COCA Conference Call – *E. coli* O157:H7 Outbreak
September 21, 2006
Patricia Griffin, MD; Karl Klontz, MD; Phillip Tarr, MD

Coordinator: Thank you all for holding and welcome to the *E.coli* outbreak update. All parties will be in a listen-only mode. Today's call is being recorded. The replay number for today's call is 888-566-0619 and will be available once the call is over and it will available until October 5. I will now turn the call over to Dr. Diana Hadzibegovic; thank you ma'am, you may begin.

Diana Hadzibegovic: Thank you, Laurie. Good afternoon. Thank you for joining us for today's special Clinician Outreach and Communication Activity conference call. This is a special COCA conference call and we will be talking about the current of *E.coli* O157:H7 outbreak related to fresh spinach. The purpose of the call will be to discuss CDC guidance for clinicians working directly with patients. We will not be providing a full account of the investigation or the outbreak. For that information, we'll refer listeners to the FDA and CDC Web site. We are pleased to have Dr. Patricia Griffin, Dr. Karl Klontz and Dr. Phil Tarr today on the call to discuss this issue. Dr. Patricia Griffin joined us from CDC. She is an internist. Dr. Griffin has supervised epidemiological investigation throughout the United States and overseas. She has authored and co-authored many journal articles. Dr. Klontz has been with FDA from 1989 where he has working as an epidemiologist for the Center for Food Safety and Applied Nutrition. Dr. Tarr is from the Washington University School of Medicine. He is the author of many publications on *E.coli* infections.

Dr. Klontz will be presenting an overview of the *E.coli* O157:H7 outbreak and FDA's role, Dr. Griffin will be providing CDC guidance for diagnosis, testing, treatment and follow-up of patient with suspected or confirmed *E.coli* infections and Dr. Tarr will talking about a clinician's perspective on interpreting guidance on treatment of *E.coli* O157:H7. We are pleased to have this presentation today. Dr. Klontz, you may begin.

Karl Klontz: Okay. Thank you very much. Good afternoon.

My mission is twofold here, first, to present an overview of the current outbreak and second, to discuss briefly FDA's role in investigation of this outbreak. But I'd like to begin by taking a moment just to commend our state and local health departments throughout the country. It's been their Herculean efforts that have allowed us the last week - not only to learn about the outbreak but to pinpoint the cause of the illnesses -- namely fresh spinach consumption.

You know, once again, state and local health departments have shown themselves to be an indispensable backbone of our country's public health system. With that, let me turn to the outbreak itself and specifically how it was recognized.

In early to mid-September, health officials in Wisconsin detected an unusually high number of persons with the recent *E.coli* O157:H7 infection. About the same time, other states were noticing smaller clusters of O157:H7 infections that exhibited a matching pattern on pulse field gel electrophoresis or PFGE -- a DNA fingerprinting technique used to subtype bacteria. The outbreak was formally identified on September 13th by OutbreakNet -- a network of public health epidemiologists who investigate food-borne disease outbreak. It became clear early on from interviews with ill persons that consumption of fresh spinach during the week prior to onset of illness was a feature shared by the vast majority of cases. In fact on September 14 -- one day after the outbreak was formally identified -- fresh spinach was implicated as the cause of the outbreak. That same day -- September 14 -- CDC issued its first health alert on the outbreak and the US Food and Drug Administration issued a press release advising consumers not to eat any fresh spinach. With the release of these two public notices, the industry and regulatory authorities began a collaborative effort to remove from the market fresh spinach and products contain fresh spinach.

Another outbreak feature that became apparent early on with the virulence of the outbreak strain, as of Sept 15 for example, of the 94 cases that had been reported by that date, almost a third had been hospitalized and 15% had hemolytic uremic syndrome. Let me now summarize then the overall outbreak covering its time, place, and person features. Now, the number I'll report will obtain from CDC's latest daily update compiled at 1 pm Eastern Standard Time yesterday, September 20. CDC will issue its next update later this afternoon and can be accessed on its Web site -- a site incidentally that offers a wide range of valuable information pertaining not only to the outbreak, but to the *E.coli* O157:H7 in general.

As of September 20th then, CDC had received a total 146 reports of infection due to the outbreak strain of *E.coli* O157:H7 in persons whose onset of illness occurred between August 2 and September 9. Cases have been reported from 23 states. Among ill persons, 76 or 52% were hospitalized, 23 or 16% developed HUS and an adult in Wisconsin had died. Cases ranged in age from 1 to 84 years with the median of 27 years and 5% where children under the age of 5 years or so.

As has been the case in many previous food-related outbreaks, most cases have been reported among females and males in the current outbreak, specifically, 103 of 146 cases or 71% are females. The outbreak appears to

have peaked between August 19th and September 5th -- a period during which 93% of the cases had onset of illness. The latest onset date among reported cases is September 9. The two states reporting the most cases are Wisconsin with 40 and Utah with 16.

On September 20th, New Mexico's public health laboratory announced it had isolated the outbreak's strain of *E.coli* O157:H7 from an open package of spinach that came from a refrigerator of a patient who had eaten some of the spinach before becoming ill. The package of spinach that tested positive was Dole baby spinach best if used by August 30. Finally, to complete this overview of the outbreak, I'd like to briefly present other evidence that helped to implicate fresh spinach as the cause.

Using a questionnaire to elicit a detailed history of spinach consumption from cases during the week before onset of illness, most recent tally of these questionnaires indicates the following: 91% of cases reported eating spinach; second, the vast majority -- 94% -- reported eating spinach raw; third, 88% reported eating a pre-packaged spinach product with the vast majority of these indicating the spinach that comes from a bag; and finally, among those who've eaten pre-packaged spinach, 97% reported eating it at home.

At this point, I'd like to briefly discuss the activities of the US Food and Drug Administration has played during the outbreak, and my comments will fall into three categories -- investigation activities, outreach and education efforts, and monitoring of recalls.

Beginning with the investigation activities, from the outset pf learning of the outbreak, FDA has collaborated with CDC and state and local health departments in a number of ways. For example, the agency has participated with CDC and the health departments in daily teleconferences during which the latest details of the outbreak are summarized.

The agency has also collaborated with CDC to design the spinach questionnaire I mentioned earlier, a tool of that has helped us understand the roles spinach has played in this outbreak. Along those lines, the FDA is working with CDC to analyze the data collected in the spinach questionnaires using information such as brand name, date of purchase, UPC code, lot numbers and so on in an effort to identify the source of spinach contamination.

This effort entails conducting so called trace backs of process whereby records are collected sequentially to elucidate the path of product associated with illness to travel from the point of consumer purchase all the way back, ideally, to the production side. At this point, to the best of our knowledge, all

brands of spinach implicated in the outbreak were grown in three counties in the Salinas Valley area of California.

Accordingly, on September 19, a team formed by FDA and the California Department of Health Services, Food and Drug Branch began investigations at nine different farms in the Greater Salinas Valley area.

Finally, in terms of investigation activities, FDA laboratories has been offered to help states test left over spinach samples collected from ill persons for the presence of *E.coli* O157:H7.

In terms of outreach efforts, the FDA continues to advise consumers not to eat fresh spinach or products that contain fresh spinach until further notice. Fresh spinach includes bagged spinach, spinach in a clamshell and loose spinach purchased from retail establishments such as supermarkets, restaurants and farmer's market. At this time, FDA had no evidence that frozen spinach, canned spinach and spinach included in pre-made meals manufactured by food companies are affected -- These products are safe to eat.

FDA has also advised commercial food establishments not to sell fresh spinach or salad blends containing fresh spinach to consumers. Such establishments have also been advised to avoid opening and minimize the handling of fresh spinach in other fresh spinach-containing products to prevent the potential for cross-contamination of other food and food contact surfaces.

These and another FDA recommendation notices may be found on FDA's Web site -- a site where one can also access the press releases FDA has issued since September 14th, daily releases and announcements and updates of ongoing volunteer recall to products containing fresh spinach.

Speaking of recalls, I'd like to complete my talk by summarizing FDA's monitoring of these recalls. To date, there had been three voluntary recalls to announce the products containing fresh spinach. They include, first, the announcement on September 15th by Natural Selection Foods, LLC of San Juan Bautista, California of products containing spinach with "Best if Used by Dates" of August 17, 2006 through October 1, 2006.

Second of recall by River Ranch of Salinas, California announced on September 17th involved the recall of spring mix containing spinach. River Ranch obtained bulk spring mix containing fresh spinach from Natural Selection Foods for processing and packaging.

And third, a recall announcement, September 19th, by RLB Food Distributors of West Caldwell, New Jersey involved certain salad products that may

contain spinach with the "Enjoy through Date" of September 20. Spinach used in their products may have been supplied from Natural Selection Foods.

Finally, it should be noted that products subjected to recall were also distributed to Canada, Mexico and Taiwan, but to our knowledge, no outbreak associated illnesses have been reported from these countries.

This completes my presentation and at this point, I'll turn the microphone over to moderator.

Diana Hadzibegovic: Thank you, Dr. Klontz. Dr. Griffin, you may start.

Patricia Griffin: Hello. I'm glad to talk to you about *E. coli O157* -- one of my favorite pathogens. So, I want to start by just giving a bit of an overview about *E. coli O157*. The press often just calls it *E. coli* and as you clinicians know, we have many *E. coli* in the gut of humans and animals that's in the environment.

E. coli O157 is a particular strain of *E. coli* that has the O cell wall antigen Number 157 and the flagella antigen that's called number 7, and it's a particularly pathogenic organism, partly because it contains a toxin that's been called Shiga toxin and that's named after Dr. Shiga and Dr. Shiga was also responsible for naming the Shigella bacteria and one of the Shigellas that we rarely see in this country actually carries a Shiga toxin.

But these organisms are very different from Shigella and I want to point that out because sometimes there's confusion that when a laboratory reports that there's a Shiga toxin present, people might think that the patient has Shigella, but when they're testing for Shiga toxin, they're testing for these *E. coli* that include *E. coli O157*.

E. coli O157 is one of the class of *E. coli* that produce Shiga toxins. There are others in this class that also caused diarrhea and can cause hemolytic uremic syndrome. It causes pretty much the same disease but *E. coli O157* is by far the most common, the most frequent cause of outbreaks and clearly the one that needs most attention - it's much more common than the others in the United States.

How common is *E. coli O157* infection in the United States? In '99, we in CDC estimated that there were about 73,000 illnesses with *E. coli O157* every year and that includes people who are diagnosed by the laboratory and people who get sick and either don't get the right stool culture done or don't even go to their doctor.

The illnesses have been decreasing namely due to changes in the contamination of ground beef and improvements in the cooking of fast food

hamburgers. And recently, we think there's been about a 29% decrease. We're still following those trends -- still plenty of *E. coli O157* in this country.

So I tried to think about some of the questions that clinicians might want to ask and we'll try to answer some of them and then not talk for too long because I want to give you a good opportunity to hear Dr. Tarr's perspective from his taking care of many of these patients and I also want to leave plenty of time for questions. What if your patient calls and says, "I ate fresh spinach in the past week or two and I'm nervous. What should I do?" The answer is just relax about it. Don't do anything.

And in particular, there's no need for the physician to get a stool culture from the patient. If a patient has diarrhea, then we recommend that a stool culture be done. This recommendation gets stronger if the patient has severe diarrhea or has bloody diarrhea.

We published our recommendations for treatment. There are Infectious Disease Society of America guidelines for infectious diseases. I did mark a guideline that was published in the CID journal in 2002. And what we say is any diarrheal illness that last more than a day especially if the patient has fever, bloody stools, systemic illness, recent use of antibiotics, attend a day care, is hospitalized, is dehydrated, has decreased urination, fast heart rate, postural signs -- any of these things -- should push you even further towards getting a stool culture.

And it's interesting in this context certainly, a fever should prompt a culture but *E. coli O157* patients tend to have little or no fever probably partly because the disease is mediated by a toxin and toxins don't always cause fevers, so we would suggest that you get a stool culture.

Also, if you have a patient who has a hemolytic uremic syndrome that's associated with preceding diarrhea or an adult patient who might have a diagnosis of thrombotic thrombocytic purpura, but if that disease is preceded by diarrhea, most of us now call that hemolytic uremic syndrome and that disease is due to *E. coli O157* until proven otherwise.

E. coli O157 causes 90% or more of those illnesses and we strongly urge you to get a culture for *E. coli O157* in any of those patients. And part of the reason to get a culture is to know what the diagnosis is and so that you think about what are the best decisions for treatment which we'll go into later.

The culture also then it gets to the public health system and this is really the only way that we detect outbreaks. It is the laboratory's report through the public health system, whenever they get an *E. coli* O157 strain, we then do

DNA fingerprinting and of those reports that enable us to detect common source outbreaks like the spinach outbreak, so it's really essential.

So one thing I thought that you might be interested in is to know in your relationship with your clinical lab, what are they doing? So if you get off this call, you might want to know what should you ask your clinical lab and I would say you would ask them, "Do you look for *E. coli O157* in every stool specimen?" And you might be surprised to hear that not all laboratories do that. You send the stool culture and it could come back negative. It doesn't mean that they look for *E. coli O157*.

In our most recent survey of a sample of national laboratories, 69% of them said they looked for *E .coli O157* in every sample using Sorbitol-MacConkey medium which is a special culture plate that they use to screen for *E.coli O157*.

First of all, if they said they don't do it, then ask your laboratory to add *E. coli O157* to their routine enteric panel. Then you're sure that when you do a stool culture they've looked for this virulent pathogen. If they say they do it, then ask them what test they do. The test that's most specific for *E. coli O157* and will give you the fastest answer is culturing on sorbitol-MacConkey agar. And we just call that SMAC. S-M-A-C with capital letters for sorbitol-MacConkey. It allows them to quickly screen, and within 24 hours, they can tell you if they have a suspect of *E. coli O157*.

Another test that's being commonly used and easier for some labs because it's more automated is an ELISA test for the Shiga toxin. If that test is positive, then you know that the patient has an organism in his or her stool that produces Shiga toxin, and that could be *E. coli O157*. It could be one of the other Shiga toxin-producing *E. coli*, some of which can cause disease as severe as an *O157*, but some of which cause only mild diarrhea.

Some of these laboratories will just report that result to you and then that's all they will do. And then they will throw this specimen away. And then all you'll know is that there's a possibility that the patient has *E. coli O157* infection. What you would like is for them to do both that SMAC agar and the ELISA test at the same time. That's a bit much and expensive for most labs to be willing to do. But the minimum that we want labs to do is when they report that a stool specimen is Shiga toxin positive, they immediately culture on SMAC so that they can tell you right away if it looks like they're growing an *E. coli O157*.

In addition, whenever they get a Shiga toxin positive or whenever they isolate an *E. coli O157*, we want those specimens or isolates sent to the public health laboratory, because we track these illnesses, and that *E. coli O157* gets further

analyzed in the public health laboratory - they get sub typed, and that's how we detect these outbreaks.

So I'm going to get a little bit into treatment of diarrhea and then soon after that we'll move to Dr. Tarr. For diarrhea in general, we do not recommend empiric antibiotic treatment, because of the self-limited nature of most of these illnesses, the cost of treatment, the potential for promoting antibiotic resistance, and whenever you give an antibiotic there's certainly the possibility of adverse drug reaction: both allergic reactions to the antibiotics and then some people will develop *C. difficile* colitis after antibiotic treatment or they may get vaginal yeast infections, so you know there are side effects in most people. By the time they go to the doctor with diarrhea, the antibiotics would not do a lot of good.

We know that antibiotic treatment is appropriate for certain subsets of people. For example, some people who have severe diarrhea and have a high risk of invasive Salmonella infection. Persons in developed countries where Shigella or Vibrio are common, and in those countries, often, we don't have laboratory support, so there's always clinical judgment on whether or not to give antibiotics as treatment for diarrhea.

The consideration has to be given to whether the patients might have *E. coli O157* infection and how to think about treatment for those people. Things that would increase your suspicion that it's *O157* infection are: the stools are bloody, the patient has severe abdominal cramps especially on the right side, and there's little or no fever, but as people in practice would know, and we've actually looked at data on people with diarrhea due to different organisms, there is no clear algorithm we have that we can put in variables like fever and the type of diarrhea and come out and tell you that it's likely to be due to one pathogen or another.

If you strongly suspect *E. coli O157*, there are some concerns about antibiotic treatment. Whenever a person has diarrhea, it's important to hydrate them. We know that there are fluid losses in diarrhea, and hydration is very important. And Dr. Tarr is going to talk more about the particular importance of hydration in *E. coli O157* infections. Also in colitis, there are data indicating that giving Imodium or loperamide can increase the risk of complications, and we do not recommend that for *E .coli O157*.

In particular, there's some retrospective data suggesting that the use of antidiarrheals could actually increase the risk of complications. With *E. coli O157*, there are some particular concerns about antibiotics, and those concerns come from looking back at people who have been treated with antibiotics. And some of these people have been more likely to develop hemolytic uremic syndrome.

There are many reasons why looking back at treatment can be a biased way of making decisions, but we've also looked at whether antibiotics have helped in the treatment of *E. coli O157*, and we haven't found any good data that patients who were treated with antibiotics actually did better.

So there's been some work in mice and in vitro also suggesting that giving antibiotics can increase the production of Shiga toxin and increase the risk of complications. So in particular for *E. coli O157*, we have concerns about patients receiving antibiotics. So if diarrhea is known to be due to *E. coli O157*, most US experts at this time would not recommend antibiotics. Most of these patients will have been ill for several days, and there's no evidence that treatment at this point is beneficial. I think I've given enough to start with.

Diana Hadzibegovic: And thank you Dr. Griffin. Dr. Tarr, you may begin.

Phillip Tarr: Drs. Klontz and Griffin provided very good background to the outbreak at hand and the general approach to patients with these infections -- the suspected or confirmed. What I'd like to do is go through a list of frequently asked questions much like Dr. Griffin did at a provider level that we found useful in our hospitals here in communicating to people treating these patients.

What is the incubation period?

In most outbreak analyses, it's been about three days. I think the range is probably very unlikely to be less than one day, and it can extend up to 10 or 12 days. That's a good working frame in my opinion, and Dr. Griffin can perhaps add more later about that. Symptoms of *E. coli* infection are generally quite painful. The profile of a patient with *E. coli* infection is non-bloody diarrhea that turns bloody between day two and four. The blood is visible to the patient or parent in about 85% of cases. Though there is a subset that fails to have any visible blood. Patients are almost never febrile when they come in for medical attention, so about half of patients in most series will report having had a fever usually during the non-bloody diarrhea phase of illness.

The abdominal pain is out of proportion to the level on what you expect with the case of gastroenteritis. Women have likened it to giving birth, a man who had it told me that it was worse than his kidney stones the year before. So pain is out of proportion to the illness. The abdomen is often quite tender. I have seen in older children, teenagers and adults the right sided pain that Dr. Griffin describes. In younger children, it's more generalized and seems to be surrounding the time of having a bowel movement.

Who should receive the stool culture?

I agree with Dr. Griffin's guidelines. And what's critical here if this hasn't been portrayed before is the link between the patients, the provider, and good rapid microbiology assessment.
Call your lab, get on the phone, speak to the microbiologist and make sure that that individual will plate the stool on sorbitol-MacConkey agar especially in the setting like this for *E. coli O157*.

Are fecal leukocytes helpful or any other rapid tests that can help you distinguish a patient at point of care?

No. About half the patients or more have no fecal leukocytes when they present the even higher acuity settings such as emergency runs.

What lab test should be obtained in addition to a stool culture at the time of presentation?

I strongly recommend obtaining a CBC, BUN, Creatinine and electrolytes on all patients with acute bloody diarrhea as a baseline. One would need to refer to those values a day or two later when the culture comes back positive. We strongly discourage giving antibiotics, as put succinctly by Dr. Griffin, there is no study that demonstrates any benefit to giving antibiotics. There are multiple studies, flawed as they are, that suggest harm in the absence of any benefit accruing to such patients and in view of multiple different studies including in adults. We discourage the use of antimicrobial agents of any class.

Now what should one do?

If a patient fits a plausible profile for an *E. coli* infection, I personally think they should be admitted to the hospital and given IV hydration. This is a thrombotic illness. The model for this is not dehydration as rota virus or cholera. The model for this is much more that of vascular occlusions leading to myocardial infarction.

And people who've died with fulminant *E. coli* related HUS, they have thrombi by all over the body. When patients present in advance of meeting a case definition of HUS, they have profound activation of the coagulation system. It won't show up on a prothrombin time. It won't show up with the CBC or show with the different tests, when they are in your emergency room or office they have coagulation activation whether or not they go on to develop HUS. A well profused body and in particular a well-profused kidney is in the host interest. We strongly encourage IV hydration with isotonic saline or equivalent crystalloid in the situation.

Laboratory tests should be obtained daily once the patient is admitted. Follow the platelet count. The trend in the platelet count will tell if a patient is resolving or getting worse. Almost all patients who we have identified early and followed for several days will have some fall in their platelet count and then will come back up and you can consider them to be out of the woods.

When does HUS occur and how will I know that my patient is recovered without these complications?

Follow the platelet count. If it is clearly rising, you are out of the woods - that's why you need more than a single value. In most recent series, HUS occurs in median of Day 8 of illness with the first day of diarrhea being at Day 1 of illness. We've seen it occur as early as Day 5 of illness and as late as Day 13. That's a reasonable window. You need not observe a patient throughout that entire window, but you do need to observe the patient daily, ideally in a hospital until you know the trend in the platelet count.

What percent of children with E. coli infection develop HUS?

Fifteen percent of children under ten in most recent series of developed HUS. And this is in a culture-proven category. I am very surprised and quite concerned that this 16% HUS rate in a group of people who are young adults, largely whom one would not expect to have such a high HUS rate.

How do I report a patient with confirmed or suspected E. coli O157 over the HUS?

It is the responsibility of the provider in most states to make that phone call. The laboratories will often do it for you. If there's any doubt, pick up the phone and speak to the local disease control authorities in the county or residence of your patients.

How contagious is E. coli O157?

In an outbreak throughout the 1990s and Dr. Griffin can elaborate, there's been about a 10% secondary attack rate. This is another reason in my opinion for hospitalizations and the institution to contact precautions people with *E. coli* infections. Even adults are biohazards.

What does one do with a patient who looks "good" when reported as stool culture becomes known?

Usually, you're out of the woods especially if you're beyond day six or seven of the illness. It will be prudent to get a CBC. And if there's any doubt about

incomplete resolution of symptoms, admit the patient, hydrate him overnight, and get a CBC the following day.

Finally, can antibiotics prevent in incubating infection?

We don't think so. In several outbreaks, most - the best of which was probably in Toronto in the late 1980s, people who had received antibiotics during an incubation period for *E.coli* had a higher risk of a poor outcome including renal failure or death. So the patient is pretty symptomatic and thinks that antibiotics might diminish this risk. We don't - there are no data to support the use of antibiotics in the situation.

I'd be happy to entertain questions according to the format of the moderator.

Diana Hadzibegovic: Thank you Dr. Tarr, Dr. Griffin and Dr. Klontz. Now we can start the Q&A session. I would like to at this point, ask the media or any media, people in the audience to hold their questions and direct them to 404-639-3286 our Media Relation Office. Let's give a chance to clinicians to ask the question. Laurie, could you please one more time tell to our audience, the replay number. And then you can start the question and answer session.

Coordinator: Yes, thank you. The replay number for this call that will be available approximately ten minutes after the call is over, the dial in number for that is 888-566-0619 that will be available until October 5 at 12 pm - sorry, 11 pm Central time.

Question: My question is what proportion of these patients present with a very mild GI symptom, but with hemolytic uremic syndrome?

Phillip Tarr: I'd be happy to take a stab with that. Is that okay, Patty?

Patricia Griffin: Yes. I also have data.

Phillip Tarr: Okay. Over the years, looking at several hundred patients with *E.coli* infection and HUS, patients with HUS who had no severe diarrhea or very mild diarrhea, probably only 2% or 3%. But there's only a moderate correlation between the severity of the diarrhea and the risk of HUS. So when can you have very mild enteric symptoms and then develop HUS? The mildness of prodrome is not a clear green light.

Question: Does cooking the spinach and how much cooking protects you from the organism?

Karl Klontz: This is Karl Klontz, Food and Drug Administration. We are told by microbiologists here in FDA that this organism is quite susceptible to heat. In

fact, one of the recommendations is if one cooks spinach at 160 degrees Fahrenheit for 15 seconds, those cells will probably be inactivated.

But this raises the larger question of whether cooking is sort of a safe way out. Currently in an outbreak setting in which a food item has been implicated as the cause, and I would really want to suggest caution in thinking that cooking clears the path and makes it safe because there are always other possible problems there, beginning with we don't really know practically what temperature we're getting our food unless we see a rolling boil or a thorough steam and so on.

The other thing is when we've got products that are known or potentially known to be contaminated - the fact that they are being handled can lead to cross contamination of counters and other foods. So, I just want to caveat that 160° for 15 seconds is the general rule of thumb with some other possible precaution.

(Q cont.): Thank you very much.

Patricia Griffin: Yes, this is Patricia Griffin, sort of dealing with that other question, I was hoping that I had our FoodNet data at hand. As you may know, hemolytic uremic syndrome is a reportable disease in many states, and in our FoodNet sites which comprise 15% of the population, we collect data on every case of HUS and so we actually do have data on the proportion that had bloody stool. I just don't have that in front of me, but I can tell you that we did a national study in the late 1980s in which we enrolled 83 people, adults and children with HUS and tried to get a random sample of people with HUS and only 73% of them had bloody stools.

That seems to me to be a fairly low proportion but I think the message here is that people with bloody diarrhea seem more likely to develop hemolytic uremic syndrome, but it's also possible in somebody who has non-bloody diarrhea.

(Q cont.): Our percentage is in the high 70s in children who have had bloody diarrhea prior to their HUS. Non- bloody diarrheas though was also categorized by families as severe usually because of the pain. Yet, only a handful had no diarrhea but we got an *E. coli O157* out of their stool.

Patricia Griffin: Right. And so, that's true also in thinking about just plain diarrheal illness if you only look for *E. coli O157* in people who have bloody diarrhea, you're going to miss a lot of these illnesses.

Diana Hadzibegovic: Thank you, next question.

Question: I work with the FDA but the questions and the opinion represent my own, not the agency, okay? I have a question: there appears to be some problem for example in Europe where a fair number of some of coliforms associated with the disease may actually be detected in the sorbitol containing agar. So the question is-I like the ELISA screening, but any thought on the subject?

Phillip Tarr: Patty, you want to go first?

Patricia Griffin: Trying to see at how to handle that succinctly. There are some *E. coli O157* that are not detected by SMAC agar. They are vanishingly rare in the United States. They're seen in some part of Europe. *E. coli O157* is just about the only Shiga toxin producing *E. coli* that we can find on SMAC agar. We can find all of them by doing an ELISA for Shiga toxin. That's one advantage of the ELISA and that you find all of those Shiga toxin producing *E. coli* including *O157.*

And it's a test that can be automated so it's easier for some labs to do than culture. So it's a fine test to do. What's important to know is that some laboratories are just getting a positive result and throwing it away. And then the clinician, in my opinion doesn't have the information that she or he needs to take care of the patient, to report to the public health authorities, deal with what you would do if you really think the person has *E. coli O157* in terms of counseling the patient, treating the patient possibly in a hospital, and counseling them about the chance of spreading the disease to another person.

So that's why we are urging people, contact your labs, if your lab says "we do the Shiga toxin test" we say that's great but we also if we tell them, if they get Shiga toxin positive, you need them to specifically look and tell you if the patient has *O157.*

(Q cont.): How about if the *O157* growth is negative shouldn't they just still send the sample over to the public health laboratory because, with these small barriers now flying across the countries and everything like that, we don't know what the future hold for us.

Patricia Griffin: Yes, we really preferred that people look for all the Shiga toxin producing *E. coli* because the others also caused diarrhea and some of them can cause a disease that is just as severe as *E. coli O157.* And we want to continue monitoring them, because at some points those could increase in frequency in this country and start causing more illness. So the best thing is truly to look for all these organisms, but while you're doing that, to be sure that you quickly make the diagnosis of *O157.*

Phillip Tarr: I'd like to amplify Dr. Griffin's comments. In the United States and Canada now and dating back as far as 1982 or 1983 when these bugs first emerged, at least emerged in our knowledge - *O157* is head and shoulders above any of the others in terms of its ability to cause renal failure or epidemics. Subsets of the others are quite pathogenic and it's quite appropriate to continue to look for them, but it should not be at the expense of rapid unequivocal identification and on forwarding of an *O157*.

Question: I'm from a State Hospital in California. I would like to ask Dr. Tarr to repeat about the following of platelets counts do I understand right that its dropped first, and how long does it drop before it rise again?

Phillip Tarr: In an uncomplicated case, it could drop for several days and then start to rise. Rather than box yourself into a set number days, it's really a day by day analysis. If the trend is down, that patient still has an evolving vascular injury that could lead to HUS; the platelet count's rising, you're out of the woods.

Question: I was wondering if there's been any preventative measures or a follow- up taken from the 2003 study that was done by the Journal of Dairy Science that showed if cows were switched from a grain diet to hay for a period of maybe a week prior to slaughter, it would reduce cross contamination? And that was actually done from the study that showed a lot of times the contamination occurs in meat packing plants and so forth. Do you have any information on that?

Patricia Griffin: Yes. I can take that question and others may want to add to it. This is not CDC data, but we're aware of that data. And there's been very good work to show methods such as the one you described, feeding hay rather than grain to decrease the excretion of *O157* prior to slaughter.

And one of the efforts that's being made is to decrease the amount of *O157* that animals are excreting when they're slaughtered because whatever they are excreting as they are waiting to slaughter also gets all over the hides of the other animals that are waiting for slaughter. And then, when the animals are slaughtered, what's on the hides can contaminate the meat. And there's actually progress being made in that ground beef is now less contaminated than it was a few years ago.

The other big thing that needs to be done is recognition that we have a huge amount of cattle manure without adequate ways to dispose of it and cattle manure contains *E. coli O157*. In old studies before, we used specialized techniques, we used to say that small proportion of cattle farms had animals with *O157*. Now, we think that virtually all the cattle farms in the United States have animals that carry this virulent pathogen. And what happens to this pathogen in the manure as if sits out in the fields? Well, you can imagine

the rain washes it down into streams and rivers and probably into ground water. And then from there, it can contaminate the environment including fruits and vegetables downstream so which the water is used in various parts of the process.

Question: My question is now that the stores have been pulling the potentially affected spinach from the shelves, and they believe this to be the positive agent. And we have been doing this for several days now and given the incubation period ranging 1-10 days, why aren't we out of the woods yet, and are we seeing a gradual resolution of this epidemic or do we expect more cases? Thank you.

Karl Klontz: This is Karl Klontz. I'll speak to part of that I'm sure Dr. Griffin and Dr. Tarr as well may have comments.

We are in an evolving mode here in terms of natural history, if you will of this outbreak. Are we out of the woods totally? I don't think so, I don't think we can say that yet, from an FDA perspective, we are placing enormous resources right now on trying to trace back the products that have been implicated in individual illnesses as part of this outbreak.

It is true in the last few days, we learned an awful lot in terms of the most likely source being in the Salinas Valley area. The epidemiology and the trace back so far seem to corroborate that that spinach indeed was grown there. But before we are comfortable placing the all clear light out, we really have some more work to do, and we want to make sure we do it judiciously and carefully, and do it right. So, that's why at this point, we are not there yet in terms of clearing the advisory on spinach.

Diana Hadzibegovic: We have time for two more questions.

Question: I'm from the San Francisco Department of Public Health and this is the question for Dr. Tarr and with an excellent set of FAQs that you shared with us. Is that available electronically or in hard copy for others to, you know, share with their jurisdiction to clinician?

Phil Tarr: Sure. What I'd like - if its okay with Dr. Griffin, I'd like to send that to her and she can disseminate it. Is that okay Pat? Or how should I best get it to you?

Diana Hadzibegovic: You can send us an email to coca@cdc.gov. One more time C-O-C-A@C-D-C.G-O-V, and we can send you information or answer.

Question: I have question for Phil Tarr and just - especially for people who present with HUS and you can no longer find the organism and the hemorrhagic *E. coli*. How long does the Shiga toxin persist and is it at that point a good idea to go

ahead and try doing the ELISA test for Shiga toxin, where it persists longer or you likely to get it after the organism is no longer there?

Phil Tarr: Very interesting questions. When a patient comes within with HUS by standard culture about 2/3 of patients were cultured negative at the time they present with HUS so that's too late to get the organism. There's a few things you can do in that situation. Number one, get on the phone where the patient might have initially presented, when they come with their HUS, it is usually a tertiary pediatric center or adult center where they may have presented three or four days before those plates may still be hanging around. Make certain they don't throw them out trying to get transferred to a good microbiology laboratory. That can sometimes involve some people skills.

Second, you should also do a rectal swab on admission. Patients with HUS frequently have an ileus or have already produced all the stool they are going to produce for a few more days. Do a rectal swab on admission and send that for an *E. coli O157* culture. It is anecdotal, but I've seen a handful of those positive and the first bowel movement two or three days later when a child has HUS, be culture negative, so try to get that done. The toxin in the stool is paradoxical, even prior to development of HUS when there's plenty of *E. coli* around. There's not much fecal free-toxin, that was published several years ago. So, looking at the stool as a target for toxins is probably too late.

I would in this circumstance, also do a toxin assay because the patient could have been cultured for a *O157* before it was missed. Or they could be among the very rare number of patients, probably no more than 5% and probably more close to 1% or 2% nationwide were truly infected with a non- *O157* Shiga toxin producing *E. coli*.

So, to review, get the original plates, do a rectal swab and set up for both the culture and the toxin assay on admission. And save some serum, serologically, you might need to look at something in retrospect.

Diana Hadzibegovic: Thank you Dr. Griffin, Dr. Klontz, and Dr. Tarr for that informative presentation. I would like to remind any listeners who did not have a change to ask a question to email that question to coca@cdc.gov - C-O-C-A-@-C-D-C.G-O-V. I would also like to remind all listeners that current information regarding *E. coli* outbreak maybe found at the CDC Website. Also, I would like to point out that this outbreak is the initial of RSS feed for the event Webpage and encourage all listeners to review the CDC Homepage and consider linking to the site via RSS to be able to automatically receive the latest information concerning CDC emergency preparedness and response activities. Thank you very much and stay tuned for our next COCA conference call.