ORIGINAL

UNITED STATES OF AMERICA
BEFORE THE FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES

In the Matter of:	:	
Enrofloxacin for Poultry: Withdrawal of Approval of Bayer Corporation's New Animal Drug Application (NADA) 140-828 (Baytril)	:	FDA DOCKET NO. 00N-1571

Monday, April 28, 2003

The hearing in the above-entitled matter commenced at 9:03 a.m., pursuant to notice.

BEFORE:

DANIEL J. DAVIDSON
Administrative Law Judge

Diversified Reporting Services, Inc.
1101 Sixteenth Street, NW Second Floor
Washington, DC 20036
(202) 467-9200

00N-1571 TR9

APPEARANCES:

On behalf of the Center for Veterinary Medicine (CVM):

NADINE R. STEINBERG, ESQ.
ROBERT M. SPILLER, JR., ESQ.
CANDACE CK AMBROSE, ESQ.
CLAUDIA J. ZUCKERMAN, ESQ.
U.S. Food and Drug Administration
Department of Health and Human Services
Office of the General Counsel
Office of the Chief Counsel
5600 Fishers Lane, GCF-1
Rockville, Maryland 20857
(301) 827-5050

Corrected as per OR 46 6/13/03

On behalf of Respondent Bayer Corporation:

GREGORY A. KRAUSS, ESQ.
ROBERT B. NICHOLAS, ESQ.
McDermott, Will & Emery
600 13th Street, N.W.
Washington, D.C. 20005-3096
(202) 756-8263

On behalf of the Animal Health Institute:

KENT McCLURE, ESQ.
1325 G Street, N.W., Suite 700
Washington, D.C. 20005

Also present:

Dennis D. Copeland, D.V.M., Director
Stewardship - Government/Industry Relations
Research & Development
Bayer HealthCare Animal Health Division
Bayer HealthCare LLC
P.O. Box 390
Shawnee Mission, Kansas 66201-0390
(913) 268-2522

C O N T E N T S

* * *

Corrected as per OR 46 6/13/03

P R O C E E D I N G S

(9:03 a.m.)

JUDGE DAVIDSON: Come to order. On the record.

By the Orders of April 10, 2002 and April 15, 2003, this hearing for the purposes of cross examination was set to begin at this time and place in FDA Docket Number 00N-1571, Enrofloxacin for Poultry: Withdrawal of Approval of New Animal Drug Application (NADA) 140-828.

Counsel, in announcing your appearances, please state your name, your address, the capacity in which you appear, and whether you have been admitted to practice before the bar or bars of any of these United States.

Who appears for the Center for Veterinary Medicine?

MS. STEINBERG: Nadine Steinberg. The address is 5600 Fishers ~~Land~~ Lane, Rockville, Maryland 20857. I appear on behalf of the Center for Veterinary Medicine and I'm admitted in the District of Columbia.

MR. SPILLER: I'm Robert Spiller. My address

Corrected as per OR 46 6/13/03

is the same as Ms. Steinberg's. I'm also appearing for the Center for Veterinary Medicine, and I'm admitted to the bar of the Commonwealth of Virginia.

JUDGE DAVIDSON: Okay.

MS. AMBROSE: Candace ~~C.~~ Ambrose. My address is the same as Nadine's. I'm also counsel for CVM, and I'm admitted to the bar of the State of Maryland.

MS. ZUCKERMAN: I'm Claudia Zuckerman. My address is the same as Ms. Steinberg's. I'm also counsel for the Center for Veterinary Medicine and I'm admitted to the bar in Maryland.

MR. KRAUSS: Your Honor, Gregory Krauss on behalf of Respondent Bayer Corporation.

JUDGE DAVIDSON: You didn't me a chance to even ask.

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

(Laughter.)

JUDGE DAVIDSON: Who appears for Bayer Corporation?

MR. KRAUSS: Your Honor, Gregory Krauss on behalf of Bayer Corporation. My address is 600 13th Street, Northwest, Washington, D.C. 20005. I'm

admitted to the bars of the States of Maryland, New Jersey, Pennsylvania, and the District of Columbia.

MR. NICHOLAS: Your Honor, I'm Robert Nicholas. I appear on behalf of Bayer, the same address as Mr. Krauss. I'm admitted to the bars of Massachusetts and the District of Columbia.

JUDGE DAVIDSON: Is there someone here for the Animal Health Institute?

MR. McCLURE: Yes, Your Honor. My name is Kent McClure. My address is 1325 G Street, Suite 700, Washington, D.C. 20005. I'm admitted to the bars of the District of Columbia and Texas, and I might add, Your Honor, that I meant no disrespect by not wearing a tie today. I have a broken arm and can't --

JUDGE DAVIDSON: That's why we didn't give you a desk.

(Laughter.)

JUDGE DAVIDSON: Are there any other appearances?

(No response.)

JUDGE DAVIDSON: Hearing none, let's move on to preliminary matters. I'll let you go first with the

preliminary matters. Ms. Ambrose.

MS. AMBROSE: Yes, Your Honor. I have one preliminary matter. I ask that I be excused from appearing on time this afternoon after the lunch break. I have a conference call scheduled with one of the witnesses who was to appear on cross examination during the lunch hour, and I'll return to the courtroom as soon as the call is over.

JUDGE DAVIDSON: Well, I'll conditionally authorize that, but we may be talking some more about that before we get into actually cross examining the witnesses.

Anything else?

MS. ZUCKERMAN: Your Honor?

JUDGE DAVIDSON: Yes, Ms. Zuckerman.

MS. ZUCKERMAN: At this time, the Center for Veterinary Medicine requests reinstatement of certain testimony and exhibits into the evidentiary record that were stricken from the evidentiary record but remain in the administrative record pursuant to Your Honor's Order dated March 3, 2003.

The March 3rd Order stated:

Corrected as per OR 46 6/13/03

"The Respondent's motion to strike testimony and exhibits set forth in Appendix D thereto relating to the Sentinel County study is granted solely for the reason that relevant information requested by the Respondent was not furnished by the Center for Veterinary Medicine (CVM) in a timely manner."

The Footnote 3 at the end of that sentence reads:

"The ruling is without prejudice to the resubmission of the testimony and exhibits at the oral phase of this hearing."

CVM seeks reinstatement into the evidentiary record of the following exhibits and related testimony that were part of Appendix D referred to in the March 3rd Order.

Exhibit B-589, which is the ~~Patent~~ Patton article, describes --

JUDGE DAVIDSON: I'm sorry, say that again, the exhibit number.

MS. ZUCKERMAN: The Exhibit number is B --

JUDGE DAVIDSON: B.

MS. ZUCKERMAN: -- as in Bayer --

Corrected as per OR 46 6/13/03

JUDGE DAVIDSON: Okay.

MS. ZUCKERMAN: -- 589, and I have copies if Your Honor --

JUDGE DAVIDSON: That's all right. Let's get them all listed first.

MS. ZUCKERMAN: B-589 is the ~~Patent~~ Patton article describing the Sentinel County study methods;

Exhibit G, as in government, 624, which is the ~~Ten-over~~ Tenover article describing the Sentinel County susceptibility test results; and

Parts of the testimony of CVM witness Fred Angulo, Exhibit G-1452 at Page 14, Lines 2 through 20 and Lines 38 through 46, which discuss the methods and the test results of the Sentinel County study.

Any concerns regarding Bayer's timely access to documents that are related to the Sentinel County study have now been mooted, for two reasons.

First, on January 27, 2003, Bayer received additional Sentinel County related information, a study protocol, and a patient questionnaire that it sought from CDC pursuant to a Freedom of Information Act request. By now, Bayer has had sufficient time, about

three months, to review the protocol and questionnaire.

Second, CVM is seeking reinstatement into the evidentiary record of only a portion of the exhibits and testimony that relate to the Sentinel County study. CVM is limiting it request to cover only information relating to the susceptibility test results from the study.

In other words, CVM is not requesting reinstatement of interview-related data on risk factors and duration of illness that were also generated as part of the Sentinel County study and that were stricken from the evidentiary record by the March 3rd Order.

As a result of CVM's narrow request, the patient questionnaire that Bayer received from CDC on January 27th is irrelevant to the exhibits and testimony CVM now seeks to resubmit.

With the exception of the study protocol that Bayer received from CDC in January, the relevant Sentinel County information has been in Bayer's possession since at least November 2002.

Bayer has had an electronic copy of the

Corrected as per OR 46 6/13/03

susceptibility test results of CDC since November, and in addition, the ~~Patent~~ Patton article, B-589, and the Ten-over article, G-624, were contained in the parties' original ~~12-A(5)~~ 12.85 submissions.

Finally, although CVM witnesses, in addition to Dr. Angulo, testify in their written direct testimonies to the susceptibility test results of the Sentinel County study, CVM is seeking reinstatement of testimony only from Dr. Angulo, who is scheduled for cross examination on Wednesday.

Therefore, to the extent that Bayer is entitled to cross examination on testimony related to the test results from the Sentinel County study, Bayer will still have the opportunity to conduct such cross examination.

Therefore, CVM respectfully requests that Your Honor reinstate into the evidentiary record B-589, G-624, and G-1452, Page 14, Lines 1 through 20 and Lines 38 through 46.

Thank you, Your Honor.

JUDGE DAVIDSON: You don't have a chair?

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

JUDGE DAVIDSON: I know you are, but I'm not. If you want to go back about 20 years --

MR. KRAUSS: Thank you, Your Honor.

JUDGE DAVIDSON: -- you want to go back about 20 years to a hearing we had on something called Catherabol, I removed somebody from the hearing because he insisted on standing up when I wanted him to sit down.

MR. KRAUSS: Your Honor, I'm happy to sit down.

(Laughter.)

JUDGE DAVIDSON: All right. Do you care to respond?

MR. NICHOLAS: I would, Your Honor.

JUDGE DAVIDSON: Okay.

MR. NICHOLAS: We would oppose that motion.

We've had a great deal of difficulty, as you know, obtaining information from CDC and/or CVM with respect to the Sentinel County study.

It's true that we did receive additional information in early January from CDC. However, we have a pending FOIA appeal with respect to additional

information for that study, which we have not received a reply to, notwithstanding many phone calls to CDC, and great efforts on our part to obtain all of the information relevant to that study so we could make a judgment with respect to the credibility of that study and the background of that study.

So we would oppose it, Your Honor, because we do not have all the information, even as of this day.

JUDGE DAVIDSON: Well, I'd like to see what's in the protocol, because based on what you've, both sides, presented to me when I was faced with this minor task of dealing with 600 pages of motions to strike and replies, all I saw was that they didn't furnish you a protocol. Since you didn't have it, I couldn't expect you to show me what was in it.

I still haven't seen it, so I don't know whether it's something that would interfere -- that's why I struck the exhibit, because, and related material, because I had no way of knowing what was kept from you.

Until I find out what it was -- and you've received it as of January 27th, so you must now have a

copy of it.

MR. NICHOLAS: Well, we've received the protocol, Your Honor.

JUDGE DAVIDSON: Yeah, and that was --

MR. NICHOLAS: But there are other many other things that we've asked for with respect to that, sir.

JUDGE DAVIDSON: Well, I understand that's a lot of things you've asked for, a lot of things you haven't gotten, and a lot of information that supposedly has come to me hasn't come to me.

I'm not criticizing anybody in particular, but from time to time, I would get e-mails saying that something was faxed to me, and I never got it, and I think I mentioned that to you on the last telephone conversation we had, group conversations.

I'm not ready to rule on this until I see what's involved. If I know, if I can see -- the basis for striking the exhibit in the first place, as I said in my Order, was the fact that they hadn't furnished you with what I considered to be important, if not vital information, being the protocol.

Now, if I see the protocol and I don't think

that that has that much of an impact on whether or not you could adequately understand the exhibit, then I might change my mind, but I haven't seen the protocol, so I still don't know where I am on this.

So I'm not ruling until I see it. No one has bothered to give it to me. It may be filed in the file somewhere, but that doesn't help me. There's a lot of stuff in this file that I'll admit I haven't looked at, and until it gets in the evidentiary record, I won't look at it.

MR. NICHOLAS: Your Honor, if I may, I'd like to request permission to respond to this motion tomorrow morning.

We will go back and be able to provide you a list of what we have not received from CVM or CDC, and so when you have the protocol, you'll have an opportunity to look at these other materials as well, and make a judgment with respect to whether Bayer has been prejudiced in its ability to examine this material.

JUDGE DAVIDSON: Sounds like a very reasonable way to proceed.

MR. NICHOLAS: Thank you, Your Honor.

JUDGE DAVIDSON: Okay. Any other preliminary matters?

MS. STEINBERG: No, Your Honor.

JUDGE DAVIDSON: Well, I have a couple. Let's see.

First of all, after I went home on Friday, apparently somebody dropped this at my door, a motion from CVM to supplement the 1285 and enter Exhibit 1801 into evidentiary record.

Now, by rule, you have 10 days to respond to that. Are you ready to respond at all at this point, or not? I'm not making you respond.

MR. NICHOLAS: Your Honor, we are preparing the response. We did get that letter from Mr. Foster from CDC. It represents, in our view, a one-sided tale, as one might expect, and we are going to present the Court with a full opportunity to understand the circumstances surrounding that.

Additionally, with respect to the documentation that we have received by CDC, we have gone back, and I am prepared to represent in that

motion that much of the analysis that's contained in the witness's testimony to Bayer is accurate and based upon data that was provided by CDC, but we will address this fully. We don't expect to wait the 10 days, but we just got this late Friday afternoon.

In addition, Your Honor, I would say that we have a motion that we will be filing today that will ask to add several recent articles to the documents.

JUDGE DAVIDSON: Do you have additional copies of this motion?

MS. STEINBERG: We have one copy.

JUDGE DAVIDSON: Well, before we finish today, I'd like you to provide one to the court reporter.

MS. STEINBERG: Certainly, Your Honor.

JUDGE DAVIDSON: I'm going to allow it into the 1285 and reserve judgment on whether it goes into the evidentiary record or not, so that you don't have to deal with the 1285 aspect in your response.

Additionally, which witnesses is this going to refer to? Are we going to need a response earlier than the 10 days?

MS. STEINBERG: No, Your Honor, I don't think

that we will.

JUDGE DAVIDSON: Okay. I have one more preliminary matter. It's a wonderful schedule you sent me, but I don't love it.

What used to be three hours is now four hours. What was two hours is now four hours. What was two hours original request is now three hours. With Dr. Kassenborg, what was three hours is now four hours -- and so on.

Now, I don't understand why your original good faith estimate was increased to show additional time. I also don't understand why I have a three-hour witness based on your latest estimate on May 5th and a witness who's supposed to take two hours tomorrow.

If I'm going to go to the trouble to put this thing on and come down here, I'd like to work. We could do both of those in one day for sure, and maybe some others.

I don't know whether you realize it or not, but I do require -- you've had enough time to prepare for cross examination.

I require cross examination to be succinct and

to move along and not to have a lot of delays involved in one question to the next question, and I do limit any redirect to what was brought up on cross and I limit, obviously, the cross to what was in direct. I've got an awful lot of direct, I realize.

So, I don't know the schedule of your witnesses. I don't know which ones are here or are not here at this present time, but I would like to do some consolidating to shorten this, work, you know, full days, and get this down to where we don't have to spend the entire time waiting for the next witness to come in tomorrow.

All right, go ahead, Ms. Steinberg.

MS. STEINBERG: I would ask that, at least for today, we keep the witness schedule as originally set. Our witness that is scheduled to appear tomorrow was not told to come today because --

JUDGE DAVIDSON: Oh, I understand that part. I issued the order the way you sent it in, but I want to make changes starting from today on.

MS. STEINBERG: Thank you, Your Honor.

JUDGE DAVIDSON: Have we got any proposals to

that, or do you need a recess to talk with opposing counsel, or do you have to check with your witnesses, or what's the story?

MS. STEINBERG: I believe we do need to check with our witnesses and make sure they'll be available here in Rockville. A lot of them, several of them are out-of-town witnesses.

JUDGE DAVIDSON: I understand.

MS. STEINBERG: We can do that now or get back to you after the lunch recess.

JUDGE DAVIDSON: I think that would be fine, after the luncheon recess.

All right. That's all I have of a preliminary nature. Are we ready for our first witness?

MS. STEINBERG: We are, Your Honor.

(The witness was sworn by Judge Davidson.)

JUDGE DAVIDSON: Please be seated, give your full name and address to the reporter, and then --

THE WITNESS: My name is Linda Tollefson. That's T-o-l-l-e-f-s-o-n.

Address is 7519 Standish Place, Rockville, Maryland 20855.

Whereupon,

LINDA TOLLEFSON

was called as a witness and, having been first duly sworn, was examined and testified as follows:

DIRECT EXAMINATION

BY MS. STEINBERG:

Q Dr. Tollefson, can you state your position for the record?

A Yes. I'm deputy director of the Center for Veterinary Medicine in FDA.

MS. STEINBERG: Your Honor, may I have permission to show the witness a document, Exhibit G-1478?

JUDGE DAVIDSON: That's her testimony?

MS. STEINBERG: Yes.

JUDGE DAVIDSON: Of course.

BY MS. STEINBERG:

Q Dr. Tollefson, could you please identify this?

A Yes. It's the written direct testimony of mine.

Q Can you turn to Page 20? Is that a photocopy of your signature that appears on the original?

A Yes, it is.

Q Since you submitted, since you signed and submitted that testimony, is there anything -- have you had a chance to review the testimony?

A Yes.

Q Is there anything in the testimony that you need to correct, typographical errors or other errors?

A Yes, there are two issues. The first is on Page 8, the paragraph that's numbered 18, and specifically, it's Lines 36 to 38. That's a mistake.

That statement now reads: "The 2001 data on Campylobacter isolates has not been available." That should be 2002. 2001 is available and is actually in the table attached to my testimony.

Q Thank you. Is there anything else?

A Yes, there is. There's one other thing. It's Page 10, the last sentence, and it's on the top of that page, the paragraph that ends on the top of that page.

It's the end of Paragraph 21, and I'm speaking to Campylobacter jejuni and coli, and identification of those, and I say -- I talk about nalidixic acid and fluoroquinolone, and the statement reads:

"This is because resistance develops first in nalidixic acid." That is actually not correct for Campylobacter. It's pretty much simultaneous.

Q Thank you. Are there any other corrections that you'd like to make?

A No, that's all.

MS. STEINBERG: Thank you. Your Honor, Dr. Tollefson is ready for cross examination.

JUDGE DAVIDSON: Okay.

MR. KRAUSS: Thank you, Your Honor. Gregory Krauss on behalf of Bayer Corporation.

CROSS EXAMINATION

BY MR. KRAUSS:

Q Good morning, Dr. Tollefson.

A Good morning.

Q I'm Greg Krauss and I'm going to conduct your cross examination today. We've already established that you've submitted testimony in this case.

You are the deputy director for the Center for Veterinary Medicine; is that right?

A Yes.

Q You're also assistant surgeon general in the

Public Health Service?

A Correct.

Q Ms. Steinberg showed you your testimony and if you'll -- you have a copy of that; isn't that right?

A Yes.

Q If you would take a look at Page 20, I think we've already established this, but that's your signature; isn't that right?

A Correct.

Q You signed it on or about December 6, 2002?

A Correct.

Q When you signed it, you made a declaration that it was true and correct under penalty of perjury, right?

A Yes.

Q Dr. Tollefson, did you draft your testimony yourself?

A Yes.

Q All of it?

A Yes.

Q Let me just explore your professional background a little bit, please.

A Mm-hmm.

Q You're a veterinarian?

A Yes, I am.

Q Do you have a Master's in Public Health?

A Correct.

Q And your Master's in Public Health emphasized epidemiology?

A Yes.

Q And biostatistics?

A Correct.

Q In your testimony, you describe yourself as a veterinary epidemiologist. Is that right?

A Yes.

Q Your testimony also states that the majority of your career in the Public Health Service has been focused on food safety issues; is that right?

A That's correct.

Q Dr. Tollefson, you're not a medical doctor?

A No, I'm not.

Q You do not have any advanced degrees in microbiology, do you?

A No, I do not.

Q You do not have any advanced degrees in veterinary microbiology, do you?

A No, I do not.

Q You do not have a Ph.D. in epidemiology, do you?

A No.

Q You are not a poultry veterinarian, are you?

A No.

Q You are not a Diplomate of the American College of Poultry Veterinarians, are you?

A No.

Q You're not a member of the American Association of Avian Pathologists, are you?

A No.

Q You are one of the designers of the National Anti-Microbial Resistance Monitoring System, right?

A Yes.

Q That's known a NARMS?

A Correct.

Q Now, the Notice of Opportunity for Hearing in this matter was filed on October 31, 2000; isn't that right?

Corrected as per OR 46 6/13/03

A That's correct.

Q And at that time, you were the director of surveillance and compliance; is that right?

A Yes.

Q Did you have a role in the decision to file the NOOH?

A Yes, I did.

Q What was your role?

A I guess I was one of the proponents that the time had come to file the NOOH, and I wrote the first draft.

Q Did you review data in coming to the decision that the time had come, as you say?

A Yes.

Q What data did you review?

A A number of -- a number of different sources of information.

One was the historical record for how we decided to approve ~~Cerofloxacin~~ Sarafloxacin and Enrofloxacin for use in poultry.

I reviewed the transcript of the Joint Veterinary Medical and Anti-Infective Drugs Advisory

Corrected as per OR 46 6/13/03

Committee meeting that took place in May of 1994.

I reviewed the National Anti-Microbial Resistance Monitoring System data.

I reviewed the Kirk Smith study.

I reviewed a number of published literature studies, also some U.K. data that had been coming out around that same time.

I reviewed the Campylobacter Risk Assessment that we were -- that was still in draft.

I don't think that's an exhaustive list, but it's a general --

Q Okay. And your testimony states that:

"Taken as a whole, the evidence requires the Center for Veterinary Medicine to act to stop the poultry use of fluoroquinolones"; isn't that right?

A That's correct.

Q Now, Dr. Tollefson, would you agree that this case is about whether Baytril use in chickens and turkeys is causing resistant Campylobacter infections in humans?

A Yes, I think that's simplistic. I would say it's about whether fluoroquinolone resistance develops

in Campylobacter in poultry and whether those Campylobacter are retained in the carcass, are transferred to humans through a food safety or a food consumption or a handling issue, and cause resistant infections in humans, correct.

Q Okay. So the ultimate question is whether, through that chain of events, use of fluoroquinolones in poultry is resulting in resistant Campylobacter infections in humans; isn't that right?

A Yes.

Q We agree, don't we, that Baytril is used for prescription use only?

A Correct.

Q And it's not used in any way for growth promotion?

A Correct.

Q It's only used to treat infections in the birds?

A I would disagree with that. The reason that I disagree with that is that the drug is administered in drinking water to a group of chickens. Some of those chickens are ill and have an infection. Others do not.

Q Okay. Well, we can get into that, Dr. Tollefson.

A Okay.

Q You would agree with me that Baytril is not prescribed to treat Campylobacter, right?

A Correct.

Q It's for, in chickens, E. coli infections, right?

A Right.

Q And in turkeys for E. coli infections and for Pasteurella multocida?

A Mm-hmm.

Q In terms of Campylobacter infections in humans, and even resistant infections in humans, for the most part, the disease consequence is diarrhea, right?

A Campylobacteriosis in humans causes diarrhea, causes cramping. Yes, I would say for the most part it's a diarrheal illness.

Q So, just to put this into perspective here, you know, sometimes in FDA proceedings we're talking about, you know, cancer risk. We're not talking about

cancer risk here, are we?

A No, we're not.

Q Sometimes in FDA proceedings, we're talking about a birth defect risk or something like that. We're not talking about that here, right?

A No.

Q We're talking about a diarrhea risk, right?

A We're talking about a risk of an adverse health event.

Q Now, your testimony states that you've examined the data and evidence, and we went through what you looked at and said it wasn't an exhaustive list, right?

A Right.

Q But what you did look at, you looked at, as you say, as a public health official, right, as a veterinarian, right?

A Mm-hmm.

Q And as an epidemiologist; isn't that right?

A Yes, that's right.

Q In your review of the evidence, in addition to what you've already testified that you looked at, did

you also look at, in general, literature on food-borne illnesses?

A Yes.

Q Did you also look at the 1998-1999 Centers for Disease Control and Prevention Campylobacter Case Control Study?

A Yes.

Q You're familiar with that study?

A I'm familiar with it. I'm not intimately familiar with it.

Q Now, Dr. Tollefson, I do not have a background in epidemiology, and you do, so I'd like to establish with you some terms.

A Okay.

Q Epidemiological terms, if you will.

A Sure.

Q As an epidemiologist, would you agree that an incidence rate for a disease consists of the number of cases over a defined period of time in a defined population?

A It's the number of new cases over a defined period of time in a defined population.

Q So it's the number of new cases of whatever the incident case, whatever it is you're looking at, the number of new cases --

A New cases, correct.

Q -- over a defined period of time --

A Correct.

Q -- in a defined population?

A Right. The other is prevalence.

Q Right. A prevalence, correct me if I'm wrong, is a snapshot in time of who may have the --

MS. STEINBERG: Objection.

MR. KRAUSS: Do you have an objection?

MS. STEINBERG: Yeah. Counsel is testifying.

JUDGE DAVIDSON: Overruled. I'll allow it. Go ahead.

MR. KRAUSS: Thank you, Your Honor.

BY MR. KRAUSS:

Q A prevalence rate would be a snapshot in time looking at a population, what's the level of disease in that population at that moment, right?

A Correct. It's the number of existing cases is an easier way to think of it.

Q Okay. Thank you.

A Mm-hmm.

Q Would you agree with me that for food-borne illnesses, incidence rates are often recorded as the number of cases per 100,000 per year?

A It depends on the organism. Yes, sometimes it's 10,000, sometimes it's 100,000. Sure. That's a rate.

Q Right. We're talking about incidence rates?

A Right.

Q Annual incidence rates are used by epidemiologists, aren't they?

A Mm-hmm.

Q And they're used to examine trends of disease incidence over time, aren't they?

A Correct.

Q Let me shift gears and go into another epidemiological term, please.

A Okay.

Q As an epidemiologist, would you agree that confounding -- are you familiar with that term?

A Yes.

Q Would you agree that confounding is the distortion of an exposure/disease association by the effect of some third factor?

A No. That's a frequently misused term. Confounding has to affect both the disease and the exposure, not just one.

I'm probably not being clear enough here, but ask your question again.

Q Are you familiar with the book, Field Epidemiology by Gregg?

A No.

Q There's a definition in the book, which I'd be happy to show you if you want to see it, that states that confounding is the distortion of an exposure/disease association by the effect of some third factor.

A Okay. I'd like to see the definition. In general, a confounding variable has to have an effect on both the exposure and the disease, which makes it very unique. There aren't that many confounding variables.

If you're talking of confounding in more of a

Corrected as per OR 46 6/13/03

use of the term in general English, I would agree with you. Okay?

Q Okay.

A Let me look at the definition --

Q I'd be happy to show it to you, Dr. Tollefson.

For the record, this is Field Epidemiology by Gregg ~~Greg~~, 2d Edition, Page 157.

A Okay.

(The witness examined the document.)

JUDGE DAVIDSON: Do I get to see it, too?

MS. STEINBERG: And also, I would like to know, Your Honor, if this is an exhibit, and if so, what the exhibit number is?

MR. KRAUSS: Portions of this book, including this page, are in the record.

MS. STEINBERG: And the exhibit number?

MR. KRAUSS: B-1912, attached to the Feldman testimony.

MS. STEINBERG: Thank you.

THE WITNESS: After that statement, he goes on to explain it, which is a better definition.

BY MR. KRAUSS:

Q Good, because I wanted to go into the explanation.

A Okay.

Q So if you could clarify it, it would be great.

A A third factor in any association may be a confounder and distort the exposure/disease association if it is, two things: associated with the outcome independent of the exposure -- that is, even in the non-exposed group -- okay, so the outcome being the disease in this case; and associated with the exposure but not be a consequence of it.

So yes, I would agree with this whole definition.

Q Okay. Well, perhaps the confusion was that I split it up, then you took care of part of my outline by doing what you just did. Thank you.

A Mm-hmm.

Q So with what you said, let me make sure I have this right here, the third factor would be a confounder if the third factor is associated with the outcome --

A Correct.

Q -- independent of exposure?

A Right.

Q Or, the third factor is associated with the exposure but not a consequence of the exposure?

A No. It's and, not or.

Q It has to be both?

A It has to be both.

MS. STEINBERG: Your Honor, may Mr. Krauss please give the book with the definition to Dr. Tollefson?

JUDGE DAVIDSON: I thought he did already.

MS. STEINBERG: He's asking questions about it without her being able to look at it.

MR. KRAUSS: I'm happy to do that, Your Honor.

JUDGE DAVIDSON: Certainly.

BY MR. KRAUSS:

Q So it's got to be both, in your opinion?

A It's got to be both. Yeah. He says that, too.

Q Okay. Thank you. Like I said, I'm not an epidemiologist.

A Yeah.

Q So, Dr. Tollefson, just as an example, there's

an example here in the Gregg book where they go through the death rate, the mortality rate in Arizona versus Alaska.

A Okay.

Q And the death rate in Arizona is 7.9 deaths per 1,000 and in Alaska it's 3.9 deaths per 1,000, so on its face, it looks like there's a higher risk of death --

A It's an age adjustment.

Q Well, that's the point.

A That's right.

Q Yeah, that's exactly the point.

MS. STEINBERG: Your Honor, can Dr. Tollefson be provided a copy of the book with the example Mr. Krauss is referring to?

MR. KRAUSS: I would be happy to.

MS. STEINBERG: Thank you.

MR. KRAUSS: Once again, we're on Page 157.

MS. STEINBERG: Mr. Krauss, do you have another copy of the book?

MR. KRAUSS: No. It's in the record, B-1912, attached to Feldman's testimony.

THE WITNESS: So it's a crude mortality rate.

BY MR. KRAUSS:

Q Right, right, without adjustment. But on its face, it would look like you would have a higher risk of death in Arizona than in Alaska, but age is associated with mortality.

A Correct.

Q The older you are, the greater the chance of dying, and, as it happens, age is associated with where you live. More people are older living in Arizona than in Alaska; isn't that right?

A Right.

Q So in that instance, age is a confounder, right?

A Correct.

Q And you have to correct for age?

A Right, and you can do that a number of ways.

Q Okay. Good.

A Okay.

Q Now, Dr. Tollefson, one of the things that you testified that you looked at in this case is the study by Dr. Smith?

A Kirk Smith, right.

Q Kirk Smith.

A Of Minnesota, right.

Q Right. One of the things that Dr. Smith finds in that study, one of his findings is that he believes there is a longer duration of illness associated with a resistant Campylobacteriosis case compared to a susceptible Campylobacteriosis case --

MS. STEINBERG: Your Honor --

BY MR. KRAUSS:

Q -- and here, we're talking about --

MS. STEINBERG: -- I have an objection to the form of the question.

JUDGE DAVIDSON: Well, let him finish the question first, then you can object. Are you finished?

MR. KRAUSS: No, Your Honor.

JUDGE DAVIDSON: Okay. Go ahead.

MR. KRAUSS: I may have to start over.

BY MR. KRAUSS:

Q In the Smith study, one of the things he finds and reports on is an association between having a resistant -- fluoroquinolone resistant Campylobacter

infection associated with the longer duration of illness compared to a susceptible, fluoroquinolone susceptible Campylobacter infection; isn't that right?

JUDGE DAVIDSON: Is there a problem?

MS. STEINBERG: Yes, Your Honor. I object to the form of the question. Mr. Krauss is describing what's in the study and should be providing a copy of the study to the witness.

JUDGE DAVIDSON: That's understandable, but the witness didn't seem to have a problem with it. Have you got a copy for her?

MR. KRAUSS: I believe I may. We will find one, Your Honor.

JUDGE DAVIDSON: While we're waiting, I'd like to remind you that I know you like to see the same thing in the record over and over and over again, but a couple of times you've asked the question, you've gotten the answer, and then you've repeated the answer for the record. And I trust the reporter. You don't have to do that.

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

(Pause.)

JUDGE DAVIDSON: Are you looking for something that's in the record?

MR. KRAUSS: No -- yes, Your Honor. It's G-589, and counsel for CVM requested that we provide the witness a copy --

JUDGE DAVIDSON: G-589?

MR. KRAUSS: Yes, Your Honor.

I'm afraid this is going to be a little bit anti-climactic, but if they want her to have a copy, then she's going to have a copy.

THE WITNESS: Thank you. What I recall is that he showed a slight difference between fluoroquinolone resistant the fluoroquinolone susceptible, but that was not a big consideration in my review of data for the NOOH, if that matters.

MR. KRAUSS: Okay.

THE WITNESS: Okay.

BY MR. KRAUSS:

Q In terms of a consequence of a resistant Campylobacter infection, the Smith report was not a big factor in your --

A No, the difference between the

fluoroquinolone, the days of diarrhea for the fluoroquinolone resistant infection as compared to a susceptible, I didn't think that was a large part of this study.

Q Okay.

A Okay. That was a question that you asked, whether --

Q I asked whether it was one of the things that he found, Dr. Tollefson.

A Yeah, and I vaguely remember that yes, it was, but the difference was not that great, and -- go ahead.

Q Okay. And did you review any other studies, in coming to your decision to file the NOOH, that related duration of, longer duration of illness to a fluoroquinolone resistant infection compared to a fluoroquinolone susceptible infection?

A No. Most of those studies were published after we began the NOOH. The Smith study was one of the earliest, and that was 1999. We were writing the NOOH in early 2000.

Q Right. Well, let me ask you this, on the issue of confounding.

A Uh-uh.

Q If -- this is an if -- foreign travel, okay, persons in the study had undertaken foreign travel.

Okay, foreign travel is associated with both resistant Campylobacteriosis and with a longer duration of illness. Would foreign travel be a confounding variable in that analysis?

A No. The foreign travel isn't causing the illness or the duration of the illness itself, so I would not call it a confounding variable.

You should adjust for foreign travel, but it's not the foreign travel itself, it's not the act of traveling that's causing either one of those, so I guess I would not call it a confounder.

Q Even though it would be associated with the exposure but not a consequence of the exposure?

A Okay, yes. It would be -- so if the person traveled to a foreign country and got the infection there, then it would be associated with the travel, but not a consequence of the actual travel. Yes, that's what I'm saying. And the outcome is not the infection, but the duration.

I still, I don't see how the travel itself affects the outcome.

Q What I'm saying is if you have a case control study, and you've got persons in your study who have had foreign travel, and they also have a longer duration of illness, and they also have a resistant infection, in that instance, if statistically, when you do your analysis, the foreign travel is associated with both the resistant infection and with the longer duration, wouldn't that be a confounder?

A I guess what I'm objecting to is that it isn't associated with both. I don't see how it can be.

Q It's a hypothetical, Dr. Tollefson.

A It's a hypothetical. Okay. If it's a hypothetical, then, yes, it would be a confounder.

Q Okay. I'm going to approach and take that.

A Okay.

Q Thank you.

A If the travel in some way gave you the illness.

Q Now, Dr. Tollefson, your career, as you said, is focused on food safety issues, right?

A Correct.

Q You make an effort to keep current on literature discussing causes of food-borne illness in the United States, don't you?

A Yes.

Q In doing so, are you familiar with the Centers for Disease Control and Prevention MMWR Reports on the Incidence of Food-Borne Illness?

A Yes.

Q Would you agree that CDC MMWR Reports on the Incidence of Food-Borne Illness are reliable?

A Yes.

Q Now, your written direct testimony -- and you have that with you at the stand, right?

A Right, mm-hmm.

Q -- on Page 3, states: "A recent reliable publication estimates 5,000 deaths and 76 million food-borne illnesses annually in the United States." Isn't that right?

A Right, the Mead, et al. article.

Q Right. And that recent reliable publication that you refer to is Mead's 1999 article?

A Right.

Q And that's G-410 in the record?

A Correct.

Q Now, that 76 million food-borne illnesses, that's not all Campylobacter, is it?

A No, no. Not at all.

Q In fact, in the Mead report, don't they estimate Campylobacter to be approximately 2.4 million cases?

A Correct.

Q So --

A And it's actually less than that, now.

Q Yes. We're going to get to that. Thank you.

So for Campylobacter, 2.4 million out of 76 million, we're talking about something like 3 percent?

A Correct. The 76 million, however, most of those are of unknown source.

Q Right.

A And some of them are viral. Campylobacter is an important bacterial cause of food-borne illness.

Q Right. But Mead's estimates, from what they can estimate versus the total, it's about 3 percent;

would you agree with that?

A Yeah, I would agree with that. That's -- Mead's article, or efforts, were the last time that CDC has tried to do this in such an extensive way. That's why it's frequently cited.

Q But isn't it true that for pathogens under active surveillance in the Mead article, he used data from 1996 to 1997 in making his estimates?

A Right, he did.

Q Now, as someone who keeps current in the food safety literature, are you aware that in April of 2002, CDC publicly reported that during the period 1996 to 2001 the estimated incidence of infection with food-borne pathogens has decreased?

A Yes.

MR. KRAUSS: In fact, I'm going to hand you Government Exhibit G-1791. Your Honor, I have an extra copy, if you would like it.

JUDGE DAVIDSON: I got it.

(The witness examined the document.)

BY MR. KRAUSS:

Q Dr. Tollefson, do you recognize this to be

that report we just talked about?

A Mm-hmm.

Q This report states, does it not, that, from the period 1996 to 2001, the estimated incidence of food-borne Campylobacter infections decreased 27 percent?

A That's correct.

Q And as you testified earlier, that previous prediction of, or estimate of 2.4 million has been changed, and now CDC says that Campylobacteriosis is less than 2.4 million, right?

A Right.

Q In fact, there's evidence in the record that says it's 1.4 million?

A About 1.4, that's correct.

Q Okay.

A Mm-hmm. There's a newer one, actually, for 2002.

Q And Campylobacter has gone down again, hasn't it?

A No, actually, it went slightly up, but not much.

Q In the exhibit that I handed you, the overall incidence as of April 2002, the overall incidence of Campylobacter infections was lower than the overall incidence of food-borne Salmonella infections; isn't that true?

A Yes, and that's still true. Campylobacter is now second. This is based on the Food Net data.

Q Right, based on the Food Net data, and in fact, it's based on Food Net data from 1996 to 2001, right?

A Right.

Q You would agree with me, wouldn't you, that a report using data from 1996 to 2001 would contain more recent data than one using just data from 1996 to 1997; isn't that right?

A That's right, but the Mead, et al. article gives peer review that morbidity, mortality -- well, it goes through a clearance process within CDC, and actually FDA also, but it's not quite as -- it's -- I don't want to call it preliminary, but it's somewhat preliminary, in the effort to get it out as soon as they can.

Corrected as per OR 46 6/13/03

Q Right.

A Which is why I think a lot of people rely on the Mead article.

Q Well, your written direct testimony states that Campylobacter has been cited as the most common known cause of food-borne illness in the United States, right?

A That's true.

Q And that is based on a 1992 article, right?

A Yes. It's probably -- yeah, it's ~~TOPES~~ Tauxe's article, 1992?

Q Right. But as of 2001, and even as you said, as we sit here today, it's no longer true that Campylobacter is the most common known cause of food-borne illness in the United States, right?

A I would agree with that. However, it's still a very important cause of food-borne illness.

Q But at the time you finalized your testimony --

A No, no, wait a minute. I said Campylobacter has been cited as the most common cause of food-borne illness. I was trying to establish that it's an

important cause.

Q Well --

A It's in the section on background on anti-microbial resistance.

Q Dr. Tollefson, before 1492, the world had been cited to be flat, and we now know that not to be true, right?

A I don't see the relevance.

Q Your testimony says Campylobacter has been cited as one of the most important causes --

A As the most common known cause.

Q -- or as the most common known cause, and on the date of your testimony, that was no longer true, was it?

A Correct. That's correct.

Q Let me turn your attention to the 1998-1999 CDC Campylobacter case control study. Now, you testified that you looked at that, okay?

A Mm-hmm.

Q Do you recall what aspects of that you looked at?

A I looked at aspects of it that were used for

the Campylobacter risk assessment.

Q Let me hand you an exhibit. This is G-1452, Attachment Number 3. This is attached to Dr. Angulo's testimony, and if I'm not mistaken, it has an independent G-number, but I can't bring it -- is it 1488, maybe, do you know?

A No, it's 1452, Attachment Number 3.

Q Right. Well, what I'm saying is, I think it has its own number now, because it's -- it's not important. We'll use this one.

A Okay.

Q Thank you. Do you recognize this report, Dr. Tollefson?

A Yes. That's an attachment to the exhibit. I didn't see it ahead of time. I recognize it as an attachment to Fred Angulo's testimony.

Q Okay. And this is a study by --

A It's a draft publication, manuscript.

Q Right. As of the time the testimony was filed in December of 2002, it was still in draft, right?

A Correct.

Q Isn't it true that data from this study on the

risk factors of Campylobacteriosis was presented as early as July 2000?

A I don't know. That makes sense. We had that data ~~of use~~ for use in that risk assessment, July --

Q I'm going to hand you what's Exhibit B-27. It's an abstract by ~~Freedman~~ Friedman, et al.

A Okay.

Q Do you recognize that?

A I don't, but it looks like it's a presentation that this manuscript would be the more detailed report.

Q Based on looking at Exhibit B-27, if you look at the citation at the end in particular, isn't it true that data from the 1998-1999 CDC Campylobacter case control study was presented as early as July 2000?

A Yes, I would have to assume that's true. This is -- it doesn't say where it was presented, but it says "Food Net Presentation." It also says Campylobacter is the most common cause of bacterial gastroenteritis in the United States.

Q That was before the 2002 article came out; isn't that right?

A 2001.

Corrected as per OR 46 6/13/03

Q April 2002, reporting on --

A Right.

Q -- data for 2001, right?

A Sure.

Q Now, you testified earlier that you were familiar with the CDC case control study in relation to its data for the risk assessment.

A Mm-hmm.

Q Am I characterizing your testimony correctly?

A That's correct.

Q Isn't it true that one of the things that the CVM risk assessment does is calculate what fraction of Campylobacteriosis cases in the country are associated with poultry, as one of the steps along the way?

A Yes. It attempts to do a fraction of the total cases.

Q For the record, there's an agreed finding of fact in this case, Bayer's finding of fact B-593, well, Bayer 593, that states that the ~~CVM BOSE~~ CVM/Vose risk assessment model relies, to calculate attributable fractions -- let me restart it and just read it directly as it is.

Corrected as per OR 46 6/13/03

"The data that the ~~CVM BOSE~~ CVM/Vose risk assessment model relies on to calculate attributable fractions came from two studies from the 1980s, Harris et al. and Deming et al." Then there's some citations.

A Right, that's correct.

Q And that's your understanding?

A Yes.

Q So for calculating the attributable fraction, what portion of Campylobacteriosis is attributable to chicken, relied on these studies from the 1980s --

A That's true.

Q -- and it didn't rely on the 1998-1999 Campylobacter Case Control Study for that --

A Piece.

Q -- piece.

A Right. That's true. And I think we took the average of those two, or something --

Q You say the average of those two. You're talking about Deming and Harris?

A Right.

Q Are you familiar with the Deming and Harris studies?

Corrected as per OR 46 6/13/03

A Vaguely.

Q You would agree with me, wouldn't you, that they're from the 1980s?

A Yes.

Q And you would agree with me, wouldn't you, that the data from the 1998-1999 Campylobacter case control study is more recent than the Deming study, right?

A Right.

Q And it's more recent than the Harris study?

A Yes.

Q Now, Dr. Tollefson, as someone with a background in epidemiology and biostatistics, do you have an understanding of what a matched odds ratio is?

A Yes. Yes, in a matched case control study --

Q Correct.

A -- is that what you mean? Okay.

Q Right.

A Right.

Q What is your understanding of what a matched odds ratio is?

A Well, the -- an odds ~~ration~~ ratio in a case control

study is the odds of the cases having the disease to the odds of the controls having the disease. A matched case control study is usually where the controls are matched to the cases on the other risk factors.

Q In a matched case control study, the matched odds ratio less than equal to 1.0 has some import, doesn't it?

A If it's less than or equal to 1.0, it means that it's not -- it's not a risk factor --

Q Would you agree with --

A -- 1.0 being null.

Q Right. If it's 1.0, the cases are as likely as the controls --

A Controls.

Q -- to, after having the exposure, to have the outcome.

A Right.

Q Okay. And with a matched odds ratio of less than or equal to 1, isn't it true that that means that the exposure is associated with a reduced risk of the disease?

A Sometimes. Sometimes it's termed as a

protective factor, but it usually -- most epidemiologists don't put that much credit in it.

Q Now, as someone with a background in epidemiology and biostatistics, do you know what a P value is, Dr. Tollefson?

A Yes.

Q What's a P value?

A It's the probability of that result having occurred. There's usually like a, if it's a P value of less than .05, it means that 95 percent of the time that finding would not have occurred by chance, so it wouldn't have been a spurious finding, for example.

Q So you would agree with me that a P value less than or equal to 0.05 is statistically significant?

A The 95 percent confidence level, yes.

Q And that's what FDA typically uses in that, right?

A I think so, yes.

Q For a P value of less than or equal to 0.01, that would be even more statistically significant compared to 0.05, right?

A Correct.

Corrected as per OR 46 6/13/03

Q In the exhibit that I gave you, which is by Dr. ~~Freedman~~ Friedman, which is G-1452, Attachment 3, isn't it true that eating poultry meat at home was associated with a lower risk of illness?

A Yes, and that was statistically significant.

Q If you would turn, please, to Page 98 of Exhibit 1452 -- and by 98, I'm using the upper right-hand corner number.

A I know.

Q Okay.

A Okay.

MS. STEINBERG: Can you repeat those page numbers?

MR. KRAUSS: 98, Nadine. It's in the upper right-hand corner.

MS. STEINBERG: Okay.

BY MR. KRAUSS:

Q Dr. Tollefson, this is a table of exposures, among other things, matched odds ratios and P values, isn't it?

A Right, it is.

Q And this ~~come~~ comes from the 1998-1999 Campylobacter

Corrected as per OR 46 6/13/03

Case Control Study?

A Right.

Q If you would now turn to Page 99, it doesn't have that table heading, if you look down the list, you see "~~8 - Chicken~~ Ate chicken prepared at home" as one of the exposures?

A Yes.

Q And the matched odds ratio is 0.5?

A Correct.

Q And the P value is 0.01?

A Correct.

Q That would mean, wouldn't it, that in this study, persons who ate chicken prepared at home were less likely to be a Campylobacteriosis case?

A Yes, that's true.

Q In fact, isn't it true that persons who did not eat chicken prepared at home were more likely to be a Campylobacteriosis case than persons who did eat chicken at home?

A The converse isn't -- no. The converse, you really can't say that, unless they actually examine it, because you're looking at a number of different

exposures.

You could say that it's statistically significantly associated with a decreased risk. Could you say that the cases -- say it again, please. I'm sorry. Ask the question again.

Q Right. Based on this finding in the ~~Freedman~~ Friedman analysis, isn't it true that persons who did not eat chicken prepared at home were more likely to be a Campylobacteriosis case than persons who did eat chicken at home?

A I can't answer that. What -- you can go through the different exposures and you can associate it, associate the level of significance with each one of these. A lot of the chicken eaten at a restaurant, for example, has a high association of illness.

You can't say that a person who didn't eat chicken prepared at home had a less -- you can't say that. They didn't ask that question.

Q But wouldn't that have been the control, in doing the match between a case and a control?

A So that --

Q Persons who did not eat chicken --

Corrected as per OR 46 6/13/03

A Did not eat the chicken --

Q -- prepared at home were more likely to be a Campylobacteriosis case than persons who did eat chicken at home.

A So you're just doing a logical converse of what the study found. I guess I'd have to say yes.

Q Dr. Tollefson, if you would look at that same table, the fourth one down, "Ate turkey prepared at home," the matched odds ratio is 0.6 and the P value is less than 0.01?

A Yes.

Q Do you see that?

A Yes.

Q So in the ~~Freedman~~ Friedman analysis, isn't it true that persons who did not eat turkey prepared at home were more likely to be a Campylobacteriosis case than persons who did eat turkey at home?

A As an epidemiologist, I would phrase it the other way.

Q Tell me how you would phrase it.

A I would say that people who ate turkey prepared at home were less likely to be a

Campylobacteriosis candidate.

Q Compared to persons who did not?

A Eat turkey prepared at home, yes.

Q Okay.

A Yes.

Q There's other risk factors here, or exposures here, under "Kitchen and food handling practices." Do you see those, Dr. Tollefson?

A Mm-hmm.

Q For example, the first one, "Had raw chicken in home refrigerator."

A Yes.

Q Would you agree with me that the matched odds ratio is 0.7?

A Yes.

Q And that the P value is less than 0.01?

A Yes. I'd also note that almost everybody had raw chicken in a home refrigerator.

Q Okay.

A It's only a few more -- go ahead.

Q Okay. And given that the matched odds ratio is less than 1.0 and that the P value is less than

0.01, wouldn't it be true that persons who had raw chicken in their home refrigerator were less likely to be a Campylobacteriosis case compared to persons who did not have raw chicken in their home refrigerator?

A Yes -- yes, and the difference is statistically significant, but it's barely, just from eyeballing it.

Q P value of less than 0.01, right?

A Right.

Q Dr. Tollefson, if you'll continue down the list, do you see the one that says, "Touched raw chickens"?

A Yes.

Q It has a matched odds ratio, does it not, of 0.06?

A Yes.

Q And a P value of less than 0.01?

A It's 0.6, not 0.06.

Q Thank you.

A And yes, the P value is less than .01.

Q So would you agree with me that, based on the ~~Freedman~~ Friedman analysis, persons in the case control study

who touched raw chicken were less likely to be a Campylobacteriosis case than persons who did not touch raw chicken?

A Yes.

Q I'm just going to do one more of these.

If you would look at the very last one in the list, and I'm sorry, the very last one in the list of "Kitchen and Food Handling Practices."

It says, "Chicken that was prepared at home required cutting while raw." Do you see that?

A Right. Mm-hmm.

Q That has a matched odds ratio, does it not, of 0.5?

A Yes.

Q And a P value of 0.01?

A Yes.

Q So based on ~~Freedman's~~ Friedman's study, isn't it true that persons who -- for persons who had chicken that was prepared at home that required cutting while raw, those people were less likely to be a Campylobacteriosis case than persons who did not have chicken that was prepared at home that was required to

be cut while raw?

A Yes.

Q The findings we just discussed, those were all statistically significant?

A Correct.

Q Dr. Tollefson, let me turn your attention to Page 2 of your testimony, Paragraph 4. Do you see, towards the bottom of Page 2, a sentence that starts with, "Resistance traits"?

A Yes.

Q And your testimony states: "Resistance traits may be passed to human pathogenic bacteria by mechanisms that allow the exchange of bacteria's genetic material."

A Correct.

Q That's your testimony?

A Under "Background on Anti-Microbial Resistance," yes.

Q Are you aware of the fact that in this case the parties stipulated, in Joint Stipulation Number 10, "The parties do not have any facts or data demonstrating horizontal gene transfer for

fluoroquinolone resistance in Campylobacter"?

A That's correct.

Q The parties also stipulated, in Joint Stipulation Number 40, " The horizontal transfer of genes conferring fluoroquinolone resistance in Campylobacter has not been demonstrated"?

A That's true.

Q Do you agree that was stipulated?

A Yeah, I agree.

Q Okay. And not only do you agree that was stipulated, you agree that that's true?

A That's true.

Q What this means is that fluoroquinolone resistance cannot be transferred from one existing Campylobacter to another existing Campylobacter through genetic exchange?

A Correct. That's correct. It's not plasma mediated.

Q Right. And it also means, does it not, that fluoroquinolone resistance from Campylobacter cannot be transferred to some other non-Campylobacter bacteria through transfer of genetic material?

Corrected as per OR 46 6/13/03

A Correct.

Q So when you say in your testimony, your testimony about resistance traits passing by exchange of genetic material, that's not relevant to Campylobacter, is it?

A That's correct, it's not.

Q Dr. Tollefson, if you'll turn to Page 3 of your written direct testimony, you refer to certain "classic studies."

A Yes.

Q Do you see that?

A Yes.

Q Those studies are ~~Homberg~~ Holmberg, G-285; Spika, G-702; ~~Taket~~ Tacket; ~~Conan Talkes~~ Cohen and Tauxe, B-252; and Edgar and ~~Bivey~~ Bibi.

A Uh-huh.

MR. KRAUSS: Now, I didn't kill another tree by making lots of copies of these. Let me just show these to your counsel, and then I want to ask you about them.

(Pause.)

MR. KRAUSS: Now, let me approach.

BY MR. KRAUSS:

Corrected as per OR 46 6/13/03

Q Let me ask you first about ~~Homberg~~ Holmberg, G-285, here. That's relates to Salmonella and not Campylobacter; isn't that right?

A Right, mm-hmm.

Q Let me ask you about G-702.

A That's Campylobacter.

Q That's not even an article by Spika, is it?

A No. The Spika article is -- they got the wrong exhibit -- is an article about Salmonella.

Q And the ~~Takst~~ Tacket article that you referenced, that has not been submitted to the docket, has it? There's no B or G number?

A I don't know.

Q And --

A It's in the 1285. Whether or not it's in the docket, that's different.

Q Well, if it's in the 1285, it would be in the docket, but maybe not in evidence?

A Okay.

Q All right. And the B-252, ~~Conan Talkes~~ Cohen and Tauxe article, this relates to Salmonella and not Campylobacter, right?

A Correct.

Q And the Edgar and ~~Bivey~~ Bibi article has not been submitted to the docket, right?

A Correct.

Q Dr. Tollefson, let me turn your attention to the joint advisory committee meeting that you referenced. I believe you testified that you were aware of the transcript from this committee meeting?

A Mm-hmm.

Q Your testimony at Page 4 states: "FDA held a Joint Veterinary Medicine and Anti-Infective Drugs Advisory Committee meeting in May 1994 to discuss the specific issue of approval of fluoroquinolones for use in poultry. There was" --

A That's not quite right. I just noticed that.

Q I'm sorry. Am I reading it wrong?

A No, no, no. That's what I said, but it was actually for use in food-producing animals.

Q Oh, so it wasn't specific to poultry?

A Uh-uh. No. I'm sorry. I just noticed that.

Q So your testimony is wrong here?

A It's wrong. It should be food-producing

Corrected as per OR 46 6/13/03

animals in general.

Q Okay. In any event, your conclusion drawn in your testimony is that there was no clear consensus among committee members as to whether fluoroquinolones should be used in food-producing animals. That's your testimony, right?

A That's correct.

Q Okay.

A There was agreement that fluoroquinolones are useful in animal medicine, that there's no clear consensus that they should be -- there's a lot of discussion about whether or not they should be approved in food-producing animals.

Q Well, in coming to your conclusion that there was no clear consensus, did you review the transcript?

A Yes, I was there, first of all, and I reviewed the transcript, and I actually talked to some of the ~~numbers~~ members in the committee.

Q The transcript is the official record, right?

A Correct.

Q And the transcript is in evidence?

A Yes, that's true.

Q And it was a public meeting?

A Right.

Q And in the official record, the transcript, which I also reviewed, isn't it true that not a single member on record in the transcript of the joint advisory committee took the position that fluoroquinolones should not be used in food-producing animals?

A Two members -- it may be semantics. It may be how you interpret that. But two members felt that additional study should be done on, and more extensive evaluation of the benefits in animals versus the risk to humans.

So they didn't -- they did not say they should not be approved, but they weren't asked that question. Okay?

Q Well, isn't it true that in the transcript, at least nine of the committee members affirmatively state there is a need for fluoroquinolones in food-producing animals?

MS. STEINBERG: Your Honor, if Mr. Krauss is going to ask the witness about what is in the

Corrected as per OR 46 6/13/03

transcript, he needs to provide a copy to the witness, and I might also add that the transcript speaks for itself --

JUDGE DAVIDSON: Yes, I think it does. It's in the record, isn't it?

MR. KRAUSS: Yes, Your Honor.

JUDGE DAVIDSON: Let me see it, and ask your question.

MR. KRAUSS: And just for the record, on this particular exhibit, the sticker page numbers are not in order, in order to make the transcript page numbers ~~bed~~ be in order.

THE WITNESS: Yes. I would agree that I think most of the members said that there is a need for fluoroquinolones in animals, in food animals.

BY MR. KRAUSS:

Q And not a single member, in response to the members saying there's a need, stood up and said, "No, there's not a need"?

A I agree with that.

JUDGE DAVIDSON: Again?

THE WITNESS: Again.

JUDGE DAVIDSON: She's agreeing for the second time.

MR. KRAUSS: Thank you, Your Honor.

BY MR. KRAUSS:

Q Now, let me turn your attention to NARMS.

A Okay.

Q You're one of the designers of NARMS, right?

A Yes.

Q And planning for NARMS began in 1995; isn't that right?

A Planning for what we now know as NARMS began in 1995. We actually started planning a resistance monitoring system a couple of years before that.

Q But your testimony at Page 2, Line 19, says planning for NARMS began in 1995?

A Correct.

Q And that was before the approval of Baytril, right?

A Correct.

Q And NARMS became operational in January 1996?

A Right.

Q That was also before Baytril was approved,

right?

A Correct.

Q The NARMS system monitors resistance in food-borne enteric bacteria, right?

A Correct.

Q There is a human component and then an animal component?

A And a retail meat component.

Q The retail meat component wasn't added until 2001, right?

A Correct.

Q When NARMS became operational in January 1996, in terms of the susceptibility testing of enteric bacteria, Campylobacter was not included, right?

A No, only Salmonella.

Q Campylobacter was not added to the human arm of NARMS until 1997, right?

A Correct.

Q And Campylobacter was not added to the animal arm of NARMS until 1998, right?

A Correct.

Q Now, let me ask you about, you have some

testimony about speciating C. jejuni and C. coli, right?

A Okay. Right.

Q I'm going to need to use a whiteboard here. Again, not only am I not an epidemiologist, I'm not a microbiologist, so I don't understand something here, and I want to clarify it.

A That's fine. It's very confusing.

Q I agree. If I understand the speciation issue correctly, NARMS will collect Campylobacter isolates -- and here I'm talking about both aspects of NARMS, human and poultry. In general, NARMS collects all Campylobacters. It doesn't -- if someone's got Campylobacteriosis, at first, they don't know what species of Campylobacter it is; isn't that right?

A Correct. Okay.

Q Okay.

A Okay.

Q And then, so you start off with all Campy. Do you mind if I use the abbreviation Campy for Campylobacter?

A No, not at all.

Corrected as per OR 46 6/13/03

Q And NARMS wants to distinguish between Campylobacter jejuni and Campylobacter coli and the other thermophilic Campylobacters; isn't that right?

A It's not NARMS on the animal side. It's FSIS.

Q Okay.

A Okay?

Q Okay.

A On the human side, I could say yes, those ~~around~~ are our NARMS partners.

Q Okay.

A Okay, but --

Q But you'd agree --

A -- distinction.

Q -- with me that somewhere in the NARMS --

A Yes, we definitely speciate the Campylobacter organisms, yes.

Q Okay.

A Okay?

Q So we were kind of stepping all over each other here for a minute. Let me just make sure I've got this right.

Somewhere in the NARMS process, on both arms

of NARMS --

A Yes.

Q -- there is an attempt made to speciate between Campylobacter jejuni and coli versus the other --

A Other thermophilic Campylobacters, okay.

Q Okay.

A Yes.

Q And the way that that was traditionally done -- I know it changed in 2001, or after 2001 -- but --

A Go ahead.

Q -- the process that was used to speciate was using nalidixic acid and cephalothin; isn't that right?

A No. No. That's not correct. As early as 1987, it was known that using nalidixic acid in the media to differentiate coli and jejuni was an error, that it was not wise, because of the increasing resistance to quinolones.

For some reason, FSIS continued to use that in their isolation procedures to find Campylobacter. The human arm never used that procedure.

Q Okay.

A Okay?

Q So I'm now going to limit this discussion to --

A The animal? That's easier. That's easier. Yeah.

Q -- the animal part of NARMS. Okay.

A Okay. So yes, you're right. For the animal part of NARMS, until 2001, they were using nalidixic acid, susceptibility to nalidixic acid and resistance to cephalothin as identification of jejuni and coli.

Q Okay.

A That's not the right way to do it.

Q Okay.

A Okay?

Q But nevertheless, NARMS was doing it?

A Yes. But no -- no. FSIS was doing it.

Q Okay.

A We didn't know that.

Q Okay. FSIS was doing it?

A Yes.

Q Okay. And so FSIS would get Campylobacter isolates in and they would have all Campy, and they

Corrected as per OR 46 6/13/03

would use nalidixic acid to speciate between the jejuni and coli on the one hand, and others --

A Yes.

Q -- primarily ~~lori~~ lari?

A Yeah, any.

Q Others?

A There's a couple others.

Q Okay. And also cephalothin, right?

A Yes.

Q I'm just going to say "C" for that. Okay? Now, in --

A Resistance to that, yes.

Q Right. So in the process, there's a split, and these over here, the jejuni and coli, they're determined to be jejuni and coli because they are susceptible to nalidixic acid --

A Correct.

Q -- and resistant to cephalothin, right?

A Yes.

Q And that's how you determine that's jejuni and coli?

A That's not how I determined it, that's how

FSIS determined it.

Q That's how FSIS determined it. Okay. And then, after this process, these same isolates are tested --

A Okay. Now, all the isolates are sent, then, to Paula. The jejuni and coli, those are sent to ARS Laboratory in Athens, Georgia.

Q Okay.

A FSIS does not do any susceptibility testing.

Q Okay.

A Okay.

Q So when you say Paula, you mean Dr. Paula Fedorka-Cray?

A Right. Correct.

Q And you're saying when they -- when those isolates arrive at FSIS on the poultry arm of NARMS, they've already gone through this process?

A Yes, they have, until 2001.

Q Right.

A Okay.

Q And now, the jejuni and coli isolates that arrive to Dr. Fedorka-Cray's lab have already been

determined through this process to be susceptible to nalidixic acid, right?

A Yes. It's somewhat of a screening test. They use a disk to select the colony, so it's not 100 percent in either case, the susceptibility to nalidixic acid and the resistance to cephalothin, but it's the majority of them.

Q So it's not 100 percent, so what you're saying is when the isolates are then chosen to be nalidixic acid susceptible, it's not 100 percent, some of them might be resistant?

A Correct.

Q But they're called C. jejuni or C. coli?

A Correct.

Q And then all of these isolates have already been determined to be jejuni --

JUDGE DAVIDSON: Excuse me, Mr. Krauss. You're playing fast and loose with my record.

MR. KRAUSS: I'm sorry.

JUDGE DAVIDSON: I mean, I know you're doing, and I understand and I appreciate the aid that you're using there, but when you say "these isolates," "this

process," the record doesn't show what you're talking about, even though I see what you're talking about and the witness sees what you're talking about.

I don't like to delay this any more than you do, but if you have to explain it again, you know, you have to go through and name the process you're talking about. Otherwise, the record is not going to show it.

MR. KRAUSS: I appreciate it, Your Honor. Thank you. So I'm going to get rid of the theses and thoses and thats.

BY MR. KRAUSS:

Q In the speciation process, using nalidixic acid as development, the jejuni and coli isolates have already been determined to be susceptible to nalidixic acid. That's why they are determined to be jejuni and coli, right?

A That's correct.

Q And then these isolates are sent to, on the poultry side now, sent to Dr. Paula Cray's laboratory --

A Yes.

Q -- for susceptibility testing?

A Right, and --

Q And they --

A -- they re-identify them as being jejuni or coli, but not --

Q Using some other method?

A Right, exactly. Yeah.

Q But they've already been determined to be susceptible to nalidixic acid?

A Yes.

Q These jejuni and coli?

A Correct.

Q And then, susceptibility testing is performed in the laboratory of Dr. Paula Fedorka-Cray, and some of these isolates are then determined to be resistant to nalidixic acid --

A Mm-hmm.

Q -- and some are also determined to be resistant to Cipro --

A Right.

Q -- even though they already have been determined to be susceptible to nalidixic acid, right?

A Right. The procedure isn't 100 percent.

Q Now, still talking about NARMS here, Dr. Tollefson, you weren't the only designer of NARMS, right?

A No.

Q In fact, Dr. Frederick Angulo from CDC was one of the designers, too?

A Yes.

Q And his role related primarily to the human arm of NARMS, right?

A Correct.

MR. KRAUSS: I don't even know if he's in the room, Your Honor, but I'm going to ask this.

BY MR. KRAUSS:

Q You respect him as a scientist, don't you?

A Yes.

Q He submitted testimony in this matter?

A Mm-hmm. Yes, he did.

Q And Dr. Paula Fedorka-Cray of USDA was also one of the designers of NARMS, isn't that right?

A Yes.

Q She's a veterinary microbiologist, right?

A She's a microbiologist, she's not a

veterinarian. Is that what she calls herself? That's fine. I don't -- she works with animal isolates.

Q Okay. So she's a microbiologist?

A Correct.

Q And she works with animal isolates?

A Yes.

Q She has a Ph.D., doesn't she?

A Yes, she does.

Q And her role was mainly with the animal arm of NARMS; isn't that right?

A Correct.

Q You testified that your testimony is based in part on your knowledge and experience as a co-author with Dr. Fedorka-Cray on several abstracts and papers; isn't that right?

A Yeah, that's right.

Q And you respect Dr. Fedorka-Cray as a scientist, don't you?

A Yes.

Q Now, Dr. Fedorka-Cray did not submit testimony in this matter, did she?

A No, she did not.

Q She was originally on CVM's witness list, wasn't she?

A Yes.

Q She was?

A Yes.

MS. STEINBERG: Objection, Your Honor.

JUDGE DAVIDSON: Yes?

MS. STEINBERG: What relevance does it have who was on our witness list?

JUDGE DAVIDSON: Well, I assume he's going to get to it sooner or later, but let him go for now.

MR. KRAUSS: I'll get to it now, Your Honor.

JUDGE DAVIDSON: Okay.

BY MR. KRAUSS:

Q Now, Dr. Tollefson, are you aware that Dr. Fedorka-Cray completed a draft of testimony for this hearing?

MS. STEINBERG: Objection, Your Honor. Relevance.

JUDGE DAVIDSON: Overruled. Go ahead.

BY MR. KRAUSS:

Q Do you want me to repeat the question?

Corrected as per OR 46 6/13/03

A No. She completed several drafts. We went back and forth drafting testimony. I actually wrote them first --

Q Okay.

A -- based on things that she had told me orally and things that we had done in abstracts and so on, as I said in testimony.

Q Okay.

A Yes. So we worked on testimony together.

Q And at some point in time, she had what was referred to as a completed draft?

A She -- the way I recall it, she thought -- she felt it was completed. We disagreed. She had added another paragraph that we thought wasn't relevant; and time ran out.

So we put most of what Paula was going to testify in mine.

Q Right.

A It has do with a lot of this stuff.

Q Right. And you reviewed the completed draft of Dr. Cray's testimony; isn't that right?

A I wouldn't call it ~~reviewed~~ reviewing it.

Q You reviewed drafts?

A Yes, definitely, I reviewed drafts.

MR. KRAUSS: Let me hand you -- first counsel, and then you -- would you take a look at this, please?

The first page -- Your Honor, let me hand her the copy.

THE WITNESS: (Examining) Yes, this is one of the drafts that I remember.

BY MR. KRAUSS:

Q You reviewed this draft?

MS. STEINBERG: Objection, Your Honor.

JUDGE DAVIDSON: Okay.

MS. STEINBERG: This document was not mailed to us.

JUDGE DAVIDSON: I understand that.

MS. STEINBERG: It's not in the record.

JUDGE DAVIDSON: I assume if it has some relevance, it will be moved into evidence.

MR. KRAUSS: It will, Your Honor.

BY MR. KRAUSS:

Q In fact, Dr. Tollefson, you testified that you recognized this document?

A Yes.

Q And you recognize this to be a draft of testimony prepared by Dr. Fedorka-Cray?

A Right, but we objected that not everything in here was factual.

Q Okay. We'll get into that.

A Okay. Okay.

Q Do you have any reason to believe that the draft, what's referred to as "Completed Draft Testimony" that's attached to the cover letter, do you have any reason to believe that it's not a true and accurate copy of Dr. Paula Fedorka-Cray's completed draft testimony that you reviewed at some point in time?

A We never had anything marked "Completed Draft," so I couldn't -- I really can't -- I don't know, because I don't know, word-for word --

Q But you reviewed drafts along the way?

A Yes, I did. I never saw this with "Completed Draft" stamped on it, but it looks, in general, sort of the penultimate draft, because we objected in one particular paragraph and some minor things.

MR. KRAUSS: Okay. Your Honor, we would move this document into evidence.

JUDGE DAVIDSON: Do you have a number?

MS. STEINBERG: Your Honor, we object.

JUDGE DAVIDSON: They haven't given me a number yet.

MR. KRAUSS: Your Honor, it would be B-1929.

(Bayer Exhibit No. B-1929 was marked for identification.)

MS. STEINBERG: We object. This is a non-witness statement.

JUDGE DAVIDSON: Well, I'm going to reserve ruling on it's admission into evidence. It will go into the 1285 file, until I hear more what we're talking about.

MR. KRAUSS: Okay.

JUDGE DAVIDSON: Because obviously, if there's something in here you think is of evidentiary nature, you have to get Dr. Cray to testify. If you think it's just something that you're going to use with respect to Dr. Tollefson's testimony, then I'll allow it. You know, that's the difference. Okay

Corrected as per OR 46 6/13/03

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

BY MR. KRAUSS:

Q Now, would you agree with me that -- I think you testified that you drafted portions of this completed draft testimony?

A Mm-hmm.

Q Would you agree that the subject matters covered in Dr. Fedorka-Cray's completed draft testimony were incorporated into Pages 9 to 12, and in particular, Paragraphs 20 to 29, of your testimony?

Take your time to look at your testimony.

A Yes, that's correct. Some of it was from Carolyn ~~Minnick's~~ Minnich's and Geraldine Ransom's testimony, from which I then, in order to help Dr. Cray with time constraints, drafted and sent to her, she looked at it, and saw it.

So I don't know if everything in here, from 20 to 29, was primarily Dr. Cray's.

Q Would it help you to have a comparison between your Paragraphs 29 to 29 and Dr. Cray's completed draft testimony?

A Well, the problem is that I'm not saying who

wrote the first -- you know, who put in what. I would say that most of what is in here, from Paragraphs 21 through 29, are in Paula's area. I'd say that. Okay?

Q Okay.

A FSIS and ~~AR~~ ARS -- the USDA portion of NARMS.

Q Now, portions of Dr. Fedorka-Cray's completed draft testimony reference certain phenomena that she and others performing Campylobacter susceptibility testing were experiencing, and she raised questions about the accuracy of the poultry NARMS results; isn't that right?

MS. STEINBERG: Objection, Your Honor.

JUDGE DAVIDSON: Okay. What are you putting it in for? Remember, that's what I said before. If you're trying to get this in the record as evidence, I got to have --

MR. KRAUSS: Your Honor, for right now, I'll withdraw my motion to move it into evidence, and I'm just going to use the document with the witness.

JUDGE DAVIDSON: All right. But you realize, my ruling means that you're talking about whether this witness's testimony is going to be affected by what was

in this document as opposed to whether or not this is going to be on the record as evidence.

MR. KRAUSS: I understand that, Your Honor.

JUDGE DAVIDSON: Okay. Thank you.

MR. KRAUSS: Your Honor, I withdraw my motion without prejudice.

JUDGE DAVIDSON: I understand, counsel.

BY MR. KRAUSS:

Q Now, let me re-ask my question, since it got interrupted.

Isn't it true that portions of Dr. Paula Fedorka-Cray's completed draft testimony referenced certain phenomena that she and others performing Campylobacter susceptibility testing were experiencing and that raised questions about the accuracy of the poultry NARMS results?

MS. STEINBERG: Your Honor, objection to the form of the question. There's no evidence that this is the completed testimony, completed draft testimony.

JUDGE DAVIDSON: I think we can solve that problem, if you stop referring to it as the completed draft testimony. It is in 1285 as Exhibit B-1929, and

Corrected as per OR 46 6/13/03

you just use that --

MR. KRAUSS: No, Your Honor, I did not make that representation. It is not in the docket as ~~D~~ B-1929.

JUDGE DAVIDSON: It is now.

MR. KRAUSS: Oh, it is now. Thank you.

JUDGE DAVIDSON: As B-1929, so if you stop referring to it as completed draft testimony, you'll obviate the necessity for objections from the other side.

MR. KRAUSS: Thank you, Your Honor.

JUDGE DAVIDSON: Okay.

THE WITNESS: Okay, but I've got another objection, as well, that's more technical.

You're asking two questions. Let me answer the first part, did she have this paragraph that talked about phenomena in isolating Campylobacter.

And that's the paragraph we objected to, because our laboratory at FDA did not have that problem. The CDC food-borne disease laboratory did not have that problem. Many other laboratories that deal with Campylobacter do not have the problem. So we

objected to her statement about "and others."

Now, your second part of your question was, doesn't that invalidate the animal NARMS data.

BY MR. KRAUSS:

Q Well, that wasn't my question. My question was, didn't she raise questions about the accuracy of the poultry NARMS results?

A Okay. And my answer to that is, I consider this, as an epidemiologist and a person used to reviewing data, as a much more minor issue than the issue with the nalidixic acid susceptible isolates only coming from Dr. Cray's lab.

So in my mind, questions were raised about the animal -- poultry isolates from NARMS before this testimony was ever drafted.

Q Okay.

A Okay?

Q When you used the word "this," you had the same problem I had earlier --

A Yeah, right.

Q -- you were pointing to something in the document, and we don't know what that is for the

record.

You apparently -- there's two issues. There's the "this" and there's the speciation. What was the "this"?

A Dr. Cray had said that she has problems in her laboratory with aggregation of colonies and mixed cultures, and those are two different issues, but the one, the mixed culture issue, we think is not really a problem. Most infections are due to a mixture of organisms.

For example, if somebody has a fluoroquinolone resistant Campylobacter infection, it doesn't mean that all of their Campylobacter are resistant, by any means. They will have a mixed infection of susceptible and resistant. Okay? So we didn't think of that as a phenomenon.

And then the issue of aggregation, other people, other laboratories have not had that problem, so we did not want to introduce that into her testimony as a major item. I mean, we just didn't agree with it.

Q What do you understand --

A Our microbiologists did not agree with it.

Corrected as per OR 46 6/13/03

Q What do your understand~~ing~~ the aggregation issue to be?

A Well, when she talks about aggregation of isolates, she was thinking that it meant -- Dr. Cray was thinking that it means that you can't speciate the isolates very easily, and that you can't susceptibility test them very easily.

Susceptibility testing of isolates is a probability issue. Okay? There's a certain number resistant, there's a certain number susceptible. Which isolate you pick from the plate has more to do with whether or not it's going to show up resistant or susceptible, until that resistance reaches something greater than 50 percent, right, as a prevalence.

So it's always -- we're sort of always underestimating resistance, if you will, until resistance becomes so common that your ~~limit~~ limits of ~~protections~~ detection are no longer there, so the aggregation issue, I just didn't think it was an issue at all, and our microbiologists didn't, either.

Q And who is that?

A Doctors Dave White, Pat McDermott, and Bob