CDC does not have a copy --

JUDGE DAVIDSON: I'll sustain the objection in part but I'll let the witness answer if you take the quotes out because we don't have any authentication of what you're saying is a quote. The words did he say it or didn't he say it, fine.

MR. KRAUSS: Okay.

JUDGE DAVIDSON: And if he wants to agree or disagree or say part -- say whatever he wants. He can testify.

MR. KRAUSS: Thank you, your Honor.

JUDGE DAVIDSON: You're trying to get to whether or not this is the meaning of what he said, I believe.

MR. KRAUSS: Yes, your Honor.

JUDGE DAVIDSON: Okay. Go ahead.

BY MR. KRAUSS:

Q Okay. Bayer proposed finding of fact number 336 says that at the 2002 NARMS annual scientific meeting you said so -- and then Campylobacter is not population-based as was pointed out so I think that for all pathogens except Campylobacter we have a

representative sample of culture-confirmed cases at the state level.

Number one, do you agree that you said that?

A I don't recall saying that precisely.

Q Do you agree with the statement contained in there that for all pathogens except Campylobacter, NARMS does not have a representative sample of culture-confirmed cases at the state level?

A I don't agree with that. I agree that NARMS Campylobacter is not population-based. I believe that the prevalence of Campylobacter observed in terms of Fluoroquinolone resistance in NARMS is approximation and represents -- is a representation of the national prevalence of Fluoroquinolone-resistant Campylobacter.

Q So it's your testimony here that you did not say that. Is that right?

JUDGE DAVIDSON: That's what he said.

THE WITNESS: Your Honor?

JUDGE DAVIDSON: What?

THE WITNESS: I'm sorry. I said I don't recall saying that. I didn't say I didn't say that. I just don't recall the precise words.

JUDGE DAVIDSON: But you also went on to say that you don't agree with that statement. That's your testimony here today.

THE WITNESS: Yes, your Honor.

JUDGE DAVIDSON: Okay.

BY MR. KRAUSS:

Q Now, Bayer proposed finding of fact number 335 says at the 2002 NARMS annual scientific meeting held in Hilton Head, 2002, you said that CDC agrees completely that there is a limitation in the NARMS sampling scheme for Campylobacter. That's why we're moving forward trying to develop a population-based collection of Campylobacter isolates.

Did you say that?

A I don't recall if that's what I said precisely, but I agree that NARMS Campylobacter is not population-based and we are moving forward to develop Campylobacter as a fully population-based surveillance system.

Q Bayer proposed finding of fact number 333 says that at the 2002 NARMS annual scientific meeting in November 2002 you said, now your question is to the

extent that the prevalence that CDC identifies in Campylobacter Ciprofloxacin resistance is representative of the country and I agree completely there are limitations in the generalization of our prevalence nationally.

Did you say that?

A Again, I don't recall saying that precisely.

Q Do you agree with what's expressed in that statement, that there are limitations in the generalizations of the NARMS prevalence nationally?

A I believe there's limitations in all surveillance systems but I believe that the NARMS prevalence of Fluoroquinolone-resistant Campylobacter approximates the presence nationally.

Q Dr. Angulo, let me turn your attention to the protocol that the states follow in selecting Campylobacter to send to states -- or to send to CDC for resistance testing. In particular, I want to focus on 1999.

Under the NARMS Campylobacter protocol, would it be true that if in any given month a state health department collected Campylobacter in the FoodNet

surveillance process, there should be at least one NARMS susceptibility monitoring sample for that state for that month? Follow that?

A No, not precisely.

Q All right. Let me break it down. If in any given month a FoodNet laboratory conducting the Campylobacter surveillance for that state has a Campylobacter FoodNet sample, at least one, 10, whatever, then there should be NARMS susceptibility samples corresponding to that same state in that same month. Would you agree with that?

A No.

Q Why not?

A FoodNet and NARMS surveillance areas do not overlap in all states. For example, there's Maryland. Maryland does FoodNet surveillance in one geographic area and they were using -- in '99, their first year in FoodNet, they were using a single Sentinel Clinical laboratory.

So while FoodNet is ascertaining all culture-confirmed cases in a geographic area, they may ascertain several Campylobacter cases because they go

to every clinical laboratory in that geographic area and for Maryland you have on the order of 35 clinical laboratories. So there are ascertained cases on all of those laboratories.

NARMS might be, following the Sentinel Clinical Laboratory, a single laboratory. So there isn't this complete overlap. That's one reason.

The second reason is that clinical laboratories select the isolates and forward them to us but the isolates have to survive to make it to us and they may be received non-viable. Campylobacter is an extremely fragile organism. It can die during transport. And we have to get it viable.

Then we have to confirm that in fact it was Campylobacter, which it usually is. And then we finally test it.

So if you look only at our test results -- I would not necessarily assume that just because we don't have a test result that we got no isolate from that lab submitted and even if the lab did not submit any isolates, I would not necessarily assume that that was contrary to the protocol because these surveillance

areas do not always overlap completely.

Q So, Dr. Angulo, taking -- Maryland was one of the states you discussed. And focusing on 1999, I've got the 1999 NARMS annual report and it's G-99. In fact, it has the cover of the NARMS 1999 annual report but then there's --

MR. KRAUSS: Who knows what's attached to it, your Honor? This is the way it was produced to us.

BY MR. KRAUSS:

Q But I went to the web and I actually have the '99 annual report tables. I put them together here in this exhibit.

And for Maryland, for example, for July of '99, the FoodNet collected 22 Campylobacter isolates. For NARMS, there are zero submissions. That doesn't surprise you, based on what you said, or does it?

A I think you're misreading this NARMS annual report. I think that's test results, not submissions. May I see the document?

Q Yes. Yes.

MR. KRAUSS: Your Honor, the FoodNet report is B-86 and I'm happy to hand you a copy if you need one.

JUDGE DAVIDSON: I've got it.

MR. KRAUSS: Okay. And the NARMS report is G-99, like I said. And because of the situation with the attachments -- and I had to get the tables off the web. I have a copy for you, if you'd like.

JUDGE DAVIDSON: All right.

MR. KRAUSS: Here you go, your Honor.

May I approach, your Honor.

JUDGE DAVIDSON: Certainly.

BY MR. KRAUSS:

Q Looking at the smaller exhibit, Table 4E is Campylobacter submissions by site and by month of collection 1999. It says page 1 of 1 in the upper right-hand -- well, they all say page 1 of 1 because they're all individual tables.

MR. KRAUSS: Your Honor, it's the last page of the exhibit.

BY MR. KRAUSS:

Q See that, Dr. Angulo? Now, on B-86, the FoodNet surveillance report, page 50 in the upper right-hand corner -- on the bigger exhibit, Dr. Angulo -- page 50 --

A I'm familiar with it.

Q Oh; you're familiar with it? Okay. July of '99 it shows 22 isolates collected for Maryland for Campylobacter and NARMS says that there were zero submitted by Maryland in July of '99.

My question is, can you explain that?

A Well, perhaps we didn't label this table very precisely and I apologize for that. But this is actually Campylobacter submission -- I think probably in the text of the NARMS annual report we explained that all the data that we're going to talk about in the report and all the tables pertain to tested isolates that are in NARMS.

So the bottom of this table is the 319 -- I think -- I would presume that -- I think that this 319 is probably the number of cases that were in NARMS that year and so although this says Campylobacter submissions for Maryland, this is probably Campylobacter submissions viabil -- those arrived viable and those tested.

So it's a combination and I would -- this probably -- the zero means in fact yes, Maryland

Corrected as per OR 46 6/13/03

contributed no isolates tested into our surveillance that month.

Now, the reasons for that are multitude and in fact this was the first year of Maryland's surveillance data and unfortunately we had a contamination problem with receipt of isolates for Maryland. It lasted for several months as we tried to figure out why the Campylobacter isolates they were sending to us were contaminated. And of course we didn't test them when they're not purified and confirmed.

So we didn't test them. The results are not in the report. And eventually we figured out the system -- or Maryland figured out why they were getting ~~contaminates~~ Contaminants and then they went back on track. So I think this series of four months of zeroes from Maryland probably reflects a difficulty we had with Maryland in them sending us pure isolates.

Q So let me make sure I have your testimony right. This table that says Campylobacter submissions in your 1999 annual report, last updated on the web March 25, 2003 -- you see that on the bottom? You're saying that's wrong.

A Uh-huh.

Q You said the table is mislabeled. It shouldn't say Campylobacter submissions, didn't you?

A No. I believe I said that perhaps it's not precise enough. It's not an incorrect statement. This title is not incorrect. Perhaps it's not precise because these are the Campylobacter submissions by the states in our collection, the 319 that we tested in 1999. That's the correct title, perhaps not precise, because Maryland submitted more isolates that we ended up testing but they turned out not to be Campylobacter or they turned out to be contaminated.

Q So CDC gets submissions that they don't report in their table. Is that what you're saying?

JUDGE DAVIDSON: I think he's already testified. There are various reasons why they don't get reported. They are not viable and there may be others. But I don't know what your question pertains to at this point.

MR. KRAUSS: Well --

JUDGE DAVIDSON: Because you said they get submissions that they don't put in their table. Other

than what you've already explained, we'll hear about it; otherwise, there's no question pending.

BY MR. KRAUSS:

Q So if a laboratory submits a sample that for some reason is not viable, it doesn't count as a submission. Is that right?

A Under what term of submission?

Q The term used in the annual report on Table 4E, Campylobacter submissions by site and by month of collection.

A When we generate the annual report tables which report the results upon the ones that are in our final collection and we generate such a table that reports who submitted how many isolates what month, that is going to reflect the ones that survived and were confirmed Campylobacter and that we actually tested. That's what they will reflect in the database.

Q Now, you explained Maryland had a problem because they were new to the program and they were having trouble, right?

A Right.

Q In that time frame, right?

A Right.

Q Oregon was an original participant, weren't they?

A Yes.

Q Since 1996?

A Yes.

Q If you look -- on the small exhibit it's the same table but if you look at Oregon for March of '99, there are zero submissions listed, right?

A Yes.

Q If you'd look at page 53 of B-86 for Oregon for March of '99, there were 40 Campylobacters.

A Uh-huh.

Q You know that without looking at the exhibit?

A I believe you. It would be reasonable that there'd be that many cases in Oregon. Oregon surveillances statewide, NARMS surveillance in Oregon is a single Sentinel laboratory. It is reasonable that that clinical laboratory would have not had any isolates of Campylobacter in the month of March and in fact would not have submitted any isolates. That's reasonable.

Q Okay. So this isn't unusual as far as you're concerned?

A Is it a viola -- or is it contrary to our guidance to the states? It's not contrary to our guidance. We would like all states to submit 52 isolates but if there's not an isolate in the Sentinel Clinical Laboratory, they have nothing to submit.

JUDGE DAVIDSON: Are you finished with this, Mr. Krauss?

MR. KRAUSS: I just have one additional follow up on this subject matter --

JUDGE DAVIDSON: No, not the subject matter, the document.

MR. KRAUSS: Oh, yes, your Honor.

JUDGE DAVIDSON: Because it's not the same as the document I have.

MR. KRAUSS: So can I give you a B number, your Honor?

JUDGE DAVIDSON: Well, for the last three pages, I think, you need another number. It's just not the same as G-99. G-99 only goes up to page 5 and it ends with the -- all of ~~juni~~ jejuni by site in my copy, I

believe. And what you gave me has three additional pages in the '99 report.

MR. KRAUSS: Right. And, your Honor, I would like to mark those as B-1931.

JUDGE DAVIDSON: Getting close to my birthday. Let's go. Come on.

(Laughter.)

JUDGE DAVIDSON: And give a copy to the reporter, please.

MR. KRAUSS: Yes, your Honor.

(Respondent Exhibit B-1931 was marked for identification.)

BY MR. KRAUSS:

Q Now, Dr. Angulo, when I asked you first about whether you would expect in any given month that a state that had collected a Campylobacter FoodNet surveillance sample, whether there should always be at least one NARMS sample, correct me if I'm wrong, you testified that that wouldn't be necessarily unusual because the FoodNet surveillance area is different than the Campylobacter NARMS surveillance area, right?

A In some states, yes.

Q Well, I'm talking about the overall program. I mean, if it's different in some states it would be different --

A Yes.

Q -- for the overall program, wouldn't it?

A Yes.

Q So that lengthy discussion that we had probably an hour and a half ago about whether the FoodNet surveillance area is representative of the United States, that's not talking about the NARMS Campylobacter area, is it?

A It is talking about the NARMS Campylobacter area. The NARMS Campylobacter area occurs within the FoodNet area.

Q But you just testified that the FoodNet surveillance area is different than the Campylobacter NARMS surveillance area, right?

A Right, but --

Q So -- excuse me. They're different. The FoodNet surveillance area is larger than the Campylobacter NARMS surveillance area, right?

A Right. But in the context of generalizing the

results to nationwide, understanding how FoodNet represents the nation in terms of the epidemiology of foodborne disease contributes to the understanding of how NARMS data can be generalized to the country as part of the important -- an important step to understanding -- to how I can get to the conclusion that the prevalence observed in NARMS is a close approximation of the national prevalence and that we're confident that the NARMS represents the national prevalence.

MR. KRAUSS: Your Honor, this would be a good place for a break if you're willing to.

JUDGE DAVIDSON: All right. I'm willing. Do you have an idea of how much you need after lunch?

MR. KRAUSS: Probably about an hour.

JUDGE DAVIDSON: Okay. My watch says it's -- by the time I finish talking it will be a quarter after 12:00, so we'll adjourn until a quarter after 1:00. I'm going to be here promptly and I expect everybody to abide by my earlier admonition.

MR. KRAUSS: Thank you, your Honor.

(Whereupon, a lunch recess was taken.)

A F T E R N O O N S E S S I O N

JUDGE DAVIDSON: Come to order. Be seated.

Ready, Mr. Krauss?

MR. KRAUSS: Yes, your Honor.

JUDGE DAVIDSON: Okay. Proceed with -- let the record show the witness is still under oath.

MR. KRAUSS: Thank you, your Honor.

BY MR. KRAUSS:

Q Dr. Angulo, let me return to the subject of proposed finding of fact number 336 which we discussed where you said you don't recall whether you said that Campylobacter sampling is a representative sample or not of the culture-confirmed cases.

MR. KRAUSS: Your Honor, I have an exhibit with which I'd like to try to refresh the witness's recollection of having said that, if I may.

JUDGE DAVIDSON: Sure.

BY MR. KRAUSS:

Q Dr. Angulo, let me -- I'm going to play a snippet for you of a tape of that NARMS conference.

MS. ZUCKERMAN: Objection, your Honor.

JUDGE DAVIDSON: I don't know how we're going

to do this on the record here.

JUDGE DAVIDSON: What have we got, first of all? You have to lay the foundation of what it is, where it came from and is there a transcript of it.

MR. KRAUSS: Yes, your Honor. There's a transcript that's attached to the testimony of AHI witness Dr. Carnavall and the transcript was authenticated in the Carnavall testimony.

MS. ZUCKERMAN: Your Honor --

MR. KRAUSS: Has counsel for the CVM heard the tape?

MS. ZUCKERMAN: No, we have not, your Honor.

JUDGE DAVIDSON: Play it for them first. We'll take a recess.

MR. KRAUSS: Okay, your Honor.

JUDGE DAVIDSON: We're off the record.

(A brief recess was taken.)

JUDGE DAVIDSON: On the record.

MR. KRAUSS: We had a problem in that we went down there to play it and CVM's counsel was there and then left and we were sitting around waiting and so we didn't get an opportunity to play it.

JUDGE DAVIDSON: All right. What's going on?

MS. ZUCKERMAN: Your Honor, CVM's counsel didn't leave. We were getting -- we have one copy of the purported transcript of this tape recording and we were getting additional copies so that we're able to follow along with the tape recording.

So I would imagine it would be another couple of minutes so that we can get copies made. Had we known before lunch, we certainly could have had the copies ready.

JUDGE DAVIDSON: Do you have any other areas of questions that you want to ask?

MR. KRAUSS: Yes, your Honor.

JUDGE DAVIDSON: And stay away from this until they're ready?

MR. KRAUSS: Sure.

JUDGE DAVIDSON: Okay. Let's do that. Ms. Zuckerman, you're handling this witness anyhow so there's no harm in not having all your counsel here.

MS. ZUCKERMAN: Yes, your Honor. Thank you.

JUDGE DAVIDSON: Okay. We're going to proceed with other areas of questioning and get back to this

particular area later.

BY MR. KRAUSS:

Q Dr. Angulo, would you agree with me that for Campylobacteriosis in the United States, there is a component of the annual prevalence that is seasonal in the United States?

A The incidence of Campylobacter in the United States is seasonal, yes.

Q And what that means is that some months over the course of a year will have a higher incidence than other months. Isn't that right?

A That's correct.

Q And would you agree with me that Campylobacteriosis in the United States peaks sometime around the third quarter of the year?

A Of course it can vary from state to state, location -- north, south there's variation. In general, across all the FoodNet sites, the FoodNet data demonstrates that seasonal -- shows a seasonality. I can't say for certain when it peaks.

Q Isn't it typical in FoodNet that you see more isolates in, say, July and August, than you do in, say,

January? Would you agree with that?

A Yes, I agree with that.

Q Would you also agree with me, Dr. Angulo, that resistance -- Fluoroquinolone resistance in Campylobacter also has seasonal features to it?

A There are variations from month to month on the proportion of Campylobacter cases that are resistant to Ciprofloxacin, varies from state to state. Some states it may not be seasonal but there are certainly variations.

Q The Smith study, which is G-589, demonstrates seasonality in terms of resistance, doesn't it?

A The Smith study is one state and yes, in that state there is a seasonal pattern of resistance. That seasonality is not the same in the other states.

Q But for Minnesota you'd agree that there's a trend such that resistance peaks -- Fluoroquinolone resistance in Campylobacter peaks somewhere around the first month of the year, wouldn't you agree?

A The proportion of isolates that are -- fluoro -- Ciprofloxacin resistance are higher in the early parts of the year than the rest of the year. I can't

say for certain it's January and I wouldn't call it a trend.

Q Let me show you the Smith study.

MR. KRAUSS: Your Honor, this is G-589.

BY MR. KRAUSS:

Q And in particular, on page 3, figure 1, the top graph.

A Uh-huh.

Q There's a peak at the change of years every year, isn't there, between '92 to '93, '93 to '94 and so on, isn't there?

A There is a consistent increase in the first quarter of each calendar year.

Q And there is a peak of resistance in the first quarter of every year when you look at the whole year, isn't there?

A That's correct, yes.

Q Now, Minnesota was a participating state in FoodNet in the year 2000, wasn't it?

A Yes.

Q And for Campylobacter sampling they were participating?

A In NARMS or in FoodNet?

Q Oh.

A Yes, to both.

Q To both. Let me hand you -- I'll give it to counsel first --

MR. KRAUSS: Your Honor, this will be B-1932.

(Exhibit B-1932 was marked for identification.)

BY MR. KRAUSS:

Q Let me hand you this Table 4E from the FoodNet 2000 annual report.

JUDGE DAVIDSON: Do you have copies for the reporter and myself?

MR. KRAUSS: Yes, your Honor. I have one for you, your Honor, and I'll get one for the court reporter.

BY MR. KRAUSS:

Q This is a table demonstrating the pathogens collected by month for Minnesota for 2000, isn't it?

A Yes. Not collected but --

Q Why don't I switch it around? Why don't you tell me what this chart represents out of the FoodNet

report?

A Right. This is the number of culture-confirmed cases ascertained in FoodNet surveillance reported by the date of isolate collection and this is for the state of Minnesota.

Q And for January there were 20 culture-confirmed cases, right?

A Right.

Q And for August there were 155 culture-confirmed cases, right?

A Correct.

Q And for January, if Minnesota was following protocol, how many Campylobacter isolates would it send to NARMS for susceptibility tests?

A It would depend upon how many weeks there were in January -- how many Mondays there were in January and there would be either four -- it would be one a week for every Monday in January.

Q So you would expect for January -- there's total confirmed 20 cases for January and they would send, depending on how many Mondays there were in 2000 in January, 4 or 5 isolates for susceptibility testing,

right?

A The second part of your statement is true but it doesn't necessarily relate to the 20 cases in the surveillance. Those 20 in surveillance -- in FoodNet surveillance, those 20 are -- we compile the FoodNet cases by the date of isolate collection but we track NARMS submission by -- for Minnesota by date of receipt at their state public health laboratory.

So it would not be true -- so the 4 in the month of January does not necessarily relate entirely or completely to the 20. They're going to be very closely related but an isolate that was collected on December 31 and submitted to the public health laboratory and they received it on January 3 is going to be in the NARMS January collection but in the December FoodNet collection.

Q Okay. For the purpose of this discussion, let's -- I'm not going to quibble over one or two or three isolates. I'm talking about the overall numbers, okay? Can we agree on that?

A Yes.

Q Okay. So for 2000 for Minnesota for January

there's 20. For February there's 42, right, that were collected, total, right?

A Yes.

Q And of those 42, in general, how many would get sent to CDC for susceptibility testing?

A The same as -- 4 or 5.

Q Okay. And for March there were 82, weren't there? 82 FoodNet collections in Minnesota for March of 2000, right?

A Correct.

Q And of those there would be 4 or 5 sent on, right?

A Yes.

Q And April --

JUDGE DAVIDSON: All right. That's enough. April -- you've got the numbers all right here on the exhibit --

MR. KRAUSS: Okay.

JUDGE DAVIDSON: -- and for each one there's going to be four or five.

MR. KRAUSS: Right.

JUDGE DAVIDSON: I'm not going to have him

asked that question over and over and over again. You want to draw your chart, go ahead.

MR. KRAUSS: All right.

BY MR. KRAUSS:

Q Let me do August. There were 155 total and 4 or 5 would have been sent on to NARMS for susceptibility testing, right?

A Yes.

Q And in total for Minnesota for 2000, for FoodNet, there were 1,079 Campylobacter isolates sent -- no -- collected in Minnesota for 2000, right?

A There were that many cases ascertained in clinical laboratories. Isolates were not collected but yes, there were that many cases ascertained in FoodNet in 2000.

Q Okay. Now, let me hand you the NARMS 2000 annual report, table 21B.

MR. KRAUSS: I have a copy for you, your Honor.

JUDGE DAVIDSON: Is this already in the record or not?

MR. KRAUSS: It is, as an attachment to the

NARMS 2000 report.

JUDGE DAVIDSON: Exhibit number?

MR. KRAUSS: I'm going to label this one as the next B number, your Honor.

JUDGE DAVIDSON: If it's already in, you don't have to. Just refer to it as the existing exhibit number. You don't know what it is? Is that the problem?

MR. KRAUSS: Yes, your Honor. I'm sorry.

JUDGE DAVIDSON: Go ahead. Give it a number.

(Exhibit B-1933 was marked for identification.)

BY MR. KRAUSS:

Q Have you seen B-1933? Do you recognize it?

A Yes.

Q It's a table for NARMS for 2000 for Minnesota. Isn't that right?

A Amongst others, yes.

Q Right. Amongst others. So the total sent to NARMS from Minnesota for 2000 were 49, right?

A Yes. Well, tested and in the final report. They may have sent more that didn't survive that were

not confirmed Campylobacter.

Q Okay.

A So that's not submission. That's testing and in the final report.

Q Okay. And of those 49, they found 12 resistant, didn't they?

A Yes.

Q And that's 24.5 percent for Minnesota for 2000 for Ciprofloxacin-resistant Campylobacter, right?

A Very close -- this is jejuni. I think we may have received a few -- about 95 percent of all Campylobacters that we receive are jejuni. Minnesota might have sent in a lari or a coli that -- so -- and this number here on the far left that you're reporting which is the FoodNet number is going to be all Campylobacter, not just jejuni.

So -- but it's -- the number on your far left column, FoodNet number, is largely jejuni 90 -- but includes 5 percent of probably additional cases. The number that you're putting there, NARMS, this 12, is only the jejuni.

JUDGE DAVIDSON: You've got to do that again

for the record. The 1,097 is everything and the 12 is only jejuni. Is that correct?

MR. KRAUSS: That's correct, your Honor.

JUDGE DAVIDSON: Okay. Go ahead.

BY MR. KRAUSS:

Q Okay. Now, in Minnesota, Campylobacteriosis is a reportable disease, isn't it?

A Yes.

Q And so they keep data on Campylobacter submissions, don't they, in Minnesota?

A In Minnesota -- Campylobacter is -- Minnesota is special because Campylobacteriosis, which is the clinical syndrome, is reportable by physicians so it is a reportable disease. They also have a -- it's also mandated that clinical laboratories forward the isolates so it's also a state mandate that the isolates be forwarded.

So it is state reportable from clinicians, it's state mandated to be forwarded by clinical laboratories. So in both instances.

Q In Minnesota.

A In Minnesota.

Q And so Minnesota, for those reasons, collects data relating to Campylobacteriosis in the state, isn't that right?

A Yes. And isolates.

(Exhibit B-1934 was marked for identification.)

BY MR. KRAUSS:

Q And isolates. Okay. Let me hand you B-1934. This is from the Minnesota Department of Health. Take a look at that.

MR. KRAUSS: Your Honor.

BY MR. KRAUSS:

Q Have you seen this before, Dr. Angulo?

A Perhaps not -- I'm familiar with this antibiogram. I made a reference to it in my testimony earlier because this is what they send to their physicians to help them treat, but I can't say for certain I've seen the 2000 report.

Q You've seen reports like this before --

A Yes. From Minnesota, yes.

Q -- from Minnesota. Yes. Okay. For 2000 for Campylobacter, would you agree with me that they had a

total of 1,028 isolates received? Do you see that in note 1?

A I do, yes.

Q Okay. So their total for the state was 1,028. Now the footnote says, if I'm not mistaken, that all 1,028 of those were resistance tested. You see that?

A Yes. But for clarity, those are not the same numbers -- 1,079 is numbers of cases. 1,028 is numbers of isolates. They're not -- the fact that they don't match up is entirely expected but some isolates don't make it to the laboratory.

Q Okay. That explains that. Somewhere between 1,000 and 1,050.

And Minnesota tested all 1,028 isolates, right?

A By a different procedure but yes, they did susceptibility testing on their 1,000 isolates. They have been doing that since 1998.

Q And they use the same definition of resistance, don't they, MIC is greater than or equal to 4 micrograms per milliliter, as NARMS does for Ciprofloxacin?

A For Ciprofloxacin they have a slightly different testing algorithm than we do at CDC. They screen their Campylobacter isolates for nalidixic acid resistance and then the ones that are nalidixic acid resistant they test additionally for Ciprofloxacin. So there's a slight laboratory procedure different that you would want to keep in mind.

Q Okay. And do they do that before they send the isolate to CDC for testing?

A No. They randomly select one isolate a week and forward it to our laboratory and judgment of speciation or resistance testing does not -- they don't -- those don't impact their selection that they send to us.

Q Okay. Now for Minnesota, when they tested all their isolates instead of just the 49 isolates that you tested, they tested 1,028, their percent resistance was what? Do you see that in the biogram? 89 would refer to susceptibility percentage, right?

A Yeah, but this is -- perhaps it's not -- I believe that the 11 percent that they report resistance is nalidixic acid resistance based on their screening.

I can't say for certain that they confirmed it to be Cipro-resistant but they report quinolone-resistant --

Q Do you see note 1, Dr. Angulo?

A Yeah.

Q They're talking about Ciprofloxacin susceptibility, aren't they for Campylobacter?

A They are reporting here advice to clinicians on what you should treat a patient with if they have a Campylobacter infection and --

Q They are? Where does it say that?

A That's the purpose of this antibiogram. It's sent to all clinicians in the state of Minnesota.

Q And this document reports that for the ~~1,028~~ 1,028 isolates collected by Minnesota -- Campylobacter isolates collected by Minnesota in 2000, there was 89 percent susceptibility to Ciprofloxacin, 11 percent resistance to Ciprofloxacin. Isn't that right?

A I don't think that's entirely precisely correct. What this is is they're advising the clinicians to expect that if you treat a patient with Campylobacter, in 89 percent of the times, the organism will be susceptible to Ciprofloxacin, that you won't

threaten the therapy.

They may be making that judgment based upon nalidixic acid results that they have done in their laboratory. I don't know necessarily that this 89 percent is a Ciprofloxacin resistance rate.

Q That's not Ciprofloxacin susceptibility as indicated in note 1?

A This is the advice to clinicians on what they should expect the Ciprofloxacin susceptibility results to be based upon their screening that they've done with nalidixic acid of the collection of their agars.

Q And the screen that they did, according to this, they found 89 percent --

JUDGE DAVIDSON: All right. Don't keep going over and over it. The distinction he wants to make has been made and you've gotten on the record 89 and 11 about 89 times already.

MR. KRAUSS: Thank you, your Honor.

BY MR. KRAUSS:

Q Now, Dr. Angulo, you testified about the 1998-1999 Campylobacter case control study, didn't you?

A Yes, I did.

Q And that was done by CDC?

A And our partners and state health departments, yes.

Q And you attached as attachment 3 to your testimony one of the reports from that, didn't you?

A Yes, I did.

Q And that's by Friedman?

A Yes.

Q Now, the 1998-1999 Campylobacter case control study, that was the largest Campylobacter case control study done in the United States, wasn't it?

A Yes.

Q And there were three analyses, based on your testimony -- three analyses of the data from that study, one by Friedman, right?

A Correct.

Q And one by Kassenborg, right?

A Correct.

Q And one by Jennifer McClellan, also known as Jennifer Nelson, right?

A That's correct.

Q And the Friedman study related to the risks of

getting a Campylobacteriosis infection in general, right?

A Correct.

Q And the Kassenborg study has to do with the risk of getting a susceptible Campylobacter infection. Isn't that right?

A The converse. A resistant effect, yes.

Q I'm sorry. Thank you. The risk of getting a resistant infection, right?

A A Ciprofloxacin-resistant Campylobacter infection, yes.

Q And the McClellan-Nelson study has to do with the human health impact of getting a resistant -- Ciprofloxacin-resistant Campylobacter infection, right?

A In a narrow sense. A duration of diarrhea.

Q Right.

A It has to do with duration of diarrhea.

Q And that is attachment 4 to your testimony, isn't it?

A Yes, it is.

Q The Friedman paper, which is number 3, that hasn't been published, has it?

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A It's in press with a journal but it has not been printed and published. It's gone through CDC clearance but it's not published.

Q Has it been accepted for publication?

A Yes, it has.

Q What journal?

A Clinical Infectious Diseases.

Q And the Nelson paper, which is attachment 4, that ~~as~~ is attached to your testimony is a draft, isn't it?

A Correct.

Q And has that been published?

A No, it has not.

Q Has that been accepted for publication?

A No, it has not.

Q And the Kassenborg paper -- are you familiar with that paper?

A I am.

Q Do you know whether that has been published?

A I know that it has not been published.

Q Do you know whether it's been accepted for publication?

A It is in -- it's also in press with the Clinical Infectious Disease supplement.

Q This morning you wanted to make some changes to the Friedman paper attached to your testimony, didn't you?

A I did, yes.

Q And were those changes corrected before it went to publication -- to the press?

A Yes.

Q Now, were any changes made to the Kassenborg draft in the process of it being accepted for publication that you're aware of?

A I'm sure many changes were made in the process of writing that manuscript but in terms of what is on the docket, I don't know whether that is one -- verbatim what is going to be in the press. You might ask Dr. Kassenborg.

Q Now, Dr. Angulo, let me direct your testimony to pages -- let me direct your attention to the testimony at pages 9 through 11. Here you're talking about risk factors for acquiring Campylobacteriosis at paragraph 11, right?

A Yes.

Q And you discuss the Friedman study in here, right?

A Yes.

Q And you also discuss -- you say that there are other epidemiological investigations to determine risk factors for spread of Campylobacter infections that have been conducted in the United States and other developed nations, and you refer to references 3 through 10 in the list, don't you? The list on page 11.

A Yes.

Q And that would be the Adak article, G-10, Eberhart Phillips, G-182, Kapperud, G-334, Neal, G-1680, Niemann, B-561, Schorr, G-1718, Harris, G-268, and Deming, G-162. Am I correct?

A I can't say for certain. I followed you but I can't accept the Niemann one. I don't know for sure.

Q The number, the B -- the letter of the number is B-561?

A I don't know what -- it's not in my testimony so -- the exhibit number is not in my testimony so I

couldn't certify that, whether it's -- I followed in my testimony every number you said but that -- I apologize. That number is not in my testimony.

Q All right. Well, that is an exhibit number for Niemann. I make that representation.

Now, you're familiar with all these articles, aren't you?

A Ah --

Q You use them as references in your testimony. You're familiar with them?

A I have an understanding of them.

Q The Adak article relates to Campylobacter infections in England and Wales, doesn't it?

A Yes.

Q And in that case control study, it was carried out between May 1990 and January 1991, wasn't it?

MS. ZUCKERMAN: Objection, your Honor. The document speaks for itself and if counsel wants the witness to discuss these documents -- these studies, would he please provide the witness with copies?

MR. KRAUSS: Yes. I'll do it, your Honor.

JUDGE DAVIDSON: All right.

MR. KRAUSS: Your Honor, to speed things up --

JUDGE DAVIDSON: I don't need it.

MR. KRAUSS: Okay. I'm going to hand the whole set to him so we don't have to keep walking back and forth.

JUDGE DAVIDSON: Are these all G exhibits?

MR. KRAUSS: Except for Niemann, which is a B-561.

JUDGE DAVIDSON: Well, give me a copy of that one. I can find the G ones. It's a different disk. That's the only reason. I don't have to switch.

MR. KRAUSS: Okay. Thank you, your Honor.

BY MR. KRAUSS:

Q All right. Let's hand you the Adak study, the Eberhart Phillips study --

MR. KRAUSS: Your Honor, could we go off the record for one second, please?

JUDGE DAVIDSON: Off the record.

(A brief recess was taken.)

BY MR. KRAUSS:

Q All right. Dr. Angulo, let me hand you G-10, which is the Adak study, G-182, which is the Eberhart

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Phillips study, G-334, which is the Kapperud study, G-1686, which is the Neal study, B-561, which is the Niemann study, G-1718, which is the Schorr study, G-268, which is the Harris study, and G-162, which is the Deming study.

MR. KRAUSS: That should allow us to go faster. I'm sorry for the delay, your Honor.

JUDGE DAVIDSON: That's all right.

BY MR. KRAUSS:

Q Now, the Adak study was a case ~~controlled~~ control study that was carried out between May 1990 and January 1991, wasn't it?

A You want me to verify that or --

Q Well, let me point you in the right direction if you're not familiar with the study. Page 2 at the top.

A It so states.

Q Okay. In terms of risk factors for acquiring Campylobacteriosis in the late 1990s in the United States, would you agree that the Friedman study is more relevant than the Adak study?

A Yes.

Q Now, the Eberhart Phillips article, that relates to a case control study in New Zealand, doesn't it?

A Yes.

Q And the Eberhart Phillips study relates to case patients from June 1994 to February 1995, doesn't it? See that in the abstract, Dr. Angulo, where it --

A It so states, yes.

Q In terms of the risk factors for becoming infected with Campylobacter in the United States in the late 1990s, the Friedman analysis is more relevant than Eberhart Phillips, isn't it?

A Yes.

Q If you'd turn to the Kapperud study that you refer to in your testimony --

JUDGE DAVIDSON: Exhibit number?

MR. KRAUSS: Yes, your Honor. G-334.

JUDGE DAVIDSON: Thank you.

BY MR. KRAUSS:

Q The Kapperud study relates to Campylobacter infections in Southeastern Norway, doesn't it?

A Yes, it so states.

Q And it relates to a case control study conducted in 1989 and 1990, doesn't it?

A It so states.

Q In terms of the risk factors for becoming infected with Campylobacter in the United States in the late 1990s, the Friedman study is more relevant than the Kapperud study, isn't it?

A I would say so, yes.

Q Now, if you'd turn to the Neal study, G-1686, this study relates to Campylobacter infections in Nottingham, England, doesn't it?

A Yes, it so states.

Q And if you look under the methods, the Neal study was carried out from June 1994 to July 1995, wasn't it?

A Yes, it so states.

Q In terms of the risk factors for becoming infected with Campylobacter in the United States in the late 1990s, the Friedman study is more relevant than the Neal study, isn't it?

A I'd say yes. I believe so.

Q Now, the Niemann study, that has to do with

risk factors associated with Campylobacteriosis in Denmark, doesn't it?

A Yes. And much more than that. Yes.

Q In terms of the overall risk factors for becoming infected with Campylobacter in the United States, the Friedman study is more relevant than the Niemann study, isn't it?

A I would not -- I wouldn't make that conclusion. They're equally relevant. We -- Jacob Niemann spent one year as a fellow -- a World Health Organization fellow in our branch immediately before he returned to do this study at which time we were designing the Friedman study.

So he had much opportunity to see the development of the questions in the Denmark study and we -- and so many of the questions that are asked in the Denmark study are identical to the questions that are asked in our study and much of the study design is identical, the lab procedures are identical and much of the supervision oversight was provided by my boss, Dr. Rob Tauxe.

So I would -- I think that although this study

was done in Denmark, it has much implications to the study done in the United States.

Q Were they sampling United States citizens in Denmark in the study, in the Niemann study?

A They may have. They sampled people that got Campylobacter in Denmark and I don't know whether they excluded U.S. citizens or not. But in terms of your question about relevance, the epidemiology of Campylobacter in Denmark and the United States, there is much in common. We have -- our cultures are very -- are relatively similar.

What is learned in the epidemiology of Campylobacter in Denmark I think would have applicability to what's learned in the United States.

Q Now, according to your testimony, the Niemann article relates to the food -- according to this citation, foodborne risk factors associated with sporadic Campylobacteriosis in Denmark. Do you see that? Is that the title of the Niemann article, number 7 in your list?

A Right, because this is not -- what you handed me is not the reference that I have -- I mean, this is

the published -- unless it's in his thesis.

Q Oh. That's the Niemann thesis that I handed you?

A You handed me the entire epidemiologic sporadic disease and Campylobacter which is the Niemann thesis, which I think might have an article in it that is cited in my reference.

Q Let me then refer only to the article that you're referring to in your cite list, number 7. That has to do with foodborne infections in Denmark, doesn't it?

A No. It has to do with sporadic Campylobacter cases in Denmark, some of which are foodborne, some of which are person to person, some of which are waterborne. I think we have the title correct and I think that's --

Q The Niemann study was conducted in Denmark, wasn't it?

JUDGE DAVIDSON: Asked and answered.

THE WITNESS: Yes.

BY MR. KRAUSS:

Q In terms of the overall risk factors for

becoming infected with Campylobacter in the United States, the Friedman study is more relevant than the Niemann study, isn't it?

A I answered that and I said that I believe they're equally relevant and the reason is because the questions are very similar, we had much input into the development of the questions and the biology of Campylobacter would not necessarily be different between Denmark and the United States. So I think they are complementary studies.

JUDGE DAVIDSON: All right. That's enough. You've answered it twice now.

MR. KRAUSS: I'm going to move on to the Schorr study, your Honor.

JUDGE DAVIDSON: I beg your pardon?

MR. KRAUSS: I'm going to move on.

JUDGE DAVIDSON: Okay. Good.

MR. KRAUSS: Thank you.

BY MR. KRAUSS:

Q The Schorr article, which is G-1718, that was relating to risk factors for Campylobacter infections in Switzerland, right?

A Correct.

Q And that has to do with the period -- the study period was February to December 1999, right?

A Correct. It so states.

Q In terms of the risk factors for becoming infected with Campylobacter infections in the United States, the Friedman study is more relevant than the Schorr study, isn't it?

A I would say yes.

Q Now, for Harris, which is G-268, the Harris study is from a single county in the United States, isn't it?

A That's correct. A single large county in the United States.

Q King County in Washington State, right?

A Correct.

Q And the Harris study took place from April 1982 through April 1983, didn't it?

A Correct.

Q April 1982 through September 1983.

A It so states.

Q In terms of the risk factors of becoming

infected with a Campylobacter infection in the United States in the late 1990s, the Friedman study is more relevant than the Harris study, isn't it?

A They're both equally relevant and for a variety of reasons, one of which is the microbiologist who worked on this study -- was related to the study, Dr. Fred Tenover, is a CDC employee and contributed to our understanding of Campylobacter and helped to design the Sentinel County study that was done in the early '90s and helped us with design of our NARMS.

So it's related to our understanding -- this was a foundational paper to our understanding which led to our development of the questionnaire for the Friedman study. So it's a complementary study to our understanding of the epidemiology of Campylobacter.

MR. KRAUSS: Your Honor, one of the articles that the witness referenced was an article that was stricken. The Tenover article. I'd like to move to strike that portion of the witness's testimony.

MS. ZUCKERMAN: Your Honor, I don't believe that the Tenover article was mentioned. Dr. Tenover was mentioned but not the article.

MR. KRAUSS: He mentioned the Sentinel County study.

JUDGE DAVIDSON: In the testimony, yeah, Sentinel County study. It's still up in the air, isn't it? So you'd better -- we don't know where it is at this point. It's out but it could be in as of Friday.

MR. KRAUSS: Right, your Honor.

JUDGE DAVIDSON: So I don't want to strike his testimony as of this point.

MR. KRAUSS: Okay. Thank you, your Honor.

BY MR. KRAUSS:

Q Now, the Friedman study had 1,316 patients in it, didn't it?

A The culture -- yes. The culture-confirmed cases in the Friedman study, yes.

Q And the Harris study had 218 patients in it, didn't it? In the abstract.

A It so states.

Q In terms of the number of patients, the Friedman case control study is more robust than the Harris study, isn't it?

A Yes.

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Q The Friedman study looked at the risks of getting a Campylobacteriosis infection in the time frame 1998 to 1999, didn't it?

A Yes.

Q And the Harris study looked at the risks of getting a Campylobacter infection in 1982 to 1983, didn't it?

A Yes.

Q So I'm going to ask you, in terms of the risk factors of getting a Campylobacter infection in the United States in the late 1990s, isn't Friedman more relevant than Harris?

A They're both equally relevant. They both contribute to the scientific data that allow us to conclude what the sources -- risk factors are for Campylobacter infection.

I wouldn't throw out this article -- again, this foundational article solely because it's 20 years old. In fact, the prevalence -- I mean, the frequency with which Campylobacter is present on ~~Alteri~~ poultry hasn't remarkably changed since -- what they find -- the risk factors they've identified here, that information still

contributes to our understanding of the epidemiology of foodborne disease.

We don't discount all previous studies simply because we did the latest study. They all contribute to a body of evidence that allow us to make judgments about appropriate interventions.

Q Let me turn your attention to the Deming article.

JUDGE DAVIDSON: Do you have a number?

MR. KRAUSS: Yes, your Honor. G-162.

BY MR. KRAUSS:

Q The Deming article -- the Deming study relates to Campylobacter infections at a single university in the United States, doesn't it?

A It does, in Georgia.

Q And the Deming study took place during the fall and winter quarters of 1983 to 1984, isn't that right?

A That is correct.

Q In terms of the risk factors of becoming infected with Campylobacter in the United States in the late 1990s, the Friedman study is more relevant than

the Deming study, isn't it?

A It is equally relevant, and this is an equally foundational article. This article was co-authored by my current boss, Rob Tauxe, who was a senior advisor on developing the case control questionnaire for the Friedman study.

It was co-authored by Charlotte Patton, who was the previous director, until she retired this last year, of the National Campylobacter Reference Laboratory. It was this paper that was the foundation of the Sentinel County study -- can I say that?

And this study was foundational and to our understanding of the epidemiology of Campylobacter which we would not discount this study nor the findings from the study contribute to our current NARMS surveillance -- I mean, all the way from the Sentinel County to the NARMS which evolved from the Sentinel County to our FoodNet case control study.

This represents an evolution of our understanding of the epidemiology of Campylobacter and I would not discount this simply because it was done over 20 -- or almost 20 years ago.

Q The Deming study had 45 students as cases, didn't it?

A It so states.

Q And the Friedman study had 1,316 cases, right?

JUDGE DAVIDSON: Asked and answered.

BY MR. KRAUSS:

Q In terms of the number of patients enrolled in the study, the Friedman study is more robust than the Deming study, isn't it?

A Yes, but robustness of a study is most important when you have negative findings. If you have a study with 45 patients and you find a significant risk factor, as strong as this risk factor was, the size of the study is relatively unimportant. The size of a study is important when you find negative findings.

So yes, the Friedman study was more robust to find some risk factors but not necessarily more robust to find what was found in the study. Robustness -- it's hard to take robustness out of context. Tell me a specific exposure and I'll tell you whether one study was more robust for finding that exposure.

Q In terms of the geographical area covered, comparing the Friedman study and the Deming study, the Friedman study was more expansive in terms of the population of the United States covered, wasn't it?

A That's correct.

Q And in terms of the population covered in the Harris study, the Friedman study population in terms of the extended United States was more comprehensive than the geographical area studied in the Harris study, wasn't it?

A Yes.

Q Let me turn your attention to your testimony regarding a retail study and here we are on the bottom of page 11 and page 12. You reference G-1528, the Rossiter study. Let me just ask you in terms of the Rossiter study, that was studying Campylobacter isolated for retail poultry, right?

MS. ZUCKERMAN: Objection, your Honor. If Mr. Krauss wants to talk about this study, I'd like him to provide the witness with a copy of it, please.

MR. KRAUSS: Your Honor, I just have a couple of questions on it. I'm going to ask him --

JUDGE DAVIDSON: Well, she's -- all right. Ask one question. If it requires him to look at the document, he'll say so and then you have to provide it to him, okay?

MR. KRAUSS: Yes, your Honor.

JUDGE DAVIDSON: Go ahead.

BY MR. KRAUSS:

Q Dr. Angulo, in the Rossiter study, do you know how the Campylobacter that was isolated was speciated?

A Well, I guess -- first, there was a abstract that was written by Shannon Rossiter from our group and she took a look at the preliminary data from this study, but I wouldn't necessarily characterize it as her study -- her abstract is certainly not the most complete analysis that we've done of this data.

And the second thing then is yes, we are familiar with the way that the three state health departments tested for isolation of Campylobacter from these retail chickens -- chickens purchased in grocery stores at their state public health laboratories and we're also familiar with how those isolates were reported to CDC and speciated at CDC because we did the

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speciation of the isolates at CDC.

Q And when you did that, I take it you did not use nalidixic acid speciation?

A We did not. We used PCR techniques -- ~~pipperate~~ hippurate -- testing, PCR testing.

Q Now, in your testimony, Dr. Angulo, you mention the Mead article, G-410, on page 7. And you mention that there's 2.4 million infections in the United States per year referenced in that article, right?

A Yes, correct.

Q And more recently CDC has come up with a new estimate of the number of Campylobacteriosis cases for 1999, right?

A Correct. We -- I want -- if -- as I think you -- as we've explained that FoodNet tracks the incidence of culture-confirmed Campylobacter cases in the FoodNet sites and FoodNet has reported a decline in the incidence of Campylobacter cases which has reflected that when we use -- the Mead article used 1997 FoodNet Campylobacter incidence as its starting point for the estimation of 2.4 million cases, if you use the -- take

in account the decline in the incidence and then use 1999 starting point, the new estimate would be 1.4 million cases.

Although this article has not been published, it's in press with Clinical Infectious Diseases but has gone through CDC clearance and has been accepted by the Journal.

Q And you also testified that CDC estimated that Campylobacter caused 124 deaths per year in the United States based on the Mead article, right?

A That's correct.

Q But for 1996 there were only 4 persons with Campylobacter infections that died in the United States, right?

A No, that's not true.

Q Would you take a look at -- attached to your testimony, attachment number 1, page 52, that's G-1452?

JUDGE DAVIDSON: What page again?

MR. KRAUSS: Page 52 of G-1452, your Honor.

JUDGE DAVIDSON: Okay.

THE WITNESS: What's the attachment?

BY MR. KRAUSS:

Q It's attachment number 1, Dr. Angulo.

A My attachment -- these are numbered at the top? I'm sorry. I'm sorry. What page?

Q 52. And at the end of the first paragraph it states four persons with Campylobacter infection died in 1996, right?

A Correct.

Q And for 1997 there was one, right?

A Correct.

Q And two in 1998, right?

A Correct.

Q And four in 1999, right?

A Correct. Your question was did four people die in the United States of Campylobacter and these are simply the death in FoodNet in our estimates using these case fatality rates, taking into account the rest of -- the generalizations to the rest of the country. In the Mead article we describe how you get to the estimate of whatever my testimony was, 124 deaths.

So I may -- the Mead article says 124 deaths but that is not -- that's nationwide based upon the

methods described in that article, and this is an article describing just what was reported and ascertained in FoodNet. Those are not the same numbers.

MR. KRAUSS: Okay. Your Honor, would this be a good place for a break for five minutes?

JUDGE DAVIDSON: Okay. You're running close to the edge, here.

MR. KRAUSS: Thank you, your Honor.

JUDGE DAVIDSON: All right. We'll take a five-minute recess, be back at 2:35 sharp.

Off the record.

(A brief recess was taken.)

JUDGE DAVIDSON: On the record.

Don't forget you have another recess coming to go through your tape recorder.

MR. KRAUSS: Your Honor, do you want to do that now or --

JUDGE DAVIDSON: Why didn't you do it while we were off the record here?

MR. KRAUSS: Before we go on, your Honor --

JUDGE DAVIDSON: I don't appreciate that.

You've all been sitting here for a five-minute recess and that's something you could have incorporated in your last request, so --

MR. KRAUSS: Sorry, your Honor.

JUDGE DAVIDSON: All right. We'll go off the record again, get it over with. Let's get back as soon as we can because you're pushing the time limits. We're not going to start at 9:30 tomorrow if you keep this kind of stuff up.

MR. NICHOLAS: Your Honor, we're happy to do this right here unless there's some particular reason --

JUDGE DAVIDSON: It's up to them. I don't want to -- doesn't matter to me where you do that. I've said that from the beginning.

Off the record.

(A recess was taken.)

JUDGE DAVIDSON: Back on the record. What do we have with this?

MR. NICHOLAS: Your Honor, we would propose playing this portion of the -- of this recording which is taken from the tape. The transcript of that tape is

attached in relevant part to witness Angulo's testimony who was at the --

MR. KRAUSS: Carnavall.

MR. NICHOLAS: -- Carnavall -- I'm sorry -- who was at that meeting, heard the presentation by Dr. Angulo and others --

JUDGE DAVIDSON: Is there an exhibit for me?

MR. NICHOLAS: Dr. Carnavall's testimony is --

MR. KRAUSS: A-199.

MR. NICHOLAS: -- A-199.

JUDGE DAVIDSON: Okay.

MR. NICHOLAS: CVM did have a motion to strike there. Your Honor denied that motion. As part of the reply to the motions to strike, we believe that's appropriately in evidence. We have the tape recording that was original.

The Center of Veterinary Medicine never requested a copy of that tape and right now, your Honor, we are prepared to play the whole tape for CVM, but that would take probably about an hour, hour and a half.

JUDGE DAVIDSON: Well, you can do that on your

own time.

MR. NICHOLAS: So we have played the portion of the exhibit that we'd like to use.

JUDGE DAVIDSON: How much are you talking about?

MR. NICHOLAS: About a minute, your Honor.

MR. KRAUSS: 46 seconds. 46.58 seconds.

JUDGE DAVIDSON: And you propose to play that for the witness and he has a copy of the transcript in front of him. Yes, no?

MR. SPILLER: Your Honor --

JUDGE DAVIDSON: I'll hear from you in a minute. I just want to hear what they're proposing.

And then you're going to ask some questions about it whether it's true or correct or what?

MR. KRAUSS: I want to see if he recognizes his voice, I want to see if it refreshes his recollection as ever having said the statement, and then I want to ask him about whether he agrees or disagrees with the statement that's said, assuming that he recognizes it.

JUDGE DAVIDSON: Okay. Now.

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MR. SPILLER: Your Honor, I think counsel has succinctly saved us a lot of time. What he wants to do is to ask the witness if he agrees with what the transcript or the purported transcript says he says, and that's already been accomplished. We don't need the tape for that.

If we did need the tape, the segment that was played for us -- we asked for the whole tape, and counsel properly pointed out that the whole tape is an hour long and the segment that they want is 47 seconds. So we have not a full transcript of what was said and that which has been referred to -- and I just made the same mistake myself -- ~~is~~ as the transcript is nowhere identified on its face as a transcript.

It is not authenticated. No one says I'm the typist, I typed exactly what was on this tape. And that which they purport to play is a digital copy, I understand, of a tape which in turn is ~~merely an audible~~ nearly inaudible and which by its own description in attachment 3 of Exhibit A-199, page 85, lines 3 and 4, it states -- even though the item is not signed -- "I recorded portions of the meeting with a tape recorder like those

used to record lectures," which brings up another point. Of course, we don't know whether it's a lawful tape. Many meetings it's perfectly appropriate to tape. Others, I presume like this one, it would not be appropriate for persons to make their own recording.

So for all those reasons, we don't know if it's authentic, we know for sure that it's not complete; we shouldn't be engaging in playing a tape which at this late date is offered, when it could have been offered and had forensics done on it some time ago to see if it's right.

The witness -- to the extent the words have been accurately transcribed, have already been read by counsel to the witness and he has already reacted to it.

JUDGE DAVIDSON: Except he said he didn't recall. He didn't say he didn't make the statement; he said he didn't recall. So under those circumstances, I ask the question, does he have the transcript in front of him or the purported transcript?

MR. KRAUSS: I don't know that he does, your Honor.

JUDGE DAVIDSON: Well, would you hand him a copy of that and let him look at it? See if that refreshes his recollection before we decide whether or not we're going to actually let him listen to the purported tape of the conversation.

MR. KRAUSS: Your Honor, what I have is a block of exactly what's on this portion of track 12, which are his words --

JUDGE DAVIDSON: Of a digitized copy of the original tape? Is that what it is, or not?

MR. KRAUSS: Yes, your Honor.

JUDGE DAVIDSON: Well, can we get some CSI people in here to go over this?

(Laughter.)

MR. SPILLER: Actually, your Honor, that's a perceptive question. You likely thought that that's the exhibit. That's what I thought when we were in the conference room. But Mr. Krauss kindly corrected me. If it's the same thing you offered us in the conference room, that's not actually the exhibit. That's something else that was prepared for you that is nowhere an exhibit and has never been shown to counsel.

MR. KRAUSS: That's correct. This is -- what I told the Judge was this is a transcription of exactly what's on track 12 that I'm preparing to play --

JUDGE DAVIDSON: But that's not in evidence.

MR. KRAUSS: The transcript is in evidence, and this is a portion of the transcript.

JUDGE DAVIDSON: The whole transcript is in evidence?

MR. KRAUSS: Yes.

JUDGE DAVIDSON: But not this piece of paper.

MR. KRAUSS: Not this piece of paper, your Honor.

JUDGE DAVIDSON: But the tape, obviously, is not in evidence.

MR. KRAUSS: Correct.

JUDGE DAVIDSON: And the tape is not the original. It's a copy of --

MR. NICHOLAS: Well, we have the original tape here, your Honor. It's just harder to hear, so we --

JUDGE DAVIDSON: Well, you say harder to hear -- excuse me for interrupting you. You say harder to hear, he says inaudible. I mean, you know, I don't

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know what it is and I don't know if I want to hear it or not, but I want to go through this first by the way I suggest it.

You show the witness that paragraph, see if that refreshes his recollection, and then I'll ask him a question and then maybe we will, maybe we won't have the tape, okay?

MR. KRAUSS: Yes, as long as by that paragraph we agree I can do it with this --

JUDGE DAVIDSON: If that's an accurate representation. Did you show it to counsel?

MR. SPILLER: Your Honor, since the exhibit is in the record, may we use the exhibit that's in the record and offer him a portion of your exhibit A-199, attachment 3, and I believe you have indicated that the particular part that you want to read is -- it's on page 88.

MR. KRAUSS: If you have it, I'd be happy for you to give it to the witness.

MR. ~~NICHOLAS~~ SPILLER: It's not my exhibit, and, I'm sorry, the copy I have has counsel's mark on it. But you can get a clean copy.

JUDGE DAVIDSON: Don't look at me. I don't have it. I have a disk. I don't have it printed.

MR. SPILLER: At the Court's direction, I will fetch a copy of this exhibit.

JUDGE DAVIDSON: Do you want to take this with you and print it out?

MR. SPILLER: I'm sure we have access and we may -- pardon me, your Honor.

JUDGE DAVIDSON: Sure. Go ahead.

MR. SPILLER: We're excavating to see if we have a clean copy.

JUDGE DAVIDSON: In the meantime, do you have any other areas of inquiry?

MR. KRAUSS: Yes, your Honor.

JUDGE DAVIDSON: Well, maybe while they're getting copies of this you can go with that, move us along.

MR. SPILLER: I apologize, your Honor. I have -- and I want to make sure that we have no extraneous marks on here.

I'm loaning to Mr. Krauss our copy of an exhibit which I believe is not in evidence -- is it in

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evidence? This one is. Okay. Exhibit ~~899~~ A-99, Attachment 3. It includes pages 85 through 89.

JUDGE DAVIDSON: Thank you.

MR. KRAUSS: Your Honor, what I would do is I, with your permission, will bracket the portions of the transcript --

JUDGE DAVIDSON: No, no. Not on his copy. You read it to him before. I heard you. You know what it is. You asked him at least once, maybe more, if that was his language.

Off the record.

(A brief recess was taken.)

JUDGE DAVIDSON: On the record. Ask him if he has seen that in print, if it helps him recall whether or not he said it. When he gives his answer, then I may have a question for him.

MR. KRAUSS: Okay. I'm sorry, your Honor. I misunderstood.

BY MR. KRAUSS:

Q Dr. Angulo, earlier I asked you whether you recalled saying that for all pathogens except Campylobacter we have a representative sample of the

culture-confirmed cases at the state level. And I believe your testimony was you didn't recall that.

Would you take a look at Exhibit A-199, Attachment 3, page 88, and see if that refreshes your recollection?

A It refreshes my recollection.

JUDGE DAVIDSON: Okay. Are those your words?

THE WITNESS: Are these my words? Again, I can't say precisely that this is what I said. I recall the context, although I can't -- I'm unable to -- I recall the setting, obviously, of the NARMS scientific meeting.

Jennifer McClellan was giving a presentation from the podium. There was a question asked. I stood up to discuss -- or to help discuss the answer to the question. The context of that question -- I don't see it -- the context with which this discussion occurred is not well-characterized, because it says all the comments by Jennifer McClellan are inaudible, but she was discussing the ability for us to use the -- our regression model to interpret the trends of -- in prevalence that were evident in the NARMS data.

And so my question, as I stood up to talk, was to provide further explanation of our ability to assess the change in prevalence over time.

I certainly was there at the meeting and I stood up and talked and I provided an explanation of the points that she was raising. I can't say for certain that these are the words that I said.

BY MR. KRAUSS:

Q In terms of the discussion that you had in response to the questions, was the general topic matter the representativeness of the Campylobacter sampling scheme for NARMS compared to other isolates that are -- other bacterial isolates that are collected?

A As I recall, the discussion was upon this -- the NARMS scientific meeting was the first time that we presented the logistic regression model which allowed us to look at the change in prevalence of Ciprofloxacin-resistant Campylobacter versus the baseline and I was discussing the ability of our sampling scheme to allow us to be confident in what that regression model was showing us in terms of the change in prevalence.

And in -- so the context where I may have discussed the sampling scheme, it was specific to ability to state that -- with confidence that the trend was routine and I remember precisely stating -- I remember this par -- I do recall this that I think our data allow the conclusion that there is an increasing trend. Equally important is the trend is going up and it's not zero.

I remember discussing the points that our sampling schemes within NARMS allows us to be confident that the prevalence of Fluoroquinolone resistance is increasing. And as you follow the testimony, these comments that I'm making here are following that discussion on the changing prevalence.

So on this part of it that you're highlighting, which is much into the discussion -- I think I see a dialogue -- much into the discussion was with the previous discussion of the context that well, how well can our sampling scheme support the conclusion of the increase in prevalence and my commentary was I was trying to make people aware that regardless of the sampling scheme, because the sampling scheme has been

consistent over time, regardless of whether you agree that the sampling scheme has limitations or not, regardless of that, because it's been consistent over time, we're confident that the prevalence is increasing.

And that's why I was discussing specifically in this paragraph you point out to comment on the prevalence and I was trying to say, well, prevalence is less important -- baseline prevalence is less important because whatever the sampling limitations contribute to that prevalence, clearly it's increasing since then.

Now, it's important to recognize the date. If you want an explanation --

JUDGE DAVIDSON: Go ahead. Nobody is stopping you. Go ahead.

THE WITNESS: Counsel is hovering.

(Laughter.)

MR. KRAUSS: I was just trying to refresh his recollection, your Honor. Apparently it's done a good job.

JUDGE DAVIDSON: It sure has.

(Laughter.)

THE WITNESS: But this was a NARMS scientific meeting in November of 2002, and since this meeting, we have done much additional exploration of the sampling basis of NARMS. And I therefore conclude, as I've stated in today's testimony, that I feel confident that the prevalence that we're measuring in NARMS is a close approximation of the national prevalence of Fluoroquinolone-resistant Campylobacter.

BY MR. KRAUSS:

Q The additional work that was done, was that done between November 22, 2002 and December 6, 2002, before your testimony was submitted?

A What date was my testimony submitted?

Q Well, the date you signed your testimony, December 6, 2002.

A Yes. There were -- some of those things were -- some of those analyses contributed to the conclusion in my witness testimony in December that allowed me to state with confidence that the prevalence -- the confidence I have of the prevalence of Fluoroquinolone resistance -- Ciprofloxacin resistance amongst Campylobacter in the United States.

Q So let me see if I've got this right. At the NARMS -- well, strike that.

Did seeing the transcript here which purports to say --

MR. SPILLER: Object to the form of the question that identifies the document as a transcript, which I think has not been established.

JUDGE DAVIDSON: All right. I'm going to sustain the objection. You read this to him before. He just read it again. I don't have to have the record say what that purports to say again.

MR. KRAUSS: Okay.

JUDGE DAVIDSON: I know your understanding of it is slightly different than the witness's and that's why you're asking this whole line of questioning.

MR. KRAUSS: Okay. Yes, your Honor. I think if I could ask two questions --

JUDGE DAVIDSON: You can ask 15 questions, but they've got to be pertinent and they've got to be to the point and they've got to not be repetitive.

MR. KRAUSS: Yes, your Honor. Thank you.

JUDGE DAVIDSON: Okay.

BY MR. KRAUSS:

Q Did seeing the sentence here about the representativeness of the Campylobacter sampling for NARMS refresh your recollection that you said this at the NARMS meeting?

A It refreshed my recollection that there was this discussion. Again, I don't recall saying these words precisely. I recall the discussion and it occurred in the context of the change in the prevalence and it was actually -- that discussion was very useful in terms of us because it was a scientific meeting where we had dialogue for us to explore those --

Q I understand.

A -- points -- some of the points that were raised at that meeting helped us direct our exploration, all of which were involved -- included in my witness testimony.

Q I understand. Would hearing a recording of the meeting refresh your recollection as to what was said? Would that be helpful to you in trying to refresh your recollection as to whether you said these words?

A I guess if I heard what I said it would help me but it doesn't -- it's the context of how these were said --

JUDGE DAVIDSON: Okay. I think the problem is that the witness has testified that the context, which is missing from the quote, the context of what -- even if it was said -- and you correct me if I'm wrong, Dr. Angulo. But even if the words were said as you recited them, the fact that they're not in context of the whole discussion changes his perception of his recollection of what he was talking about at the time.

I've heard him say it more than once, so I don't know why we keep going through this.

MR. KRAUSS: All right, your Honor. Could --

JUDGE DAVIDSON: Now, I will allow, if you think it's important, on your own time, you can have -- after we've adjourned, you can have Dr. Angulo listen to your version and see if it helps him. And if it does, then you can report back what the results were. But counsel would be present.

I don't want to go into it here because it messes up my record to put a recording on that I don't

know what it is or where it came from.

MR. KRAUSS: Thank you, your Honor.

JUDGE DAVIDSON: Did I characterize your --

THE WITNESS: I guess the -- may I make a --

JUDGE DAVIDSON: Sure. Go ahead.

THE WITNESS: My last comment is that the whole intended purpose of the NARMS scientific meeting was to have a casual and frank discussion amongst all stakeholders about the limitations and strengths, and we were freely answering questions in a dialogue format.

We had no idea that there was a tape recorder in the room. No one asked for permission to tape anything, and I had no idea that I should -- that the words that -- that all this discussion would be -- I thought we were talking amongst stakeholders about what were the strengths and limitations, where were we going, what was work in progress.

We revealed that we were working on these issues, some of which we resolved in time for my witness testimony, and it was not the context of a taped scientific meeting that I knew my comments would

be taped.

BY MR. KRAUSS:

Q Dr. Angulo, when you say stakeholders, that includes scientists, right?

A Yes.

Q And scientists with backgrounds in epidemiology, right?

A Yes.

Q Now, let me turn your attention to your testimony, page 10, lines 36 to 44. You report a population attributable fraction for eating chicken in a restaurant and for eating turkey in a restaurant, don't you?

A Line 36?

Q 36 to 44.

A Yes. We also talked about non-poultry meats in a restaurant.

Q Right.

A Right.

Q And a population attributable fraction does not necessarily indicate anything about causation, does it?

A I had an explanation of this this morning, but it's the same point that in a case control study where you have evidence of an exposure being associated with an outcome, you can measure that by a point estimate, whether it be odds ratio or risk ratio, and that point estimate, estimate of effect, estimate of association, can be translated with additional information about the -- evidence about -- about information about the proportion of the population exposed.

But anyway, that point estimate can be translated into a population attributable fraction or an etiological fraction, same term, and so it's the same issue as before.

Causation is a body of evidence that leads to a conclusion of causation. A demonstration of a strength of an association is one of the pieces of evidence that lead to causation. Population attributable fraction is another piece of evidence that leads to causation but not everything that has an association would I conclude is causal, so not everything that has a population attributable fraction would I say is causal.

In this instance, though, there's a body of scientific evidence that shows that eating chicken is a risk factor for getting Campylobacter so taking the step from that association to causation is -- can be made.

Q Now, Dr. Angulo, at page 16 of your testimony -- of 17 --

MR. KRAUSS: Indicates I'm getting closer to the end, your Honor.

JUDGE DAVIDSON: It won't stop you from going back to page 4, will it?

(Laughter.)

MR. SPILLER: Excuse me, your Honor, Mr. Krauss. I'll try to make this my last interruption. We were just talking about sort of transcripts that are done and I don't suggest that Dr. Cox is making a transcript but I wanted to understand whether we are recording words to be used later in this hearing, whether there is other computer work going on here --

JUDGE DAVIDSON: Wait a minute.

MR. KRAUSS: I think the court reporter is.

JUDGE DAVIDSON: Yeah, but what's going on?

Is there a tape recorder going over there? If there is, I want it.

MR. COX: No, I think he's asking about my computer, sir.

JUDGE DAVIDSON: Well, I want to see -- what's going on with that? I can't see you, so -- first of all, identify yourself for the record and stand up.

MR. COX: This is Tony Cox. I'm taking notes, actually not having to do with the proceeding.

JUDGE DAVIDSON: Well, then you can take it outside.

MR. COX: Or I can turn it off.

JUDGE DAVIDSON: If you're not paying attention to this proceeding, I don't know why you're in here.

MR. COX: Oh, I'm paying good attention --

JUDGE DAVIDSON: Well, maybe you're better than most of us, but if you're taking notes about something else then I don't think you're giving full time and attention to what's going on here.

Turn it off and we can go on.

BY MR. KRAUSS:

Q Now, Dr. Angulo, at page 16, lines 9 to 23, you say that -- you give the opinion that Fluoroquinolones are, in your opinion, less effective for resistant Campylobacter infections, right? In general, that's the subject matter of that paragraph?

A Yes.

Q And in support of that you reference three studies. Is that right?

A Yes.

Q That would be the Smith study, the Nelson study and the Niemann study, right?

A Correct. Yes.

Q Now --

A I also reference the Sentinel County study in my testimony.

MR. KRAUSS: Your Honor, that's not in the record.

JUDGE DAVIDSON: If it's in his testimony it's in the record.

MR. KRAUSS: It's been stricken.

JUDGE DAVIDSON: The Sentinel County study is

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not, but the testimony is.

MR. KRAUSS: I think the testimony related to that has been stricken, your Honor.

JUDGE DAVIDSON: You're right. I apologize. Go ahead.

MR. KRAUSS: Thank you, your Honor.

BY MR. KRAUSS:

Q Now, Dr. Angulo, in terms of measuring any extra days of diarrhea in comparing a Ciprofloxacin-resistant Campylobacter case to a Ciprofloxacin-susceptible Campylobacter case, do you have an opinion as to whether the median or the mean number of days is the appropriate measure?

A We'd want to look at both. Both would be appropriate. If we're talking about -- it's whatever your -- impact on duration of diarrhea. Duration can be measured by mean, ~~medium~~ median, range. It's all -- there's a variety of measures you can measure to difference in durations.

Q Did you participate in discussions at CDC as to whether the median or the mean would be the -- a more or less effective measure for the extra days of

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duration of diarrhea?

A For the Nelson study, yes. Not for the Niemann study nor for the Smith study.

Q Okay. But --

A I'm co-author of the Nelson study so we certainly discussed the outcome measure.

Q And did you draw any conclusions as to whether the median duration of diarrhea would be a good indication of severity or not, as opposed to the mean?

A We actually report both. We report most results with the mean but we also comment that the median is equally useful to look at differences in duration.

Q Now, with respect to the Smith study -- and I have -- do you still have a copy of that up there, G-589?

A I don't believe I received --

Q I thought I gave it to you earlier. If I didn't, I'm sorry. Here, Dr. Angulo. I'm sorry.

A Thank you.

Q Now, in the Smith study, in terms of the measure of duration of diarrhea, comparing ~~resistance~~ resistant

Campylobacter infections to susceptible infections, it does not control for foreign travel, does it?

MS. ZUCKERMAN: Objection, your Honor. The document speaks for itself.

JUDGE DAVIDSON: Well, it's all right.

THE WITNESS: I'm sorry. I'm not an author of this study and I could read it, what it says but --

BY MR. KRAUSS:

Q But you rely on this study in your testimony for the proposition that Fluoroquinolone-resistant infections have a longer duration compared to susceptible infections and I'm trying to get your understanding or familiarity with how the study was done as an epidemiologist which you are. Do you know whether -- whether you know whether you controlled for foreign travel.

A I guess this was -- this article was published in the New England Journal of Medicine, which is a premier medical journal. I'm certain it was well-reviewed by peer review and -- but I did not either look at their analysis in terms of their data set and repeat their analysis, nor did I -- am I intimately

familiar with how they modeled all -- the entire -- to get their outcome, although I'd be happy to read it and give a review.

But perhaps -- I'm comfortable with the conclusion -- I'm confident the conclusion, because of the status of the Journal and the status of these researchers, but it's not my research, per se.

JUDGE DAVIDSON: But the question was do you know whether you control for foreign travel or not. And it's a simple answer. It doesn't matter, as far as I'm concerned, whether you know or not.

THE WITNESS: I don't know for certain.

JUDGE DAVIDSON: That's fine. That's the answer to the question.

MR. KRAUSS: Thank you.

BY MR. KRAUSS:

Q Now, for the Niemann study -- let me turn your attention to the Nelson paper. Now, you worked with Ms. Nelson on her thesis, didn't you?

A I was her field advisor.

Q Right.

A Yes.

Q And on her thesis, you suggested that she conduct a survival analysis, didn't you?

A So we're not talking about her article, we're talking about her thesis, which --

Q G-1679.

A I'm familiar with this thesis. It was done in the year 2000.

Q And you were the field advisor.

A Correct.

Q And you suggested that she conduct a survival analysis?

A Yes, because there were people in the data set that were censored because they still had diarrhea at the time of interview and we were exploring to see if any Cox proportional hazard model or survival analysis might not yield more precise estimates.

So we embarked upon this experiment to see if we would find this to be useful. This was very early in our analysis of the data set.

Q And when you say the data set, this is data from the 1998, 1999 CDC Campylobacter case control study, isn't it?

A The Nelson study. Correct.

Q It used data from the --

A Yes.

Q -- from the 1998, 1999 CDC Campylobacter case control study, right?

A Yes. And as we've discussed, three sub-studies of that. This is close -- most analogous with the Nelson analysis, although by the time we did the Nelson analysis the data set had changed slightly in terms of being cleaner and we certainly had a much more sophisticated understanding of the data set by then in the year 2000.

JUDGE DAVIDSON: Off the record.

(A brief recess was taken.)

JUDGE DAVIDSON: Go ahead, Mr. Krauss.

MR. KRAUSS: Thank you.

BY MR. KRAUSS:

Q Now, in the McClellan thesis, there was no statistical difference in duration of diarrhea between people with Fluoroquinolone-resistant Campylobacter infections and people with Fluoroquinolone-susceptible Campylobacter infections. Isn't that right?

A That was a very naive analysis but that is correct. Very incomplete analysis.

Q And in the thesis -- when she did the -- calculated a hazard ratio, the hazard ratio for the association between Ciprofloxacin resistance and duration of diarrhea, adjusting for age, sex, residence, FoodNet site, education, and household income, and stratified by race, the differences between a resistant infection and a susceptible infection was not statistically significant, was it?

A Perhaps not. Again, this was in year 2000 and it was a very -- very early in our understanding of this data set. I guess the -- to emphasize, purpose of her thesis was not to find the dominant risk factors, per se. We were just trying to see what Cox proportional hazard model --

Q Dr. Angulo, you answered my question. Thank you.

A -- just to see if the Cox proportional hazard model would contribute to our understanding and the outcome was we didn't find the Cox proportional hazard model to be useful, which is why we don't use it in any

further analysis after this date. It achieved its purpose.

Q Now, for the Nelson paper -- that's the same researcher, right? She was Jennifer McClellan and she became Jennifer Nelson?

A That's correct.

Q Attachment 4 is her paper, right?

A Correct.

Q And she found that when not adjusting for antimicrobial or antidiarrheal medication use, there was no statistical difference in the mean duration of diarrhea between patients with a Ciprofloxacin-resistant infection compared to patients with a Ciprofloxacin-susceptible infection, isn't that right?

A That is correct.

Q Now, turning to the Niemann paper, which is B-561, is this the Niemann paper that you refer to in your testimony?

A I don't believe so.

Q Then I'm not going to ask you about it. Now, let me -- actually, I'm going to reverse myself, Dr. Angulo. Let's just take a look at the Niemann thesis.

Are you familiar with the Niemann thesis?

A I am.

JUDGE DAVIDSON: Do you have an exhibit number?

MR. KRAUSS: B-561.

BY MR. KRAUSS:

Q He found, didn't he, that -- in looking at the duration of illness between resistant infections and susceptible infections, that actually there was a longer duration of illness for susceptible infections than resistant infections, didn't he?

A Is that -- are you reading that from somewhere?

Q Will you turn to page 200, Table 3 where it lists duration of illness, median days, for resistant infections it was 9 days, for susceptible infections it was 10 days, right?

A I believe this is just descriptive. It's not -- this is just a simple description of what was found but it's not his final conclusion. When he models the duration of diarrhea then you have -- then the differences would be different.

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But yes, in terms of -- yes.

JUDGE DAVIDSON: Just answer the question.

THE WITNESS: It so states on page --

JUDGE DAVIDSON: Okay.

THE WITNESS: -- table 3.

JUDGE DAVIDSON: What's the next question?

BY MR. KRAUSS:

Q And Niemann found that the duration of illness was not different between cases with a Ciprofloxacin-resistant infection and a Ciprofloxacin-susceptible infection, didn't he?

A No. It was my understanding in talking to Kare Molbak ~~Karl Mollbach~~, who is -- as I cite this I believe in my testimony -- a personal communication with Dr. Molbak ~~Mollbach~~, it's my understanding that in their final analysis they found a difference of duration of 5 days between the resistant infection and the susceptible infection.

Q That difference was not statistically significant, was it?

A I don't know -- I --

Q You don't have basis to know one way or the

other?

A I don't know.

Q If you'd look at page -- I'm going to give you the number in the upper right-hand corner, the sticker number of 193, for Niemann, the last paragraph on the page, he says the duration of illness was not different between cases with Ciprofloxacin-resistant infection and a Ciprofloxacin-susceptible infection, right?

A And he also says the next sentence, too, which says, however, when stratified on treatment Fluoroquinolones or other kinds of unknown antibiotics, the duration was longer for cases with resistance.

Q Right. But those patients received antibiotic treatment because they were having a longer duration of illness anyway, weren't they?

A No.

Q Turn to page 133. Dr. Niemann found that the data suggests that more severe symptoms, i.e., longer duration of symptoms, were the incentive for initiation of antibiotic treatment. So they were having a longer duration of diarrhea so that's why they got treated, right? Isn't that what he says?

A Where are you citing?

Q At the bottom -- right above predisposing factors. That paragraph. However --

A I'm sorry; what page number?

Q 133.

A Now we've gone to a different article, have we not?

JUDGE DAVIDSON: Okay. Who's asking the questions here?

MR. KRAUSS: I'll withdraw that question.

JUDGE DAVIDSON: Thank you.

BY MR. KRAUSS:

Q Now, Dr. Angulo --

MR. KRAUSS: Dr. Angulo, I have no further questions for you. Thank you.

THE WITNESS: Thank you.

MR. KRAUSS: Subject to redirect.

JUDGE DAVIDSON: Ready for you. Do you want to change chairs, or if you don't have any questions --

MS. ZUCKERMAN: Yes, please.

JUDGE DAVIDSON: Okay. Go ahead.

Off the record for a few seconds while you

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change chairs.

(A brief recess was taken.)

JUDGE DAVIDSON: On the record.

Let's go.

REDIRECT EXAMINATION

BY MS. ZUCKERMAN:

Q Dr. Angulo, Mr. Krauss asked you about the results in the studies looking at duration of diarrhea when not adjusting for antidiarrheals. Can you explain what would happen if the analysis had adjusted for antidiarrheals?

A Yes.

Q Please explain.

A As I described, our evolutionary understanding of the data set -- but the outcome that we are trying to measure is duration of diarrhea and it's very clear -- it was very clear before we did the analysis, it's also very clear in the data set -- but it clear a priori ~~apriority~~ that taking an antidiarrheal medication, especially a prescription antidiarrheal, Immodium, would have a major consequence on the duration of diarrhea.

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So we found it essential to include in the model ~~apriority~~ a priori in our analysis to deal with the impact and the major impact of using an antidiarrheal. Because of course the antidiarrheal drug shortens the duration or in fact can impact the duration of diarrhea.

So we have always from the beginning thought about the need to -- how to manage that effect. So we have tried it from several different processes. The one way that we have managed it is looking at the data set.

The data set starts with 858 observations. There are 740 cases that there are information about duration of diarrhea because sometimes when you interviewed people, they still had diarrhea or not. In that 740-person data set, the difference between diarrhea between the resistant and the susceptible was seven days versus eight days. It was not statistically significant as I responded to -- but it had a P value of .1.

But then if you subset those 740 and look at only the 421 who had taken no antidiarrheal medication,

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of those 421 people who took no antidiarrheal medication, then you find a significant difference between resistant and susceptible strains, 7 days versus 9 days with a P value of .05.

Q I want to ask you again about the duration of diarrhea analysis but this time I want to ask it in terms of foreign travel. In your opinion, is foreign travel a confounder for Ciprofloxacin-resistant Campylobacter infections?

A Again, it's important to -- ~~apriority~~ a priori ital confounders and then confounders that are in the data set. Before we did the study, ~~apriority~~ a priori ital -- we would not think that international travel would be a confounder because the definition of confounder is it must be an independent risk factor for the outcome and associated with the exposure.

We're talking -- the outcome is duration of diarrhea. It's hard -- we don't have -- we don't appreciate and do not appreciate a situation where international travel would impact the duration of diarrhea. The strains of Campylobacter that you acquire on international travel is -- particularly

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because most of the people in our study -- many of the people in our study that traveled traveled to Europe.

These strains -- we don't understand why there would be a difference in duration of diarrhea ital associated with international travel. So ~~apriority~~ a priori we did not think international travel was a confounder.

And also, then, when we start -- when we do a ~~multi-variant~~ multivariate -- when we do our analysis and if you put antidiarrheal medication into the model account for the strong effect modification of antidiarrheal medication, then in the various different ways that we have tried to look at international travel, it does not appear as a confounder because it is not associated with the outcome. It's not an independent risk factor of duration of diarrhea.

Accordingly, if you don't put antidiarrheal medication because international travel is associated with taking an antidiarrheal -- so you have a line -- an association between international travel and taking the antidiarrheal and antidiarrheal is an independent risk factor for the outcome, and we know international travel is associated with the exposure of interest, so

if you did not put antidiarrheal in the model, you would think that the data is telling you that international travel is confounded because it would look like it was associated with the outcome and would look like it's associated with the exposure, but it's only associated with the outcome through antidiarrheal medication.

It is not an independent risk factor for the outcome. In fact, it's just a proxy for taking antidiarrheal medication.

Now, this has been manifest in our analysis because then, as I described, there were 421 people that have taken -- that did not take antidiarrheal medication and in those 420 people, there's already -- there's a difference in duration of diarrhea between the 7 days and 9 days.

Those same 421 people, if you look at people that took no antibiotics and no antidiarrheal medication, which there are 67 people, the difference in duration of diarrhea between the resistant the susceptible is -- resistant infection is 12 days duration, susceptible is six days duration, and there's

a statistically significant difference between those two.

So -- and importantly, of those 67 people that did not take antidiarrheals and did not take antibiotics, none of them traveled internationally. So on that stratified analysis, international travel does not contribute to this marked effect that we see between the duration of diarrhea -- between the resistant strains and -- people infected with resistant strains and people infected with susceptible strains.

However, to more completely understand the impact of international travel, we did a ~~multi-variant~~ multivariate model, not just stratified analysis. We did a ~~multi-variant~~ multivariate analysis. We started with the 858 people in our data set. We did a logistic ~~aggression~~ regression, a multi -- I'm sorry -- analysis of ~~variants~~ variance regression model and we put the different variants in.

And if you put international -- I'm sorry -- if you put taking an antidiarrheal into the model, then when you enter international travel it does not contribute to the model at all. It doesn't stabilize the model, it doesn't change the points estimates

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significantly.

So international travel does not appear to be a confounder in our data set on ~~multi-varied~~ multivariate analysis as long as antidiarrheal medication is in the model.

There is a limitation of international travel in our data set and that limitation in our data set is that of the 858 people that were in our data set, approximately 100 of them were not asked the international travel question.

They were not asked that question on a relatively random process because they were not asked that question if they were not asked the set of exposure questions in our questionnaire, which they were not asked if, by the time we interviewed them, it was after 21 days from the culture collection date.

So there was a hundred people that were randomly -- relatively randomly not asked the travel question. So we have done additional statistical analysis which is called multiple imputations where we have imputed the travel status for these 100 people where the travel status is unknown and put that in the model to see even if we -- we wanted to make sure that

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when we see that international travel is not contributing to the ~~multi-varied~~ multivariate model, we wanted to be certain that that effect was not simply because there's much -- that there are unknowns in the travel.

So we imputed them, ran several iterations. All the iterations we run we never are able to make international travel contribute to the final ~~multi-variant~~ multivariate model.

So I would say with confidence that in our data set, both ~~apriority~~ a priori and, before we even did the study, we didn't think international travel would be a confounder and then when we did the analysis, it does not appear to be a confounder in our analysis.

Q Switching topics now to FoodNet and NARMS incidence and prevalence, respectively. In response to Mr. Krauss's questions earlier on FoodNet and NARMS, you had testified that the incidence of Campylobacter declined over the period between 1997 and 2001.

Mr. Krauss also asked you about the representativeness of NARMS with respect to Campylobacter. Can you explain what the relationship is between the prevalence of Fluoroquinolone

Campylobacter and the changes in incidence of Campylobacteriosis in the United States?

MR. KRAUSS: Objection, your Honor. That's outside the scope of the cross examination. All we discussed was the incidence of Campylobacteriosis in general. We didn't discuss the incidence of Fluoroquinolone-resistant Campylobacteriosis with Dr. Angulo.

MS. ZUCKERMAN: Mr. Krauss did ask questions about the prevalence of -- in NARMS. That was a substantial portion of --

MR. KRAUSS: I didn't -- sorry, your Honor.

JUDGE DAVIDSON: Did you want to say something else?

MR. KRAUSS: I'm sorry, your Honor.

JUDGE DAVIDSON: You want me to change my ruling? Okay. I'm going to sustain the objection.

First of all, the witness has gone to great lengths to explain almost everything he's been asked so if you're asking him to do it again, I don't appreciate that.

If he wants to add something to his testimony

that he hasn't already given us more than once, I'd appreciate that. Otherwise -- I mean, I don't blame the witness. You keep asking the questions, both sides, and he keeps giving the same answers. And he explains in great detail on how it affects his confidence.

All right. You can proceed to the next question.

MS. ZUCKERMAN: Thank you, your Honor.

THE WITNESS: There's some --

JUDGE DAVIDSON: Go ahead.

THE WITNESS: Well, there is something I neglected to say but I don't know if you want --

JUDGE DAVIDSON: Well, is it in response to the question, which I don't even remember at this point? You've been talking for five minutes.

THE WITNESS: Yes, your Honor. It is, your Honor.

JUDGE DAVIDSON: Okay. Go ahead.

THE WITNESS: Well, the -- FoodNet allows us to track the change in incidence over time and as I've described, in FoodNet, the incidence of Campylobacter

has declined 33 percent. NARMS allows us to track the change in prevalence of resistance over time and NARMS has shown -- as I described in my testimony, NARMS has shown us that the prevalence of Fluoroquinolone resistance or Ciprofloxacin resistance among Campylobacter has increased 150 percent.

The new data -- or the new analysis is we're able to merge those two data sets to ask the question, that is, what is the change over time of the incidence of Fluoroquinolone-resistant Campylobacter. And Campylobacter is declining, prevalence resistance is increasing. What happens at this intersection? And in fact, when we do that analysis, the intersection is that the approximately -- there is -- in 2001, the incidence of Fluoroquinolone-resistant Campylobacter is approximately 50 percent higher than the incidence was at baseline.

JUDGE DAVIDSON: Now, you say new data. Is that included in your testimony or is that something that happened since you signed your testimony?

THE WITNESS: It's since my testimony.

JUDGE DAVIDSON: Well, that causes a problem

for everybody involved, so you shouldn't -- I mean, I know it's interesting and valuable information but how is the other side supposed to be prepared and respond to something that you haven't testified to previously?

MR. KRAUSS: Your Honor, I move to strike the testimony.

JUDGE DAVIDSON: Granted. Motion is granted.

MR. KRAUSS: Thank you, your Honor.

MS. ZUCKERMAN: Well, I have one final question and before I ask it, perhaps I ought to request permission to ask it because it has to do with the Sentinel County information. This is something that was discussed when Mr. Krauss was questioning and given the fact that Dr. Angulo is here and available to resolve any issues of questions about isolates, where they came from, the protocol, the study, he's here and he's able to provide those answers.

So we can do that now and I can also give you a copy of the protocol that I believe Mr. Nicholas was going to provide yesterday but did not.

JUDGE DAVIDSON: Give me some more of what's involved in this question.

MS. ZUCKERMAN: What would be involved is the number of isolates -- in fact, we have a flow chart that was prepared by CDC recently. It's a flow chart that shows the sample numbers initially that were collected and how that relates to the samples that were discussed in Dr. Angulo's testimony. Only the susceptibility results and the numbers of samples and where they came from.

JUDGE DAVIDSON: I have a problem because I don't understand why it's coming in now and wasn't put in originally. I mean, right now I know it's all stricken.

If you were somehow asking him questions that were going to clarify something that was -- the wrong impression that was left by his testimony or by the cross examination, then maybe I'd allow it subject to it all being stricken if we don't allow the Sentinel County study but based on what you've told me, I don't see anything like that.

I see you're trying to get something additional into the record that wasn't here before. Am I wrong?

MS. ZUCKERMAN: Well, as I understand it, there was confusion expressed by Bayer in the motions to strike about the Sentinel County study and what it represented. There was no confusion on the part of CVM or CDC about that study.

JUDGE DAVIDSON: Well, then why do you have to clarify it now? In other words, if you're satisfied that what you presented was accurate and good evidence, and I'm going to rule on whether it comes in or not probably on Monday, what's the point of adding to it at this point something that isn't already in the record? That's my problem.

In other words, are you enlightening or modifying -- I shouldn't say modifying -- doing away with inconsistent -- no, that's not right either -- explaining something -- an improper inference that was left on the record by cross examination or are you just bringing in additional information?

MS. ZUCKERMAN: The cross-examination did not involve talking about the numbers of isolates from the Sentinel County study.

JUDGE DAVIDSON: Then why are you -- then

there's no redirect on that.

MS. ZUCKERMAN: Your Honor, the reason why I mentioned it is because Dr. Angulo was right here and I know that the ruling --

JUDGE DAVIDSON: I understand that, but you -- the problem you're creating for me is if he comes in with new material that wasn't previously in the record, then where does that leave me as far as their opportunity to then come back with additional witnesses, additional testimony, to combat what he's putting on the record now? And I can't do that. We'll never end the proceeding. At some point it's got to stop.

As I have said, if this testimony is designed to clarify a representation or material that was brought out on cross that you think has an improper inference, that's fine. But if you're going to bring in information that you could have brought in before, whether it wasn't available at the time his testimony was prepared, then that's a whole 'nother process, not the fact that the witness is here now.

MS. ZUCKERMAN: Understood.

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JUDGE DAVIDSON: Okay.

MS. ZUCKERMAN: I have no further questions.

JUDGE DAVIDSON: All right.

MR. KRAUSS: Your Honor?

Judge Davidson
~~MS. ZUCKERMAN~~: I didn't let her ask anything, hardly.

MR. KRAUSS: I know, but he did mention a couple of things that had a couple of --

Judge Davidson
~~MS. ZUCKERMAN~~: Couple?

MR. KRAUSS: Yes, your Honor.

JUDGE DAVIDSON: We'll see how far we get.

MR. KRAUSS: Okay. Thank you, your Honor.

JUDGE DAVIDSON: Ask questions, don't make speeches.

MR. KRAUSS: Thank you, your Honor.

RECROSS EXAMINATION

BY MR. KRAUSS:

Q Dr. Angulo, on redirect, you testified regarding the 12 days versus 6 days of difference between Ciprofloxacin-resistant infections and Ciprofloxacin-susceptible infections in those people who took an antidiarrheal. Do I have that right?

A No.

Q Who did not take -- okay. Thank you.

MR. KRAUSS: I have no further questions. Thank you, your Honor.

JUDGE DAVIDSON: I'm sure you don't have any redirect on that.

MS. ZUCKERMAN: I certainly don't, your Honor.

JUDGE DAVIDSON: All right. Now, do we have any preliminary matters here -- not preliminary -- any housekeeping matters to take care of? I have one if you don't have any. All right. Well, I have two, as a matter of fact.

If you still -- I'm directing you as far as that recording is concerned, if you're still interested in pursuing that, the witness is probably not going to be here but as far as any authentication or having the witness listen to it on your own time, when we adjourn here, I'll direct the witness to spend a couple of minutes or so with you to listen to that 47 seconds to see if it helps him.

But that's just if you still want to pursue that. As we've got it now, he's refreshed his

recollection from the written word and I've explained for the record, at least once, I'll do it again, that I can't allow the tape itself into evidence because I'm not sure of the authentication or the fact that it's not the original tape. It's something that was digitized afterwards.

And while I'm not technically up to snuff on what that means or doesn't mean, it raises too many questions for me to try to deal with it.

All right?

MR. KRAUSS: Yes, your Honor.

JUDGE DAVIDSON: That's one. Two. Yes, ma'am.

MS. ZUCKERMAN: Your Honor, may I comment to --

JUDGE DAVIDSON: Sure.

MS. ZUCKERMAN: We have -- CVM will be preparing other witnesses for tomorrow, and my concern is that if it's determined that Dr. Angulo will need to listen to more than the 47 seconds --

JUDGE DAVIDSON: All I'm interested in is the 47 seconds to see if he recognizes his voice. You can

report back he did or he didn't. He's already testified to what the import of it was and he went in detail -- lengthy detail as to why in his position it was taken out of context, it was a whole different approach.

The words themselves he doesn't recognize precisely, but if you can report back to me, and both sides will be there, that he does recognize his own voice, that's all I want to hear.

MS. ZUCKERMAN: Thank you, your Honor.

JUDGE DAVIDSON: The rest of it I've already understood.

Yes, sir.

MR. KRAUSS: We understand, your Honor.

JUDGE DAVIDSON: All right. Now, my other housekeeping matter is that I know the room is small, I know we're cramped, but I don't want anybody sitting where I can't see them anymore. As of tomorrow, there will be no chairs over here below the bench. They'll all be on that side.

If you want my explanation for that, it is I allow a lot of leeway to people who attend these

hearings but I don't allow them to read newspapers or do other things in the courtroom while my proceeding is going on. And with all due respect, Dr. Cox, I know you can do more than one thing at one time, but not in my courtroom.

Okay. Thank you. We're adjourned until 9:00 a.m. tomorrow morning.

MR. KRAUSS: Thank you, your Honor.

MS. ZUCKERMAN: Thank you, your Honor.

(Whereupon, at 4:15 p.m., the hearing was adjourned, to reconvene at 9:00 a.m. on Thursday, May 1, 2003.)

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