Walker. So we objected. We did not want to keep that in the testimony.

Q But isn't it true that Dr. Fedorka-Cray, on the susceptibility to nalidixic acid issue, was prepared to testify in this case:

"Thus, by use of susceptibility to nalidixic acid as a criteria for selection, isolates would have been expected to be susceptible to nalidixic acid and therefore also susceptible to fluoroquinolones. However, a percentage of the isolates were resistant to nalidixic acid with additional fluoroquinolone resistance observed for some of the isolates.

"This suggested that either sensitivity was not absolute as defined by clinical laboratory standards or that other phenomena were occurring."

MS. STEINBERG: Objection, Your Honor.

JUDGE DAVIDSON: Sustained. You're reading into the record testimony that is long, and convoluted, and may or may not have been received in evidence in this case if I had a chance to rule on it, but the witness, the person you're trying to get the testimony in from is not here, not before me, and this witness

can say yes, she was prepared to testify to that, but she doesn't have to answer, as far as I'm concerned.

Move on.

MR. KRAUSS: Okay, Your Honor. Please allow me to approach it one different way here?

JUDGE DAVIDSON: Go ahead.

MR. KRAUSS: The witness has already testified that she had reviewed --

JUDGE DAVIDSON: I understand.

MR. KRAUSS: -- some drafts.

JUDGE DAVIDSON: But you're still going in an area which is putting stuff in the record which I can't rely on, because I don't have this witness in front of me. She's not subject to cross examination.

You're trying to back-door, and get stuff on this record which doesn't help, so you're wasting our time with it unless you think you've got something really important here, as I said before, as it reflects on this witness's testimony only; and yet you read a long passage of what she was prepared to testify to, and I believe that's contrary to what my ruling was.

MR. KRAUSS: Thank you, Your Honor.

JUDGE DAVIDSON: Okay.

BY MR. KRAUSS:

Q When you reviewed Dr. Fedorka-Cray's draft testimonies, like you testified that you did, was there information in the draft testimony relating to the speciation of Campylobacter isolates with nalidixic acid?

A Yes.

Q And --

A This.

Q Right.

A Yes.

Q And did that testimony that you reviewed, the draft, did it say that, based on your recollection, did it raise an issue as to whether sensitivity was absolute or not?

MS. STEINBERG: Objection, Your Honor.

JUDGE DAVIDSON: Sustained. You're still doing the same thing. I can't help what she said or didn't say, but it's not before me.

If you want to get this witness to change her testimony or alter it in some way based on what that

says, fine, but you're already asked her that and she said she didn't agree with it, so I don't know -- move on to something else, please.

MR. KRAUSS: Thank you, Your Honor.

BY MR. KRAUSS:

Q Dr. Tollefson, let me turn your attention to Table, the table in your testimony on Page 12.

A Mm-hmm. In Paragraph 29.

Q Right. Now, this table relates to poultry NARMS, doesn't it?

A Correct, only poultry NARMS.

Q Now, at the beginning of your testimony when you were being questioned by Ms. Steinberg, you made a correction to your testimony regarding the 2001 poultry NARMS?

A Correct.

Q And you say that that has been published?

A Yes, it has, in abstracts and presentations. What I changed was on Page 8, because I said that 2001 data were not available yet, but it's really 2002, which is repeated in the table.

Q Yes.

A Not yet available, not published.

Q Okay. So the 2001 data are available, right?

A Yes.

Q But they're not published?

A Well, it depends on what you mean. Dr. Cray has presented at meetings on that data, so they're public, and they're also -- they've been confirmed. They're not preliminary. Okay?

NARMS works on a calendar year system, so now we're in April 2003, all the 2002 isolates have been received, possibly not all susceptibility tested; but then we go back and check and, you know, make corrections, and so on. Then, that data is available in the reported audit.

So I'm not sure what you're asking. Published in a peer review journal, I don't believe so.

Q Let me clarify.

A Okay.

Q Isn't it true that, for other years, for the animal isolates, the veterinary isolates from NARMS, there's a final --

A Report.

Q -- report?
A Yes.
Q And that gets disseminated?
A Right, it's on our web site.
Q Right. And that's disseminated as a final report?
A Right.
Q That has not happened to the 2001 poultry NARMS for Campylobacter; isn't that right?
A That's correct.
Q Now, looking at your table, isn't it true that over the time period 1998 to 2001, there were changes in the sources of the whole carcass rinsates used to collect Campylobacter isolates?
A Yes.
Q And isn't it true that over the time period 1998 to 2001, different geographic areas were represented in the poultry NARMS sample?
A No, we actually don't know that.
Q Well, for example, in 2001, isn't it true that the isolates were from the eastern lab only?
A Yes, but that doesn't represent poultry

slaughtered in the eastern part of the country. FSIS has three labs, but what they receive is based on their load.

Q Okay.

A So they could be getting isolates from all over the country, and they do get isolates from all over the country.

Q Looking at your table, comparing 2000 to 2001, isn't it true that the sources of isolates from 2000 were different than the sources of isolates in 2001?

A Not really, not enough to make a difference. The sources are all from the FSIS regulated, federally regulated slaughter plants.

What we had available in '98, '99, and 2000 were programs where FSIS was actually looking at Campylobacter. It's the same kinds of chickens as are in their Salmonella program. Okay.

So what happened is once they stopped looking specifically at Campylobacter, we had to use their Salmonella program chickens, but they're the same chickens. I mean, it's all the chickens going through the federally inspected slaughter plants.

Q Have you done a comparison between the sources of chickens from the broilers nationwide young chicken study and FSIS chicken monitoring program that was the source of the 2000 isolates and the Salmonella program rinsates, eastern lab only, that was the source of the 2001 isolates?

A What we had in 2000 were not just the broilers. We also had the whole chicken ~~laundry~~ monitoring program, so it was everything. Okay?

Q Right.

A Okay. And then in 2001, the Salmonella program rinsates are everything, potentially everything. What we actually receive, we don't know.

Q My question was whether anybody did a comparison study between the sources for the 2000 and the sources for the 2001?

A All right. Let me answer it another way. Our sources of isolates come from federally inspected slaughter plants, which is Food Safety and Inspection Service of USDA. We do not know where, like which plant is sending in which isolate from what kind of chicken. We don't know. That's all blinded. We do

not have that information.

The reason we, FDA, consider it a valid sample is simply because of the numbers. We get -- all the Salmonella rinsates that they're doing have an equal probability of coming into the NARMS program, if that explains it better, but we couldn't do a comparison, because we don't know.

Q Okay. And now you've answered my question.

A All right. Thank you. I'm sorry.

Q Nobody did such a comparison?

A No. No. That's not possible.

JUDGE DAVIDSON: Excuse me, Mr. Krauss. The witness has been on for over an hour-and-a-half, and since we just had some exodus from attorneys, I think maybe it's time for a break, if it's okay with you. If you want to ask a few more questions, first, find a convenient, place, that'll be okay.

MR. KRAUSS: I'm happy to break here, Your Honor.

JUDGE DAVIDSON: All right. We'll take a 10-minute recess.

(A brief recess was taken.)

JUDGE DAVIDSON: Counsel for Bayer is not here at the moment, but I had a question directed to counsel for CVM which is procedural in nature.

There was a reference made to G-589, and what I need to know, since I think somebody is not giving me all the information I need, not from your standpoint, but from -- come on in. It's all right. No problem. We're just talking about G-589. I want to know whether it's in evidence or not in evidence.

MS. STEINBERG: It is in evidence.

JUDGE DAVIDSON: That's what I was afraid of. The people who did my disks here so that I could follow along --

MS. STEINBERG: Would you like a copy of it? I have a copy.

JUDGE DAVIDSON: That will be fine. Thank you. But I've got to get another disk made up here, because they didn't do what I asked them to do.

While you were out, we decided that the case doesn't have to go on anymore.

(Laughter.)

MR. KRAUSS: Who says prayers can't be

answered, Your Honor?

JUDGE DAVIDSON: No, I was just talking about -- we're on the record -- I was just talking about the fact that the disks that were prepared for me by the dockets people didn't include all of the evidence that I asked them to, so I'm going to have to get some changes on that.

So you'll have to bear with me when you refer to things that are on the record, and you have to tell me whether it's in evidence or just in the 1285 when you're referring to it, and you have to give me an opportunity to try and find it someplace.

MR. KRAUSS: Okay, Your Honor.

JUDGE DAVIDSON: Because I had asked them to give me a disk that showed all of the evidentiary record with the strikes, and what they gave me was just everything from my Order with motions to strike, so there's a lot of stuff not here.

Okay. Proceed.

MR. KRAUSS: Thank you, Your Honor.

BY MR. KRAUSS:

Q Dr. Tollefson, returning now to the table at

Page 12 of your testimony, you're looking at the year 2000 and the year 2001, in particular.

In the year 2000, the isolates were speciated using nalidixic acid and cephalothin, right?

A Mm-hmm, yeah.

Q And that was not done in 2001, right?

A Correct.

Q Let me turn your attention to Page 19 of your testimony, in particular Lines 23 and 24. It refers to fluoroquinolone resistance among Campylobacter found on chicken and turkey carcasses from the animal arm of NARMS prior to 2001. Do you see that testimony?

A Mm-hmm.

Q Isn't it true that the animal arm of NARMS did not test fluoroquinolone resistance among Campylobacter found on turkey carcasses before 2001?

A (Examining) It must be true. We must have had turkey from epidemiology studies. Yes, you're correct. That's a mistake.

Q Your testimony here is not correct?

A It's not correct.

Q Dr. Tollefson, turning to the human arm of

NARMS, if you will, your testimony states that one of the goals and objectives of NARMS is to provide descriptive data on the extent and temporal trends of anti-microbial susceptibility in enteric organisms from the human and animal populations.

A Right.

Q Is that right?

A That's correct.

Q Now, would you agree with me that NARMS could not establish causal trends?

A NARMS alone cannot establish causal trends.

Q Now, focusing on the human arm of NARMS, NARMS -- the human of NARMS does not collect any data, other than maybe age and a patient ID, from Campylobacter patients who submit their stool samples; isn't that right?

A Correct. There's limited demographic information.

Q And that limited demographic information does not include, for example, whether the patient who is submitting their sample may have used a fluoroquinolone or any other antibiotic before they submitted their

sample, right?

A Correct.

Q So published reports from NARMS that report the percent of human isolates that are fluoroquinolone resistant, human Campylobacter isolates that are fluoroquinolone resistant, those numbers don't exclude patients who may have taken an antibiotic or -- fluoroquinolone or any antibiotic -- before they submitted their sample?

A That's correct.

Q And that limited demographic information also does not include whether the person who's submitting their stool sample and then the Campylobacter isolates for susceptibility testing may have undertaken foreign travel prior to submitting, or prior to getting their Campylobacter infection; is that right?

A Correct.

Q So published reports from NARMS regarding the percent of Campylobacter isolates that are fluoroquinolone resistant includes persons who got their Campylobacter infection through foreign travel?

A We don't know that. First of all --

Q You can't exclude them, because you don't collect the data; isn't that right?

A I don't believe you get Campylobacter infections by foreign travel. You get it from -- they may have been traveling in the week before showing signs of Campylobacteriosis. It's true, we do not exclude those people from NARMS. There's no -- it's a public health surveillance system. There's no way to exclude them.

Q So, for example, NARMS would not exclude isolates from persons who had traveled to, say, Mexico, prior to having their Campylobacter infection?

A Correct.

Q And it wouldn't exclude persons that may have traveled to Spain before they came down with their Campylobacter infection?

A Correct.

Q They wouldn't exclude --

MS. STEINBERG: Objection.

JUDGE DAVIDSON: That's enough. It wouldn't exclude any of them.

MR. KRAUSS: Thank you, Your Honor.

(Laughter.)

BY MR. KRAUSS:

Q In fact, isn't it true that NARMS doesn't collect any data that would allow for determination of the source of the Campylobacter infection?

A Correct. It's simply a surveillance system.

Q Now, in your testimony you testified that in 2003, all 50 states and three local health departments will participate in NARMS?

A That's correct, as of now.

Q That's not true for Campylobacter monitoring, is it?

A No. Campylobacter is very difficult and unique, and you should use Dr. Angulo's testimony for that.

Q Okay.

A Which I think I referred to when I talked about Campylobacter. It changes, year to year.

Q Okay. So when you testified that for most of the period relevant to the hearing on fluoroquinolones 27 state and local public health departments representing 63 percent of the U.S. population

submitted isolates to the CDC for inclusion in NARMS, that wasn't referring to Campylobacter monitoring?

A No, that's in general. Campylobacter is a small part of NARMS.

Q Right. So you're not suggesting for the purposes of this hearing that 27 states representing 63 percent of the population were submitting Campylobacter isolates?

A No. For Campylobacter participating public health laboratories. See written direct testimony of Dr. Angulo, farther down in the paragraph.

Q Right. But I wanted to talk about your testimony.

A Mm-hmm. That's fine.

Q Now, from -- you have a list on Page 7 of participating states that participate in NARMS, right?

A Correct.

Q Now, Hawaii didn't submit any Campylobacter isolates from 1996 to 2001, did they?

A No.

Q And neither did Kansas?

A I don't think so. I'd have to look at Fred's

testimony.

Q Louisiana didn't submit any, did they?

A No, I don't think so.

Q Maine didn't?

A I'm telling you, I'm going to have to look at Dr. Angulo's testimony to see which states were participating in NARMS over those years.

Q Okay.

A Which states were participating for Campylobacter in NARMS over those years.

Q Okay.

A They did change each year.

Q Let me short-circuit this a little bit so Judge Davidson will be happy.

Isn't it true that for all the time that NARMS has been collecting human Campylobacter isolates, it collected from, at most, nine states and not 27?

A Yes, that's true. Sentinel Laboratories within the states.

Q Let me turn your attention to the human NARMS sampling scheme.

A Okay.

Q Now, according to your testimony, for Campylobacter, participating public health laboratories select and forward the first Campylobacter jejuni or Campylobacter coli isolate received in each laboratory each week to CDC for susceptibility testing; is that right?

A Yes. That's what they send to CDC.

Q And the sampling scheme is different for other enteric pathogens that NARMS monitors, isn't it?

A Oh, yeah, absolutely. Campylobacter is much more expensive.

Q How does the fact that Campylobacter is much more expensive impact the sampling scheme?

A Well, we needed to limit the number of Campylobacter isolates that we could do in NARMS because of the cost per isolate, if you will. Think of it that way.

Q So for Campylobacter monitoring through human NARMS --

A Right.

Q -- the sampling scheme is limited?

A It's limited, right. Now, Campylobacter also,

not all states isolate that organism, which is another reason why we only do some of them.

Q The most it's ever been is nine?

A Yeah, and it probably won't be more than that.

Q For ~~non-typoid~~ non-typhoid Salmonella, NARMS, participating NARMS public health laboratories select every 10th isolate, right?

A For Salmonella ~~typing~~ typhi, correct.

Q I thought it was ~~non-typing~~ non-typhi.

A No. No. Where are you?

Q Page 7 of 20, Line 26.

A Oh, okay. Right.

Q It's ~~non-typing~~ non-typhi?

A Right. Now, that's -- okay. For most of the time that was true. It's not true anymore. It's changing.

Q Okay.

A But if you're going to compare it to Campylobacter -- is that what you're trying to do?

Q Yes.

A Yes. It was every 10th.

Q Okay. And for Shigella, participating public

health laboratories that are participating in NARMS, sent every 10th Shigella, right?

A Correct.

Q And for E. coli 157, they sent every fifth isolate, right?

A Right.

Q So -- and for Campylobacter, it's the first of the week, right? One week?

A Right.

Q So for a participating public health laboratory, let's say that laboratory gets 100 isolates in a week of Salmonella, it would send 10 for susceptibility testing in NARMS?

A It would send 10 to CDC, correct. They not all be susceptibility testing.

Q They would send 10?

A Right.

Q To CDC?

A Right.

Q And that same lab, if in a given week it receives 100 Campylobacter isolates, in that one week, it would send one isolate for susceptibility testing --

A Correct.

Q -- is that right?

A That's correct.

Q And so in that example, for the Salmonella, every one of the isolates that's sent represents 10 other isolates, right?

A Right.

Q And in the Campylobacter example, that one isolate would represent 100 isolates, right?

A That's correct, in that hypothetical example.

Q Right. And then, in that same scenario, if a participating state laboratory received 50 Salmonella isolates, it would send five, right?

A Mm-hmm.

Q And if it received 50 Campylobacter isolates, it would send one?

A One, in that week.

Q So still, for the Salmonellas, it's representing -- every one isolate sent represents 10, right? And in this instance, the one isolate from Campylobacter represents 50, right?

A That's right.

Q Going the other way, let's say that a participating state laboratory receives 200 Salmonella isolates, it would send 20 for testing, right?

A I agree.

Q And --

MS. STEINBERG: Your Honor, this line of questioning has been asked --

JUDGE DAVIDSON: Where are we going with this, Mr. Krauss?

MR. KRAUSS: Your Honor, I'm trying to demonstrate that the sampling is not representative in Campylobacter versus --

JUDGE DAVIDSON: Well, it's in the testimony -- 10, five, one. I mean, go to your brief. I mean, it's here. There's no question. If you want to get from this to somewhere else, fine, but don't keep giving me more examples of --

MR. KRAUSS: Thank you, Your Honor.

JUDGE DAVIDSON: I think we can all figure what a 10th, 5th, 20th, 20 percent, 10 percent, and 1 percent of the samples, with your example, but there's

no need to go through it any more.

MR. KRAUSS: Thank you, Your Honor.

JUDGE DAVIDSON: If you want to draw some conclusion from it, go right ahead.

BY MR. KRAUSS:

Q Dr. Tollefson, do you agree that the frequency of Campylobacteriosis in the United States over time in a given year varies, month to month?

A We think so, yes. We think there's some kind of seasonal variation.

Q Okay. And in that seasonal variation, would you agree with me that typically the peak for human Campylobacteriosis is sometime in July-August time frame?

A Correct.

Q Would you agree with me that there's a seasonality to the --

MS. STEINBERG: Your Honor, objection. This is beyond the scope of Dr. Tollefson's testimony.

THE WITNESS: That's true.

JUDGE DAVIDSON: Where are you doing --

MR. KRAUSS: Your Honor, she's --

JUDGE DAVIDSON: Just tell me where you're going, so I'll know.

MR. KRAUSS: May I approach?

JUDGE DAVIDSON: Sure.

(Counsel approached the Bench.)

(Counsel conferred with the Judge.)

BY MR. KRAUSS:

Q Dr. Tollefson, would you agree with me that fluoroquinolone resistant Campylobacter, that there's evidence that fluoroquinolone resistant Campylobacter also varies over time, over the course of a year?

A I don't know that.

Q Isn't it true that in the study by Kirk Smith, he found a higher level of fluoroquinolone resistance in the winter months, say January?

A I'd have to refresh my memory. I think he found more --

Q I have it here. I'm sorry, Dr. Tollefson.

A Yeah. Oh, that's right, with notes on it.

MS. STEINBERG: Your Honor, I object. Again, it's beyond the scope of the testimony and Dr. Smith's exhibit speaks for itself.

JUDGE DAVIDSON: I understand. I'm going to allow it for a while yet, because the basis of the witness's testimony is the reliability of the studies. There's where he's going.

MS. STEINBERG: Thank you, Your Honor.

JUDGE DAVIDSON: We'll let it go.

(Pause.)

MR. KRAUSS: Dr. Tollefson, let me approach with our battered copy of Dr. Smith's study; and in particular, I'm referring to Page 3 of G-589. This is in evidence, Your Honor.

BY MR. KRAUSS:

Q And if you take a look at the draft that demonstrates, over time, percentage of resistant isolates -- would you take a look at that?

A Uh-huh, that it increased over time, by year and by quarter.

Q Do you see that there's a peak in every year?

A Yes, and it flows with the total. At the bottom is the total number, and these are the resistance levels.

Q Right, and the resistance levels, as

demonstrated by the draft, on Page 3, the top draft, Figure 1, doesn't it demonstrate a peak in resistance in a regular pattern at the beginning of every year?

A Yes. I'm not aware of others --

Q But you agree that that's what this shows?

A Yes.

Q Are you aware that the human NARMS data as reported by quarter shows a higher level of resistance consistently in the first two quarters, compared to the last two quarters?

A It generally shows a higher level of resistance, yes, for six months, same thing. Yes.

Q For Campylobacter?

A For Campylobacter, I agree.

Q So that would be, besides the Smith article, another reference that resistance in Campylobacter is seasonal; would you agree?

A I guess. Yeah.

Q Now, I think I already asked this, but since I was interrupted, I need to make sure I did. I'm sorry.

Didn't you agree that, overall, Campylobacteriosis peaks sometime in the summer?

A Yes.

Q Now, if during the peak in the summer -- you would agree with me, wouldn't you, that during the summer months, a participating laboratory collecting NARMS Campylobacter isolates would get more isolates than, say, in January?

A Probably, yes.

Q Let's say in January the lab got 100 isolates and -- I'm sorry. In July, the lab got 100 isolates and in January it got 25 isolates, for the sake of our discussion.

A Yes.

Q In both instances, if it received those isolates in a week, it would send one, one isolate, right?

A Correct.

Q And then the human arm of NARMS would get those isolates and include it in their yearly sample, right?

A Most of them. Sometimes the participating labs send too many, or whatever.

Q And then, human NARMS typically will get

somewhere around 50 isolates from each participating site, if they're sending one a week, right?

A Right.

Q And in those 50 isolates in our example, one might be from the 100 in July, right?

A That's correct.

Q And one might be from the 25 in January, right?

A Yes.

Q And the peak in resistance is in January, right?

A Right, but --

Q And each of those would be given --

A Equal weight.

Q Yes.

A That's how surveillance systems, what we call surveillance systems are done. Now --

Q But you don't disagree that that's what's happening?

A No, I don't disagree that it's happening. I disagree with the implication of a large effect.

Q Would you agree that NARMS does not calculate

-- the NARMS program does not calculate an incidence rate?

A Correct.

Q Let me finish my question, for the record. NARMS does not calculate an incidence rate of fluoroquinolone resistant Campylobacteriosis in the United States?

A Correct.

Q All NARMS does is report a percentage of the collected isolates that it has determined to be resistant, isn't that right -- Campylobacter isolates?

A Correct. Correct.

Q Now, you've already agreed with me, Dr. Tollefson, that one of the purposes of NARMS, in your opinion, is to track trends in antibiotic resistance in enteric pathogens over time; isn't that right?

A That's correct.

Q And you've agree with me today that annual incidence rates are used by epidemiologists to examine trends of disease incidence over time, right?

A Yes, or prevalence -- or prevalence rates.

Q Right. Both.

A Right.

Q Right. Incidence or prevalence.

A Okay.

Q And you've agreed with me today that CDC MMWR reports on incidence of food-borne illness are reliable, right?

A Yes.

Q In your opinion, are the annual percentages of fluoroquinolone resistance in Campylobacter that are reported by human NARMS, are they representative of the national proportion of Campylobacter cases that are resistant infections?

A In my opinion, yes.

Q So isn't it true that if you assume that human NARMS data are representative of the national proportion of Campylobacter cases that are resistant infections, and you use the reliable CDC MMWR data on the national incidence of Campylobacteriosis, you can calculate an annual incidence rate of fluoroquinolone resistant Campylobacteriosis cases -- you don't agree?

A No, because, first of all, I want to talk about prevalence, not incidence. We're not talking

about incidence here.

MS. STEINBERG: Your Honor --

THE WITNESS: There's only one way to do that.

MS. STEINBERG: Your Honor, the question asked for a statistical analysis. It's beyond the scope of the testimony.

JUDGE DAVIDSON: Well, she's already attempting to answer it, so -- I mean, you know, you got to get your witness to know that when you object, she's supposed to stop talking. But if she wants to keep talking, that's her business.

MS. STEINBERG: Thank you, Your Honor.

JUDGE DAVIDSON: What was the answer again?

THE WITNESS: Well, we're not dealing with incidence rates, or incidence of fluoroquinolone resistant Campylobacteriosis or anything else.

BY MR. KRAUSS:

Q I thought you said that if NARMS reports 14 percent resistance, fluoroquinolone resistance in Campylobacter --

A It's not a representation of the incidence rate of fluoroquinolone resistant NARMS (sic). That's

what I answered. It is a representation of the prevalence rate of fluoroquinolone resistant Campylobacteriosis in the U.S.

Q For that year?

A Okay.

Q Let me make sure I get this right. NARMS reports, let's say, 14 percent fluoroquinolone resistance in Campylobacter for a given year. Okay? Let's take that.

A Okay.

Q Would it be your opinion, then, if that's the report, and if it's representative of the proportion of Campylobacter cases in the country that are resistant, that of all the Campylobacter cases in the country, you tested them all and you'd have 14 percent resistance?

A Approximately.

Q So isn't it true that you can take what you just said would be a national prevalence of the amount of the amount of fluoroquinolone resistant Campylobacter cases in a given year and use that with the incidence rate of all Campylobacteriosis cases in a given year, and calculate an incidence rate of

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fluoroquinolone resistant Campylobacteriosis cases in the country?

MS. STEINBERG: Your Honor, again, it's beyond the scope, and I think that most of that has been asked and answered.

MR. KRAUSS: Your Honor, this witness designed the NARMS system. I'm asking her what the --

JUDGE DAVIDSON: I'm going to allow it.

THE WITNESS: No. That's the answer. No.

BY MR. KRAUSS:

Q Okay. Now let me just --

JUDGE DAVIDSON: ~~Which~~ would you care to explain?

THE WITNESS: Yeah. Can I explain that?

JUDGE DAVIDSON: Absolutely. Go right ahead.

BY MR. KRAUSS:

Q Go ahead and explain.

A NARMS is a public health surveillance system. We designed it so that it has a good probability of detecting resistance should it exist in each of these several food-borne pathogens, and it's based on practicality, above all else.

Now, what it's capable of doing is, if you

believe that Salmonella in California is no different than Salmonella in Maine -- Salmonellosis or Campylobacteriosis or any food-borne disease -- and we know that it isn't, it's based on representative, in general -- we try to make them as geographically diverse as possible in the case of Campylobacter. In the case of everything else, we've got all 50 states represented.

We take a limited number of samples to give us an indication of the prevalence rate of resistance among these food-borne disease pathogens.

Now, your issues about seasonality and resistance varying with seasonality is true. We've looked at that, and we think the impact is very minimal.

That doesn't mean that we're going to say that in 2001, we got 19 percent fluoroquinolone resistance in Campylobacter in humans, that it's absolutely 19 percent, but it's approximately one-fifth, or approximately 15 percent, or whatever. It's not exact. It's a public health surveillance system. Okay.

Q But those are -- human NARMS does publish what

it believes to be a percentage of all Campylobacteriosis cases in the country in a given year?

A Right. It's an indicator of what's out there throughout the U.S., yes.

Q Right. Right.

A Okay. But that's something, it's technically very different from incidence.

Q Okay. Well --

A Okay. You need an analytical epidemiology study to determine incidence rates.

Q It's your position, is it not, that if human NARMS for 1997 reports 13 percent fluoroquinolone resistant Campylobacter on the human side of NARMS, that all of the Campylobacteriosis cases in 1997, of all of them, 13 percent of those, best estimate based on human NARMS, were resistant?

A Were fluoroquinolone resistant.

Q Right.

A Approximately 13 percent, right.

Q Okay. Now, if CDC, in their MMWR reports, report that there's 25.2 cases of Campylobacter per

100,000 people in that year, it's your position, is it not, that 13 percent of those, give or take, as good or as accurate as human NARMS can be, 13 percent of those would be resistant infections, right?

A Correct.

Q Okay. Dr. Tollefson, if you could look at the two exhibits that I gave you, G-1791, and the other MMWR exhibit that I gave you, G-748 -- I gave that thank you, didn't I?

A No, I don't have 748.

MR. KRAUSS: All right. My apologies. Your Honor, this is Government Exhibit 748, and I believe it's in evidence.

BY MR. KRAUSS:

Q Now, Dr. Tollefson, if you take a look at G-748, on Page 2, Table 1, do you see a table that's the incidence of diagnosed infections for pathogens through the Food Net --

A Yes.

Q -- surveillance network?

A Right.

Q Okay. And you see the Campylobacter is listed

there for '96, '97, '98, '99, and 2000, right?

A Yes, right.

Q And these are incidence rates, right?

A Right, but through Food Net.

Q Through Food Net.

A Right.

Q And so CDC has estimated, for example, for 1997, that there were 25.2 cases of Campylobacteriosis per 100,000 people in the United States for the year 1997?

A Right.

Q From what you testified about earlier, human NARMS, the human side of NARMS reported 13 percent human resistance, right?

A Right.

Q So isn't it true that if, for 1997, the incident rate is 25.2 per 100,000, and NARMS reports 13 percent resistance, it's your position that 13 percent of each of these 25.2 infections would be resistant infections?

A Approximately, yes.

Q So that would give us a resistant incidence

rate, if we multiply 13 percent by 25.2, we'd get 3.28.

A Okay.

Q Yes?

A I wouldn't call it an incidence rate, the problem being that Food Net is an active surveillance system, that's more statistically robust, to get new cases of disease as they arise in the population. NARMS is not. The Campylobacter, they're all Food Net sites, sometimes. Sometimes they're not. But it's a Sentinel Lab system.

I would not call that an incidence rate. I wouldn't put my money on that number. Now, if you're asking me is it approximately that, fine.

Q Okay.

A I guess I don't know what you're trying to get to.

Q Well, just allow me to go through this.

A Okay.

Q So would you agree that, then, for 1997, the good estimate of the number of fluoroquinolone resistant Campylobacter cases per 100,000 people in the United States that were resistant would be 3.28 per

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100,000?

A Okay. Yes.

Q All right. Now, if you'll take a look at G-748 for 1998, CDC reports an overall incidence rate for Campylobacteriosis of 21.4, doesn't it?

A Yes.

Q And the human NARMS system reported for 1998 14 percent resistance, didn't it?

A Right.

Q So we could get a good estimate by your testimony, a good estimate of the number of fluoroquinolone resistant Campylobacter infections per 100,000 people by taking 14 percent of 21.4, couldn't we?

A Approximately, yeah.

Q And so that would be 3.0 cases of resistant infection per 100,000? It's actually 2.996, but I rounded ~~founded~~ up.

MS. STEINBERG: Your Honor, objection. The witness shouldn't be required to do a calculation on the stand without a calculator --

MR. KRAUSS: Your Honor, I'm handing the

witness a calculator.

JUDGE DAVIDSON: No, that's all right.

THE WITNESS: It's approximate.

JUDGE DAVIDSON: We'll let it go for now. If there's a problem with the calculations, you'll let me know, I'm sure.

MR. KRAUSS: Thank you, Your Honor.

BY MR. KRAUSS:

Q For 1999, Dr. Tollefson, if you would take a look at Exhibit G-748, Page 2, Table 1, CDC reported an overall incidence rate of Campylobacteriosis in the United States of 17.5 per 100,000, didn't they?

A Yes.

Q And your human NARMS system for 1999 reported a resistance rate of 18 percent, didn't it?

A Yes.

Q We could get a good estimate of the number of fluoroquinolone resistant Campylobacter cases in the United States for 1999 per 100,000 by taking 18 percent of 17.5, couldn't we?

A Yes.

Q And that would be 3.15.

A Okay.

Q And if you take a look at Exhibit G-748 for 2000, CDC reported, did they not, an incidence rate for Campylobacteriosis of 20.1 cases per 100,000?

A Right.

Q And your human NARMS system for the year 2000 reported resistance of 14 percent; isn't that right?

A Right.

Q So we could get a good estimate of the level of fluoroquinolone resistant Campylobacter infections per 100,000 people in the year 2000 by taking 14 percent of 20.1, couldn't we?

A Mm-hmm.

Q Yes?

A Yes.

Q And that would give us 2.81, wouldn't it?

A Mm-hmm.

Q Yes?

A Yes.

Q Now we'll need to move to Exhibit, Government Exhibit 1791, and there's a table on Page 5?

A Yes.

Q In this CDC MMWR report, CDC reports an overall incidence of Campylobacter in the United States of 13.8 cases per 100,000, doesn't it?

A Yes.

Q Your human NARMS system reports for 2001 resistance of 19 percent, doesn't it?

A Right.

Q We could get a good estimate of the number of fluoroquinolone resistant Campylobacter cases per 100,000 in the United States in 2001 by multiplying the 19 percent by 13.8, couldn't we?

A Yes.

Q That would be 2.62, wouldn't it?

A Right.

Q So from 1997 to 2001, the good estimate that we can calculate for the number of fluoroquinolone resistant Campylobacter infections per 100,000 people in the United States in each of those years, except for 1999, it's gone down, hasn't it?

A The rate has gone down.

Q Right.

A Correct.

Q And it's gone down from, in 1997, 3.28, to 2001, 2.62, right?

A The rate has gone down, correct.

Q And that rate is a good estimate of the number of --

JUDGE DAVIDSON: All right, asked and answered.

MR. KRAUSS: Okay. Your Honor, I'm going to take you at your word that once we got up to noon and I was at a good place for a break, I'd take a break.

JUDGE DAVIDSON: Absolutely. You always take me at my word. What kind of way is that to talk on the record?

(Laughter.)

JUDGE DAVIDSON: All right. I think an hour is more than enough for lunch.

MR. KRAUSS: Yes, Your Honor.

JUDGE DAVIDSON: And it's now -- all right. We're adjourned -- I'll give you a little bit more -- adjourned 'til 1:15.

(Whereupon, at 12:05 p.m., a luncheon recess was taken.)

AFTERNOON SESSION

JUDGE DAVIDSON: Come to order. Be seated, please.

Have you found out anything about the witnesses?

MS. STEINBERG: Your Honor, we did have discussion during the lunch break, and in reliance on the earlier Order, it would be difficult to produce witnesses on other days than already ordered, and we would jointly ask that we keep to the Order.

JUDGE DAVIDSON: That order that I issued so long ago, right? Was it last Friday or Thursday?

MS. STEINBERG: Well, Your Honor, we talked, in order to come up with a joint proposed schedule, and that schedule accommodates all of the witnesses' other obligations.

JUDGE DAVIDSON: Okay. Good enough.

MS. STEINBERG: Thank you.

JUDGE DAVIDSON: Getting a little higher. There's still another chair coming, I think.

(Laughter.)

JUDGE DAVIDSON: Feeling much more confident.

(Laughter.)

JUDGE DAVIDSON: I did want to point out, I forgot earlier, that somewhere along the line, did either of you, did either side get some kind of special dispensation from the Commissioner on ignoring my Orders?

Don't get excited. But I've noticed that the last month or so, I'm getting motions without draft Orders. People just forget about that. That's a requirement in this proceeding.

MS. STEINBERG: I'm sorry, Your Honor. I don't know if that applies, but I'm very sorry --

JUDGE DAVIDSON: No, you can check. It applies.

MS. STEINBERG: No, I mean --

(Laughter.)

MS. STEINBERG: I'm sorry about that.

JUDGE DAVIDSON: And I'll add another requirement. See, just because I have -- see, before, I had no help. Now, I got part-time help, so you think you don't have to bother. But it has to be in MicroSoft. It has to be e-mailed to me along with the

paper, in MicroSoft. What is that, Word, MicroSoft Word or something?

MR. SPILLER: Word, as opposed to WordPerfect?

JUDGE DAVIDSON: Right.

MR. SPILLER: Okay.

JUDGE DAVIDSON: So that I can -- so that if I agree with you, I can just send it out without having to work on it.

Yes, sir.

MR. NICHOLAS: You know, we've been doing that as a result of the discussion some time ago. The problem has been that many of the attachments we don't have in electronic form, so we did, in fact, file a motion this morning to enter into the documented record several additional articles. That motion was e-mailed to you.

JUDGE DAVIDSON: I saw it.

MR. NICHOLAS: But the -- usually, we've been delivering, hand-delivering copies to the Dockets --

JUDGE DAVIDSON: Right, you have to.

MR. NICHOLAS: So I have a copy for you.

JUDGE DAVIDSON: Oh, thank you.

MR. NICHOLAS: I have given a copy to CVM.

JUDGE DAVIDSON: And the draft order?

MR. NICHOLAS: Yes, there's a draft order attached to it, as I believe there always is, but I could be wrong.

JUDGE DAVIDSON: I think maybe you are; but I could be wrong, too. I tell everybody I may not always be right, but I'm never in doubt.

(Laughter.)

JUDGE DAVIDSON: Let's proceed.

MR. KRAUSS: Thank you, Your Honor.

BY MR. KRAUSS:

Q Good afternoon, Dr. Tollefson.

A Good afternoon.

Q Referring back to your written direct testimony, there's a portion of the testimony on Page 18 that refers to other effective drugs approved by CVM, and I believe your testimony is, "There are other effective drugs approved by CVM to enable the drug and poultry industries, working together with veterinarians, to treat each of the diseases and specific bacteria for which Enrofloxacin was approved

in poultry."

Is that your testimony?

A Yes, that's correct.

Q In fact, in your testimony you refer to a chart that was attached to CVM's responses to interrogatories; isn't that right?

A Right.

Q And that was attached to Interrogatory Response Number 87?

A Correct.

Q And you attached that chart to your testimony?

A Yes.

Q I've got a blowup of the chart here.

A Okay.

Q And this is the one from the interrogatory answer, but it would be identical to the one attached to your testimony.

A Yes, that's the same one.

Q Now, we agree, don't we, that Baytril is approved to treat E. coli infections in chickens, right?

A Mm-hmm.

Q And E. coli and Pasteurella multocida infections in turkeys, right? And, Dr. Tollefson, as a veterinarian, are you aware that the types of infections that Baytril is used, prescribed to treat can occur in chickens and turkeys older than one to three days old?

A Yes.

Q In fact, are you familiar with the testimony of some of the veterinarians that Bayer has -- the witnesses that Bayer has called and submitted written direct testimony for?

A Yes.

Q And you're aware that there's testimony and evidence in the record that these diseases happen in the growout houses of these chickens and turkeys, right?

A Yes, sometimes.

Q So these drugs here that are approved for day-old turkeys, for example, or day-old chickens, that approval wouldn't be applicable to turkeys in the growout house that are older than one to three days old, would it?

A If they're used according to their label, correct.

Q Right. And so the same with the day-old chickens and one-to-three-day-old turkeys, right, and the one-to-three-day-old chickens, right?

A Mm-hmm.

Q You're aware, are you not, that the parties have stipulated that individual bird treatment, in other words once the birds are in the growout house and there's 20,000 chickens, it's not practical to individually treat each of the birds?

MS. STEINBERG: Excuse me. Can Mr. Krauss provide a copy of that information to the witness, and can you let us know what number?

MR. KRAUSS: Thirty-six.

(The witness examined the document.)

MR. KRAUSS: For the record, the stipulation is:

"For commercially grown broiler chickens and turkeys in the United States, it is neither feasible nor practical to administer Enrofloxacin on an individual bird basis."

BY MR. KRAUSS:

Q Now, Dr. Tollefson, as a veterinarian, would you agree that, not just talking about Enrofloxacin, but any drug that would be injected for the treatment, that that would not be practical to administer on an individual bird basis to 20,000 chickens in a growout house?

A Yes, I would agree.

Q And the same with turkeys in a growout house?

A Yes.

Q You agree with that?

A Yes, I do.

Q So it wouldn't be practical to inject, so these wouldn't be applicable for treatment, right?

A Right.

Q And as a veterinarian --

JUDGE DAVIDSON: Excuse me. These?

MR. KRAUSS: I'm sorry.

JUDGE DAVIDSON: I know. It's a problem. But see, that's not going to be in the record, that chart.

MR. KRAUSS: It's attached to her testimony, Your Honor.

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JUDGE DAVIDSON: Right, but the lines you drew through, when you say "these," it confuses the record.

MR. KRAUSS: I understand. I'm sorry.

JUDGE DAVIDSON: But I think it's pretty clear what you're talking about, so just go ahead. I'm sorry I said anything.

MR. KRAUSS: Thank you.

BY MR. KRAUSS:

Q Now, Dr. Tollefson, as a veterinarian, are you aware that there's a high degree of tetracycline resistance in E. coli isolates cultured from poultry?

MS. STEINBERG: Objection, Your Honor. That's assuming a fact that's ~~no~~ not in evidence. Is there something to point to or lay a foundation?

MR. KRAUSS: Other than the evidence that's been submitted to the record?

MS. STEINBERG: Lay a foundation.

MR. KRAUSS: She's a veterinarian. Your Honor, I'm asking her whether or not she's aware of this.

JUDGE DAVIDSON: All right. She can answer.

THE WITNESS: I know there's some resistance.

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I don't really know what.

BY MR. KRAUSS:

Q Have you reviewed the testimony of the veterinarians, the veterinarian witnesses that Bayer submitted -- you testified you did review that, right?

A Yes.

Q Did you review the testimony of Dr. John Glisson ~~Glysson~~?

A Yes.

Q He's the acting associate dean of the University of Georgia School of Veterinary Medicine; is that right?

A Yes.

Q When you reviewed his testimony, do you recall that he testified that tetracycline treatment of E. coli is usually ineffective or poorly effective because of widespread resistance to tetracycline among avian E. coli isolates?

MS. STEINBERG: Your Honor, Dr. Glisson's ~~Glysson's~~ testimony speaks for itself, and Dr. Tollefson's recollection of Dr. Glisson's ~~Glysson's~~ testimony --

JUDGE DAVIDSON: I'm going to sustain the

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objection.

If you want to ask her if she knows about certain things, and does she agree or disagree, that's one thing, but don't recite other testimony of record again and again and again.

She admitted that she's aware of some degree of a problem with tetracycline, as far as resistance is concerned. Now you're trying to get Dr. ~~Glysson's~~ Glisson's testimony on the record again with this witness to approve it or disapprove it? I don't understand.

MR. KRAUSS: Well, she testified that she has reviewed Dr. ~~Glysson's~~ Glisson's testimony.

JUDGE DAVIDSON: I understand that.

MR. KRAUSS: Okay .

BY MR. KRAUSS:

Q Do you, Dr. Tollefson, do you have any knowledge or evidence that tetracycline, that there's not a high level of tetracycline resistance in avian E. coli isolates such that tetracycline treatment is ineffective or poorly effective?

A I don't -- I don't know. You're asking me if I -- could you repeat the question?

Q Do you have any knowledge or evidence that tetracycline -- that there are not high levels of tetracycline resistance in avian E. coli isolates such that tetracycline treatment of E. coli is ineffective or poorly effective? Do you have any evidence?

A That it isn't? That -- I --

MS. STEINBERG: Your Honor, I object to the form of the question. There were a lot of double negatives, and honestly, it's confusing.

JUDGE DAVIDSON: All right. She can answer it. She doesn't know. Okay.

THE WITNESS: I don't know. I don't know. Let's --

MR. KRAUSS: You don't know.

THE WITNESS: I don't know.

JUDGE DAVIDSON: Excuse me.

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

JUDGE DAVIDSON: Very important interruption. Off the record.

(A discussion was held off the record.)

JUDGE DAVIDSON: Are we all here? Okay. Back on the record. I apologize for the interruption.

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MR. KRAUSS: That's fine, Your Honor.

BY MR. KRAUSS:

Q Dr. Tollefson, you've testified that you've reviewed the testimony of Dr. ~~Glysson~~ Glisson; isn't that right?

A Yes, I've read it.

Q Do you have any reason to disbelieve his testimony with regard to tetracycline resistance in E. coli isolates that he's observed?

A What -- I was somewhat confused by his testimony, because there are other tetracyclines that would be able to be used under ~~ADUCA~~ AMDUCA, under the extra-label use laws, so I wasn't sure if all the tetracyclines were a problem or not. I don't know that personally, and I did not go into it in depth.

Q Okay.

A So I can't answer that with yes or no.

Q Let me ask you this, Dr. Tollefson. Are you aware that, from your review of the testimony, that practicing poultry veterinarians in this case have testified that there are no practical alternatives to Baytril for treating these diseases of poultry?

A Yes, I know that -- yes.

Q What drugs are you aware of that are being used by practicing poultry veterinarians that are practical and effective to treat E. Coli infections in broilers older than three days old and E. Coli or Pasteurella multocida infections in turkeys older than three days old?

A I don't know.

Q You don't know of any drugs?

A No, I don't, I don't -- I can't answer that question. It's not my area of expertise, and I don't know what practicing veterinarians, poultry veterinarians are doing.

Q But you testified that there are other effective drugs --

A Right.

Q -- that can be used?

A Correct.

Q But that was outside your area of expertise?

A No. You asked me do I know what poultry veterinarians are actually using. I know what has been approved for those specific diseases, which is what you

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asked us to answer in Interrogatory Number 87, and I also know that, under the extra-label use provisions of the Animal Drug Use Clarification Act, other anti-microbials can be used.

Now, what they're actually using, I do not know, and that's what you asked.

Q That's what I asked. So that's what I'm asking you -- approved drugs and drugs available under AMDUCA ~~ADUCA~~, do you know of any that are being used by practicing poultry veterinarians to treat these diseases?

MS. STEINBERG: Your Honor, asked and answered.

JUDGE DAVIDSON: Yes. She said she doesn't know what they're doing now. Move on.

MR. KRAUSS: Okay.

BY MR. KRAUSS:

Q Now, Dr. Tollefson, you testified about reviewing the Kirk Smith study, G-589.

A Mm-hmm.

Q I'm not going to ask you specifically about the document or anything, but there was a case control

study that he performed, or a case study that he performed, that ultimately got into that article, G-589. You agree with that, right? That was the basis of the article?

A Case study?

Q Or case control study?

A I -- okay. Go on. Go ahead and ask the question.

MS. STEINBERG: Your Honor, can Mr. Krauss provide Dr. Tollefson with a copy of that?

JUDGE DAVIDSON: He did before.

MR. KRAUSS: Can we go off the record one second?

JUDGE DAVIDSON: Off the record.

(A discussion was held off the record.)

JUDGE DAVIDSON: Back on the record.

MR. KRAUSS: Your Honor, it's G-589.

THE WITNESS: Case comparison study, he calls it.

MR. KRAUSS: Okay.

BY MR. KRAUSS:

Q Now, this is a study that you testified that

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you reviewed as part of the process of coming to the decision to issue the NOOH, right?

A Mm-hmm.

Q Did FDA audit the study?

A No, we did not.

Q Did FDA review the protocol for the study?

A No. The study took place ahead of time. I mean, it already had taken -- had already taken place.

Q Okay.

A Okay.

Q Did FDA get the raw data from the study?

A No. We spoke to Kirk Smith about the study and about the possibility of getting the raw ~~did~~ data. We did not. I'm 90 percent sure we did not get it.

Q Even though the study had already been performed by the time the NOOH was issued, did you review the protocol, even though it would have been after the study was done? Did FDA review the protocol?

A I don't recall.

Q And FDA did not get the raw data, right, you said?

A Correct.

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Q So you couldn't have done any kind of an audit of the raw data?

A No, we did not.

Q Or any kind of an analysis of the raw data, right?

A Correct.

Q Did FDA perform any independent assessment of the validity of the Smith study?

A By independent, you mean someone other than FDA employees?

Q Did FDA conduct an assessment of the validity of the study?

A I guess that's inherent -- I would answer that that is inherent in our evaluation of the study.

Q So you evaluated the study?

A Yes.

Q And that was based on what? Based on the paper?

A In talking to Dr. Smith, and actually even before the study, and Dr. Bender, and so on, the co-authors ~~ops~~.

Q So this evaluation that you did didn't involve

a review of the protocol and --

A Well, we did review the protocol. When you asked that question -- I mean, we looked at the protocol, we talked about the protocol, we talked about what they did.

Q Okay. Your evaluation didn't involve anything with looking at the raw data, is that right?

A No, it did not.

Q Was there a written protocol?

A Yes, to my recollection there was a written description of what they did. I would call that a protocol.

Q And FDA reviewed that as part of the evaluation of the Smith study?

A We discussed it as part of the evaluation of the Smith study, right. We didn't do a written evaluation of it, if that's what you're looking for.

Q But you looked at a written protocol? There was a --

A We met with the authors of this study, and -- I cannot recall. Okay?

Q Was there a written protocol or not?

A I cannot recall.

Q Did you ever see a written protocol?

A I --

MS. STEINBERG: Your Honor, asked and answered. He's badgering the witness.

JUDGE DAVIDSON: Sustained.

BY MR. KRAUSS:

Q Now, Dr. Tollefson, let me turn your attention to the CDC Campylobacter case control study, and ask you kind of the same questions here.

JUDGE DAVIDSON: Got a docket number? I mean, exhibit number?

MR. KRAUSS: Yes, Your Honor. Yes. One aspect of it is G-1452, Exhibit 3 -- Attachment 3.

JUDGE DAVIDSON: More? Others? Other aspects?

MR. KRAUSS: I believe it's also G-1488, and there's discussion of it in the Kassenborg testimony.

JUDGE DAVIDSON: Okay. That's 1460?

MR. KRAUSS: Yes. And there's another aspect of it, Your Honor, that I believe is Attachment 4 to G-1452, the Angulo testimony.

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JUDGE DAVIDSON: Okay. Proceed.

MS. STEINBERG: Your Honor, if Mr. Krauss is going to ask Dr. Tollefson about those specific documents, can he please provide them to her?

MR. KRAUSS: Well, I've already provided 1452, Attachment 3, and that should be sufficient, Your Honor, to handle the questions, I believe.

JUDGE DAVIDSON: Okay.

BY MR. KRAUSS:

Q Now, Dr. Tollefson, is it your understanding that the CDC Campylobacter case control study was analyzed by, for different aspects, by different CDC epidemiologists?

A Correct.

Q And, for example, Dr. ~~Freedman~~ Friedman --

MS. STEINBERG: Your Honor, this is beyond the scope of Dr. Tollefson's testimony.

MR. KRAUSS: Your Honor, she testified that she reviewed the CDC Campylobacter case control study as part of the decision for bringing the NOOH, if I'm not mistaken.

JUDGE DAVIDSON: All right. I'll let it go.

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But, you know, there are going to be other witnesses in this proceeding besides Dr. Tollefson.

MR. KRAUSS: I understand that, Your Honor.

JUDGE DAVIDSON: And, you know, you keep referring to things that Dr. Smith did and Dr. Angulo, and they're going to be here, too. Okay? Go ahead. I'm just reminding you --

MR. KRAUSS: Yes, Your Honor.

JUDGE DAVIDSON: -- of something you already know.

MR. KRAUSS: I'll speed it up, Your Honor.

JUDGE DAVIDSON: Okay.

BY MR. KRAUSS:

Q So Dr. ~~Freedman~~ Friedman, her part of the analysis was the risk factors of getting a Campylobacteriosis infection; isn't that right?

A Yes, I believe that's right.

Q And Dr. Kassenborg, her part of the analysis was the risk factors of getting a fluoroquinolone resistant Campylobacter infection; isn't that right?

A Correct.

Q And there's a report by a Jennifer McClellan,

also known as Jennifer Nelson, right, and her part of the study was the differences between, or the consequences of a resistant infection versus a non-resistant infection, right?

A Right.

Q Now, with respect to the CDC Campylobacter case control study, and those three analyses, did FDA audit those studies?

A No.

Q Did FDA review the protocols of those studies?

A I don't know.

Q Did FDA get the raw data from those studies?

A We got, yes, we got some of the raw data of those studies.

Q Okay. From any particular of the three studies or what do you recall?

A From the case control data set.

Q Did FDA audit the raw data that it did receive?

A No.

Q Did FDA do any assessment of the validity of

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those studies? And by those studies, I mean ~~Freedman~~ Friedman, Kassenborg, Nelson/McClellan.

A No.

Q Dr. Tollefson, I'm a little bit confused about one thing that you said earlier today, and that is with respect to the most recent publication from CDC MMWR with respect to Campylobacter incidence.

A Mm-hmm.

Q I believe you testified that, for through 2002, Campylobacter incidence was up. Is that what you said?

A I thought it was, slightly, yes.

Q Slightly up?

A But I don't have a --

MR. KRAUSS: Let me hand to you -- and Your Honor, this is B-1924, and it's attached to our motion. This just came out April 18, 2003, and it's Attachment 3 to the motion. I'm sorry. It may be Attachment 2. I was given bad advice, Your Honor.

BY MR. KRAUSS:

Q Dr. Tollefson, we already established -- I believe, you have the document G-1791 -- that for 2001,

Campylobacter, overall incidence was 13.8; isn't that right?

A Right.

Q And B-1924, on Page 6 of 8, the table does not have a table number, but would you agree with me that the Campylobacter incidence is 13.37 overall?

A Yes. Well, that's what the table says, but hold on, because I didn't use the draft of this.

Yeah. If you look at Figure 1, it looks like it's going up slightly, but I agree, that must not be right, because the number is slightly down.

Q Right. So going into, from 2001 to 2002, Campylobacteriosis incidence in the United States has gone down, correct?

A Yes.

MR. KRAUSS: Thank you. Your Honor, with that, I have no further questions of this witness, at this time.

JUDGE DAVIDSON: Do you have redirect?

MS. STEINBERG: Yes, we do.

Your Honor, at the outset, we had talked about switching tables for redirect.

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MR. KRAUSS: Perhaps we should go off the record quickly, Your Honor?

JUDGE DAVIDSON: Off the record.

(A discussion was held off the record.)

REDIRECT EXAMINATION

BY MS. STEINBERG:

Q Dr. Tollefson, I only have a few questions for redirect. I would like to clear up a couple of questions from the cross examination.

On cross examination, you were asked whether you agreed that Campylobacteriosis is mainly a diarrheal disease or the main effect is diarrhea, and I wanted to ask you whether there are other symptoms of Campylobacteriosis?

A Yes. Diarrhea is only one of the symptoms. There's cramping, there can be bloody diarrhea. It's -- it can be a very severe illness.

Q Are there common complications from Campylobacteriosis?

A Yes, there are complications that can range from minor to very severe, like reactive arthritis and Guillain ~~Guilliam~~-Barre, which is a paralysis.

Q I also wanted to ask you a question about G-410, which is the ~~lead~~ Mead document.

A Yes.

Q Do you need a copy of that?

A No.

Q How often does CDC produce a document like that, a comprehensive survey?

A A comprehensive review of the Food Net, of the food data, food-borne illness data, not very often, usually about every seven to 10 years.

Q Is Exhibit G-410, that ~~lead~~ Mead article, the most comprehensive study to date --

A Yes.

Q -- the most recent comprehensive study to date?

A Yes.

Q Do people still cite to it as the most recent comprehensive study?

A Yes, they do.

Q Does the fact that Campylobacteriosis is now reported as the second most common bacterial diarrheal disease for enteric gastroenteritis, does that play a

part in the factor that's an important food-borne disease?

A It's only slightly below Salmonellosis. It's still a very important food-borne disease in humans in the U.S.

Q I have a couple of questions for you about G-1452, Attachment 3.

A Mm-hmm.

Q Do you still have a copy of that?

A Yes, I do.

Q Mr. Krauss asked you to agree that people who did not eat chicken at home were more likely to be Campylobacter case than people who did eat chicken at home.

What about people who do not ever eat chicken? Are people who eat chicken at home more likely to be a Campylobacter case than people who, for example, eat cheese sandwiches at home?

A You can't answer that from the data set, from the Attachment Number 3, G-1452, but it gets to the question of what is protective, really, and it's unlikely that people would be -- who eat cheese

sandwiches -- would be less likely than people who eat chicken at home to get Campylobacteriosis.

Q In fact, in the list on Pages, beginning on Page 98 of Attachment 3, G-1452, and going on, are there, in fact, situations where chicken is considered a risk factor for acquiring Campylobacteriosis?

A Yes, there are.

Q Could you point out some of those to us, please?

A Yes. Chicken prepared -- just going down the list -- on an outdoor grill at a large social gathering, that's statistically significant.

Chicken in a restaurant. Turkey prepared at a restaurant. Broiled chicken prepared at a restaurant. Chicken wings prepared at a restaurant. There are many.

Q And I notice that you mentioned turkey, which was going to be one of my questions, so are there also situations where turkey presents as a risk factor for acquiring Campylobacteriosis?

A Yes. It looks like ate turkey prepared at a restaurant and ate oven-roasted turkey prepared at a

restaurant are both, and there's also contact with animals. It discussion say chickens or turkeys. Yes.

Q Turning attention to two other exhibits, G-285 and B-252, Mr. Krauss asked you about those two exhibits, and asked whether it was true that those two exhibits dealt with Salmonella rather than Campylobacter?

A Correct.

Q What did you cite those exhibits for?

A This was in my testimony under the heading of "Background on Anti-Microbial Resistance," and the purpose of it was to describe how food-borne pathogens may be transmitted from animals to humans. It's not meant to be specific to Campylobacter.

Q Would the transfer of resistant bacteria from animals to humans be different if you're talking about Campylobacter as a bacteria rather than Salmonella as a bacteria?

A No, no different.

Q Now, I want to turn to the issue of -- I guess the chart is gone -- the first chart that Mr. Krauss had drawn about Paula Cray's lab and the various

problems with speciation.

A Okay. Right. I have that in my testimony.

Q What is the net result of using nalidixic susceptibility and resistance to cephalothin in speciation?

A The net result is that Paula Cray's lab received a biased data set in that they were more likely to be susceptible to ciprofloxacin than resistant to ciprofloxacin.

She, in other words, received a sub-sample, if you will, until 2001.

Q Thank you. Mr. Krauss also had a chart up there with a calculation of the incidence rates, and various other things.

Did his chart take into account any changes in the population during the years on the chart?

A No.

Q Does that matter for his calculation?

A Yes.

Q Can you explain why?

A What he was trying to -- well, I don't know what he was trying to show. But he was indicating that

since the incidence of Campylobacter was decreasing, then proportion -- then the incidence of resistant Campylobacter was also decreasing.

However, if the population is increasing over time, then the absolute numbers may or may not be decreasing.

Q Do you still have G-589 with you, Dr. Smith's study?

A No, I don't.

Q Maybe a copy would help.

Dr. Tollefson, was Dr. Smith's study published?

A Yes.

Q In what journal?

A In the New England Journal of Medicine.

Q To your knowledge, is that a peer review journal?

A Yes.

Q I have one more question on the MMWR.

A Mm-hmm.

Q Do you have both of the exhibits --

A Yeah, I do --

Q -- G-748 and G-1791?

A Yes.

Q Mr. Krauss's last questions concerned whether or not Campylobacter has gone up from 2001 to 2002.

I'd like to start with Exhibit G-748 and ask you, on the first page, under the heading "2000 Surveillance," whether or not this indicates the number of Campylobacteriosis cases for 2000?

A Yes.

Q Can you tell us what that was?

A It was 4,640.

Q And then turning to G-1791?

A Yes, there, 2001 is 4,740 Campylobacter --

Q So did the number of Campylobacteriosis cases go up from the year 2000 to 2001?

A Yes.

MS. STEINBERG: Thank you. May I have a moment?

JUDGE DAVIDSON: Certainly.

(Pause.)

MS. STEINBERG: I don't believe that the witness has a copy of this. This was in the motion

that Mr. Nicholas handed to us this afternoon. It is marked as Exhibit B-1924, and I'd like to bring it to the witness, if that's okay with you, Your Honor.

JUDGE DAVIDSON: Go ahead. Go ahead.

BY MS. STEINBERG:

Q This is on Page 2 of B-1924, and under the title, "2002 Surveillance," can you tell us what the number of Campylobacteriosis cases is there?

A 5,006.

MS. STEINBERG: Thank you. At this time, Your Honor, I have no further questions on redirect.

MR. KRAUSS: Your Honor, I have a brief recross.

JUDGE DAVIDSON: Go ahead. Go ahead.

MR. KRAUSS: I can do it from right here.

JUDGE DAVIDSON: Oh, you're so kind. That's all right. Would you like to move?

MR. KRAUSS: No.

RECROSS EXAMINATION

BY MR. KRAUSS:

Q Dr. Tollefson, I'll work backwards. Ms. Steinberg just asked you about the numbers of cases of

Campylobacteriosis using these MMWR reports, and it's G-1791, G-748, and B-1924.

Now, it's not your testimony here today, is it, that the overall incidence of Campylobacteriosis from 2000 to 2001 to 2002 is increasing, is it?

A No.

Q In fact, those numbers that Ms. Steinberg asked you about is the laboratory culture confirmed cases, isn't it?

A Yes.

Q And that would depend on how many people go to a doctor, right?

A Correct.

Q And get a culture, right?

A Correct.

Q And then have that culture be confirmed, right?

A Correct.

Q Now, with respect to the analysis that you and I walked through on the incidence rates -- you called it an incidence, or Ms. Steinberg called it an incidence rate -- you didn't want to call it an

incidence rate, right?

A (Shakes head.)

Q On that analysis, your testimony, when Ms. Steinberg was asking you about it, was that if the population changes, the numbers can change; isn't that right?

A The absolute, the total numbers can change.

Q Right. Are you aware of any analysis that's looked at the population changes in Food Net case control -- I'm sorry -- Food Net areas for which Campylobacter are sampled and performed a calculation to determine a rate of fluoroquinolone resistant Campylobacteriosis in the United States?

A No, that's not what I was referring to. I was referring -- if you're going to go to a rate, which is a population-based number, then it would be the population throughout the U.S., not in Food Net sites. Right?

Q Right. But what we walked through together it was incidence rates of Campylobacteriosis in the United States per 100,000.

A Correct.

Q And you said, well, if the population changes, the numbers can change.

A No, no, total numbers.

Q Total numbers meaning?

A How many cases, not rates, cases.

Q Okay. Oh, so the rates are accurate?

A Yeah. Yes.

Q Okay. Thank you. Now, one last thing. You testified regarding the symptoms of Campylobacteriosis and about the complications --

A Mm-hmm.

Q -- when Ms. Steinberg was questioning you, and I was kind of surprised, because you referred to reactive arthritis as a common complication. That's not true, is it?

A No.

Q Reactive arthritis is not a common complication, is it?

A No, but that's not what I said. I said some complications include. Ms. Steinberg asked me the question as to common, but I did not say that it was common.

Corrected as per OR 46 6/13/03

Q Okay. And that would be true of ~~Guilliam~~ Guillain-Barre Syndrome, too, isn't it?

A Correct.

Q ~~Guilliam~~ Guillain-Barre Syndrome is not a common complication?

A No, it is not.

MR. KRAUSS: Nothing further, Your Honor.

JUDGE DAVIDSON: Okay. I just have one little question, not -- it doesn't have great import, but I wanted to find out, because I read your -- do you have your testimony in front of you?

THE WITNESS: Mm-hmm.

JUDGE DAVIDSON: I was confused by Page 3, starting on Line 19, when you say all three bacteria can cause severe food-borne illness in humans, even though they are non-pathogenic in animals.

THE WITNESS: Correct.

JUDGE DAVIDSON: Now, even though the Commissioner of FDA, in years gone by, has said that I have lot of expertise scientifically, I deny it. I don't have any. Okay.

So then we go down to Line 46, where it seems

to me you're saying that E. Coli caused mortality. Now, if it's non-pathogenic, how could it cause mortality?

THE WITNESS: It's a respiratory pathogen in that case, of chickens.

JUDGE DAVIDSON: Oh, so it is pathogenic, but not --

THE WITNESS: Right, it's not a food-borne, it's not an enteric pathogen.

JUDGE DAVIDSON: Gotcha. Thank you very much.

THE WITNESS: Sure.

JUDGE DAVIDSON: You're excused.

(The witness was excused.)

MR. KRAUSS: Thank you, Your Honor.

JUDGE DAVIDSON: Now, any other housekeeping matters before we --

MS. STEINBERG: No, Your Honor.

JUDGE DAVIDSON: Okay. Now, do we have a problem tomorrow with meeting at 9:30 instead of 9 o'clock? Anybody unhappy about that?

MR. KRAUSS: No.

MS. STEINBERG: No.

JUDGE DAVIDSON: Okay. We're adjourned until 9:30 a.m. tomorrow morning.

(Whereupon, the hearing was adjourned.)

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