So we have been talking to companies to say hey, you know, can you donate and send us samples, where we will blind them, or we'll get a third party to blind them, for example, and then look at how the technology can be used to track contamination within a food plant, within a processor and things like that, and at the same time also used to track contamination that might be coming in through ingredients, and also monitoring of a production environment.

So if you use sanitizers, do you want to

know how effective that sanitizer is? Does it change the ecology of a food production plant in terms of the microbial ecology that might be in that food plant.

So if you use a certain sanitizer, do you change that bacteria from one resident strain to another? But also at the same time, do you also induce evolutional changes to the bacteria as well, that causes it to become a lot more virulent, so to speak?

And at the same time, you know, spoilage events, can we predict spoilage events out of it?

The technology also has the ability to also prevent outbreaks. And you can see form the numerous talks over the last day or so that the technology has the power and resolution right now to predict events a lot quicker. And some of the things that FDA has been working on, and CDC, was to try and get time of results to be shortened.

So I think here helps them to be a lot more targeted. And we understand where they are coming from. Helps them to be more targeted in their

recalls. You know, how many of you have seen some of the recalls out there? I think there was one in Europe where they thought that Spanish cucumbers was attributed to the outbreak, right. And then after that, people were dumping out cucumbers. And then they say, well, it's not Spanish cucumbers.

We have the same thing here in the U.S., too. There was the outbreaks with, I think it was with green onions, where they said well, it was initially Florida tomatoes, and then it shifted to California and then, and so forth.

I think it puts the industry a little bit uneasy that way. So here, I think the regulators now has the power now to provide a lot more targeted and a lot more focused type of recalls, and actually prevent financial losses as well, to companies, so they don't have to dump out products just because they thought it was a suspected product that might be in the market.

So some of the initiative, or the objectives that what we want to achieve her in this private-public partnership here is to try to promote

that technology to the industry. We want to collaborate with the food companies here, along with the regulator, side by side, on the research side of it, to see how this technology can be used, can be pushed out and used by all.

The research and laboratory services, I think, is one. You saw Mansour's presentation. There are people out there. I think the larger companies may have the capability to actually do this in-house, but look at the smaller companies as well.

So now they need to have someone on staff trained in order to interpret some of these results. So it can be a financial cost for them to have that manpower within their company.

So having some sort of third party, where they can go to, to help interpret the results, or help decipher some of the results that the regulators are giving them, that would be helpful.

We started off initially thinking that we could get pathogens from industry. And we were definitely pretty wrong, because no company said they would be willing to give us anything that might be

pathogens. So we started adding on environmental isolates as well, and I'll touch on that one a little bit later.

And also, with some of the environmental isolates and the sequencing projects that we have, basically also, our charter here is to contribute to the database, to GenomeTrakr.

So just to highlight in terms of where whole genome sequencing is going, I saw listed a couple of various projects that is happening at IFSH right now. It may or may not have all three elements, but I think the one that I'm really excited about is the last one there, where we are looking at environmental monitorings. Right.

So the first one here that I have here listed was pulsed light. So here we wanted to look at how pulsed light, for example, when it's used for surface decontamination, changes different types of ecology. Can certain strains of bacteria be a lot more resistant to pulsed light to -- than others?

And then, what is the changes in terms of the genetic makeup when you use that technology?

It shouldn't be the role of plasmid in the second one. It should just be regulation of toxin production for *Clostridium botulinum*, and what they are looking at in terms of, can certain types of acid and all that trigger or regulate toxin production for *Clostridium botulinum*?

Clostridium botulinum has always been, toxins analysis has always been either using the ELISA methods or the mouse bioassay. But I think if you can go into whole genome sequencing and start predicting toxin production in certain types of foods, I think this gives that power now to, rather than just using ELISAs or the mouse bioassay, which are all very expensive to do.

Alfalfa seeds, for example, I think in the last few years we have seen outbreaks in sprouts. So is there a way of actually looking using sequence information here to have a more targeted approach in terms of how monitoring can be done with the irrigation water that's using in sprout production?

So I'll touch on the last one a little bit towards the end here, on environmental isolates. All

right.

So with whole genome sequencing in production environment, I think that approach there, what we would -- what we are looking was definitely, hygiene is definitely essential in food production. And there are papers out there, for example, this one that was published this year by Rodrigues, for example, looked at 16S rRNA, and actually showed that in milk, for example, high somatic cell counts can always lead to abundance of certain types of bacteria in that sample.

And also the ecology of the processing environment can also influence food quality at the end.

So with food plants as well, food plants can also potentially harbor very unique bacterial ecology in the food plant. And there are literature out there that shows, for example, like sprouts and certain types of fresh produce, there are abundance of certain types of bacteria in them.

Can we utilize those types of information here to help sort of track a potential contamination?

And what is the food commodity, for example, that might be, potentially be implicated in outbreaks, so basically predicting the outbreak a lot -- operating issues a lot quicker before an outbreak actually happens.

So that project that I was talking about, we are really excited about how it was going, was because we finally got a company that says yeah, we will do this, but we have to blind a lot of this information here.

So, you know, a lot of the administrative stuff and the logistics are still being sorted out. But what we thought was, here, you know, to look at how sanitation, how effective it is, looking at samples that might be taken, sent to IFSH for sequencing. And then we will definitely discuss some of the results with the company first before uploading them onto the database.

But it will also require some sort of, sort of removing of certain identifiers and in certain datasets and things like that from that information as well. But again, we are still trying to tease out

some of those.

But so the challenge here that we are seeing is can we use the technology to determine how effective, or can we determine harborage points within a processing facility as well? So if you remove something, you are always upsetting that balance, that microbial balance in that facility.

So can we predict changes, for example, in that facility? And also, basically it allows them to be a lot more targeted in their food manufacturing process, and also provide much more information to their food safety plan as well.

So, with that, I'll leave it as that. I just want to acknowledge so the IFSH and IIT collaborators. Behzad and Melissa are the ones that are running the facility. They've been hard at work trying to establish that capability, and also responsible for those projects as well.

I also wanted to acknowledge the FDA collaborators as well, who are -- most of them are here in the room, for providing us with the expertise and a lot of the discussion.

So if you want to hear more about our future, sort of, events where we will have the discussion with FDA and industry, do let me know and we'll try and keep you in the loop.

So, with that, thank you.

(Applause.)

DR. SHAW: Thank you, Alvin.

And then we have one last speaker in this session before we go to lunch, and that is Vanessa Coffman.

MS. COFFMAN: Good afternoon. My name is Vanessa Coffman, and I don't have a fancy title anymore because I gave it up to go back to school. So I'm actually a Ph.D. student currently. I'm at the Johns Hopkins University. I'm going to finish up in a few months.

And my dissertation work focuses on industrial hog farming and the different respiratory health implications to workers and community members. And we're using a community-based participatory research approach to collect that data.

And I am also a fellow at the Center for a

Livable Future, although these are my own views and not that of the Center's. That's me.

Can I have the next slide? The next slide.

So I wanted to talk a little bit about consumers, in general. So we all are consumers, of course. But we have a different interest in food safety than I believe the majority of people in the U.S. do. We're more educated on the topic; we have a vested interest, right.

So there was a study that came out this year from Michigan State University, and it was a poll online of a thousand different consumers throughout the U.S. It's nationally representative.

And they asked, "Using a 1 to 5 scale where 1 is not concerned at all, and 5 is very concerned, how concerned are you about the safety of the food available for purchase in your community compared to other communities?" And 50% said they were very concerned.

They also asked, "How often do you seek information about where your food was grown and how it was produced?" And about 50% of people said that

they rarely or never looked for this information, although half of people were looking for this information at some point.

They further asked, "Please tell me whether you think the following statement is true or false. Genetically modified foods have genes, and non-genetically modified foods do not." Two-thirds of people got this correct, and hopefully all of you did as well. But unfortunately, a third of respondents didn't get this correct.

So we need to think about what information we're putting out there, how we're putting it out there, and how consumers are consuming that information.

They then asked, "Using a 1 to 5 scale," so the same scale, "where 1 is you do not trust at all, and 5 is completely trust, how much do you trust the following individuals or groups when it comes to the health and safety of food?"

Now, I must say, the way that they have presented their data, 4 and 5 are together, 1 and 2 are together, and 3 is not shown. But I'm pretty

happy, because academics, 60% of people trust us to provide them information that is correct.

And when it comes to government scientists, 50% of people trust the information that is given by government scientists. And I'm sorry, industry folks; only about a third of people trust you.

There's another poll that came out in 2017, and this is from the Pew Research Center. This is also nationally representative data from 4,000 people. And they found that 1 in 6 Americans both actively seek out and frequently consume science news. So some people seek it out. Some people actively consume it, and then 17% of the population does both.

And when they asked people where they got their information from and if they thought that that information they were getting was reliable, so the yellow bar here is the facts gotten right the majority of the time, and the red bar are news outlets that cover those facts.

So people said that they went to science and technology centers and museums, 12%, to go look

for information about science. And they were pretty confident, 54% of them, that they were getting accurate information.

If we go down to something like science podcasts, 12% of consumers got information from science radio programs or podcasts, and they thought that 28% of that was -- 28% of people found that the facts were right most of the time.

And if we see documentaries, people are consuming more information from documentaries. And if we look at science forums, people are looking at science forums -- about 11% of people consume their news from science forums.

And government agencies, we see it's just a little bit lower than science forums, although people are more confident in the information they're getting from government. So that's a good thing.

I'd also like to talk a little bit about the literacy rate in the U.S. This is pretty surprising, I think, to a lot of people. This is pretty hard to read. I did take out some of the cells, so -- but it's still pretty data-heavy so I'll

just explain what's going on.

The -- so we have prose literacy here, document literacy in the middle, and quantitative literacy on the far-right side. And we see that about 14 -- somewhere between 14 and 11% of people in the U.S. are below basic when it comes to document literacy, and about 20% below basic when it comes to quantitative literacy.

And if we break this out by race and ethnicity, this might not surprise you, more whites have higher literacy rates than other ethnic groups, and this is both in document and quantitative literacy.

And as we move through our educational system, more people, the higher educated you are, the more literacy you have, and the less education, the lower the literacy that you have.

So moving into talking about consumer groups and what consumer groups think about whole genome sequencing, so stepping away a little bit from consumers themselves, so I found it to be really positive.

I'm looking at the *Federal Register* announcement for this meeting. "All whole genome sequencing data will continue to be uploaded to a federal database" -- sorry -- "that is readily accessible to all food safety and public health partners and stakeholders, including consumers."

This is really great, to have this transparency and the availability to consumers, but are we able to actually consume that information? Is that going to be in a format that is readily usable by consumers?

And so, also thinking about a unique database for food safety, I've heard a lot through the last day or so, about using NCBI, but will there be a food safety-specific database that's easily used by all the people who are interested in using this data?

Whole genome sequencing will definitely increase consumer confidence in results and safety, especially if we can show, through epidemiology, that cases are going down, outbreaks are going down, and that we're doing a better job to protect the health

of the public.

And we've heard a little bit about this. So decreases in illnesses and outbreaks, we might actually see an increase in outbreaks. How are we going to communicate that to the public? What does that mean? We really need to talk about getting ahead of outbreaks and making the caseload smaller.

The whole genome sequencing seems to be rapid. Can we make it faster? How do we streamline this? How do we improve our ability to get ahead of these outbreaks?

And, of course, it's a sensitive and specific test. And we want to be able to track antimicrobial resistance. Antimicrobial resistance is a huge problem in the U.S. and in the world, and consumers are really understanding this. You know, there are so many headlines in the news every day about antimicrobial resistance.

And how can we start to think about not just single pathogens that we're interested in, but how can we look for a whole host of different pathogens in our food, and make sure that we're

really getting ahead of outbreaks?

So, of course, there's some drawbacks. Who can upload information to these databases, and what quality controls are there? Will this translate to significant improvements in public health? I believe so, and it seems like everyone else in this room agrees. But how are we going to track that? How are we going to communicate that? What does that actually mean? How does that translate?

Transparency: Transparency seems like a great advantage, but we've heard a lot from our industry stakeholders that they don't want to upload t a database. They're worried about regulatory action. How can we help protect them and protect consumers at the same time?

And what happens when the system fails? Inevitably, every system fails. Is this going to be a human error? Is this going to be a computer problem? What happens when we don't trust this data?

We are working, in our lab, on the bioinformatic bottleneck that we perceive to be there. You have so much data available. How are you

going to crunch all this? Who's going to crunch all this? How are we going to train all the people who need to be able to analyze this data? And I think this goes back to developing an efficient reference database.

Something that I'm interested in and nobody has spoken about yet, is a new definition of adulterants. If you can say that you have *E. coli* O157:H7, but it doesn't have the attaching and effacing LEE gen gene, does that count as an adulterant? Do you need to recall that product? Is it going to make somebody sick?

And as this technology advances, we've heard the idea of next-gen, next-gen sequencing. Just getting to this point has been very expensive and time consuming, and are we going to come to the point where we've had all these public meetings, we've invested all this money, and now there's new technology, and we need to upgrade to that new technology and have a whole host of other meetings, and invest, and train people on that?

And this brings me to Moore's law. So

Moore is one of the cofounders of Intel, and he hypothesized that as technology advances, it gets smaller, it gets cheaper, it gets faster. And Moore predicted that it would follow in this manner. But we see that the cost of sequencing a genome is decreasing exponentially.

So just wrapping up, and thinking about the path forward for consumers and for consumer groups, we have to ask ourselves some questions.

Do we communicate? I think the answer is obviously yes. We communicate, and we just need to think about what we communicate, who we're communicating to, and in what manner do we communicate.

If people are consuming information from blogs, and they're consuming it from podcasts, and they're consuming it from documentaries, you know, maybe publishing isn't the best way to communicate to people who actually consume food and make decisions with their dollar. You know, we need to meet people where they are.

And thank you for your time and attention.

And I didn't use up all my time. So I guess if there's questions I would take them, or we can break for lunch early.

DR. SHAW: So thank you, Vanessa.

And so what we are going to do, since we do have a few minutes before lunch, we're going to take some questions from the audience for any of our speakers.

And so I think if our speakers who are present, if you wouldn't mind coming up to the front, up on the panel. And we'll do a quick Q&A before we go to lunch.

So while we're assembling, do we want to do the question that's from the -- from online?

DR. ABLEY: Yes. We have one question from online right now.

Instead of only applying WGS in response to repeat positives in a facility, would you recommend running WGS on all isolates from all routine environment samples taken, and raw product, to determine the microbial ecology of that facility? At what time frame between repeat positives would you

recommend applying WGS?

DR. SAMADPOUR: I usually tell my clients that you don't need to turn every sample into a Ph.D. thesis. So there is a time and place for doing work like that. If you want to do an initial investigation, you know, you want to do a mapping, you understand your environmental flora, you can do work like that in the beginning.

And then, as Angie mentioned, your job at that point is to monitor intensively, and eliminate not only the positive spot that you had, but all the root causes that resulted in that. And that's what people don't really, you know, take seriously often.

The question should be, why is it there? How did it get there? What are the root causes for it being here? And by addressing those, then you can really start to take it to a point where it becomes very irregular, or not frequent events.

There is definitely some -- and whole genome sequencing may be an overkill. You could do any manner of subtyping that would give you the same information. So it has to be a gradual approach, and

kind of measured.

DR. SIEMENS: I'll second that. And the reason, one of the reasons that I mentioned before that we had previously done some PFGE work on *Listeria*, and it was really, the work that we did was to validate the principals and practice of sanitary design and our GHPs that we had in our facilities.

And essentially what it ended up doing was, all of the papers that had been written about product flow, and people flow, it actually validated that those were the right principles on a day-in, day-out process control that I needed to do.

So if you know those, and those have been validated, there's no reason to do it on an ongoing basis. If you don't understand how organisms travel through your process, or that the control practices that are in place impact, then I would go back and do it more on an investigational basis and take a look at it.

But as an ongoing monitoring piece, it does not give you any information than some of the other either species level or even, you know, those kinds

of things. You can do a control program without going to a genetic level.

DR. McENTIRE: If I can just add, all of these things also cost money. And so if you know, for example, that you're working within an operation where -- Angie mentioned they're validating sanitary design in their practices. If you know that you have poor sanitary design, I would recommend putting money at improving deficiencies, known deficiencies, rather than doing testing to see what you have. So it's -- you know, it's a balancing act.

DR. SHAW: So do we -- oh, we have a question.

DR. CARRILLO: Hi. Is this on? Yeah. Dr. Siemens, you alluded to, you know, bias of the database, or I think that was you, and interpretation of the database. And I agree, that is a big problem, that we don't have nearly enough food samples in there.

How would you propose -- you know, could there be a partnership between industry, regulatory agency to develop some properly sampled databases so

that we can address this, so data isn't misinterpreted?

DR. SIEMENS: That's a really great question. And I'm not sure, right at the moment because, you know, part of the reason that we're here is to understand the dynamics of if you are contributing in food sources, what are the potential regulatory and/or compliant actions that can be.

We've talked about the fact that once you're in the database, you know, the metadata, in some cases, in some public-facing are not available, but we still have it. You mentioned ATIP, right, in Canada. What's the availability of that if you go through the legal Freedom of Information in the U.S., right? What is that?

And there's a lot of those questions that I think has to be continued dialogue on, before we start getting the voluntary, you know, increase of non-regulatory-type samples and analyses put into the database. I think that's the reason why you haven't seen the rush today, because there's still some pieces in there that we don't understand the

dynamics. So that's a continued dialogue question.

DR. SHAW: Peter, did you --

DR. LEE: I think also, from our industry members as well, I think what they are telling us is that, you know, is there -- can there be some sort of guidance or a policy development there in terms of how those sequences will be used and deposited. And is there sunset clauses there as well?

You know, how long is this, the sequences going to stay on the database? And, you know, it looks as though it's going to stay forever, but then, what -- you know, can it be implicated in something which happen 15 years later down the track. All right.

So if they find an outbreak today but they cannot link it to anything, right, then 15 years down the track and they find the same strain in a plant, then what happens there?

So, you know, so I think that there's still some more work to be done there on policy and usage of the database and sequences.

DR. SAMADPOUR: One other problem with

metadata is that you can read too much into it. For instance, let's say you have a *Listeria monocytogenes* that came on corn. Has nothing to do with corn. The contamination, in all likelihood happened in the field, animals impacting the -- around culture commodities.

And then we see exactly the same *Listeria* in another place that got onions from, and they have a shared field with the plant that was -- had the corn.

So if you have, let's say, if you in a fermented -- dry fermented meat operation, and you find *Salmonella* or *Listeria*, chances are it came from, you know, pork, raw pork that went to many other places, or spices could bring the same thing in.

So just because you have a tag in that database doesn't mean anything. The ultimate source of microbial contamination, aside from some propagation that you see in plants, is going to be fecal material, human and animal.

MS. COFFMAN: That's a very interesting

application, though. If you are finding two different crops and they are contaminated, and they're in the same field, then you have the ability to go into that field and make some corrective actions, right?

DR. SAMADPOUR: It goes to, okay, what are the animals that are impacting, and then what's the radius of activity for these animals. So, again, it's a very complicated issue, and just having it tagged in the database does not mean much.

DR. SHAW: So I wanted to follow up on something that Vanessa mentioned. And she was rightly to point it out, and we haven't really talked about it yet, is that traditionally when we think about a pathogen, as microbiologists, we've sort of lived in this genospecies serotype sort of paradigm.

And I'm wondering what the panelists think about what whole genome sequencing in the future may sort of, how it may impact that, that sort of paradigm that we've been working with all these years.

DR. SAMADPOUR: It's changing it. We are

moving a lot of organisms from one group to another group based on -- this is an amazing shortcut that now you have to do proper taxonomy.

DR. SIEMENS: We've already started that discussion in non-O157s, right. I mean, when we really got in and started looking at the body of non-O157s as described by, you know, kind of the level of identification we have, we got in and realized there's a lot of them that doesn't have the ability to cause illness, missing one of those components, you know, in there.

And -- but today, if they're at this level, they're an adulterant. I do think it will advance. And the technology, and somebody mentioned about the cost and technology and the timing, you know, when is that technology going to catch up that you can get a result as quick?

We should have that conversation, because if it's found in there, and it's not going to -- it doesn't have the attachment gene, or it doesn't have the ability to produce toxin, the possibility of illness -- I don't ever say anything's zero, is very

limiting.

So you no longer have a potential public health outbreak. Shall I be held at the same regulatory compliance implications as if I have a bug that has the ability to produce illness?

So I do think it's going to advance that conversation. The other piece of it is, I still think we ought to look at some dose response pieces as well. There is just some differences in organisms and its ability to cause illness. Whole genome sequencing does not get us into that.

And so, do we walk away from some of this discussion on dose response as we move forward with organisms, and as we find more? So I think that's another component that gets tied in to this conversation.

DR. SAMADPOUR: And we had a situation with STECs, that we wrongly called them Shiga toxin-producing *E. colis*, fully knowing that most of them are non-pathogenic. And some of us were arguing that we should call them EHECs instead of STECs, and define the virulence factor components.

So I look at that as a kind of artifact of using the wrong nomenclature. But now we have the ability, and with the example I gave you on *Vibrio cholerae.*

Immediately we go in and do whole genome sequencing and now we are defining these pathogens not by classical microbiology, but do they have the ability, for example, is it a *Clostridium botulinum?* Does not have the toxin gene? Don't worry about it.

So we now have that added ability to have the shortcuts to do a lot of things that we couldn't do and with changing taxonomy also.

MS. COFFMAN: So thank you. I did present a lot of questions without a lot of answers, so I'm glad to have this opportunity to have these conversations.

I am concerned that if you do find an O157, but you don't have the genes that encode for, let's say, attachment, they you release that product and something bad happens.

DR. SAMADPOUR: Okay. There are known virulence markers. Just because something is O157

does not mean anything. All it means is that it has the O antigen, number 157. We have O157 that are intra-pathogenic. They have only the eae, or mostly eae -- alpha eae.

We have situations that we have the O157, we have gamma eae. At that point we hold the product, because of the fear that it may have lost its toxin genes. So these type of decisions are not done flippantly. There is a -- we go with the FSIS definition of the pathogen. And based on that, we follow the protocols and then we make disposition decisions.

Angie, do you want to --

DR. SIEMENS: No. I -- we make those decisions today. What your comment is, is not any different than the decisions that are made today around the definitions and what he just mentioned.

I still have a possibility of something that I have released that's negative, that may, because of just the difficulty in sampling product, and running analyses, that there are products that, you know, go through the system that are negative

that cause outbreaks.

So that is not any -- your comment is not any different than what we deal with in reality today.

DR. SAMADPOUR: There is a fear of sending a positive or something that could make people sick, and they are always very conservative in making the decisions.

DR. SHAW: So, Jennifer, I'll give you one. Did you want to say something?

DR. McENTIRE: No. No.

DR. SHAW: Okay. So --

DR. McENTIRE: I want to hear what Martin --

DR. SHAW: Oh, so Martin -- so we'll take one question from Martin, and then we'll -- I promise we'll break.

DR. WIEDMANN: Okay. This is a follow-up to this question, and specifically for Vanessa.

What would it take for consumers or the general public or politicians to accept that we have sufficient scientific evidence, for example, to say

that some *Salmonella*, given X, Y, and Z genetic markers are not virulent, and regulation follows?

I don't want to discuss the science, because it's tricky, but we'll get it right. And for some of you have already shown it as you can get it right. But what would it take, or would it be seen as a relaxing of the standards, because that's the trick?

MS. COFFMAN: I mean, I think that a lot of consumers would see that, and a lot of consumer groups would see that as a relaxing of the standards. However, if you have sound science, which we are definitely getting there, and we are understanding day by day, more and more, then you know, there's a possibility for discussion.

But I think the problem, and that I just mentioned, is that most people would say, well what happens when you get it wrong?

DR. SAMADPOUR: There is something else that can be done and probably should be done is to re-examine the taxonomy, and maybe move them out to another group, the ones that are truly don't have the

virulence factor determinants to be a pathogen.

DR. SHAW: So I think that was a really interesting conversation. And it's just sort of how technology sort of moves our conversations along, and how we think about things as microbiologists. It's sort of this constant sort of movement.

But anyway, so we are at 12:30. We are going to break for lunch. I just have a couple of things.

Remember, the cafeteria is down the hall. And I also want to put in a plug. So today, if you didn't know and you wanted to take a little -- you wanted to get some fresh air, today is the last day of the, sort of, USDA Farmer's Market that we do every, sort of, spring and summer season.

And so if you wanted to take a walk over, there's some special events happening because it's the last one. And if you have never, sort of, seen the Farmer's Market, it's next to the Whitten building like on the east side of the Whitten building. So if you're looking this way, it's on the right side.

So take that opportunity if you want to take a little walk. And I think we're going to be back at 2:00.

(Whereupon, at 12:33 p.m., a lunch recess was taken.)

A F T E R N O O N S E S S I O N

(2:05 p.m.)

DR. SHAW: Okay. I think we're ready to go. We've got our logistics together. I hope you had a good lunch. Maybe you took a walk down to the Farmer's Market.

So, anyway, I think we started some good discussion before we went to lunch, and then we're going to sort of continue in that vein with our next speaker, who is the -- Ms. Roberta Wagner, who is the Assistant Administrator for the Office of Policy and Program Development.

She will be talking about the interaction of WGS and FSIS's current policy and future policy development, and will be moderating a roundtable to discuss many of the topics that we've heard about for the last day, day and a half now. And so I'm going to turn it over to Roberta.

MS. WAGNER: Okay, thank you.

First of all, welcome. Welcome back from lunch. I hope you're wide awake. I don't have a PowerPoint presentation because the one I provided,

Uday told me it was too messy to put up, so you're just going to have to listen to me through talking points.

For those of you that don't know me, I've been in the public health regulatory arena for about 30 years now, 28 at FDA, and I'm going on almost 2 years at FSIS now.

So I do think I have a unique perspective because I've been in both FDA and FSIS. I started FSIS on the Field Operations side for a year, and then I came over to Policy just about 6 months ago when Dr. Engeljohn retired a little bit sooner than we thought he was going to retire.

So this has been a huge learning curve for me. I am going to stick to some notes, just because I'm still actually learning the language over here at FSIS, but I still think I can, I'll make some salient points.

And I am going to have a little bit of a diatribe here because I -- honestly, in listening over the last 2 days, and thinking about this a little bit, I honestly do think that FDA and FSIS

will likely approach the use of whole genome sequencing, with the exception of outbreaks, a little bit differently.

And I think there's a number of reasons for that. So I just think it's the right forum to kind of bring that up and remind people that we have a very different regulatory foundation and law, and it dictates the way we do business. It dictates how often we're in establishments. And so it really has framed the way we do business.

And I just want to point that out, because I think it's important. I think you're going to hear me say perhaps different things than you heard Steve or others say yesterday about how FDA is using whole genome sequencing, so I just think this might be the right time to kind of remind people of the differences between FSIS and FDA.

So -- and again, what I'm going to do today is I will talk to you a little bit about how FSIS is using whole genome sequencing. I'm going to point out where I believe we have some pretty solid policy, and where we likely need to relook at our policy and

see if we need to fill some policy gaps.

I'm going to talk to you about things we've been talking about internally, kind of future applications and how we may use whole genome sequencing in the future. And I don't want the industry folks to get excited. This is all -- when I talk about future applications for whole genome sequencing, it's hypotheticals at this point.

It's just things we've been throwing around. And you're not going to hear anything different than you've heard through the other presentations, quite frankly. But I just think this might be a good time to reiterate.

We're going to get ready for a roundtable discussion. So some of this can be used as memory-joggers, so when we come up here and we start discussing what we've heard over the last day or two, I think, and we'll have some great topics. So I'm going to do some of this as memory joggers.

So I wanted to start by reiterating a few points that we heard yesterday, or I should say over the last day and a half now. Whole genome sequencing

is a powerful tool that will replace traditional methods for routine microbiology characterization and subtyping of foodborne pathogens. And FSIS will certainly use it in that way.

It is a tool that can characterize bacterial pathogens with far greater accuracy, I've heard the word precision, granularity, I mean, there's been a lot of words used around that, than previous methods such as PFGE.

It's a tool that holds promise of being able to facilitate an in-depth understanding of harmful traits and pathogens such as bacterial virulence, and of course, antimicrobial resistance.

I also want to reiterate an important point made yesterday regarding how important it is for all stakeholders, so that's all of us sitting in this room and participating in this meeting, to continue to collaborate, coordinate, share and openly communicate, harmonize, standardize, these are all the words we've heard over the last year and a -- or the last day and a half, and assure data quality regarding the use of whole genome sequencing.

And I want to emphasize the importance of the Gen-FS partners continuing their work together. You really are out there to make sure we have a unified front in terms of the use of whole genome sequencing data, particularly in the food safety arena. So I just want to put that out there.

And again, before I kind of jump in to how FSIS is using whole genome sequencing and where we are relative to policy development, as I mentioned, I've worked in both FDA and FSIS, and in both organizations I started out in Field Operations, on the ground -- boots on the ground, folks -- and then moved over to Policy. I did that in FDA. I did that now over at FSIS.

First of all, you know, we are alike in that we are both public health regulatory agencies, FDA and FSIS. Our mission is to protect public health, and relative to food, it's to reduce foodborne illness. That's what we're about.

With that said, there is a lot of differences, and again, as I mentioned, that's grounded in law and regulations. So let me go

through some of those.

You're aware we regulate different foods. I mean, I think we say that often enough, but these foods have different risks associated with them. They have different groups that consume them at different rates. So we are different in that respect. There's different risks associated with the foods that we regulate.

Of course, FSIS regulates raw meat, and now that includes Siluriformes fish, and poultry. And then we also do egg products. And then all the -- you know, most of what we're doing is the raw meat, so that has some -- you know, that has some challenges in and of itself, but then we do also have kind of those non-ready-to-eat that kind of look like ready-to-eat products, ready-to-eat products, etc.

And then on the FDA side, they regulate basically all other foods. So -- and it's about 80% of the foods that are consumed in the U.S., FDA regulates. And their foods are a mix of raw, and they also do a lot of ready-to-eat foods, kind of your -- so they do the raw fish, but they also do

cooked fish, shellfish, raw shell eggs, raw fruits and vegetables now, non-ready-to-eat and ready-to-eat food ingredients, and many ready-to-eat processed foods. So that's kind of the FDA world.

There's a vast difference in the number of FDA establishments that have an assigned inspection frequently versus the number of establishments that have to be under what we call continuous inspection or once per production shift inspection on the FSIS side.

So, for FSIS, we have about 6,000 official establishments. Those are our slaughterers and our processors. And I will say that warehouses and distributors in the FSIS world are not routinely inspected, with one exception, and those are these, a small subset of the warehouses that are ID warehouses.

Our inspection frequencies are dictated by our laws, so the Federal Meat Inspection Act, the Poultry Products Inspection Act, Egg Products Inspection Act. They tell us how often. Our inspection frequently are dictated in those laws.

And according to those laws, we have to have FSIS inspectors in slaughter establishments, so all meat and poultry slaughter establishments, basically during all hours of operation. So FSIS has to be present onsite.

And relative to those further processors, those just processing, we have to have inspectors visit and do inspection tasks in those facilities once per production shift, so basically daily, at least once daily.

So in addition to that, FSIS conducts weekly meetings with establishment management. So we have in-plant personnel in those establishments, or you have those going and visiting processors, and once a week they have to meet with establishment management.

So they are having conversations. And this is an opportunity for that, those in-plant inspectors and their managers to talk to the establishment about non-compliances, about positive samples, what are you going to do with these positive samples.

I would also say they, the establishments

and USDA-FSIS, they get their results, sampling results emailed to them basically real-time. At the same time we get the results and they've been cleared, they're getting the results. They get emails through their LIMS system.

They also get quarterly reports of all their sample results, and that way they can trend if they choose to, once a quarter. So our establishments have a lot of information coming to them, that we expect them and require them to do something about pretty much immediately.

Okay. So in contrast, FDA -- and maybe my numbers are a little off. Somebody can correct me if I am. But when I left a year and a half ago, we had over 60,000 domestic establishments that require to be -- that were required to be inspected under a mandated minimum inspection frequency.

And that inspection frequency was established under the Food Safety Modernization Act. It is a minimum inspection frequency, and it basically is that those establishments need to be inspected once every 3 years if they've been

designated as high risk, and once every 5 years if they have been designated as low risk.

And -- but with that said, FDA, a lot of states are doing contract inspections for FDA. I think about half of the inspections, food inspections, establishments inspections that FDA reports out on annually are now done by the states. So those states are helping FDA, usually to exceed that minimum inspection frequency.

So, again, there is no routine conversation or opportunities for routine conversation between FDA inspectors and plant establishment management. In fact, if you're hearing from FDA, it's likely not a good thing, quite frankly. So --

Let's see. What else can I say in here? Our sampling models are completely different. Basically, FSIS inspectors collect thousands of regulatory samples of product. We focus on product sampling for pathogen testing annually.

And what they're doing is they're collecting those samples to verify that the HACCP systems in those establishments are continuing to

work, that the establishments are producing unadulterated product, or that they're meeting pathogen performance standards, which means we're really looking to see if they're maintaining process control where applicable.

We do have pathogen reduction performance standards, for example, for *Salmonella* in poultry establishments, slaughter establishments.

There is a limited environmental sampling done on the FSIS side. And, of course, we do focus that to our ready-to-eat food product establishments.

In contrast, FDA, in the domestic arena, and I should make that clear. You know, we both have to resort to border sampling relative to imports. But in the domestic arena, FDA has been focusing on environmental sampling, taking environmental swabs. And again, they focus on ready-to-eat establishments but may venture into others as well. They do collect for-cause product samples, but it's on a very limited basis.

But with that said, where we are alike is both FDA and FSIS do collect product samples to

establish prevalence baselines. So FDA, it's a little bit newer. Maybe they're not even doing it anymore, but I know when I left, we were focusing on getting some prevalence baselines for certain high-risk commodities, and FSIS does that routinely.

Lastly, we have very different enforcement approaches. We don't have different enforcement tools, necessarily, but our approaches are very different. We both do take -- we do progressive enforcement, so we'll put you on notice first before we move up to something more severe than that.

But while we take a progressive enforcement approach on the FSIS side, it really is the locals, the districts and those inspectors that can independently -- they're empowered to independently take some pretty strong enforcement very quickly.

They can suspend establishments from inspections, which has the effect, for those that know the FDA side, of an injunction. Because you legally cannot operate if you don't have inspection in those facilities.

So our inspectors, they can note things.

They can literally elevate that to a frontline supervisor and make that decision. No OGC needs to be called. Headquarters doesn't need to be called. It happens very quickly. But at the same time, they typically resolve the issue fairly quickly, as quickly as possible so we can get those establishments back up and running.

And then on the FDA side -- and I worked in the compliance arena quite a bit on the FDA side -- when we're going to even issue, take an administrative action on the FDA side, like issuing a warning letter, there were often -- there's some direct reference warning letters where the districts could issue them, but often they had to come into the center for approval, and the center would have to go to the Office of General Counsel for approval, so just to issue a warning letter. So they're taken very seriously.

And then, of course, seizures, injunctions and prosecutions, you have to work through the Office of General Counsel and FDA for those.

So all of that to say, if it seems like FDA

and FSIS may be taking a different approach relative to how they're using whole genome sequencing, I think there's reasons for that. And I think it's okay, too, quite frankly.

So how has FSIS been using whole genome sequencing? FSIS, like FDA, has been using it in the outbreak investigation or response arena. I believe we have solid policy established regarding the use of -- you know, initially, it's PFGE, but it morphs into whole genome sequencing quite nicely, some of the policy we have out.

It's in the *Federal Register* notice. We put out a *Federal Register* notice in 2012. It really is talking about your raw product, your non-ready-to-eat product, but it makes it very clear when we will consider something associated, a food associated with illness and when a product becomes adulterated because of that, because again, one big difference -- and boy, I'm still getting used to this -- on the FDA versus FSIS side is we do raw meat. *Salmonella* is not an adulterant.

It only becomes an adulterant when that

product is associated with illness. So we've made that very clear in the *Federal Register* notice. And we made it very clear, kind of, what the threshold of data is to link that non-ready-to-eat or raw product to illness.

FSIS, again like FDA, is also using -- so that's a reactive manner. When we're, you know, using whole genome sequencing for food, foodborne outbreak response, something's already broken down in the system. So I consider that being -- using it as, in a very reactive manner.

We are also using it like FDA in a proactive manner to identify harborage in food processing establishments. We are starting to use it on a more limited basis when warranted to detect evidence of repeated introduction of a strain into a non-ready-to-eat food environment, such as through animals coming into the slaughter establishment.

You've heard a little bit more about that from other folks. I think it applies to produce as well. You have -- you kind of have -- it's transient, because it's coming in from that field;

it's coming in from the animal. It may not actually be harboring in the facility. It's just coming into the facility more than once, maybe quite a bit.

So we're starting to use it to identify those instances. And then we are using it, again, in a limited fashion to assess whether we're having cross-contamination issues in some of our facilities.

FSIS communicates any -- you know, if we have evidence of harborage, during our weekly meetings and, you know, through their emails, the industry and the establishments understand that very quickly. And then they know they are required to take action as appropriate.

Our inspectors are to verify that they've taken appropriate corrective actions. Typically, we will go in and do some environmental sampling ourselves when we see harborage. So we'll do that. We likely will collect additional product samples as well, to make sure that, you know, what's in the environment isn't making its way into the product.

And again, I think -- we believe that our policy around harborage, we do have industry

guidelines out there. Folks seem satisfied with it, but we really do want to take a step back, particularly after this meeting, and look at it again, see if there's any areas we need to clarify.

We'll probably interact with the industry to see what they have to think about that. And I also think we might have to revisit our instructions to our inspection personnel out there, to make sure they're clear.

So, again, what my office does is we do both what I would call operational policy, so it really is setting up those instructions for field inspectors. We want consistency out there to the extent possible with, you know, 9,000 inspectors. But we do that in my office as well as general policy setting.

Relatedly, I do want to mention that FSIS is working on developing procedures for reporting evidence-based whole genome sequencing data to the industry. We've heard comments that how are you going to do that. So we are working on that.

In addition, we do continue to work closely

with FDA to more systematically evaluate whole genome sequencing data as it pertains to our dual jurisdiction facilities.

So, and those dual jurisdiction facilities, I can tell you, in the, probably last year and a half, we have supported each other in taking enforcement type actions, because FDA has the environmental samples and FSIS has the product samples. And with whole genome sequencing, we are making connections.

So again -- and we're looking at harborage. And we're able to identify harborage. So we're dealing with those facilities in a more systematic way because we're talking to each other and we're sharing the sequence data.

So in addition to how we've been using whole genome sequencing, as I just described, so we've been using it for outbreak response, for kind of harborage, cross-contamination, depend -- you know, determining if animals are bringing a particular strain into the facility on more than one instance.

I do want to touch on some of the things we're thinking about. And again, Dr. Goldman touched on some of these yesterday.

So FSIS believes we could use whole genome sequencing data to evaluate long-term or industry-wide trends which may result in the need to revisit existing policy, or the development of new policy.

So I'm just going to list a few of the potential applications for kind of doing these long-term evaluations or industry-wide trending that we are considering. And again, we've already heard a lot of these from others that have presented at this meeting.

So we are looking at novel and recognized AMR genes in *Salmonella*, *Campy*, generic *E. coli* and *Enterococcus* species. We're looking at subtyping distribution in animal species, products, global geographic regions. And we're not looking at, we're thinking about looking at.

We're thinking about looking at the presence or absence of pathogenicity islands or genes associated with STEC, *Salmonella*, *Campy*, and *Lm*, and

then the presence or absence of genes associated with resistance to commonly employed intervention. We really think that this -- there's a real possibility, and we really want to delve into that piece.

So we want to look at -- what we're hearing is that some of these pathogens are becoming resistant to some of our interventions. So they become heat resistant, pH resistant, resistant to chlorine, so they can survive high levels of chlorine.

So we want to use it in that way, too, to figure out maybe some of our interventions are no longer going to be usable. And we need to move on, so we want to look at that.

Such evaluations and trendings, of course, were not possible with PFGE. It is possible with NGS or whole genome sequencing. If we were to use data in this manner, we believe we would need to answer the following questions and modify or develop new policy based on the answers to those questions.

So we're already thinking, if we were to do this, what are the questions we're going to have to

answer?

And so some of those questions are, how will we use those results? So we did the trending analysis, the long-term analysis; how will we use those results generated to influence the design of future exploratory or baseline studies conducted to determine the need to set or modify performance standards?

Or how will we use them to influence sampling programs, lab detection methods, risk assessments, attribution measures?

And hypothetically speaking -- and I want to say that, because I don't want folks leaving and saying, Roberta said -- if we were to look at the presence or absence of pathogenicity islands or genes, kind of those virulence genes associated with STEC, *Salmonella*, *Campy*, and *Lm*, we might need -- and a question we would have to ask ourselves is, do we need to define or redefine adulterants, adulteration based on the presence or absence of virulence genes for pathogens, for example?

And others have mentioned that today.

Might we have to look at that in the future?

When contemplating future uses of whole genome sequencing, FSIS has also been thinking about how we would use it as a tool to further evaluate pathogen-positive sampling data that we have for individual establishments.

So now we often use that data to basically calculate percent positive rates and determine if folks are meeting performance standards, pathogen reduction performance standards.

So, obviously, with whole genome sequencing, we could do a lot more than that with those positive results. And so, what we're thinking, again, you know, we could look at those results in the context of, for a specific establishment, are the pathogens we're seeing, are they pathogen lineages historically associated with outbreaks?

So, you know, CDC has -- these are, for example, Salmonellae that have caused illness before. Might we look at *Salmonella*-positive isolates from specific establishments and say, hey, that's a particular strain that has caused illness, or no,

that's one that really hasn't, and might we use that in some way?

You know, basically again, if we might look at this relative to pathogenicity islands genes, gene combinations associated with virulent strains, the presence of genes associated with resistance to antibiotics, antimicrobials, and commonly employed interventions.

So, again, just taking a step down, we have positive isolates that have been sequenced from specific establishments and what can we learn about those.

And again, the way we would likely use it is share it with the industry. It's kind of -- you know, it's part of what we know, and let's just continue -- you know, we're about continual improvement in these establishments. And again, how can we further reduce the presence of pathogens in the food products that we regulate?

So, again, if we were to do this, there's a couple of questions. You know, there's a main question we would have to answer. And again, based

on the answer, we may have to establish policy or make changes in existing policy.

So how should such data influence the level of concern and subsequent assignment of agency resources to such things as follow-up samples, public health risk evaluations, food safety assessments and enforcement?

So, again, this was this whole ideal of not -- you know, we might learn through whole genome sequencing that all Salmonellae aren't the same, all STECs aren't the same, you know, all *Lm* isn't the same, and might -- how might we use that information to make decisions on how we're going to utilize, for the Agency, our resources? There's other ways I'm sure the industry would use that information.

Just wanted to mention that FSIS signaled, in a February 2016 *Federal Register* notice, and the beginning of the title was, "New Performance Standards for *Salmonella* and *Campy* in Non-Ready-to-Eat Chicken Parts," and it moves on to comminuted chicken and turkey products.

We mentioned, and we kind of signaled in

that *Federal Register* notice how we will use whole genome sequencing data to prioritize and then assign inspection resources in establishments. And I just wanted to read it really carefully.

Again, what I have found is FSIS, they put pretty much everything they're doing in the *Federal Register.* So if you want to know what we're doing or what we're thinking, go to the *Federal Register*.

So in that particular *Federal Register* notice, it states in part that FSIS will schedule a public health risk evaluation, possibly a food safety assessment, and those are -- for FDA folks or those that are regulated by it, those are full-blown inspections. Okay. So that's what we're talking about there, with sampling, environmental sampling.

So we might -- we'll basically schedule those based on FSIS test results for establishments that do not meet pathogen reduction performance standards, for establishments that have produced products with repetitive *Salmonella* or *Campy* serotypes of public health concern, or repetitive antibiotic-resistant *Salmonella*, and for

establishments with *Salmonella* or *Campy* PFGE patterns or whole genome sequences as they become available, matching those patterns or sequences found in recent outbreaks, or epidemiologically linked to illnesses.

So I just want to point out that we are signaling how we're going to be using whole genome sequencing in current -- and this is actually from a year ago, *Federal Register* notices.

So let me close by stating that again, Dr. Goldman mentioned this yesterday, whole genome sequencing technology is in our 5-year strategic plan. It's in our action plans. First develop capacity, then move on to developing the compliance and enforcement strategies, looking at other applications for the technology. More to come. It's evolving.

We recognize that whole genome sequencing improves on PFGE's ability to detect and confirm illness clusters, and as such, FSIS is using whole genome sequencing data to detect clusters, potentially representing outbreaks or incidence of harborage, and is developing procedures for reporting

results directly to establishments.

FSIS also recognizes that whole genome sequencing provides an unprecedented ability to characterize pathogen isolates, and that we can use these data to understand temporal, geographical, or industry-specific trends, enhance our sampling programs, pathogen-detection methods, and risk assessment attribution studies, and ultimately, food safety policies.

And we understand that establishment-specific results can be used to prioritize assignment of agency resources, so again, just summarizing everything I just said about some potential applications in the FSIS world.

And lastly, we also recognize that establishments can use whole genome sequencing results to inform the design and verification of HACCP controls and supply chains.

So let me see where I'm at. So what I wanted to do next, because we are going to have the round table. We have 12 esteemed stakeholders that are going to come up here, a very diverse group. And

we want to pose some questions to them and kind of get their perspectives around that.

But before we do that, I just want to -- I want to read through a list of my take-homes from the public meeting. And so this is -- these are mine. Hopefully some of them are yours as well. And I do want to mention, I'm not a microbiologist, so if I misused any terms in the micro world, I apologize. I'm a chemist by degree. So apologize there.

But anyway -- and again, I want to do this to just spark our memories so when we have the roundtable up here, and you know some of this is fresh in your mind.

So what I heard over the last day and a half, we need standardization, harmonization across all whole genome sequence networks relative to whole genome sequence metadata, data reporting, analytics tools.

And around analytics tools, I heard that we need web-based easy to use tools. And then we also need standardization and harmonization around the interpretation of the data.

I heard that all stakeholders need to continue to communicate, collaborate, learn together, share together in multiple venues and forums.

I heard that, you know, we -- I think we heard over and over again how powerful a tool whole genome sequencing, new generation sequencing is, but that we need to use it in combination with other evidence, data, information, and we need to use it in the context of the questions that we're trying to answer.

Whole genome sequencing will likely change how we define and characterize hazards. And again, you know, a lot of folks talked about, you have whole genome sequencing data, you need to consider, you know, things like chain of pathogen transmission, gene expression, environment, food matrix production environment, and many more when you're using that whole genome sequencing data. So you need to put it in context.

We must develop and follow data quality standards, particularly as data is being uploaded into public centralized databases.

Investments in training are crucial to ensure consistency in data interpretation. We need to address this live/dead cell issue. We need to address the sharing of data, so we could have -- basically, so we can continue to grow the sequence database. And folks brought up that we really need to get those food sample sequences into that database.

And if we can do this, if we can figure out a way to get more and more sequences into NCBI for example, what a powerful tool we have to improve food safety. So we need to overcome these hurdles of, you know, industry being concerned of being penalized in some way if they upload sequences for pathogens.

With that said, you know, I do want to mention -- and I'm speaking for FSIS here, that we are certainly open for further discussions on creating a safe harbor for industry, so they can use this new technology.

We want them to use it, of course, to enhance and advance their food safety systems. We want to encourage its use, not discourage its use, so

we really do want folks to come to the table and let's really try to sit down and tackle this issue of perhaps how we might create a safe harbor as the industry is learning how to use, or is experimenting with whole genome sequencing.

One thing I took home from this is we had no food lawyers present. I think we really need to get the food lawyers at the table. There seem to be an awful lot of legal questions. You know, when -- if I upload, what's going to happen to me? Should we sunset data, etc., etc.

So, you know, maybe that's the next discussion. We need to have some discussions with the food lawyers out there, and get their thinking.

We need to establish policy around retrospective investigations. We heard that today. We heard this is a great tool for other things besides those we've talked about during this meeting, such as shelf life studies, causal spoilage analysis, determining if pathogens in raw materials are seeding the environment, so repeat transient pathogens.

Or are they resident harborage? We could

do some more work around that, understanding how pathogens move through the processing environment, learning the microflora of the processing environment. So we heard many, many different uses for new generation sequencing and whole genome sequencing.

As a regulator, what I heard very clearly is that we need to establish clear policy regarding the use of whole genome sequencing and whole genome sequencing data, and we need to publish those in something, a compliance guideline or something like that.

And last two, we need to figure out what and how to communicate relative to whole genome sequencing to consumers. So we need to consider the consumers in all of this. What should we be telling them? How can we explain this in kind of a plain English way that's not overly complicated?

And then maybe when we do move to suggesting that certain Salmonellae -- well I can't use Salmonellae. I can use -- I'll pretend I'm from FDA. Certain Salmonellae aren't an adulterant. It

might be easier for them to understand. So I think we got to pave the way for that.

And then we need to -- and the last take-home, we -- what I heard was we need to very deliberatively and thoughtfully move forward with using whole genome sequencing data. So we need to do it very carefully.

So, with that, I don't know, is Bill down there? Am I supposed to move on to the roundtable, or --

Are you doing that part or am I doing it?

DR. SHAW: Okay. So yeah. So thank you, Roberta, for giving us your perspective.

And then I think we're going to bring up the panelists, and you know all who you are. So you want to -- you want me to read them out, Peter?

So Martin Wiedmann, and then John and Steve and David, and then Bill and Jorgen and Jennifer, and Mansour, and Tommy. There's Tommy. And who am I missing? Suelee?

MS. WAGNER: Okay. And what question do you want?

Okay. So, first of all, we have a great diversity of folks sitting at the table, and I think we're going to ask you, we'll just start at that end, and introduce yourselves.

And I want to say thank you for taking time out to do this. We appreciate it. Again, I think we have a real diverse group.

DR. GOLDMAN: David Goldman, FSIS.

DR. KLIMKE: Bill Klimke, NCBI.

MS. COFFMAN: Vanessa Coffman, Johns Hopkins Center for a Livable Future.

DR. WHEELER: Tommy Wheeler, USDA ARS.

DR. BESSER: John Besser, CDC.

DR. WIEDMANN: Martin Wiedmann, Cornell University.

DR. McENTIRE: Jennifer McEntire, United Fresh Produce Association.

DR. SAMADPOUR: Mansour Samadpour, IEH.

DR. MUSSER: Steve Musser, FDA-CFSAN.

DR. ROBBE-AUSTERMAN: Suelee Robbe-Austerman, APHIS and NVSL.

DR. SCHLUNDT: Jorgen Schlundt, GMI and

Singapore.

MS. WAGNER: Okay. And what I think I want to ask you to do, I'm going to put you on the spot a little bit. So I think the majority of you have been here for the majority of the meeting. I'm sure you had to step out here and there.

I think Jennifer, you came in today. Were you here yesterday?

DR. McENTIRE: I was at FDA yesterday.

MS. WAGNER: Okay. So that's okay then.

What I think we want to do is, can you just share a learning from the last day and a half? And so that's part one.

And then part two, where do you think we need to have additional discussion?

So, I mean, I don't know about you, but my head is spinning. And, you know, it's where like where do we even start? So that's why I think we want to pick your brain a little bit on kind of what are those next topics we likely will have to meet around.

And I don't care which side. David, you

could start.

Oh, you have the microphone. Go ahead. You can start.

DR. GOLDMAN: I'm sorry. Okay.

(Off microphone comments.)

MS. WAGNER: No. Yeah. I was going to say, I want you in the middle so you can, you know, liven it up as we go afternoon.

DR. GOLDMAN: I think I'll be quick to try to set a model here, because there's a lot of us up here. And a lot of what I will say has been said by FSIS in various talks throughout the meeting.

One of the things that I note and have noted in previous discussions is, the more we know, the less we know, in some respects. There are lots more questions. Whereas I think maybe 5 years ago, just for me, personally, I thought it would pretty straightforward. We'd see -- we have a goal in mind; we'd get there fairly readily.

It's much more complex than that, and I think we all need to appreciate that. And a consequence of that is that as Roberta just said, and

it's a good chance to echo, we're necessarily deliberative as a regulatory agency. We're going to be even more so with this particular issue because of the complexity. So I think that's one takeaway.

In terms of next steps, I think it was really hard and challenging to pull together a meeting with the breadth of participation we have here today, although it was hugely beneficial. I think we need to have more discussions, maybe with smaller groups representing some of the same broad audience, but more of what's been occurring already around the world.

And if we could replicate this sort of a meeting sometime in the future, I think we'll need to do that as well.

MS. WAGNER: Next.

DR. KLIMKE: I think I heard some people say that they think we need more sequencing, and I'm looking forward to seeing those sequences deposited at NCBI.

MS. COFFMAN: I've been really impressed, and I want to applaud everyone who's been working on

this issue, because you can tell, obviously, that you all care and, you know, we're really going to, hopefully, make some headway on foodborne illness in this country and around the world. So it's a very exciting time, and I appreciate all your hard work.

As someone who's about to graduate with a Ph.D. in epidemiology, I'm really excited to hear that you guys still value epidemiology. So that's great. And I wonder how we can take our epi findings and translate those into something that is digestible for the consumer.

DR. WHEELER: I think one of the things that I learned is that we're about to have a lot more information about some of these pathogens than we've had, and there are going to be a lot of opportunities to take advantage of that. And we just have to fine tune how is the best way to do that.

And I also think that there's a lot of questions still out there that are really not answered yet. And I think there's some work that we need to do to get to that point, to understand, you know, how much variation is out there, and what's the

distribution of that variation. And that really can end up impacting how some of this data is going to be interpreted.

DR. BESSER: There's all these different agencies and different terms and different new technology terms. But I think I'm coming away from this with a little more appreciation how, below the surface, we're more on the same path than we thought we were.

I think we're all headed in the same direction. I think I have a little more appreciation for some of the industry concerns. And my understanding that not all of this will ever be understandable was reinforced by this meeting.

DR. WIEDMANN: I think I've come away with being very encouraged about some of the data we've seen and the move we've seen to being able to use whole genome sequence data to redefine what is a pathogen and ultimately what is an adulterant.

And I'm very encouraged by some of the FSIS data I've seen on comparing food isolates to human isolates to get at some of the issue of *Salmonella*

Kentucky, which has always been intriguing to some of us, and how application of these tools to redefine pathogens of concern or whatever we're going to call it in *Salmonella* might move us to a better point where we can better address this pathogen where we have not made much progress.

DR. McENTIRE: I've been encouraged at the openness, just in having the discussion and then surfacing many of these issues.

And Roberta, I was particularly pleased to hear your openness to consider the opportunity to develop safe harbors, because I think that that will allay a lot of industry concerns. And then we'll be able to move forward much more readily.

DR. SAMADPOUR: Angie and Jennifer did a good job talking about some of the industry's concern. Something that may be useful is to have a similar educational symposiums.

In the next year there are several industry-specific meetings, the poultry industry, beef industry, and FSIS and FDA regulated. It would be nice to take this to the industry and educate

various members of the food industry on the technology, what it does, what it cannot do, and make sure that they understand that, you know, doors you have used are not there, you know, no one is going to make a decision without clear epidemiology, and there is always going to be a scientific discussion.

DR. McENTIRE: That's a great suggestion.

DR. MUSSER: So, first of all, I'd like to thank everyone that organized this public meeting. For those of you not in the federal government, putting on public meetings is a very heavy lift. It's not something you just decide to do and have it happen.

And in addition to organizing it, just putting it on day to day is a very difficult task. So my hat's off to you, FSIS, for pulling this off, and thanks very much.

For my part, I've learned once again that we are still not communicating very well, that there are a lot of points that we need to communicate better, that we continue to need to reach out to our industry, regulated industries and explain how we're

using this technology, and what it means to them, and to us, as well as the public.

We, as a federal government, are often criticized for this, and not doing a very good job at it. So we will continue to -- for me, it reinforced I got to pay for more seminars. I got to pay for more, not really public meetings, but symposia.

I think we're going to have another in, at IFSH in the spring time, probably another one following that. We'll continue to have them as long as we have interest in people attending.

And finally, I think my concerns about data analysis and software availability continue to be reinforced in that there's many ways to get to the same answer, but that in many cases, we don't even have a way to get to the same answer. So a software bottleneck still exists in how we use them, so we need to work in that area as well.

DR. ROBBE-AUSTERMAN: So I'm really excited about the opportunity of whole genome sequencing being a point of interaction of agencies at the time of need, and allowing for that efficient

communication during outbreak investigations.

And I also -- although I haven't been involved in these meetings, I run the core at NBSL, and watched the FDA start whole genome sequencing and see how far everybody's came since 2011. And it's been impressive how fast this technology has rolled out and how quickly everybody has come to work together.

So I think it's going to continue, and it's also so impressive of how much inherent knowledge that we've gathered just with this little *Listeria* project that was done for a couple of years where everybody decided to focus on that. And I think it'll kind of continue to do this with all the pathogens that we evaluate.

MS. WAGNER: Thank you.

DR. SCHLUNDT: Yeah. I'd like to say that I'm very encouraged that there is this, I think, general recognition that this is an international issue. It should not be a national issue, not even in the U.S., because we have this opportunity that we can actually use this as a global machine.

And then I would just have one warning because even though I also agree that it's fantastic how quickly it has been moving forward, especially in the U.S., if we are moving forward too fast, without coordinating what we are doing, we might squander this, I think, rather fantastic opportunity that we might end up with a global machine and a global solution to a lot of different things that would not only help countries outside the U.S., but would actually also help the U.S. consumers because more than half of your food, you import from elsewhere.

And if you had a common system, based on whole genome sequencing and metagenomics, by the way, I think we have to mention that also, that would really be to the benefit of the consumers, and I would also say the food producers in the U.S., especially if it was around the world.

MS. WAGNER: Okay. Now, what -- I'm going to look at some other folks. What question do you want me pose up here? We have 15 of them.

I guess I'll do one question. I have a list of 15 questions. Is there a topic that you

really want the panel members to address, any of you, in particular? Is there just something you really want to hear from -- hear about from everybody on the panel?

(Off microphone remarks.)

MS. WAGNER: Okay. So what I'm asking is, is there a topic that you would really like everybody on the panel to address? Any of you. Because otherwise I have a list of questions, but I really want this to be about you, too.

(No response.)

MS. WAGNER: Nobody has any burning desire? Okay. What are key next steps, in your opinion, for the regulatory community?

DR. MUSSER: You pointed to me --

MS. WAGNER: No, no. You don't get to --

DR. MUSSER: -- because I have the microphone.

MS. WAGNER: You don't get to pass the baton. Everybody has to answer.

DR. MUSSER: You know, for -- at least in FDA's case, we have a number of activities we're

pursuing. One is, we are preparing -- we understand that communication, education and training are very important. And as a result, we're preparing a number of training videos that we'll post on our website for people interested in learning how to use software, various software approaches, various -- you know, if you want to see how we do sequencing or, we do sequencing, how we do the analysis.

We're even going to enlist NCBI and have them do a little video on how to use their software and how the database works.

In addition to that, we're going to continue to look at expanding partnerships, both domestically and internationally, particularly internationally because as Jorgen correctly points out, we import a lot of our food.

We're going to work very -- continue to work very hard on adding partners to the contribution of the -- contribution to the database. This has really been a huge effort on our part, to get people to contribute to the database.

We've been to WHO. We're going to FAO in

the fall, trying to establish partnerships with international organizations and governments and academia to raise awareness about submitting samples and the fact that we all get our food from around the world. We live in a global food commodity system.

And so if we have an outbreak in the United States, and it comes from an import, there's a good likelihood that someone else is importing the same food and their citizens may be getting ill as well, so how we approach that issue.

And then we will continue to try and develop software solutions that are available free of charge, and maintain our relationship with NCBI, because that's also free of charge.

It's expensive to set up these computer systems, and it's really nice to have a partner like NCBI that doesn't charge us for all of the computing and all of the data analysis, and all of the software development that they do.

And, you know, I would encourage you, if you have a lot of information and you want to talk to them, they're a great group of people to talk to

about, I'd really like to see a tool like this, I'd really like to see this in my data stream.

They have all the data and the ability to look at it. So I think that's something we will continue to pursue. So that's probably enough for me.

MS. WAGNER: Okay.

DR. SAMADPOUR: You know, from what I see in the field, we have different types of events that can impact a food company. So we have investigation for cause. This is when epidemiological data indicate that a company may be linked to an outbreak.

So by the time they are contacted, CDC has done a lot of work. They have established -- state health departments and CDC have established a linkage. They called FSIS. Then FSIS or FDA, depending on the industry, will get involved. And they have to go and do now their own internal investigation as to why this thing has happened.

And in that scenario, next-generation sequencing is a tool that was used in the beginning of the process, maybe to make the connection. But

what the regulatory agencies need to do to establish better protocols for communication, to be able to give them the data, answer the questions.

And in my experience, they have been very good, actually, in situations that we have been involved. There are phone calls, you know, we request records. They are immediately supplied, provided. And there is some level of delay once in a while because labs are behind or, you know, there is not enough resource to process some samples.

But from a point of view of what the industry or what regulators should be doing is better communication at that level, and a lot of it is already there.

Then you go to situations where, you know, you are doing your food safety assessment, or FDA is sending a team to look at a food safety system that may or may not include taking samples, and other sorts of samples, there is a level of delay in that regard, that sometimes samples are taken, products have to go on hold. There is a delay that could cause and does cause economic harm.

So some level of coordination that labs are in the loop and they are going to give a positive or negative result in couple of days, an expedited way of dealing with this to prevent economic damage, that's going to be essential.

Under what protocols will you go in and start taking samples? Because the moment you go in during production and take samples, they have to go on hold. They cannot release products.

Now, if it's peanut butter, you know, it lasts for like 10,000 years. Many of the people have products with shelf life of 14 to 17 days. In that case, you know, there's a lot of economic damage that can be done.

So more sensitivity in that part is really important, and established protocols. How do we go there? How do we collect the samples? What type of samples will we take? Would it impact the industry, and do they have to go on hold? And if they are going to go on hold, what are the protocols for giving them the results much faster?

After that, not much has changed. We used

to, you know, use PFGE to make the connections and look at our databases and stuff like that. And now you're using whole genome sequencing, which is actually better, because of the more specificity. So false clustering is not going to happen as much as we had it before.

So, again, better communications and some better protocols as, you know, when you know that you are going to impact them in terms of products on hold and stuff like that.

DR. WIEDMANN: Maybe three sort of hopefully pretty quick ideas. I think one of them is more clarity around when, where and how whole genome sequencing and next-generation sequencing data are used to define unhygienic conditions.

We talked about harborage, but harborage doesn't -- one could argue it doesn't always mean unhygienic conditions. Mansour threw us a curve ball with, you know, it's introduced, and it survives over 2 to 3 years.

Some people could argue survival over 2 years indicates unhygienic conditions because you

haven't got a system in place that eliminates it that quickly. Some people might argue otherwise.

In some facilities, some might argue that constant reintroduction, if you have a ready-to-eat facility that produces under what should be very high levels of hygiene, might be a problem, per se.

So how do we define that across different industry, different facilities?

Number two, and more specific for FSIS is really -- and I think it was mentioned multiple times, can we come up with a performance standard that's not percent positive carcasses or percent positive samples but is adjusted for public health potential in *Salmonella*, and use that to manage *Salmonella* more?

And one thing that hasn't been mentioned that I think we're going to need at some point is, can we move towards a risk assessment that looks at presence of genes in a food sample, or presence of genes in a commensal organism, a non-pathogen, obviously a specifically antimicrobial resistance gene.

If I find an exotic antimicrobial resistance gene that would have huge potential to cause drug-resistant infections in a food a gene, I don't know, is it a live or dead organism, what do I do what that food? Is it a public health hazard? How do I react?

What if I find a commensal that has one of these antimicrobial resistance genes? It's not a pathogen; what's the public health risk associated with that? How do we deal with it?

These data are going to be created, intentionally or as a byproduct, as we do metagenomics, etc. Once we have these data, how do we react on them?

Industry is going to need guidance. Regulator is going to need guidance. And I don't think we want to make those decisions ad hoc for the first time we find a bunch of hits for an antimicrobial resistance gene in a metagenomics sequence.

DR. WHEELER: I think I would have to say that we definitely need a little more clarity in

developing the policies and -- that are going to come around, how exactly whole genome sequencing is going to be applied, and communicate that clearly.

And along with that is, you know, how to address, you know, some of the issues such as what -- some of the shortcomings, such as long-read and short-read, and what does that really mean, and what is that information that you're not getting, and how does that reflect on how you interpret that data?

I think there's questions about, across the system that we need to address relative to how much variation do we see. And, you know, several comments have been made about there's -- you really can't set a specific cutoff for what's the same and what's different but -- and clearly that's going to vary among organisms, but more clearly, how is that going to be addressed in the policies, going forward, I think need to be defined.

DR. WIEDMANN: We need a consumer communication strategy around whole genome sequencing, all aspects of it, because otherwise we're not going to be able to utilize it fully. It's

going to be the next GMO. Maybe we have a great tool that we can't use.

MS. COFFMAN: Thank you. I thought I had already hit on that, but yes, absolutely. So yes, let's get the messaging right about the science.

DR. MUSSER: So I just want to follow up on something I -- that Jennifer reminded me of this morning in her talk, and that is that, at least in FDA, and I'm certain FSIS, when we do an inspection of your facility, or we have any kind of regulatory or other communication with you as an industry, you have a right to that data. And moreover, you have a right to understand what the data means.

So I encourage you always to please contact us if you have questions about this. If you get a letter from us, or you get a communication from an inspector and you don't understand it, don't go away and say oh, I just feel, you know, particularly impugned by this and I don't know what to do.

It's our responsibility to make sure that you understand this. And believe me, we really do want to work with you in understanding what this

information means and how you can apply it to make food safe, because at the end of the day, you're in business to provide a safe product for your consumers, and we're, we have the same concern. We want to have you producing safe food.

So we're in this together, and we would, want to make sure that you understand all of the information.

DR. SAMADPOUR: This is a very important point that a lot of members of the industry don't understand that they can have a conference call with FSIS, with CFSAN, by just asking the district, during emergencies.

And when I tell them that, they kind of think that they have to go and, you know, okay, so how do we do that? Do we have to hire attorneys to do that for us? It's a matter of just calling the district and asking for it.

And I think the more you guys advertise that, that you know, you are available during all these crisis and emergencies to them, I think that's a very valuable resource.

MS. WAGNER: Yeah. I mean, I -- two points I want to make for the FSIS piece. Obviously, if -- and the establishments that are under our jurisdiction understand this, but if they don't understand, don't agree with anything that's happening out there relative to our inspectors, we have an appeals process. So it just works its way up through the system. So you can use that.

And what we've been doing during outbreak investigations is we have been having -- usually in the FSIS world, if a food's implicated we have to have a -- we go to a recall committee. But we'll usually have, we've been having pre-conversations with the industry just -- and actually, very early conversations when we might have an implicated food product, but we really don't have a common source yet, it's kind of going in a couple of directions.

You know, we're having conversations with those folks before we even, you know, move into any other conversations, so --

And during the -- we have -- industry was in recently, and we -- they said, you know, sometimes

we have data that kind of refutes what you're saying. And we said, we want to see it. Give it to us. Explain it to us. We will take that under consideration.

So we are having -- we have pretty open discussions, and very fluid discussions when we're going through these situations, where we're trying to implicate a food with illness.

DR. McENTIRE: Roberta, if I can just add a -- Steve, I appreciate your comments and your offer, and I have found, over the past couple of years, a better relationship with FDA, and in particular, in embarking on these conversations and having that open line of communication.

I think, from the industry, individual members who see FDA so infrequently -- which is in contrast to FSIS -- you know, FDA-regulated industry rarely is inspected, doesn't have that expectation of an open line of communication with the Agency.

So I think that it's very intimidating when anyone from the Agency shows up. So there's a natural reluctance and fear to question that person,

that I don't think is a reflection on the willingness of FDA to have that conversation. I think it's just kind of the environment in which the community's been raised.

And so I do view part of my role as an association representative as serving as a liaison. I know my other association colleagues try to provide that same service to their members, to facilitate that discussion and with the hopes that eventually I can take myself out of it because the relationship has been established.

But I don't think we're quite there yet, but I certainly appreciate the, you know, the willingness of FDA, and certainly FSIS as well, to have that conversation with regulated industry.

MS. WAGNER: But I would also add -- I mean, and I know this happened on the FDA side as well as the FSIS side, we often have CDC at the table because we usually go over the epi data with the establishments as well. And they created and generated the epi data, so who best to speak to it?

So, you know, I think that's a real -- I've

been around for a long time, and that's a real change over the last 5, 6 years, you know, really bringing CDC to the table to explain their part of the puzzle rather than us speaking for them during these meetings. So --

DR. GOLDMAN: I guess I should say something since you asked about what the regulatory agencies need to do.

I think it's been very clear in this meeting, and certainly FSIS has had almost a dozen opportunities at smaller venues, usually trade association meetings, to hear from the industry, very clearly, that unless there's a safe harbor, and unless we surmount these regulatory legal issues, the conversation's going to have a premature end.

And I think we just have to acknowledge that. I mean, it's been said here clearly. And I think the burden is really on FSIS to forge a way forward there.

I think that we have, we've been struck with the allure of the fact that the industry does orders of magnitude more testing than FSIS does, and

probably many more orders of magnitude than FDA-regulated -- or FDA does.

And so, you know, we've said, you know, we'd like to see your data, or give us your data, or at least, at the very least, send it to the NCBI database. Well, it's not quite that easy, and I think we hear clearly that it's not that simple. So we have to somehow get past that. And we need to do some work on our side to do that, I believe.

DR. BESSER: I would just like to say, repeat what I said yesterday, that we actually did, have created a safe harbor for exactly this reason, which is a Voluntary.net at the University of Georgia. And a lot of the intricacies of maintaining this firewall with all the FOIA laws and all the other laws, have been worked out already.

So at a minimum, this can be used as a model. And there's several large food producers involved in Voluntary.net. Many industry members are nervous about, how strong is this firewall; are we really protected? But several large food producers are very adamant that they find this an incredibly

useful tool for assessing the risk of their findings.

So if there's a possibility that their products are making people sick, they want to know quickly, to stamp out the problem before it becomes a big issue.

And so I think what we have is a cultural problem, or an education problem, or a trust problem. But I think the mechanisms are there, and at a minimum, we have a model that we can always work on.

MS. COFFMAN: So then I have a question for the industry stakeholders. What does need to be done to make other people upload their data into this protected safe harbor? You know, consumer groups have been asking for data around antimicrobial resistance. We get met with so much pushback. But if it's beneficial to you, why not use it, and what are the reasons? And what can we do about it?

MS. WAGNER: I'll let the industry folks can answer that.

DR. McENTIRE: I think that, in large part, it is getting the attorneys involved and understanding how strong is that firewall, having

that trust established, having case studies, perhaps, of where industry has voluntarily uploaded their data and has not suffered adverse consequences, has not been penalized, case studies where it's been demonstrated to be beneficial to the company itself.

I think right now it's viewed as very one-sided. We see the benefit to the agencies, but it's less clear how a company would directly benefit. And so I think that it's -- in having some early adopters move forward and be willing to share their stories, and have their attorneys support those stories, that that'll probably be what I perceive it will take to evolve to that state.

DR. BESSER: I would be happy to provide the names of the early adopters, but I think I'm going to ask their permission first.

DR. SAMADPOUR: I think the drive -- there are two different things. One is that there are food companies that want to have a place to send their samples to get the subtyping results, to see whether they have harborage in their space or not, in their food production facility. And I think that was the

main driver for Voluntary.net, and then to start having a larger database and then see how things are moving.

What the other utility is, I have what I know to be a harborage situation, or repeatedly I see the same organism. At that point, one of the concerns that maybe your client has is, is this thing, has it made anyone sick? What kind of situation are we in?

In that case, there are two options. One is, you know, to give it to someone who has a portal to do the work and upload. The other one is to -- that there are several companies that can get the isolate, do the whole genome sequencing and download the Listerias, and then do a comparison.

So that venue is also available, for these two different types of cases.

MS. WAGNER: So then it's really, it's the laboratories uploading the sequences. So you don't know which establishment --

DR. SAMADPOUR: Yeah. So you don't necessarily need to put the client's strain --

MS. WAGNER: Yeah. No. You have the lab --

DR. SAMADPOUR: -- there. You bring in the CDC data, the human strains, and then you do your comparison, if you have the --

DR. WHEELER: I think one of the direct benefits to the companies is potentially that by populating the database and getting more isolates in there, we start to learn what we don't yet know, which is how much variation in sequence is there out there in certain products, and how often do we see a individual sequence around in different places and over time and space.

And once we get that kind of information established, then it becomes more clear how definitely you can make attribution. Because we've heard a lot of talk today and yesterday about how, you know, you have ranches, and you have feed lots, and you have processing plants, and they have a lot of the -- plants have a lot of the same sources of animals.

And if there are specific sequences that

are coming from locations to multiple places, then you potentially -- and we have some preliminary data that demonstrates that, that you're going to see the same sequence in multiple places over time and space.

And so then it becomes less risky for you to have your sequences in the database and contribute to the learning process when it becomes more and more clear that a single isolate isn't necessarily going to have specific risk, or as much risk.

DR. WIEDMANN: I think there are two ideas of safe harbor. One of them is Volunteer Net. I want to be able to search CDC database. I have a zone 3 positive. I know my distribution path. I want to know whether that organism caused disease cases that are consistent with the distribution at the time of contamination I have.

That's there. That can be done. I'm not sure the human data are accurate enough that I can ask. My distribution is these three states. Can I map, with time, that there were cases over the last 6 months? If there is, then that's really all that is needed.

The second one is for industry to know, if they do subtyping, whole genome sequencing, that they know that they're not going to be forced, through some mechanism or another, to turn those data over. And then, you know, FDA, FSIS, whoever, is going to analyze them and then prove something to them that they don't want to see and use the data for something they were not generated for.

So those are both, you know, fall under the definition of safe harbor, potentially, but they're slightly, or maybe very, very different types of requests.

I think what Tommy said, and the challenge there is that industry's worried about that if industry acts, let's say, produce processor put all the data in there and then there's a match, how do we know the match is the produce, not the cows that were, you know, grazing next to the produce?

And whoever populates the database first, or with more data, is more likely going to be implicated. So no one's going to want to start, unless we put a baseline in there with everything

across at a high level, that people are comfortable with.

DR. MUSSER: So maybe a bit of history here. We -- when we first started doing sequencing, the first people we approached to add data to the databases was industry. We reached out to a number of the larger industry partners that we have, and they all said no.

We didn't immediately understand why that was, but a lot of it's based in law and what they're required to do. So, for example, most of our industry doesn't test for *Lm* at their facilities. They test for *Listeria* species, because if they test for *Lm*, and they have -- obviously, if they're sequencing and they note more than it's just *Lm*, that they probably -- that there's a reporting requirement for that.

Likewise, if they've gotten something in a product, and it's positive for a pathogen, you know, they're -- there's a recall and a reporting burden on that.

And so that's the -- there's the legal

issue. And then the other issue, which I think is probably more overriding for the regulated industry, at least for FDA, is civil litigation.

So everything is fine, well and good when you're dealing with the regulatory agency. You know, you might get a letter, or you might have to do some cleanup. You might have to do a recall, which no one wants to do. But really no one wants the civil litigation problem, because with civil litigation, everything is discoverable.

When did you know it? What did you record? Who did you give it to? And if it went Voluntary.net, I can guarantee you that all of that will be subpoenaed. There will be no safety; there will be no firewall. We've looked into this.

If there is an outbreak where people are injured and there's civil litigation, it's all discoverable. So it's a when you knew it and what you did about it problem. And this has been the fundamental problem with industry uploading data.

There's a number of other very positive things that industry has done with this, but the fear

about uploading sequences is, what happens if someone gets sick and it's linked to the sequence and I get drawn into civil litigation.

DR. SAMADPOUR: A couple of points here. One is that there is another use in situation where the industry may want to actually put this strain in. And when they are about to make a decision themselves as to the extent of a recall, then the pathogen has been discovered in product that is in chain of commerce.

There is a lot of value to be able to go in and see if you have matches to, you know, historical matches. And that could make a difference between recalling a month of the product versus, you know, a year and a half of the product. So that's something that I could see as a kind of a, you know, need that can be addressed.

The other thing is that sometimes we read too much into whether there is one base difference or five or ten. The mechanism is what's important. There is a biological clock. And then Martin kind of started talking about that.

It's really, is a function of how many times these things are multiplying, how many generation times they have had, how many replication cycles they have had. And that's what we are measuring. And that's what determines the number of mistakes that -- or changes that we are detecting.

And so you cannot really look at these things in absentia. You can have a same strain going to 10 places. In one place it is highly evolving; it's growing. It's a very good environment. You are going to find a lot of differences. And that place is going to have the huge problems that we may not find because, guess what, there are like more SNP differences that we thought, right.

And in another place, if it's immobilized and it's not growing, then it's going to be an exact match, and they may get into trouble. So just, we should not lose sight of the molecular basis of these changes that we are seeing.

MS. WAGNER: You know, the one thing I was thinking, you know, and some of the work we want to do is really around the product and the environment.

And I think folks are very nervous about putting that in with the clinical data.

So just thinking about, is there a way that certain of that data could be separated? Because I think that's the real issue here. It is. I don't really have a problem if you're -- you know, I'm doing my sampling, I'm, you know, implementing my environmental sampling programs, or product testing programs.

That's not the issue. I want to know where is it going, how is it moving through this -- those -- it's when it -- you put it in combination with that clinical sequencing data that it becomes a problem.

So maybe we need to think about, is there something we can do around -- you know, just so we can build up the database and we can do some trending. The industry could actually use the data. We could use the data. So --

I mean, the illness piece is the critical piece, I get. But maybe that's -- if we want to think about it, maybe that's the piece. Is there a

way to disconnect that in some instances? That's all I'm saying.

DR. BESSER: I just want to clarify a few things. I don't know all the details of how Voluntary.net works, but my understanding is, is that the data is anonymized before it gets into the database. Actually, the manager of Voluntary.net does not have access to that data. Therefore, it cannot be what you -- if it was subpoenaed, they'd get anonymized data.

If -- the CDC can ask for permission to see if there's any matches. They can say yes, there's a match. The database manager then sends a message to the entire contributors to Voluntary.net and said, whoever had Isolate ABC, if you would like CDC to have permission to see that strain, contact me.

So it's -- the manager actually doesn't even have access to that information, if I understand it correctly. And also, the database manager at Voluntary.net has access to the full data of PulseNet, not that minimum dataset that you've seen, so the clinical data, the dates, the states, not the

patient identifying information.

And the last piece I wanted to say is that we've seen a slide quite a bit that suggests that where we want to go to is detecting outbreaks before they occur. And in order to do that -- well first of all, there's only a subset of outbreaks where that's possible, and those are the outbreaks where we are aware, there are vehicles that we're aware of causing problems.

Probably a lot of the vehicles out there causing problems are unrecognized at this point. And so we're always going to have a tremendous number of outbreaks with new vehicles. And, you know, just the last year, the last 2 years, the list is very long with new vehicles.

But even among those vehicles that we recognize, I think the only way to have data in advance of human cases is to have the information from industry and all the regulatory agencies. I don't see any other way to achieve this goal of detecting outbreaks before they occur.

DR. SCHLUNDT: Could I add? I understand

that I'm in the U.S., but surely this must also be about protecting consumers. I mean, we've only been -- consumers. We are basically only talking about protecting the industry here. I thought that this was, the basic purpose was to protect consumers, avoid consumers, American consumers and other consumers from dying from eating food.

There must be something there. I realize this, that if a good industry starts putting something up, they will be punished, and that's not a good thing. But that could be solved, for instance, by government saying that you have to do something.

Now, I know that's not always the way you do in the U.S., but still, you can actually learn things from other countries, even in the U.S., I think. So that's the first thing.

The other thing is, now we are only talking about outbreaks. Outbreaks are only accounting for maybe 5 to 10% of all the disease burden. So if we are talking about protecting consumers from dying from eating the normal food, we should also talk about the sporadic cases, which whole genome

sequencing will really also give us something to do, to actually prevent these diseases in the future if we really want to.

So I think you're -- there needs to be some sort of high-level discussion, and at some stage, political level have to be involved, because all of you in regulatory agencies here, you will refer to the law as it is now, but politicians in the end will say, we want to protect the consumers, I think.

And if they see a new opportunity -- and this is a new opportunity -- I think that they will also act on that at some stage. So then we are back to being able to explain this is simple language, not because politicians are stupid but because we tend to always use too many words, like I just did.

DR. SAMADPOUR: Okay. If I'm -- I may be able to answer that issue. If you look at the mechanism where we have pathogens, pathogens come from pathogen testing programs, and when they are for products, it's always test and hold, meaning product is under hold, and we do the testing.

And if we find the pathogen, the product is

diverted to a safe end, which is a landfill or cooked, in terms of if it is beef product. So from that point of view, product is -- consumer is protected.

Jennifer here said, not always. There are always exceptions. We are still finding Darwinism at work in some segments of food industry, which we say, okay, what happened? Oh. I released my product and I sent a sample to be tested for pathogens. And again, that's a situation where, by law, they have to call FDA or FSIS, let them know, and they're going to have an immediate recall.

So we are not talking about these. Any pathogen event will protect -- or pathogen detection event results in protecting consumers, or people will go to jail.

We are talking about different. The fear is, if I do my routine pathogen testing and give this strain, or put it on this database, someone is going to say well, I find a match 5 years ago. How to deal with that, that is really the holdup.

But from every other aspect of the work,

consumers are protected because pathogen testing results in -- they're compelled to let the government know if the product is not under their control.

DR. SCHLUNDT: Yeah, but pathogen testing doesn't work. We know that.

DR. SAMADPOUR: And -- but your -- if you don't have pathogen testing, then you don't have anything to put on this database anyway. Correct?

DR. SCHLUNDT: No. The issue is, we will not solve the food safety problems by end-product testing or product testing in the line because then we would have to test everything.

When we have low -- I mean, they -- I mean, we have tons of papers about that. So we are not solving things by testing food. I mean, you have to go Havelaar et al. and all these other papers. This is not helping.

DR. SAMADPOUR: It's a catch-22. You have to have a pathogen to do whole genome sequencing, and put it on that database. That comes from this pathogen testing that, in your words, is not working. But everything else is a dream. I mean, food safety

is not done through pathogen testing. Food testing is through validated processes. Pathogen testing is verification that we do to verify that everything happened the way it did, correct?

But you are not going to be able to put anything in that database if we haven't done the pathogen testing, despite the fact that pathogen testing, in itself, may not make food safe. It's not its function.

DR. SCHLUNDT: Yeah. But the point is, you will populate the database by doing strategic testing by smart people here in the agencies saying, how many strains do we need from each production in here. That's sensible, smart testing instead of stupid testing.

DR. SAMADPOUR: The agencies, FSIS has their own surveillance. FDA has their own surveillance programs. There is not enough budget to do that, and there are times that they were doing things, and the industry got together, and they got rid of the program, which is -- what was it? The Leafy Green, correct?

That's a FDA program that was looking at market surveying and trying to establish a base, and that was taken away because the budget was taken away. It became a political issue.

MS. WAGNER: Yeah --

MS. COFFMAN: So --

MS. WAGNER: Go ahead.

MS. COFFMAN: Well, I wanted to jump off a point that my friend from Singapore made. We don't have enough clinical testing, and that is also another stakeholder that's missing from the panel today.

You know, if people are getting sick and they're going to see their doctor, which we all know is a small proportion of people that do, are they going to be tested, and is that going to be done by whole genome sequencing, which can then be uploaded into a database?

MS. WAGNER: I can tell you I recently went to the doctor for a foodborne outbreak illness, and they gave me the kit. And I was like, you have got to be kidding. That's all I have to say. I felt

horrible, and I was like, I am not doing that.

But anyway, I mean, the one point I want to make, too, is industry does a lot of testing, end product testing, on the FSIS side, you know. I'm not sure what's going on with the FDA side now. But end product testing and environmental testing, and they do it voluntarily, quite frankly.

So the one thing I wouldn't want to happen is if we went to the politicians and we basically regulatorily forced them to provide testing records if they were testing, because they won't test. I mean, that's reality. So you kind of have this fine balance going on as well.

DR. McENTIRE: I just wanted to note, to put things in perspective, that as we look at the burden of foodborne illness in the United States, I think we go a long ways by encouraging people to wash their hands.

You know, it's -- the majority -- we're talking like all foodborne illness is because of production, because of farming operations and processing facilities. And we know that, in

actuality, that is not the case.

So even if we can impact food contamination at the point of production, that still, that does not, that will not address all foodborne illness.

DR. BESSER: You know, it was brought here what the definition of an outbreak. I think it's a really interesting question now. I think we're stretching the definition of an outbreak. The data shows that 5% of cases in the United States are outbreak-associated. 95% of cases are sporadic cases.

I think if we redefine an outbreak, and perhaps in nicer terms, as something that we could do something about, be it chronic contamination being in a true epidemiological point source, I think it would be the other way around. It would be 95%, some of which is washing hands, but a large proportion of which is things that we can control.

We can't control, you know, how people wash their hands so much, but we can control the flaws in the industrial food production system. That's something we can do. And probably, a large burden of

our illness is due to things that we can do something about.

And so I think that this process, investigating outbreaks which are events or realizations that there's a cluster of diseases, can take us a long way towards the ultimate goal, which is protecting consumers, which is exactly what you're after.

So I think, every gram of food that's consumed in the United States is tested, because it's consumed.

MS. WAGNER: Okay. I'm --

DR. BESSER: It just doesn't skip up the --

MS. WAGNER: I'm getting the evil eye up here, so I think -- thanks a lot. Great conversation. I hope the folks in the audience enjoyed this as well. I know I got a lot out of it. So thank you so much.

(Applause.)

DR. SHAW: Yes. Thank you to our panelists. And now we have -- we're moving into our public comment period. And so if there are folks in

the audience that want to make a public comment, we have the two microphones in the audience.

And then also, I just want to remind everything -- you know, if you haven't been to a public meeting in a while, there is also an opportunity to make written comments. So, you know, we had a *Federal Register* notice that announced this meeting. You know, comments can be submitted in a written format, too.

And our first, Betsy.

DR. BOOREN: Hi. Good afternoon. Betsy --

DR. SHAW: Oh, and as Betsy, who knows the drill, name and organization before you start speaking.

DR. BOOREN: Great, thank you. Betsy Booren, OFW Law.

I think -- you know, as I look at the title of this public meeting, and we're trying to improve public health and food safety, I think one component here, and I'm going to quote Dr. Goldman, we know what we know, but we know -- we know we now know not a lot. Somewhat -- I think that's sort of what David

said.

The point that I'm getting to is, Americans get food in a variety of different ways, and they're getting food increasingly in ways that our distribution chain is struggling with. I'm talking e-commerce. I'm talking this technology and the amount of food prepared in retail stores and restaurants.

And so one of the discussions that has not occurred in this meeting, and it's probably not appropriate for this meeting, but I want to put on the record is, as we evolve and have these continued conversations about improving public safety using this tool, I think that is a very important part on determining where contamination comes from and how it contaminates food.

We've all talked about, it's coming from food-producing facilities that are putting product into commerce. We are getting food in new and different ways, and what does that mean? What does it mean for e-commerce? What does it mean for food kits? And that also stretches our boundaries with

who regulates that food at a federal, state, and local level.

And I think that's a really important thing that we need to capture in this discussion. We're a little premature now, but as we move forward, that's increasingly going to be a very important part of ultimately having a measurable effect on public health.

DR. SHAW: And then I also just wanted to make a comment. Those of you who are attending the meeting online, you can make a comment. You know, on the online version we will capture that. But make sure you include your name and the organization, and so we can have that for the public record.

Any other public comments in the room?

MR. ROACH: Yes. I'm Steve Roach from Food Animal Concerns Trust. And I really appreciated these 2 days of meetings, and actually coming on the back of the NARMS meetings as well, both. I found I've learned a whole lot from this, with -- I work with a consumer organization, and we're trying to understand what whole genome sequencing means for us.

One of the things -- I did want to make a couple of points about things that I -- have been touched on, but probably maybe we'd like to lift up a little bit.

I think probably for us, one of the most important things is starting to talk about source attribution. And so that could be -- source attribution, so what -- so how do we find attribution of the clinical isolates? Where are they coming from? What food sources are they coming from?

But I also think source attribution, the representative from Cargill talked about oh, well it may not be harbored in the plant, but it maybe bring -- being -- come into the plant from similar sources.

From our perspective, as the end consumer of the product, it's just as bad if it's harbored on the farm as it's in the plant if it eventually comes to us. So I think it's, how do we actually address some of those before we get to the plant, particularly with the meat side, which is what my organization is concerned with.

So source attribution, as something that a plant could help, okay, you know, we know this set of farms is causing problems. And then once we know there's a problem we can try to manage it a little bit.

Another thing that we're interested is in identifying emerging resistance. And I think this tool will be very helpful for that. We don't know where we're going in the world with resistance. Hopefully we won't have routine *mcr-1*. It'll stay at these really micro levels. But I think it's something that we can use these tools to look for.

And the final concept that I thought was important, this idea of redefining what is an adulterant. I think that is correct, because what we want to do is -- and for risk management, you want to find the bad things, the real hazards, and not get them confused with things that aren't hazards.

But I would say, you know, there may be cases where we need to define new things as hazards. So -- and I think we need to talk about it. What do we think about *mcr-1* in food? And *mcr-1* in *E. coli*,

it's a non-pathogenic *E. coli*, but it could easily pass it on to a pathogenic *E. coli*. And the CREs are another area.

And I don't have an answer to that. And I don't know what I would tell a plant if you find *mcr-1* or CRE *E. coli* in your, you know, in your processing. What do you do? I think it's something we really need to talk about. Or a farm, if you have a farm and you find large numbers of your animals may end up having these.

I think there -- the Ohio farm that found the -- I think it was a CRE, they had quite a few animals that actually contained it. So I think, what do we do about these, is a conversation we need to have.

DR. SHAW: Any other public comment?

(No response.)

DR. SHAW: With that, I think, you know, I'm going to turn thing over to Uday to sort of wrap up for us.

DR. DESSAI: Thank you, Bill.

Okay. So it looks like it's over, but it's

not quite over, because this is just the beginning. This is the beginning. This is the beginning of the dialogue on that continuum that Dr. David Goldman was talking about.

So what we heard today, it's rich information over the last 2 days -- actually, last 4 days, NARMS and now WGS. And I think we have a lot to process.

We made good notes of all the points that we received, candid points, very, very honest points, and we'll be working on those, and working with you on those, because we want this open dialogue to continue through this continuum, because just like one of the presenters said, PFGE was just the chapter length, whereas WGS is reading ever letter.

So when you read every letter, there is too much information. And digesting that information, making it palatable, communicating it and saying what it means is very important. We have long ways to go with that process.

Now, it's needless to say that technology is moving extremely fast. This wasn't there 10 years

ago. Today it's in my hand, and we do such high-level processing in this. So don't be too surprised that whole genome sequencing could be easily manageable in the next 5 to 10 years.

So before I proceed to one of those slides, let me thank everybody who participated in the meetings. Those of you who flew from overseas and never got a wink, actually, really thank you. And our Gen-FS partners who decided that this is a good idea to share the stage with FSIS in doing this, thank you all.

And last but not the least, but everybody who came here, as well as those online, really, thank you very much. I think there is a lot that we learned in this meeting.

You will get -- I think Bill said, you will get an opportunity to submit your comments, and have conversations if you need to. And all the transcripts which are being made, those will be available to you at, in due course of time.

Particularly the staff in Policy, Field Operations, as well as Public Health Science will be

looking at those comments, and we will do our best to capture those high points from today's discussion.

Now, the NARMS meeting which happened 2 days ago was -- actually, our Secretary came to basically tell his message to the NARMS people.

For this meeting, Under Secretary for Food Safety came to open the meeting. We also have our Administrator here to close the meeting in a little bit.

But before that, let me take you to a quick slide to put things in perspective. And that is, like David Goldman said, learning, small goals, applications is where we are today. And basically, we rely more on -- and less investigation. That's what you heard a whole lot about it, and that application and prevention, we are talking about.

But think of that circle there. A lot of things need to be done before we kind of reverse the process. And more application and prevention will be our focus as we go through these 2020 through 2030 Healthy People objectives.

And a lot of big goals can be set maybe in

the next whatever number of years. That's why I have the questions over there. And what will happen is, more data, more tools, more analytics, more risk assessments, which are required, as well as more guidance, regulations, all that will happen with collaboration.

Collaboration, I think, is a key for the success of whole genome sequencing, for us to get right down there where the foodborne illness is. If I take an example of FSIS, we have about 325,000 salmonellosis to contain in -- annually, until we reached 2013. And depending upon what we achieve, we'll have our next target.

But the bottom line is, we have a lot of work to do. And the success will come out of collaborations.

So thank you again, and over to our Administrator, Paul Kiecker.

MR. KIECKER: So I know that everyone's in a hurry and getting ready to go, so I won't take a whole lot of your time.

For those of you that don't know, my name's

Paul Kiecker. I'm the Acting Administrator for FSIS, and I want to really thank everyone for showing up and participating in the meeting today.

I think that it's obvious that FSIS is dedicated to modernizing the methods and strategies to protect the nation's food supply. The Agency's position to address the 21st century's public health challenges by building on prior successes, leveraging our collaboration with partners, including those that are here today, so we can proactively ensure that food products we regulate remain safe to eat.

We have made great strides in implementing whole genome sequencing at our labs, and FSIS is already conducting whole genome sequencing on all isolates that are regulatory samples that are collected.

The results from our whole genome sequencing will help us by characterizing bacterial genomes with greater precision than ever before. That will help us accurately identify and respond to outbreaks, conduct efficient tracebacks, study environmental harborage and the movement of pathogens

within establishments.

We also want to make sure that we are considering -- that we are coordinating with others in the scientific and regulatory community in developing and using this technology.

When developing and implementing and interpreting whole genome sequencing, we have been and will continue to work closely with FDA, CDC, NCBI to ensure standardized laboratory methods, analytical pipelines and communications regarding whole genome sequencing.

As you have heard over these last 2 days, FSIS has many food safety initiatives underway to meet our regulatory objective and ensure food safety.

I want to make a special -- say a special thank you to anyone that has participated in the meeting, people that were on the panel, people that presented information here, anyone that was involved in setting it up. And I think we should give them all a round of applause.

(Applause.)

MR. KIECKER: Once again, thank you all for coming. Have a safe trip back. Thank you.

(Applause.)

(Whereupon, at 3:54 p.m., the meeting was concluded.)

C E R T I F I C A T E

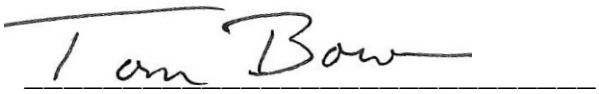
This is to certify that the attached proceedings in the matter of:

USE OF WHOLE GENOME SEQUENCE (WGS) ANALYSIS TO IMPROVE FOOD SAFETY AND PUBLIC HEALTH

Washington, D.C.

October 27, 2017

were held as herein appears, and that this is the original transcription thereof for the files of the U.S. Department of Agriculture.



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