

ORIGINAL

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

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In the Matter of:	:	
	:	
Enrofloxacin for Poultry: Withdrawal	:	FDA DOCKET NO.
of Approval of Bayer Corporation's	:	00N-157E
New Animal Drug Application (NADA)	:	
140-828 (Baytril)	:	
	:	
-----	x	

Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland

Tuesday, May 6, 2003

THE HEARING in the above-entitled matter
commenced at 9:30 a.m., pursuant to notice.

BEFORE:

DANIEL J. DAVIDSON, Administrative Law Judge

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2000N-1571

TR 15

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C O N T E N T S

WITNESSES:	DIRECT	CROSS	REDIRECT	RECROSS
Mary Bartholomew	731	734		
Louis Louie Cox, Jr.	835	836		

RESPONDENT EXHIBITS:	IDENTIFIED	RECEIVED
1924 - Attachment to motion	915	915
1925 - Unidentified document	915	915
1926 - Unidentified document	915	915
1927 - Granoff, et al. study	915	915
1942 - Study on Restaurant Spending	759	
1943 - Today's Special: Nutrition Information	766	

GOVERNMENT EXHIBITS:		
1806 - MIT transcript of Cox	852	
1807 - Harvard transcript of Cox	855	
1808 - Letter from ASA to Cox	858	
1809 - 4/99 Cox letter to Voxe	866	
1810 - Second day of transcript	873	877
1811 - Cox paper	885	

P R O C E E D I N G S

1
2 JUDGE DAVIDSON: Okay. Are there any
3 preliminary matters?

4 MR. SPILLER: The Center has no preliminary
5 matters, Your Honor.

6 MR. NICHOLAS: I do, Your Honor. Bob
7 Nicholas.

8 First off, we attempted to hand-deliver to you
9 yesterday the docket, our reply. I'm not sure whether
10 you got it or not.

11 JUDGE DAVIDSON: I got it.

12 MR. NICHOLAS: Secondly --

13 JUDGE DAVIDSON: It was not just a reply; was
14 it?

15 MR. NICHOLAS: No. It was a reply to the
16 motion and in addition --

17 JUDGE DAVIDSON: Another motion. Come on.
18 It's not your fault. You're all doing it.

19 MR. NICHOLAS: And Mr. Krauss has one or two
20 matters.

21 JUDGE DAVIDSON: All right. Mr. Krauss.

22 MR. KRAUSS: Good morning, Your Honor.

1 Gregory Krauss on behalf of Bayer.

2 Yesterday I promised just to give you an
3 update on the "B" documents that I used and whether
4 they were in evidence. In fact, they are all in
5 evidence. B-44, B-881 and B-934 are all in evidence.

6 JUDGE DAVIDSON: Thank you.

7 All right. Here's what I have for you. I
8 received admittedly confusing e-mail and then I managed
9 to figure out what was involved in and look at the
10 material. Correct me if I'm wrong. What it's talking
11 about is correspondence back and forth concerning
12 Freedom of Information Act requests and other requests
13 from Bayer to CVM and other government agencies, I
14 guess, and there appears to be some disagreement as to
15 what was happening, what did happen, what did not
16 happen, et cetera, et cetera.

17 But the latest motion from Bayer indicates
18 that they have no objection to government's G-1801
19 coming in and Bayer 34, 36, 37 -- I forget.

20 MR. NICHOLAS: It's 1937 to 41, Your Honor.

21 JUDGE DAVIDSON: "B." 37 to 41 comes in,
22 because it all deals with the same subject matter.

1 Well, I'm going to let you decide.

2 First of all, if you want them all in, which I
3 don't see the need to, but if you want them all in,
4 including 1804, which I did not allow in yesterday,
5 which deals with the same kind of thing -- okay.

6 If you don't want them in, that's fine with
7 me, too. They stay in the administrative record and if
8 there becomes a particular issue as to what was or
9 wasn't then maybe that will rise to the level of
10 evidence.

11 As far as I'm concerned, it's just procedural
12 correspondence which may or may not affect the evidence
13 in this proceeding.

14 So by the close of business today, you can
15 tell me what you've decided during one of the recesses.
16 If you want extra, I will let you get together and
17 confer whether you want them in or out. Personally, I
18 would just as soon leave them out. It would be the
19 same for everybody and they would be in 1285, as I
20 said.

21 Okay. Now we have another appearance ready?

22 MR. BATES: Good morning, Your Honor.

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1 JUDGE DAVIDSON: State your name, address, and
2 capacity in which you appear and the long list of bars
3 in different states and the United States Government
4 you've been admitted to.

5 MR. BATES: My name is Jeffrey Bates. I'm
6 with McDermott, Will & Emery. I can be reached at the
7 ~~firm in~~ ^{firm's} Washington address as well as 28 State Street,
8 Boston, Massachusetts, which is our Boston office,
9 02109.

10 I'm admitted to practice law in the State of
11 Massachusetts or, as we like to say, the Commonwealth
12 of Massachusetts, as well as a number of courts,
13 including in the federal courts, Registry of
14 Commonwealth.

15 JUDGE DAVIDSON: Okay. Thank you.

16 MR. BATES: And oh, one last point. I'm
17 appearing on behalf of Bayer.

18 JUDGE DAVIDSON: Oh, I did not know that.
19 Okay. We're ready for Dr. Bartholomew.

20 MR. SPILLER: The Center calls Mary
21 Bartholomew.

22

1 Whereupon,

2 MARY BARTHOLOMEW

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

5 JUDGE DAVIDSON: All right. Please be seated.
6 Give your full name and address to the reporter and
7 then await counsel's additional questions.

8 THE WITNESS: My name is Mary Joann
9 Bartholomew. My address is, Center for Veterinary
10 Medicine, HFV 105, 7500 Standish Place, Rockville,
11 20855.

12 MR. SPILLER: May I approach the witness, Your
13 Honor?

14 JUDGE DAVIDSON: Certainly.

15 DIRECT EXAMINATION

16 BY MR. SPILLER:

17 Q Dr. Bartholomew, I'm handing you a document.
18 Can you identify that, please, for the record?

19 A Yes. That's my witness testimony with my CV
20 attached at the back.

21 Q And is your testimony Exhibit G, like "Golf,"
22 1454?

1 A Yes, it is.

2 Q And is your CV Exhibit --

3 JUDGE DAVIDSON: 1404.

4 MR. SPILLER: Thank you, Your Honor.

5 BY MR. SPILLER:

6 Q G-1404?

7 A Yes, it is.

8 Q And referring to Exhibit G-1454 and page 20,
9 is that a copy of your signature?

10 A Yes, it is.

11 Q Since the date that you signed this, have you
12 had the opportunity to look through it to see whether
13 or not there are errors that require correction?

14 A Yes, I have.

15 Q And did you find any?

16 A I found one that I would like to correct at
17 this time.

18 Q All right. Tell us what page that's on.

19 A It's page eight, line 16.

20 Q All right. I have page eight, line 16, and I
21 notice that material is double indented. Is that a
22 quote of something else?

1 A Yes. That's a quote from a book chapter
2 that --

3 Q All right. So am I correct that the
4 correction you're offering today is to your testimony -
5 - we're not presuming to go back and change the book.
6 Is that right?

7 A That's right.

8 Q Okay. Tell us what that correction is.

9 A The fraction of 45.2 percent should be 48.2
10 percent and the fraction 70 percent should be 66.7
11 percent.

12 Q All right. And do these figures also appear
13 in the Center's Risk Assessment that's G-953 in this
14 record?

15 A The corrected numbers I gave you appear in the
16 risk assessment document.

17 MR. SPILLER: Thank you, ma'am.

18 No further questions, Your Honor.

19 JUDGE DAVIDSON: The witness is ready for
20 cross.

21 MR. BATES: Thank you, Your Honor.

22

1 CROSS EXAMINATION

2 BY MR. BATES:

3 Q Good morning, Dr. Bartholomew.

4 A Good morning.

5 Q Have you testified or been qualified as an
6 expert witness before?

7 A I have not testified as an expert witness; no.

8 Q And your field of expertise is biostatistics;
9 is that correct?10 A That's correct. I'm a biostatistician at the
11 Center.12 Q Could you tell us what that field is, what
13 your expertise involves?14 A Statistics involves the analysis of data,
15 looking at what are appropriate methods for analyzing
16 and interpreting what data are telling you and --17 Q And where do you get the data for the work
18 that you do?

19 A Data come from many places.

20 Q Maybe you could give me some examples.

21 A Well, are you talking about my work as a
22 reviewer at the Center or --

1 Q Let's talk about that.

2 A As a reviewer at the Center for Veterinary
3 Medicine, I review new animal drug applications, and
4 the data received are data presented by drug sponsors
5 with drug applications. It appears as studies that
6 they have conducted for the purposes of demonstrating
7 the efficacy or safety in some way, shape or form.

8 Q Thank you. Now, let's shift a little bit.
9 You are joint author of what we will call the CVM risk
10 assessment. I think that's G-953. Is that what that
11 is?

12 A I believe that's the exhibit number.

13 Q And you were joint author of that?

14 A Yes, I was a joint author. It was a team
15 effort. There were many people at the Center and
16 outside the Center also involved in the team effort of
17 constructing, gathering data, constructing risk
18 assessment, and then writing the risk assessment
19 document.

20 Q There was a lot of statistical data in that
21 document, as I recall.

22 A There's a fair amount of data; yes.

1 Q And the data, let's talk about where you got
2 some of that. For example, did you get some of that
3 from census data?

4 A Census data were used; yes.

5 Q And did you get some from data published by
6 non-governmental organizations?

7 A There were literature data that were used for
8 the risk assessment.

9 Q I see. And whether or not it was in the
10 model, is it also true the FDA, Food and Drug
11 Administration is trying to get information on
12 restaurant use and so on and trying to get that through
13 the National Restaurant Association?

14 A As far as I know, the FDA is not gathering
15 information from the Restaurant Association.

16 Q So you've been at CVM since 1990?

17 A Yes, I have.

18 Q And you have already said you were joint
19 author of the risk assessment, CVM risk assessment.
20 When I use risk assessment I mean CVM risk assessment.
21 And so you know why and how and when that assessment
22 was performed?

1 A Most of that information I am aware of; yes.

2 Q And you are also, as I recall from CV, on a
3 EPA Office of Water panel that's evaluating microbial
4 risk assessments for water?

5 A That's correct.

6 Q So you know something about the microbial
7 contamination of water?

8 A To the extent that it was discussed at the
9 workshop panel, yes.

10 Q And something about EPA's efforts to regulate
11 that problem?

12 A Somewhat; yes.

13 Q Just a few last preliminary questions. Do you
14 have any degrees in microbiology?

15 A No, I don't.

16 Q In that field, microbiology, any professional
17 certifications?

18 A No, I do not.

19 Q And let's switch now to risk assessment. Any
20 degree in risk assessment?

21 A No. I have certificates from a couple of
22 short courses that I have taken.

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1 Q Thank you.

2 Let's speak a little bit more directly about
3 the risk assessment. Can you tell us when that risk
4 assessment was begun, when work on it was begun?

5 A Yes, I can. It was in the summer of 1998.

6 Q And can you tell me when it was finished?

7 A I would say that we put the final version with
8 correction on our website on January 5th of 2001. I
9 would consider that a completion date.

10 Q And you said, with corrections. Can you
11 explain what you mean by that?

12 A Yes. We had put the final version on the
13 website in October and when it was up on the web, it
14 was noted that there had been an error in the
15 spreadsheet. There were a couple of places where the
16 ~~sales~~ ^{cells} were pointing between a data
17 point from 1998 and connecting to a data point for
18 1999, and that was found through the efforts of one of
19 our ~~stakeholders~~ ^{stakeholders}, and when we found that out we
20 corrected it and put the revised version up on the web.

21 Q Do you recall if you also deleted a study?

22 A I do recall that there was a study deleted but

1 that was not at that time. That was deleted between
2 the December, '99 which was called the draft risk
3 assessment.

4 We had a public meeting and after the public
5 meeting, we went back and did revisions and worked on
6 it and we dropped one of the case control studies; yes.

7 Q Which study was that?

8 A It was a study by Hopkins from Colorado.

9 Q Now, is it correct that when you did the risk
10 assessment, you used data from the 1998, 1999 CVM case
11 control study?

12 A Yes, we did use data from the KPK case control
13 study; yes.

14 Q And from the point of view of relevance and
15 quality as biostatistics, how would you evaluate this
16 study?

17 A I would say that the CDC study was a large,
18 well conducted study and that you will need to look at
19 what you're using it for with respect to how it was
20 collected.

21 Q So with that background, let's talk about what
22 you were trying to accomplish with this study. Was

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1 your purpose to try to quantify the likelihood that
2 humans in the United States might be impacted by
3 domestically acquired fluoroquinolone
4 campylobacteriosis which is attributable to use of
5 Baytril in chickens?

6 A Yes.

7 Q And did you try to accomplish that purpose by
8 seeking to quantify the number of persons in the U.S.
9 population who in 1998 or 1999 got ~~campylobacterial~~ *campylobacter*
10 infections from eating chickens that were resistant to
11 fluoroquinolone campylobacterial infection that were
12 domestically acquired, that were not due to prior
13 fluoroquinolone treatment in people who sought care
14 from a health care provider and were prescribed the
15 fluoroquinolone? If you want that read back in parts,
16 we can do that.

17 JUDGE DAVIDSON: We can?

18 MR. BATES: I will repeat it or perhaps we can
19 get the --

20 JUDGE DAVIDSON: Well, how about breaking it
21 down? There's just too many things in there.

22 MR. BATES: All right.

1 Your Honor, perhaps if I just put some bullets
2 on the board.

3 JUDGE DAVIDSON: Only if you remember that
4 that is not going to go into the record and when you
5 refer to it you can't say, "this here" or "that." You
6 have to state what it says.

7 MR. BATES: I understand. Okay. I'm just
8 going to do it for the convenience of the witness and
9 myself.

10 JUDGE DAVIDSON: Okay.

11 MR. BATES: So we know exactly what we're
12 talking about.

13 BY MR. BATES:

14 Q So the first part is, we talked about what the
15 purpose of the study was.

16 What I'm trying to see if we both can agree on
17 is how you tried to accomplish that purpose.

18 So first seeking to quantify -- pardon my
19 writing -- the number of persons in the U.S. who in
20 1998 and 1999 got campylobacter infections from eating
21 chicken that were resistant to fluoroquinolone, not to
22 the prior treatment of fluoroquinolone, sought care

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1 from a health care provider and were prescribed
2 fluoroquinolone.

3 I'm not trying to confuse. I'm just trying to
4 make sure I have all the pieces.

5 A Would you go back to the first part of your
6 question? Are you asking specifically about the use of
7 the 1998, 1999 campylobacter case control study and
8 efforts --

9 Q No. I'm sorry. We talked about what the
10 purpose of the study was and now I'm trying to
11 understand the means that you were trying to use to
12 accomplish that purpose quantitatively.

13 So I'm just trying to take the various sort of
14 interlocking steps to see if I'm understanding how you
15 tried to accomplish that purpose.

16 So my question is, in trying to accomplish the
17 purpose we just discussed, were the steps I just
18 covered in ~~the~~^{my} questions accurately describe the way in
19 which you tried to accomplish this?

20 A There is one step, basic step that I think you
21 left out and that is that you have fluoroquinolone
22 resistance that's not attributed to prior treatment and

1 it was also not attributed to foreign travel.

2 Q Okay. So we are on the same page here, more
3 or less.

4 A More or less, yes; and I think that one that -
5 - you are only going down the path of looking at the
6 human aspect of this and this is a risk assessment
7 model that has two parts and there was what was the
8 human health part and then there was the exposure part.

9 Q That is right. Thank you. That's exactly
10 right.

11 So with that in mind, I'm going to talk with
12 you a little bit about the model itself and the risk
13 assessment itself. And would you like to have a copy
14 in front of you?

15 A That would be very helpful. Thank you.

16 MR. BATES: May I approach, Your Honor?

17 JUDGE DAVIDSON: Yes.

18 MR. BATES: This is Exhibit G-953.

19 JUDGE DAVIDSON: Okay.

20 BY MR. BATES:

21 Q There you are. Why don't you have a quick
22 look at that just to make sure.

1 (The witness examined the document.)

2 A Yes.

3 Q That's it?

4 A Yes, that's it.

5 Q Just so we're clear on what we're talking
6 about, the risk assessment, the analysis stops with the
7 quantification of the number of these people that were
8 prescribed fluoroquinolone. It does not go on to ask
9 how many of those people did or did not respond to
10 treatment. Is that correct?

11 MR. SPILLER: Objection. The question assumes
12 a fact not in evidence. We should let the witness say
13 when it stops.

14 MR. BATES: I have no objection.

15 JUDGE DAVIDSON: Okay.

16 THE WITNESS: I'm sorry. I didn't understand
17 the objection. Would you explain?

18 MR. BATES: I'll do my best to; and if I get
19 it wrong, I'm sure my colleague will help me.

20 BY MR. BATES:

21 Q Am I right that the last step in the
22 qualification, risk assessment, was the number of these

1 cases where people were prescribed fluoroquinolone; am
2 I correct?

3 A Yes.

4 Q So you didn't take the next step, which might
5 have said how many of those people might have
6 responded, did or didn't respond to treatment?

7 A No. We describe that in the risk assessment,
8 why we didn't do that.

9 Q Okay.

10 MR. BATES: Your Honor, if I may draw some
11 pictures here. I would like to do that.

12 BY MR. BATES:

13 Q So is it fair to say that at least logically,
14 if not chronologically, the first step in the process
15 was to try to estimate the number of cases of
16 campylobacteriosis in the entire U.S. population?

17 A That's correct.

18 Q So we can just sort of draw this over here.
19 We're trying to get the universe of campy cases in the
20 U.S. population. We don't actually have a study of the
21 whole U.S. population that gives us the number of
22 cases?

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1 A That's right.

2 Q So am I right that what you did was to take
3 the FoodNet ~~attachment~~ ^{catchment} data on a number of cases and
4 then extrapolate that to come up with the number of
5 cases for the U.S. population?

6 A Yes. We do that. CDC does that, also.

7 Q And so, when we are working with many things
8 but certainly with diseases, it is correct, isn't it,
9 that when one wants to sample from which one
10 extrapolates to be representative of the population
11 that it is trying to investigate?

12 A Yes, that's a general principle.

13 Q Especially in diseases.

14 So let's say, for example, one wanted to know
15 whether the sample which had a lung cancer rate --
16 whether that rate was similar to be extrapolated to the
17 U.S. population, you would want to know whether
18 consumption of cigarettes, for example, was similar to
19 consumption of cigarettes for each population? Is that
20 fair?

21 A Yes.

22 Q So that's why you said on page 32 -- and

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1 you're ^{welcome} ~~welcomed~~ to look at this if you like.

2 A Page 32?

3 Q Well, I want to give you the pages in the
4 model, the exhibit pages in the record.

5 A I see. Okay.

6 Q And on that page it says the "ideal
7 extrapolation of FoodNet data ^{incidence} ~~incident~~ rates to the
8 U.S. population would require knowledge and
9 distribution of risk factors that affect the rates of
10 diseases.

11 A Right.

12 Q And that's another way of saying what I just
13 said about lung cancer and smoking?

14 A Yes.

15 Q And you did an analysis of the representatives
16 of the sample; is that correct?

17 A Yes, we did.

18 Q And you used some basic demographic factors,
19 rural versus urban, age, sex and race. Is that
20 correct?

21 A Yes.

22 Q You came up with more or less, 177 million

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1 cases in 1998 and 104 million cases in '99 -- 1.7
2 million in '98 and 1.4 in '99?

3 A I'm sorry. You're asking two questions there.
4 You're asking about the representativeness of the
5 samples and we did display in Table 1.1 that ~~detachment~~ ^{the catchment}
6 area is fairly consistent with the U.S. population.

7 Q On that basis, you then extrapolated? I'm not
8 trying to write down of course how big this big circle
9 is.

10 And in 1998, you estimated about 177 million
11 cases --

12 MR. SPILLER: The form of the question.

13 BY MR. BATES:

14 Q I'm sorry. 1.77 million.

15 MR. SPILLER: Can you specify? We request
16 that counsel identify the page and part where that
17 occurs.

18 MR. BATES: I'm sorry, Your Honor. These were
19 about the only two numbers I could remember without
20 looking them up.

21 Well, let's see if I've got the right place.

22 BY MR. BATES:

1 Q If you would please turn to page 44 of Exhibit
2 G-953; and at the bottom of that page you will see that
3 there is a -- call it a small table. Do you see that
4 table?

5 A Yes.

6 Q And it gives a mean estimate for 1998 at about
7 1.77 million. Is that mean estimate for what is
8 calculated that would be the number of cases in that
9 big circle here for 1998?

10 A Yes; that would be the number.

11 Q And just below that, the line that starts,
12 "1999," the mean for that one is one million, three
13 hundred seventy-six and so on?

14 A Yes.

15 Q And that's the guesstimate for the total
16 number of cases that you developed for 1999?

17 A Yes.

18 Q So for '98, 1.77; '99, 1.4, more or less? Is
19 that a fair statement?

20 A Those are the means; yes.

21 Q Now, we talked a moment ago about the use of
22 the 1998, 1999 CDC case control study. At page 103 of

1 your risk assessment, in the carryover paragraph, the
2 last sentence, that says that the data from this study
3 -- and this study here means the 1998, 1999 CDC case
4 control study? Is that correct?

5 (The witness examined the document.)

6 THE WITNESS: That's correct.

7 BY MR. BATES:

8 Q And it says the data from this study will
9 provide "updated risk factor information from which
10 etiological fractions would be identified," is that
11 correct?

12 JUDGE DAVIDSON: If that's what it says. I'm
13 waiting for something to come out of all of these
14 questions. You're repeating what is already in my
15 record.

16 MR. BATES: I understand.

17 BY MR. BATES:

18 Q So if we had risk factors from this study, we
19 could then use those as we talked about a moment ago to
20 test whether our sample is representative or not?

21 A I don't see how that would be possible because
22 it implies that you know what the distribution of risk

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1 factors is in the entire population if you are trying
2 to do the test that's representative of, and I don't
3 see how we could possibly know that.

4 Q Well, I don't want to be too hard here. I
5 talked a little bit about cigarette consumption versus
6 lung cancer.

7 If the CDC study that we're talking about said
8 that eating chickens or other meats in restaurants was
9 a risk factor, wouldn't we want to know whether the --
10 the frequency with which people ate in restaurants and
11 the sample was similar to the frequency of the U.S.
12 population overall?

13 A I'm not sure that I agree with that, because I
14 don't know the details of that, whether or not
15 restaurant chicken consumption is the sole ~~determinate~~ ^{determinant}
16 of what we would be looking for.

17 We were concerned about exposure to chicken
18 through various ~~sorts~~ ^{sources}, not just through restaurant
19 consumption of chicken.

20 Q Do you know whether the CDC study that you
21 refer to now has been completed?

22 MR. SPILLER: Object to the form of the

1 question. Can you specify which CDC study that you are
2 referring to?

3 MR. BATES: I'm sorry. I will be glad to do
4 that.

5 BY MR. BATES:

6 Q We're talking about the 1998 CDC study that
7 you said in the risk assessment is going to be looking
8 at risk factors.

9 A Yes.

10 Q Has that been completed?

11 A I don't know for sure whether that has been
12 completed. I have not seen a published article based
13 on that study to date.

14 Q Well, let me show you attachment three to
15 Exhibit G-1452 and ask if you recognize that.

16 A Yes. I see that this is a CDC draft article.

17 MR. BATES: May I approach, Your Honor?

18 JUDGE DAVIDSON: Yes.

19 BY MR. BATES:

20 Q And if you turn to the back of the study,
21 you'll see a table near the end, and that is table
22 four, is it not?

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1 JUDGE DAVIDSON: Page number?

2 MR. BATES: That is Exhibit page number 101.

3 JUDGE DAVIDSON: Thank you.

4 BY MR. BATES:

5 Q That is a table attempting to show risk
6 factors; is that right?

7 A It says, "^{multivariate}~~multi-varied~~ analysis and derived
8 population, attributable fractions, Campylobacteriosis,
9 case control study, 1998, 1999."

10 Q And ^{population attributable}~~population, attributable~~ fractions, is
11 that the same thing as etiological fractions we're
12 talking about?

13 A Yes.

14 Q So in that document from CDC there's a table
15 which tries to identify the risk factors that we were
16 just talking about?

17 A Yes. They are analyzing risk factors.

18 Q All right. And one of those for chicken is
19 eating in restaurants; is that correct?

20 A Yes.

21 Q And then that is the only one for chicken; is
22 that correct?

1 MR. SPILLER: I object to the form of the
2 question. It states as a fact something not in the
3 record and contrary to the cite of the table.

4 BY MR. BATES:

5 Q Pink chicken. Undercooked. I'm sorry. I'm
6 looking for ^{population attributable} ~~population, attributable~~ fraction,
7 etiological fraction for chicken. The only one here --
8 am I right?

9 A No. There's ^{"Ate"} ~~"A,"~~ undercooked or pink chicken."

10 JUDGE DAVIDSON: ^{"Ate"} ~~"A,"~~ chicken prepared at home"
11 is another factor.

12 BY MR. BATES:

13 Q I'm sorry. I'm talking about the etiological
14 fraction. So we have ^{"Ate"} ~~"A,"~~ undercooked or pink chicken,"
15 and we have chicken at a restaurant?

16 A Yes.

17 Q Just by way of comparison, the chicken at a
18 restaurant fraction is said to be 24 percent and the
19 pink is 3 percent; is that right?

20 A Yes.

21 Q So why wouldn't we want to know, when we're
22 trying to do with this extrapolation, whether the

1 sample was a good basis from which to extrapolate
2 whether people throughout the U.S. were eating at
3 restaurants at a similar rate to the people in the
4 sample?

5 MR. SPILLER: Your Honor, I object to the form
6 of the question, why wouldn't we want to know. The
7 "we" isn't defined. I don't believe there has been any
8 testimony that we wouldn't want to know anything.

9 JUDGE DAVIDSON: Sustained.

10 BY MR. BATES:

11 Q If you want to know whether the sample that
12 you're using accurately predicts for the whole in one
13 of the risk factors, in fact the largest for chicken,
14 quite a lot, is eating chicken in a restaurant,
15 wouldn't you want to know whether the frequency of
16 eating out in restaurants in the sample was similar to
17 the frequency of eating out at restaurants for the
18 whole U.S. population?

19 A If you were interested specifically in
20 restaurant chicken consumption, perhaps; but I think
21 that we established with Dr. Angulo that the FoodNet in
22 the case control study would be representative of the

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1 U.S. population.

2 Q I'm not challenging whether it is
3 demographically now. I'm referring back to the
4 statement involved.

5 If you knew about the risk factors, you would
6 want to use those to help us understand whether the
7 sample is representative?

8 MR. SPILLER: I object to the form. It's not
9 a question.

10 JUDGE DAVIDSON: Overruled.

11 You're going back to one of your first
12 ~~question~~^{questions}, when you read from the witness' testimony or
13 from the -- I can't remember at this point.

14 MR. BATES: This was from the model.

15 JUDGE DAVIDSON: From the model. Ideally you
16 started? Is that it?

17 MR. BATES: That's correct.

18 JUDGE DAVIDSON: It took us a long time to get
19 there; didn't it?

20 Why don't you refresh your recollection of
21 that and then ask her the question?

22 MR. BATES: I'll be glad to, Your Honor.

1 BY MR. BATES:

2 Q So if you go to page 103. I'm sorry. I'm
3 sorry.

4 JUDGE DAVIDSON: Back in G-953.

5 BY MR. BATES:

6 Q Yes. It's page 32. Sorry.

7 MR. SPILLER: I'm sorry, Mr. Bates.

8 MR. BATES: Exhibit 953.

9 MR. SPILLER: Okay.

10 THE WITNESS: Page 32. Yes.

11 BY MR. BATES:

12 Q And the first full paragraph, the point that
13 says, "The ideal extrapolation of FoodNet incidence
14 rates to the U.S. population would require knowledge of
15 the distribution of risk factors that affect the rate
16 of disease."

17 And my question is, in light of that
18 observation, would you agree with me that we would want
19 to examine whether the rate of eating at a restaurant
20 in the sample is similar to the rate in the U.S.
21 population?

22 A I would agree that that would probably be one

1 of many.

2 Q Fine. So let's see if we can do that.

3 Now, Dr. Bartholomew, what I have just done is
4 clip up a map of the United States. Now, I wonder if
5 you could tell me which states were in the FoodNet
6 sample for the 1998, 1999 time period, the example in
7 your study?

8 A I would have to look them up in the risk
9 assessment. I cannot spew them off.

10 Q All right.

11 A It says -- and I'm reading at the bottom of
12 page 34, in Table 1.3 or Table 1.4, the State of
13 California; Connecticut.

14 Q State of California. Connecticut.

15 A Georgia.

16 Q Georgia. Now, as for Georgia, is that the
17 whole state, or just part of it, or both?

18 A I don't recall.

19 Q Okay. Go ahead.

20 A Maryland. Did I say that?

21 Q Maryland. No. Okay. Maryland.

22 A Minnesota.

1 Q Minnesota.

2 A New York.

3 Q New York.

4 A And Oregon.

5 Q Oregon.

6 So at least geographically speaking, it's a
7 big part of the center of the country here that is not
8 represented in the FoodNet; correct?

9 A Yes.

10 MR. BATES: Your Honor, I would like to mark
11 for the record Exhibit B-1942.

12 JUDGE DAVIDSON: Copy for the witness. Copy
13 for myself. Copy for counsel.

14 MR. BATES: Can you reach that? I'm sorry.

15 (Respondent Exhibit 1942 was
16 marked for identification.)

17 MR. BATES: Your Honor, this is a study on
18 restaurant spending that we obtained from the National
19 Restaurant Association.

20 MR. SPILLER: Excuse me. Form of the
21 question. Can we ask the witness if she recognizes it
22 and let her characterize it if she is --

1 MR. BATES: I will be glad to.

2 BY MR. BATES:

3 Q Dr. Bartholomew, I am handing you a copy of
4 what has been marked as B-1942. Do you recognize that
5 document?

6 (The witness examined the document.)

7 A No, I don't.

8 Q Can you tell me what it says it is?

9 A It says it is a Restaurant Spending, Consumer
10 Expenditure Survey in 1998.

11 Q Can you tell me who did it?

12 A National Restaurant Association.

13 Q And a moment ago you testified, if I recall,
14 that you didn't know if the FDA relied on such studies
15 by the National Restaurant Association; is that right?

16 A Yes.

17 Q I wonder if I could show you a document and
18 see if that might refresh your recollection.

19 JUDGE DAVIDSON: Do you have copies?

20 MR. BATES: I do.

21 (The witness examined the document.)

22

1 BY MR. BATES:

2 Q Can you tell us what that is?

3 A I can tell you that it says it's from
4 www.fda.gov, and I'm not sure what it is. They
5 specialize in nutrition information. I am not sure
6 what this is.

7 Q Go to the last page and look at the bottom of
8 the page. What does that tell us about the --

9 MR. SPILLER: Objection to the question. The
10 witness has already said that she doesn't recognize it,
11 and there's no testimony that it is within the scope of
12 her direct.

13 MR. BATES: Your Honor, I take counsel's
14 point. I would like to move the restaurant study on
15 the grounds that as it shows in this document from the
16 FDA, the FDA does rely on studies such as this from the
17 National Restaurant Association on how Americans spent
18 their food dollars.

19 JUDGE DAVIDSON: Well, I'm not the FDA, but
20 it's a pretty large organization, and the Consumer
21 Magazine is certainly not the kind of thing we rely on
22 in my cases as far as factual information.

1 I get a copy of the Consumer Magazine every
2 time it comes out. It's got a lot of interesting
3 tidbits in it, but it's nothing that qualifies as
4 evidence.

5 MR. BATES: With all due respect, Your Honor,
6 I believe this is a study of restaurants in the United
7 States. It was not just in a magazine.

8 JUDGE DAVIDSON: I know. Who did that?

9 MR. BATES: I beg your pardon?

10 JUDGE DAVIDSON: You tell me the Restaurant
11 Association of America did that. Does that qualify as
12 evidence in my case? And if it is, why didn't you
13 introduce it? This witness certainly didn't rely on
14 it.

15 You're cross-examining a witness and you're
16 trying to put evidence in the record which I don't even
17 think qualifies as evidence. Now, I could be wrong, if
18 you show me where it does qualify as evidence; but you
19 should submit it yourself, not through this witness.

20 MR. SPILLER: Your Honor, since there has been
21 a motion, if it's going to be in evidence, if it's
22 going to be entertained, could I have voir dire on this

1 document?

2 JUDGE DAVIDSON: Well, let's wait and see what
3 he has to say.

4 MR. BATES: I would like to move the
5 introduction of this document.

6 JUDGE DAVIDSON: You did that already.

7 MR. BATES: Let me state the grounds. One of
8 the kinds of evidence that is admissible as evidence is
9 evidence by market studies that people in the industry
10 and people in the public rely upon. That is a fairly,
11 I think, straightforward proposition ⁱⁿ ~~on the~~ evidence
12 ~~cause~~.
law

13 Secondly, the document we're talking about
14 here is in fact a study of restaurant spending.

15 Thirdly, in issuing regulations, that is what
16 this document pulled from the website does -- issuing
17 regulations, effective May 2, published August, 1996,
18 in the Federal ~~Registrar~~.
Register

19 In explaining those regulations in this
20 document that I handed you, Your Honor, it says: "This
21 is important considering more and more Americans are
22 spending their meals outside home."

1 "According to the National Restaurant
2 Association, Americans are spending 44 percent of their
3 dollars outside the home in 1996." And so on.

4 So this is the kind of evidence that is
5 admissible. It is also the kind of thing that FDA has
6 itself relied upon; and certainly if there are
7 questions about the weight of the evidence, we can have
8 argument about those.

9 But this is, as I say, evidence from a market
10 study, from a business source that the public and the
11 industry rely. It is something that the FDA in the
12 past has relied on and I believe it would help the
13 trier of fact in considering this case.

14 JUDGE DAVIDSON: You still haven't answered my
15 question about why you introduce that with this witness
16 when she says she doesn't recognize it. She didn't
17 testify about it, and it's cross-examination.

18 You have a case in chief that you presented.
19 You presented me with all evidence. If this was
20 reliable evidence that you wanted put in your case, why
21 wasn't it put in earlier?

22 MR. BATES: I think the reason I'm trying to

1 examine on it now is the discussion in the case so far
2 about the --

3 JUDGE DAVIDSON: I understand your reasoning
4 for putting it in. I don't understand why it wasn't in
5 before.

6 If you bring it in at the last minute that you
7 claim is viable and interesting -- and I might glean
8 something from it if I were to review it but it has
9 nothing to do with this witness, per se, and should
10 have been put in, if you thought it was important,
11 evidence right at the outset.

12 MR. BATES: Well, it does have to do with this
13 witness.

14 JUDGE DAVIDSON: Only because you want to get
15 to the representativeness aspect.

16 MR. BATES: We need to do that in order to
17 understand whether this universe is correctly defined.

18 JUDGE DAVIDSON: That's what you need to do,
19 you think; but I'm not satisfied that this is where
20 this belongs at this time. I will let counsel for CVM
21 respond to your motion.

22 MR. SPILLER: Your Honor, we oppose the

1 motion. The witness has testified she didn't rely on
2 this. She didn't even recall it. It is clearly not in
3 her written direct testimony. It is clearly beyond the
4 scope of her written direct testimony and therefore not
5 fair cross, anyway; and a ludicrous standard that this
6 is a document of a kind relied upon by FDA would enable
7 truckloads of documents to come in if that were
8 allowed.

9 FDA properly as a scientific agency relies on
10 millions of documents every year.

11 There is no indication that this witness, the
12 testimony that we are cross examining today, relied on
13 this.

14 It should not be received in evidence.

15 JUDGE DAVIDSON: You want to mark the second
16 one 1943?

17 MR. BATES: Yes, sir.

18 (Respondent Exhibit 1943 was
19 marked for identification.)

20 JUDGE DAVIDSON: It will stay in the
21 administrative record, but it's not going to be in my
22 evidentiary record.

1 MR. BATES: Thank you, sir.

2 JUDGE DAVIDSON: All right. That's my ruling.
3 B-1942 and B-1943 are not received in evidence.

4 MR. BATES: Just to resume, could I ask the
5 reporter to read back the witness' answer to the
6 question that I was given to whether restaurant data
7 would or wouldn't be relevant? I'm trying to move on.

8 JUDGE DAVIDSON: All right. Off the record.

9 (A discussion was held off the record.)

10 JUDGE DAVIDSON: Okay.

11 MR. BATES: Ready to proceed?

12 BY MR. BATES:

13 Q So we talked, Dr. Bartholomew, you and I did,
14 about the first step in the model, trying to estimate
15 the total number of Campylobacteriosis cases in the
16 United States for these two years.

17 Was the next step in the model to try to
18 estimate the portion of those cases that was
19 attributable to chicken?

20 A Yes.

21 Q And that is what we were talking about a
22 moment ago when we spoke about attributable risks and

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1 etiological fraction; is that right?

2 A Yes.

3 Q Okay. We are going from total numbers to
4 somewhat smaller numbers this time, percentage of cases
5 out of the whole which are attributable to the
6 chickens; is that right?

7 A Yes.

8 Q I gather from a biostatistical point of view
9 this is a little bit complicated and rather than me
10 trying to say it myself, let me just refer you to
11 something in your testimony. I'm sorry. The model.
12 This is at page 102 of the model. And when I say the
13 model, I'm referring to Exhibit G-953.

14 If you look at the point under assumption one,
15 it says, "Discussion Number One." There's a statement
16 that says, "One limitation ^{of} ~~is~~ epidemiological tools
17 used to determine the attributable ^{risk} ~~risks~~ or etiological
18 fraction."

19 Is it those cases that were exposed to the
20 risk factor of interest even though the exposure may
21 not have been a cause of the disease, could be
22 included in the calculated level of risk thereby

1 potentially overestimating the actual level of risk?

2 So with that statement in mind, it's possible,
3 isn't it, that some of the cases in my attributable
4 risk circle may not actually have been caused by
5 exposure to chickens?

6 A Yes. Exposure to chickens. I would agree that
7 there may be some that are miscalculated.

8 Q And with regard to this particular part of the
9 model and its significance, am I right that you all did
10 a sensitivity analysis to get some sense as to which
11 variables were likely to affect the outcome analysis?

12 A We did sensitivity analysis and I can't speak
13 to the results without looking at them because I don't
14 recall.

15 Q Okay. Let's do that.

16 Actually, I'm going to move on, because that's
17 in the record.

18 JUDGE DAVIDSON: Thank you.

19 BY MR. BATES:

20 Q So based on what we just said, we could
21 multiply the total by this percentage, the etiological
22 fraction but we're not actually following a true causal

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1 change; is that correct?

2 A I thought ^{fill} about this question some and what we
3 had established ~~ACRIONI~~ ^{a priori} based on other literature,
4 based on a history of information that chicken was
5 causal and when we set out to do the risk assessment,
6 we were trying to quantify to what extent; and so, the
7 causality was not established by the calculation of
8 population, attributable fraction. That was a fraction
9 that we used as a quantification but we did not say,
10 uh, huh, because it's a certain percent, that's
11 causation. We knew that from a body of information
12 that was collected beforehand.

13 Q Just so that we are on the same page, we could
14 both agree with that and still agree that the number of
15 cases that results from this multiplication may be an
16 overstatement?

17 JUDGE DAVIDSON: Asked and answered. We did
18 that already.

19 BY MR. BATES:

20 Q An etiological fraction that you derived from
21 the 1980's; is that correct?

22 A That's correct.

1 Q And do you recall in the model expressing some
2 reservations about those studies?

3 MR. SPILLER: I apologize, Mr. Bates, for the
4 interruption. You said from some 1980 study. Did you
5 mean studies within the 1980's or did you mean
6 literally 1980, one year?

7 MR. BATES: 1980's, plural.

8 MR. SPILLER: I apologize for the
9 interruption.

10 THE WITNESS: Would you go back to the
11 question, please?

12 MR. BATES: Yes.

13 BY MR. BATES:

14 Q You and I just agreed, I think, that the
15 etiological fraction that we're talking about is based
16 on some studies from the 1980's?

17 A Yes.

18 Q And I was just asking whether in the risk
19 assessment you expressed some reservations about those
20 studies.

21 A Yes, we did.

22 Q And we talked before about the recognition in

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1 this document that the CDC case control studies was
2 underway?

3 A Yes.

4 Q And I take it it was the view expressed here
5 and your view that when those data came in, one could
6 use those to calculate the etiological fractions?

7 A That was expressed in the document. Yes.

8 Q And the model that was used -- the 1980's
9 studies resulted in a 57 percent fraction --

10 MR. SPILLER: Objection to form. Eighty
11 versus '80's.

12 JUDGE DAVIDSON: Eighties.

13 MR. BATES: I'm sorry.

14 BY MR. BATES:

15 Q The 1980's studies resulted in a 57 percent
16 ~~reduction~~ ^{fraction}; is that correct?

17 A Well, to be precise, there were two studies.
18 One had a population attributable fraction of 48.5 and
19 the other had a fraction which was 66.7 percent; and we
20 recognized that those studies were based on samples.
21 We incorporated uncertainty about them; and because we
22 didn't know which one was the better estimate, we

1 modeled between the two of them so that the mean
2 estimate from the model was 57 percent. But you have to
3 understand that that is a distribution. That's the
4 central value but there was a whole range of population
5 attributable fractions considered there.

6 Q I understand. So we talked a moment before
7 about Exhibit G-1452 which was the CDC draft study we
8 talked about. Do you have that handy?

9 A I think you must have taken that back.

10 MR. BATES: Your Honor, may I approach?

11 JUDGE DAVIDSON: Certainly.

12 BY MR. BATES:

13 Q This is Exhibit G-1452 that we were discussing
14 earlier.

15 MR. SPILLER: Excuse me. Mr. Bates, did you
16 mean attachment three of G-1452?

17 MR. BATES: Thank you. Attachment three of G-
18 1452.

19 BY MR. BATES:

20 Q Will you turn to page 23, please? It's
21 actually page 101 in the exhibit.

22 A Yes.

1 Q This is the table we were discussing before
2 about population attributable fraction?

3 A Yes.

4 Q And this said that the "^{Ate}~~A~~" chicken prepared in
5 the restaurant¹ has a population attributable fraction
6 of ²⁴~~44~~ percent?

7 A Yes.

8 Q And if you go down to I guess the fifth entry
9 from the bottom of that table it says, "^{Ate}~~A~~" chicken
10 prepared at home."

11 A Yes.

12 Q And there is no population attributable
13 fraction for that; is that correct?

14 A That's what it says in this table. Well, let
15 me take that back. I don't know. I don't see what the
16 code is for "N/A." Is that not available or not
17 applicable? I'm not sure what that is; but I do see
18 there's not a number in that column.

19 Q And if you go to the column that says "AOR" it
20 says .7 for the chicken prepared at home?

21 A Yes.

22 Q And specifically, what does that suggest when

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1 you have an AOR that's less than one, I guess?

2 A That suggests that in the study, if you ask
3 cases if they had eaten chicken at home and you ask
4 controls if they had eaten chicken at home then the
5 proportion of cases who would respond, "yes, I ate
6 chicken at home" would be more than the proportion of
7 the -- I'm sorry. Did I say cases? The controls would
8 have a higher proportion of people who said "yes, I ate
9 chicken at home" than the cases would have.

10 Q So am I right that we have sort of competing
11 risk factors here? We have one set of risk factors for
12 chicken at a restaurant that says there's a risk, that
13 cases for disease more frequently from exposure to
14 controls. You have the reverse of that at home.

15 A If that is what the data indicate.

16 Q So if we were just working with these data,
17 the 24 percent number, fraction, couldn't be projected
18 across all chicken because when you ate it at home the
19 relationship switches. Is that correct?

20 A I think what it's saying is that cases were
21 more likely to have eaten chicken at a restaurant and
22 controls were more likely to have eaten chicken at

1 home.

2 Q So if we are trying to get overall chicken
3 numbers, we have to find some way to reconcile those
4 things, things going in different directions? Is that
5 right?

6 A I think your statement is correct, and I think
7 there's an awfully lot of other things that need to
8 happen, too. A case control study can only answer
9 questions that have been asked.

10 So if you notice that those population
11 attributable fractions -- there will be some things
12 that are not addressed but they don't -- I'm trying to
13 add up in my head -- that there will be some things for
14 which you will not have the answers.

15 Q I understand.

16 So in order to get at that, what if one tended
17 to do a correlation between chicken consumed and cases
18 in the FoodNet database to see what that relationship
19 might be and if it turned out that the number of cases
20 had decreased as the amount of chicken consumed
21 increased, would that suggest that the relationship
22 observed at home might be more accurate than the

1 relationship observed in a restaurant?

2 MR. SPILLER: I object. It's beyond the scope
3 of direct. I don't believe this is in the written
4 direct testimony. It seems to be an extrapolation of
5 what someone might wish were there, but I believe it
6 wasn't.

7 MR. BATES: If I may, Your Honor. The model
8 says if we had these data we would use them. I'm not
9 trying to figure out how we would use them because we
10 do have them; and in fact, I believe we had them before
11 the January data.

12 JUDGE DAVIDSON: You say, you believe we have?
13 Are they in the record?

14 BY MR. BATES:

15 Q Dr. Bartholomew --

16 JUDGE DAVIDSON: I asked you a question.

17 MR. BATES: These data were available July of
18 2000.

19 JUDGE DAVIDSON: Which document?

20 MR. BATES: This is attachment three to G-
21 1452.

22 JUDGE DAVIDSON: So it's already in the

1 record?

2 MR. BATES: Yes.

3 MR. SPILLER: As a draft, if I may, Your
4 Honor. It doesn't mean that the data is in the record.

5 JUDGE DAVIDSON: All right. Overruled. I
6 will let you go a little bit further with this; but if
7 the witness is not comfortable with this because it's a
8 draft or because she didn't review it, then you have to
9 stop.

10 MR. BATES: All right. I understand.

11 JUDGE DAVIDSON: All right. Go ahead.

12 BY MR. BATES:

13 Q Dr. Bartholomew, I was asking you about a
14 potential way of trying to understand whether the risk
15 factor associated with eating in restaurants would be
16 more powerful than the risk factors associated with
17 eating at home because they point in different
18 directions.

19 I'm going to ask you now, did you review Dr.
20 Cox's testimony in this case?

21 A I have read Dr. Cox's testimony; yes.

22 Q That's fine. I'm going to show you page 29

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1 from that testimony.

2 JUDGE DAVIDSON: The exhibit number?

3 MR. BATES: The exhibit number, B-1901. It's
4 attachment one and it's page 37 to attachment ¹~~29~~ in the
5 document.

6 BY MR. BATES:

7 Q Would you take a look at that page? Is there
8 a graph on that page?

9 A There is a graph.

10 Q And does that graph purport to show the
11 relationship between the consumption of chicken overall
12 and cases of illnesses negatively related? The more
13 chicken you eat the less illness you had?

14 MR. SPILLER: Objection. Beyond the scope.
15 I, too, eagerly await the cross examination of Dr.
16 Cox's written direct testimony but this witness is
17 being asked about the contents of Dr. Cox's testimony
18 and that's not her testimony; so, it's beyond the
19 scope.

20 JUDGE DAVIDSON: I assume it's preliminary to
21 something.

22 MR. BATES: Yes, it is, Your Honor. I'll get

1 right to the point.

2 JUDGE DAVIDSON: Why are you asking the
3 question when it's in there? It states it.

4 Let her look at it. You don't have to read it
5 into the record. Ask your questions.

6 BY MR. BATES:

7 Q So does that graph -- strike that. I'll just
8 -- if we were to find that there was a negative
9 relationship between consumption of chicken overall in
10 cases, that would suggest that the risk factor for
11 eating at home here which is less than one would be
12 more representative on the whole than the risk factors
13 of eating at restaurants which points in the other
14 direction?

15 A I'm not sure whether I agree or not. I have
16 not thought this over.

17 One thing that should be clear is that what is
18 associated with developing campylobacteriosis is the
19 contact and exposure to campylobacter, and there may be
20 some aspects of cooking at home that would permit
21 people to kill campylobacter more so than other -- it
22 depends how people cook it.

1 Q Well, then this will be quite quick. There
2 are studies, aren't there, including the one that you
3 deleted from the record that showed that the overall
4 risk of consuming chicken is in fact what I might call
5 negative? That is to say, the cases ate less chicken
6 than the controls?

7 MR. SPILLER: Objection. The question calls
8 for speculation about of what was in a study that is
9 not in the record.

10 MR. BATES: Well, I believe it is, Your Honor.
11 It's B-35. We just talked about it earlier, the one
12 they deleted from their model.

13 JUDGE DAVIDSON: Well, is it or isn't it? I
14 mean, I don't have a repository here.

15 MR. SPILLER: I will yield to the description
16 of it as a document. The question said, that was
17 deleted from your record.

18 MR. BATES: Risk assessment. Risk assessment.

19 MR. SPILLER: It was not in the risk
20 assessment documents but it is a --

21 MR. BATES: Your Honor, B-35.

22 JUDGE DAVIDSON: As long as I know it is of

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1 record, you can answer the question, if you know.

2 THE WITNESS: As I recall, the Hopkins study
3 could be interpreted as having a population
4 attributable -- you know, I don't remember whether it
5 was specifically chicken or undercooked chicken that
6 was very similar to the Harris study so that we would
7 have reported it as being -- and we did in the draft
8 risk assessment document as being confirmatory of the
9 same value that the Harris study had.

10 The reason we dropped it had nothing to do
11 with what it told us. It had to do with: We went back
12 and tried to recalculate population attributable risks
13 and we found discrepancies in the numbers presented in
14 the table. We could not rectify the numbers; and so,
15 therefore, we thought that the results might be
16 unreliable.

17 MR. BATES: Well, Your Honor, I'm not going to
18 ask her to read something that's in the record.

19 JUDGE DAVIDSON: All right. Thank you.

20 BY MR. BATES:

21 Q There was a study in 1987, in Dubuque, is that
22 right, G-564, by ^{Schmid}~~Schmidt~~, et al.? Do you remember that

1 study? It's G-564.

2 A Excuse me. Say that again.

3 Q Are you familiar with the Schmidt, et al in
4 Dubuque, Iowa, 1987? It's Exhibit G-564.

5 A I can't say that I recall it.

6 Q So you don't know whether that found risks one
7 way or the other?

8 A No.

9 Q Are you familiar with the Ikram study in
10 Christchurch, New Zealand from 1992, G-370?

11 A Yes.

12 Q Am I right that that said there was no -- they
13 found no positive correlation between eating chicken
14 and --

15 JUDGE DAVIDSON: Excuse me. What is that
16 exhibit number?

17 MR. BATES: It's G-370. I'm sorry. G-307.

18 JUDGE DAVIDSON: I don't have a 370.

19 MR. BATES: It's 307, I believe.

20 JUDGE DAVIDSON: Thank you.

21 THE WITNESS: Do you have a copy of that
22 paper?

1 MR. BATES: Your Honor, I can do this, but I'm
2 afraid it will waste time, to show her things and ask
3 her to read. I'll be glad to do it if --

4 JUDGE DAVIDSON: Well, that's where it belongs
5 if you're just showing her things and asking her to
6 read them. If you have a question concerning what's in
7 there and whether or not it affects her testimony, show
8 it to her, have her read it, ask her if it changes her
9 testimony or what you want to ask her about it.

10 MR. BATES: All right. Let's do that. We
11 will just try to do this as quickly as possible.

12 BY MR. BATES:

13 Q Let's start with the Ikram study from
14 Christchurch, New Zealand.

15 JUDGE DAVIDSON: G-307; correct?

16 MR. BATES: That's right.

17 May I approach, Your Honor?

18 JUDGE DAVIDSON: Yes, sir.

19 BY MR. BATES:

20 Q Here's a copy of the study. And would you
21 look at the table on -- I guess it's page two of the
22 exhibit. Do you see that? Table one.

1 A Oh, table one? Okay.

2 Q Right. And it says that the risk factors for
3 Campylobacteriosis infection associated with poultry.
4 Do you see that? And then it says, "chicken." And it
5 shows that the odds ratio is less than one?

6 A Yes.

7 Q So we do have the Ikram study and odds ratio
8 for all chicken is less than one; is that correct?

9 A And I see that we have, when eaten at a
10 friend's house it has an odds ratio of 3.1.

11 Q I understand. What we're trying to focus on
12 here is whether we can get -- the question is whether
13 all chicken is positive or negative risk when we have
14 the CDC study pointing in two different directions.
15 I'm trying to see if there are other studies that would
16 help us shed some light on this. So I'm looking for
17 all chicken.

18 We talked quickly a moment ago about the
19 Hopkins study that was deleted. That's Exhibit B-35.

20 JUDGE DAVIDSON: Why do you keep saying it was
21 deleted?

22 MR. BATES: I'm sorry.

1 JUDGE DAVIDSON: We had an objection based on
2 that that it was only deleted in the risk assessment
3 and not from the record.

4 MR. BATES: There were two Hopkins studies.
5 I'm trying to focus on that.

6 JUDGE DAVIDSON: I know; but when you say
7 "deleted," you confuse me.

8 MR. BATES: Okay.

9 JUDGE DAVIDSON: Give me the number and I'll
10 tell you whether I like it or not.

11 MR. BATES: B-35.

12 JUDGE DAVIDSON: B-35?

13 MR. BATES: "B" as in Bear, 35.

14 JUDGE DAVIDSON: You'll have to give me a copy
15 of that. I only have one disk here and --

16 MR. BATES: Very well, Your Honor.
17 I'm handing it to the witness, Your Honor.

18 BY MR. BATES:

19 Q And would you turn to page two of the exhibit,
20 please, and the beginning of the second full paragraph?
21 It says, "Ill persons were less likely than either set
22 of controls to have eaten chicken." Then we also

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1 worried about undercooked. Overall, ill less likely
2 than either set of controls to have eaten chicken.

3 MR. SPILLER: I'm sorry. I'm having trouble
4 finding the word "overall" there. Are you quoting
5 that?

6 MR. BATES: I'm sorry. What I read was: "Ill
7 persons were less likely than either set of controls."

8 MR. SPILLER: And for completeness, would you
9 offer the witness the next --

10 MR. BATES: I already did that. I said, "more
11 likely to have eaten chicken that was undercooked."

12 What I'm trying to drive at is what we are
13 looking at when we look at all of the controls and
14 cases in the study, not just bits and pieces because we
15 have a bits and pieces problem with the cases and
16 the --

17 JUDGE DAVIDSON: What is the question?

18 BY MR. BATES:

19 Q What we have seen in these two studies, then,
20 when you look at all the cases, when you look at all
21 the cases put together as opposed to subgroups, overall
22 chicken is more like eating at home than it is eating

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1 in a restaurant?

2 A Would you please repeat the question? When
3 you look at?

4 Q When we try to understand whether there is a
5 risk factor associated with eating all chicken, not
6 just eating it in a certain place -- and we have the
7 CDC study that says if you eat at home it's less than
8 one and if you eat at a restaurant it's more than one.
9 Am I right that these studies shed some light on
10 whether overall, regardless of where you eat the
11 chicken, the odds ratio is negative?

12 (The witness examined the document.)

13 THE WITNESS: I think that the studies
14 demonstrate that some ways of eating chicken are risky
15 and others are less risky.

16 BY MR. BATES:

17 Q Now, let's look then at Exhibit G-564, which
18 is the -- I believe, the ^{Schmid} ~~Schmitz~~ study in ^{Dubugue} ~~Dubugue~~ that
19 I was referring to a moment ago.

20 Your Honor, do you have that on your --

21 JUDGE DAVIDSON: Yes, I have it. Thank you.

22

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1 BY MR. BATES:

2 Q I'm handing it to the witness.

3 So if we look at this study, which was in
4 ~~Debuque~~ ^{Dubuque}, I believe, in 1987 -- would you turn to page
5 3? I'm sorry, page 4. And in the discussion section
6 near the bottom in the right-hand column, the next to
7 the last full paragraph, it says, "We found no
8 epidemiological association with consumption of
9 chicken," correct?

10 MR. SPILLER: Did you say right-hand column
11 near the bottom?

12 MR. BATES: I did.

13 JUDGE DAVIDSON: "Although we found"?
14 That's -- although -- I see.

15 MR. BATES: That's correct.

16 JUDGE DAVIDSON: Okay.

17 BY MR. BATES:

18 Q And -- just to move along -- are you familiar
19 with the recent case control study in England by
20 Rodriguez --

21 MR. SPILLER: I'm sorry, Your Honor, I
22 apologize for interrupting. I think the witness has

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1 already testified that she was not familiar with this
2 study and that it was not cited in the risk assessment.
3 Counsel may recall that. If she isn't and if it's not,
4 then I think we're beyond the scope.

5 MR. BATES: Well, it's an exhibit in evidence,
6 Your Honor. I -- want to ask her one question --

7 JUDGE DAVIDSON: Well, I don't have any -- you
8 can ask the question, but I don't understand the last
9 question. You said -- I know what you're trying to do,
10 but you're leaving my records in shambles here. You're
11 point out -- and you start reading, and you ask the
12 witness to read it, and then you move on to something
13 else. You don't have any question about that, then why
14 does she have to look at it?

15 MR. BATES: So when we -- I'll -- let me ask
16 about the Rodriguez study, then I'll ^{ask} ~~ask~~ the question.

17 JUDGE DAVIDSON: All right.

18 BY MR. BATES:

19 Q So the ^{Rodrigues} ~~Rodriguez~~ study, would you look at
20 the --

21 A I don't have it.

22 Q This is Exhibit G-17 --

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1 JUDGE DAVIDSON: She didn't; there's no
2 question. That was the problem. That's what I just
3 said. There was no question asked.

4 BY MR. BATES:

5 Q When one looks at the ^{Rodriguez}~~Rodriguez~~ study, and
6 these other studies that we just talked about --

7 JUDGE DAVIDSON: Do you have the number?

8 MR. BATES: G-1711.

9 JUDGE DAVIDSON: 1711?

10 MR. BATES: Correct.

11 JUDGE DAVIDSON: I need a copy. Hate to tell
12 you, but, you know, the people that prepared this --
13 CDs for me -- gave me five of them, and this one
14 doesn't go up to G-1711.

15 Thank you. Now let's -- the question is?

16 BY MR. BATES:

17 Q The question is when we look at the ^{Rodriguez}~~Rodriguez~~
18 study, which in the abstract says, "No statistically
19 significant risk associated with consumption of
20 chicken," other than -- nor with reported domestic
21 kitchen practices. We look at this study, we look at
22 the other studies we just talked about -- we get, do we

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1 not, a picture that says, "Consumption of chicken per
2 se isn't a risk"?

3 A And I think that we've stated that consumption
4 of chicken, if it had no campylobacter on it, is not
5 a -- is not a risk.

6 Q Well, these chickens had campylobacter on
7 them, didn't they?

8 A We don't know that, do we?

9 Q We do. I direct your attention to Exhibit G-
10 564, this -- study on page 4.

11 A What is this --

12 MR. SPILLER: Object to the form of the
13 question. We're talking about these chickens in the
14 context of Exhibit G-1711, and the witness has been
15 questioned about their campylobacter status. Counsel
16 testified, "We do;" and now we're off to another study.

17 MR. BATES: No, the same study. This is the
18 ~~Schmitz~~ ^{Schmid} study we just talked about --

19 JUDGE DAVIDSON: Well, now you were in the
20 ~~Rodriguez~~ ^{Rodriguez} study.

21 MR. BATES: I'm sorry. I was talking about
22 all the studies that we just mentioned. You asked what

1 my question was, Your Honor -- if you put them all
2 together, don't we get that picture?

3 JUDGE DAVIDSON: All right. And her answer
4 was, I think, that we do if you're just talking about
5 certain chickens, but not if you consider all the
6 chickens -- chicken -- I'm sorry. I won't even try.

7 What was your answer?

8 THE WITNESS: My answer was that if chicken
9 has campylobacter, it's a risk factor.

10 JUDGE DAVIDSON: And then you said, "Well, it
11 does, doesn't it?"

12 MR. BATES: Well, look at page 4 --

13 JUDGE DAVIDSON: Is this all the studies?
14 They all -- all these studies that you referred to that
15 you put on the record, portions of, referred to
16 portions of, deal with chickens that have
17 campylobacter? That's the import of your statement,
18 which is not testimony in this case.

19 MR. BATES: Let's then -- take your point --
20 let's talk about the studies, what they say about
21 whether there is campylobacter on the chicken.

22 JUDGE DAVIDSON: All right.

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1 BY MR. BATES:

2 Q Exhibit G-564 has the one-year study of
3 epidemial campylobacteriosis in mid-western cities?

4 A And this is an article that I'm less familiar
5 with than some of the others.

6 Q Well, just look at the -- doesn't it say --
7 MR. SPILLER: Object -- form of the
8 question --

9 JUDGE DAVIDSON: Page 4, right-hand
10 paragraph --

11 BY MR. BATES:

12 Q Page 4, right-hand column, where we were
13 reading before --

14 JUDGE DAVIDSON: The paragraph that starts
15 with "Although we found" -- did you find it --

16 BY MR. BATES:

17 Q Did you find it, doctor?

18 A Yes.

19 JUDGE DAVIDSON: Okay.

20 BY MR. BATES:

21 Q That statement says, "Large numbers of chicken
22 carcasses at retail stores were ^{Contaminated} ~~contamination~~" --

1 A Yes. And I need to say that we're still
2 finding that today, but the problem -- or the question
3 is "What is the campylobacter status at the point of
4 ingestion," so that if you find, as you do cooking at
5 home is not coming out as a strong risk factor, it's
6 because probably people at home are taking better care
7 to cook their chicken so that the campylobacter are
8 killed by the time they eat them.

9 Q So you're suggesting there's something going
10 on in a restaurant that's different than going on at
11 home?

12 A I'm suggesting that people at home take better
13 care.

14 Q Restaurant cooking practices are less good
15 than home cooking practices and that would explain the
16 difference of --

17 A Well, I don't want to point my finger at all
18 restaurants. I think some restaurants take care also.

19 Q In either event, what you're -- am I right
20 that what you're suggesting is that we're trying to
21 understand cause here. You've got what's known to
22 statisticians as a feedback problem, is that right?

1 Do you know what a feedback problem is?

2 A No.

3 Q Well, let me put it in my own words. You've
4 got eating chicken in a restaurant, resulting in an
5 increased risk factor of disease. It might be that the
6 problem is the chicken, or it might be the problem is
7 the restaurant doing something to the chicken.

8 Is that correct?

9 A I -- that's a difficult one to answer. It's
10 hard to imagine the restaurant doing something to put
11 campylobacter on the chicken.

12 Q It is? Well, what about ill food handlers at
13 restaurants? Big problems.

14 A No. And when I say no, I mean compared to the
15 amount of campylobacter that are coming in day after
16 day on chicken.

17 Q Just stay with me. Ill food handlers in
18 restaurants is a problem, regardless of the big or
19 small.

20 MR. SPILLER: Beyond the scope of direct.

21 MR. BATES: Excuse me --

22 JUDGE DAVIDSON: It's fairly obvious. The

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1 witness has already agreed to that. I don't know why
2 you're pushing it.

3 BY MR. BATES:

4 Q So we know -- let's go back to the ^{CDC}~~eye~~ draft
5 1452. It's attachment 3. And if we look at Table 4 on
6 page 101, and we also see that eating non-poultry meat
7 in a restaurant has a risk factor of 21 percent. Do
8 you see that?

9 A Yes.

10 Q That's similar to the etiological fraction for
11 chickens in restaurants, right?

12 A That's correct.

13 Q Well, doesn't that cause you to wonder whether
14 there's something going on in a restaurant that's
15 independent of whether it's chicken or meat -- because
16 they both have similar risk factors?

17 MR. SPILLER: Object to the form of the
18 question as it presumes independence when the
19 restaurants incorporate both chicken and other meat.

20 JUDGE DAVIDSON: All right. I'm going to
21 sustain the objection. I think you've beaten this
22 horse enough. The record speaks for itself. You have

1 the data. You have an opportunity, in brief, to make
2 whatever argument you please. Move on to something
3 else.

4 BY MR. BATES:

5 Q So when we do the -- we were just talking
6 about the etiologic fraction of the total number of
7 campylobacter cases. And when you do your calculation,
8 is your next step to try to estimate the number of
9 those campylobacter cases which are resistant?
10 So if I were to draw another circle inside my second
11 circle -- we're trying to do next. Is that correct?

12 A That's correct.

13 Q And the quantification that you're doing
14 here -- you are going from all cases, to chicken cases,
15 to resistant cases.

16 A May I make a suggestion --

17 Q Yes.

18 A -- that that circle should --

19 JUDGE DAVIDSON: Excuse me. The circle is not
20 in the records, so don't believe that.

21 THE WITNESS: Okay.

22 JUDGE DAVIDSON: He just -- what he said was

1 fairly clear --

2 THE WITNESS: Supposition --

3 JUDGE DAVIDSON: -- he stepped from total
4 population to the chicken to resistant.

5 THE WITNESS: Okay.

6 MR. BATES: Did I get something wrong? Do you
7 want to clarify that?

8 JUDGE DAVIDSON: No, she was just worried the,
9 I think, the circles; but they're not in the record.

10 THE WITNESS: Where are they placed? Where
11 it's placed.

12 BY MR. BATES:

13 Q So what happens to the formula that you use,
14 the multiplication? When you've got a situation like
15 eating chicken at home, which -- where the fraction is,
16 well, reversed or negative? How do you factor that
17 into this multiplication?

18 A Well, as you know, we didn't do it that way.
19 We had an overall factor attributed to chicken which we
20 were not separating out. This is eaten pink, this is
21 eaten at a restaurant, this is -- we had a global
22 value.

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1 Q I understand, but when you -- I'm just trying
2 to -- in the risk assessment, you said if one had these
3 data, one could use them to do the calculation. I'm
4 now trying to understand how one would do that.

5 A Well, just as I said, we would have used all
6 the various attributable fractions and come up with a
7 global attributable fraction that we would apply.

8 Q Got it. ^{And} ~~At~~ if that fraction turned out to be
9 less than one, or negative, then what would you end up
10 doing?

11 A It would not turn out to be -- you cannot have
12 an attributable fraction that's negative. You can have
13 an odds ratio that's less than one, but you cannot have
14 negative risk.

15 Q If the odds ratio were less than one, then
16 what would you do?

17 A Well, this is supposition and I think that, as
18 we've seen, it -- the global estimate would not be.

19 Q Well, we're going to argue that in the brief,
20 so I'm just trying to understand what you would do if
21 an odds ratio were less than one.

22 MR. SPILLER: Objection --

1 BY MR. BATES:

2 Q How would you make this -- how would you make
3 it work?

4 MR. SPILLER: Objection. I'm educated by my
5 witness. I now recognize the question invites
6 speculation.

7 JUDGE DAVIDSON: Yes, but I think she can
8 answer it. If you did come up with that kind of less
9 than one, what would it mean? It's just hypothetical;
10 it doesn't mean that you're saying that that is the
11 result.

12 THE WITNESS: If an odds ratio were less than
13 one? That -- an odds ratio less than one still does
14 not imply a zero risk. It means that a certain -- that
15 the cases are less at risk, perhaps, than -- or I
16 should say that the controls were less at risk, but it
17 still does not imply zero risk. So I'm struggling to,
18 right now, to think about what it would be. It would
19 be a non-zero value, but not very large.

20 BY MR. BATES:

21 Q So if you had -- if you had an odds ratio less
22 than one, and you took -- you then tried to multiply --

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1 resistance times something less than one, how do you
2 get a value from that? That's what I don't understand.

3 MR. SPILLER: Again, objection. Not merely
4 speculation, but speculation multiplied now.

5 MR. BATES: I'm not pursuing it, I'm
6 just trying to get sense.

7 JUDGE DAVIDSON: All right. With that double
8 ~~slip~~^{flip} of the chart, is this a convenient place? The
9 witness has been on the stand almost three hours --
10 almost two hours.

11 All right, we'll take a 10-minute recess.

12 (A brief recess was taken.)

13 MR. BATES: Dr. Bartholomew, ready to resume?

14 THE WITNESS: Yes.

15 BY MR. BATES:

16 Q Now just to try to pick up about where we left
17 off, when we were -- we were going from the total
18 ~~indication~~^{etiologic} fraction issues, which was dependent on the
19 year you picked, which was roughly 1.7 million and 1.4
20 million, and we're going to the percentage of those
21 that were campylobacter cases attributable to chicken.

22 A Yes.

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1 Q Yes.

2 A Yes.

3 Q Thank you.

4 A I'm sorry.

5 Q No, no, that's -- we're trying to get this
6 right. And in your model you use 57 percent.

7 A That's the mean value.

8 Q Would you agree with me that if, as you
9 suggested in the model, we use the new ^{CDC}~~EVC~~ data, that
10 number might be 24 percent or it might be even lower?

11 A I would not agree that we would have
12 disregarded totally other information so that 24
13 percent was restaurant dining. I think we would have
14 looked around for what else, because, as you know, our
15 consumptions -- the way we use consumption is not
16 individuals sitting around ^{ingesting}~~injecting~~ chicken. We were
17 talking about the exposure of the population to the
18 chicken, with a lot of implication of secondary
19 transmission and that sort of thing.

20 So I'm saying that we would -- if we would use
21 the ^{CDC}~~EVC~~ data, we would not just pick up that 24 percent
22 and run with it. There would be other modeling that

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1 would need to transpire also.

2 Q Including the fact that when eating at home,
3 the number goes the other way.

4 A Yes.

5 Q So then the next step in the process is to try
6 to estimate the number of those chicken cases which are
7 resistant. Am I right, or have I got that wrong?

8 A Yes.

9 Q I got it right. To try to estimate the number
10 of those chicken cases which are resistant, is that
11 correct?

12 A The number of cases that are from chicken and
13 are ~~Fluoroquinolone~~ ^{Fluoroquinolone} resistant are --

14 Q So you needed -- you have 57 percent here. It
15 might be less than that based on the new study. Yes?

16 A Yes.

17 Q And now you've got to get a percentage for
18 this next fraction?

19 A Right.

20 Q Am I right that the way you do that -- I'm
21 going to draw another circle, so -- if you just said,
22 well, we're going to look at the -- all the resistant

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1 cases -- this -- is that right?

2 A Right.

3 Q And then did you say and we're going to pull
4 out of there the cases that -- I'm drawing a small
5 circle inside the big circle -- you pull out of that
6 the number of cases that were attributable to foreign
7 travel.

8 A Yes, conceptually, that's what went on, mm-
9 hmm.

10 Q Then you said, am I right, that you said we're
11 also going to pull out of that the number of cases --
12 and I'm drawing another circle that's smaller -- that
13 were related to prior treatment --

14 A Yes.

15 Q Then am I right that you said everything else
16 is chicken?

17 A Yes, we did.

18 Q Well, we now have the ~~Preidence~~ ^{Friedman} study. That
19 what we've been talking about, the ~~Preidence~~ ^{Friedman} study. The
20 ~~CDC~~ ^{CDC} study that we've been talking about -- Exhibit G-
21 1452 -- an attachment to Exhibit 1452.

22 And am I right that that is a risk factor in

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1 Table 4, that we've been talking about, at page 101,
2 for drinking water?

3 MR. SPILLER: Objection to form. Misstates
4 the record. If counsel is referring to the seventh
5 line down, it has a different title.

6 MR. BATES: Let me be real precise.

7 BY MR. BATES:

8 Q "Drank untreated water from a lake, river, or
9 stream." Do you see that?

10 A Yes, I do.

11 Q And do you recall in the risk assessment,
12 making the statement that there is resistance to
13 campylobacter in water?

14 A I don't recall that. Could you point it out
15 for me?

16 A Well, why don't you look at page 49 to 50, and
17 in particular -- it's G-953, pages 49 to 50.

18 A Yes, I see that.

19 Q Yes. So we do find ^{Fluoroquinolone}~~Floroquinolone~~-resistant
20 campylobacter in water, do we not?

21 A It appears that in the effluent from abattoir
22 and sewage purification plants, they do find it.

1 Q And that water often goes into lakes and
2 streams and so on, is that correct?

3 A I hope not too much of it.

4 Q We'll let another agency worry about that.

5 My only point is should we have another circle
6 of some size -- I don't know how big it is -- for
7 resistant cases from water?

8 A Well, I think that we concluded that poultry
9 farm runoff would also be attributable to use in
10 chickens.

11 Q Based on what, do you remember?

12 A We discussed with our microbiologist -- and
13 that our conclusion was that without selection
14 pressure, use of fluoroquinolones, you very rarely find
15 resistant campylobacter.

16 At the time that we did the risk assessment,
17 the fluoroquinolone use in poultry was the only
18 agricultural fluoroquinolone approved; so that that
19 would be the selection pressure, considered to be the
20 largest one for creating the resistance in water. So
21 we attributed that to chicken also.

22 Q But your own report says, does it not, that

1 there was 11 percent resistance rate in -- I'm reading
2 from page 50 -- 11 percent resistance rate coming from
3 a sewer treatment plant that did not receive meat
4 processing solution. That's not run-off from chicken,
5 is it?

6 A I can't say. And as I said, it was an
7 assumption that we made that most of it was --

8 Q I agree with that. I'm just trying to
9 understand whether there might not be other things that
10 one would want to subtract in order to get a picture of
11 what that fraction might be.

12 A Well, the water is not treated with
13 fluoroquinolones, so that it would ostensibly come from
14 either the use of the fluoroquinolone in the chicken,
15 or fluoroquinolone -- the use in people. And we had a
16 little blurb for taking care of fluoroquinolone use in
17 people also, which --

18 Q But that was part of treatment, yes? That's
19 getting a prescription. That's not coming out of a
20 waste water treatment?

21 MR. SPILLER: Objection to the form of the
22 question, which presumes that effluent from humans that

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1 had been treated would not survive sewage treatment.

2 Counsel describes them as separate, not established.

3 JUDGE DAVIDSON: I'll sustain the objection.

4 BY MR. BATES:

5 Q When you said that you pulled out prior
6 treatment, tell me what you meant by that?

7 A We estimated, from the 1998-1999 campylobacter
8 case control study, that proportion of the resistant
9 isolates that was due to either travel or prior
10 fluoroquinolone use; and we applied that proportion to
11 ~~Norm's~~ ^{NARM's} data so that we could have an annual update.

12 And in doing so in a risk model, you use
13 distributions, so that you have variability -- you
14 incorporate the possibility that the number that you're
15 using is that number, or some other number. So you
16 have uncertainty about it.

17 Q Just to be clear, though, what you were trying
18 to do was to identify the number of resistant isolates
19 that resulted from someone taking a prescription.
20 That's what this circle I drew was all about, is that
21 correct?

22 A That's correct.

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1 Q You weren't trying to identify resistant
2 campylobacter that came out of a waste -- treatment?

3 A Not specifically, no.

4 Q So wouldn't we want to, if we could, try to
5 account for some portion of resistant campylobacter
6 that wound up in the environment, got in the water, and
7 people were exposed to it?

8 A I don't know. I suppose if your focus was
9 that, campylobacter in water, that you might want to do
10 that, yes.

11 Q And returning to page 101 of attachment 3 to
12 Exhibit G-1452, which is the Table 4 that we've been
13 discussing, I think you pointed out to me that there's
14 something -- some portion of the ~~proposition trivial~~
15 risk which is not attributed to anything?

16 A Would you repeat the citation, please?

17 Q Yes, certainly. It's Exhibit G-1452,
18 attachment 3.

19 JUDGE DAVIDSON: Page 101?

20 MR. BATES: Page 101, Table 4.

21 BY MR. BATES:

22 Q And my question was do you recall testifying

1 that there's a portion of the etiologic fraction that's
2 not attributed to anything?

3 A Yes.

4 Q And would I be right that that's more or less
5 25 percent, if I had those numbers on there, that's
6 unattributed to anything?

7 A I haven't done that addition, but I'd say it's
8 about that, okay.

9 Q So this picture that I drew over trying to
10 understand what sources other than chicken we should
11 subtract in order to get the chicken number -- are you
12 saying that, with regard to the unattributed 25 or less
13 percent, there are no resistant cases in that portion?

14 A I would say that in 1998-99, that we had
15 attributed all of the domestically acquired resistance
16 to chicken; so if it was not chicken-associated, then
17 ostensibly it would not have been resistant.

18 Q So when -- with that -- I guess I asked a
19 different question. You answered -- with regard to
20 that 20 percent, the assumption you made says there
21 were no resistant campylobacter provided by the 25
22 percent?

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1 A Well, as I -- one thing that you said was that
2 the source was not ^{known} ~~know~~ for that 25 percent.

3 Q Right.

4 A And to the extent that something in that 25
5 percent was not chicken-associated, then there would --
6 then it would not have included ^{resistance} ~~resistant~~. But there
7 is -- there's uncertainty here. We don't know what
8 that 25 percent --

9 Q There may or my not be other things that have
10 to come out of this -- is that --

11 A You are looking at the pool of resistant
12 bacteria there, right?

13 Q Correct. I tried to go from -- I thought the
14 way that you tried to come up with a fraction for
15 multiplying times the number of chicken cases was to
16 say, well, what are all of the resistant cases, and
17 let's pull out foreign travel, pull out prior
18 treatment. We talked maybe we should pull out a
19 little -- of the water.

20 A Yes.

21 Q And so there might be some things in this
22 other attributed portion that we might want to pull out

1 too.

2 A Well, you're looking at a table that's
3 developing a population-attributable fraction for
4 campylobacter cases, not for resistant cases.

5 Q I understand that. I'm just trying to say one
6 has to assume, therefore, in this 25 percent, there's
7 no percentage of resistance; because if there is, one
8 would want to pull it out in order to make sure you
9 have the right number.

10 A I guess I'll go back to what I said earlier.
11 To the extent that the unknown portion is -- was a
12 source other than chicken, that there would be no
13 other -- I'm having trouble making these two things
14 match because here we're talking about attribution of
15 campylobacter, and there you're talking about
16 attribution of the resistance. And so I'm having
17 trouble making your two statements match.

18 Q All right, let's try this. We have this 25
19 percent unknown.

20 A Unknown with respect to where they got their
21 campylobacter, yes.

22 Q Right. And we have -- in addition, we have

1 population-attributable fractions for non-poultry meat
2 and -- other things, on Table 4. Is that correct?

3 A Yes.

4 Q And so we know that campylobacter comes not
5 just from chickens?

6 A That's true.

7 Q And we know, at least in the case of water
8 that there sometimes resistant campylobacters in water;
9 and water is one place where people get campylobacter.
10 Correct?

11 A Yes.

12 Q And that's why we may not be sure how big it
13 is, but there's a fraction here that we would know if
14 we pulled it out?

15 A Twice I've said I'm not sure that it belongs
16 to other than chicken or human use --

17 Q We'll go over that. But if it turned out that
18 some of these other sources that we just talked about,
19 the unattributed ones, the non-poultry meat and
20 restaurant, and so on -- had some resistant
21 campylobacter -- in that case, it wouldn't be from
22 prior treatment, then one would want to pull those

1 things out as well. Yes?

2 A If you had sources that you could justify, I
3 think you would want to pull them out. Now, our risk
4 assessment was very clear about what it was assuming.
5 It was assuming that the -- what the selection
6 pressures were. And so I -- I mean, I could answer
7 your question in the hypothetical that if you knew of
8 something else as a selection pressure, you would want
9 to account for it.

10 Q And if one -- that would mean that the
11 percentage that you got would go down some, yes?

12 A If I were subtracting out, yes, it would have
13 to mean that.

14 Q In your work on the EPA water panel, have you
15 become familiar with a study that the U.S. Geological
16 Survey is doing on pharmaceuticals and streams in the
17 United States?

18 A Not through that. I'm aware of that study to
19 the extent that I know it's out there. I haven't
20 studied it.

21 Q And are you aware that the results of that
22 study have been recently published?

1 MR. SPILLER: Objection. Beyond the scope of
2 direct. Way beyond.

3 MR. BATES: Your Honor, I would -- I have
4 marked Exhibit B-1945, which is a --

5 JUDGE DAVIDSON: You have an objection
6 pending. Care to respond to it?

7 MR. BATES: I'm sorry.

8 JUDGE DAVIDSON: You have an objection
9 pending. Now you're going to start marking papers?
10 That doesn't -- that doesn't -- that's not the way I
11 operate.

12 BY MR. BATES:

13 Q You've testified --

14 JUDGE DAVIDSON: Now --

15 MR. BATES: All right.

16 JUDGE DAVIDSON: I want you to respond to the
17 objection.

18 BY MR. BATES:

19 Q A moment ago you just testified that the
20 resistance in water came from --

21 JUDGE DAVIDSON: You're still back on that, is
22 that it? I'm ruling -- I'm sustaining the objection.

1 I don't want to see any more business with respect to
2 what we're going to take out, what we're not going to
3 take out. The record speaks for itself. If you have
4 those things in the record, you can put it in the
5 brief.

6 You've gone through with this witness 15 times
7 or more the fact that certain things had to come of her
8 calculation. She stands by her calculation. She
9 hasn't changed that. We understand it has limits, and
10 she has put in the assumptions, and you can take it
11 from there.

12 I don't understand why we're wasting hours on
13 this particular aspect of it.

14 Now if you move on to something else, I'll be
15 happy to listen to you. If you want to stay with this,
16 you've finished your cross-examination.

17 MR. BATES: No, one or two more --

18 JUDGE DAVIDSON: Okay, thank you.

19 BY MR. BATES:

20 Q So we go through our calculations -- we start
21 with a -- we go to the campylobacter, we go to --

22 JUDGE DAVIDSON: Just --

1 BY MR. BATES:

2 Q -- and then we go to --

3 JUDGE DAVIDSON: -- excuse me. I thought I
4 just said I don't want to hear any more about that. I
5 mean, if you want to explain to me what you're doing,
6 I'll be glad to listen; but to go back through this
7 over and over again -- and you've asked the same
8 questions more than once -- because I realize the
9 witness is not giving you the answers you'd like to
10 hear; and she may not be totally responsive. But we're
11 in an area where I don't think we're getting much for
12 the record. And that's my problem.

13 MR. BATES: I'm just trying to get to --

14 BY MR. BATES:

15 Q We talked before about the final step in the
16 calculation.

17 JUDGE DAVIDSON: No, you're talking to me now,
18 not the witness. What are we doing?

19 MR. BATES: I'm -- I'm simply trying to recall
20 the process by which we get to the final step of the
21 calculation -- focus on the final step.

22 JUDGE DAVIDSON: It's not in her testimony?

1 MR. BATES: Excuse me?

2 JUDGE DAVIDSON: It's not in her testimony?

3 MR. BATES: The final step --

4 JUDGE DAVIDSON: The process by which she got
5 to her calculation?

6 MR. BATES: It is in her testimony.

7 JUDGE DAVIDSON: Then why do you have to
8 recall it?

9 MR. BATES: I'm not going to go through the
10 detail; I'm just trying to get to the end -- I'll be
11 happy to start with the end point.

12 JUDGE DAVIDSON: Well, if you have something
13 that you're going to ask her about that, that's fine.
14 You can start at the end point, ask her the question,
15 and move on.

16 BY MR. BATES:

17 Q So the end point of the calculation was, as I
18 think we discussed, that you estimated the number of
19 cases that were fluoroquinolone-resistant of chicken
20 that were prescribed fluoroquinolone?

21 A Yes.

22 Q And I think, recalling what we talked about

1 before, that you did attempt to estimate a number of
2 those cases where there was a treatment -- is that
3 correct?

4 A That's correct.

5 Q And did you attempt to estimate the number of
6 cases where a bacterium was susceptible, where there
7 was a treatment failure?

8 A No.

9 Q Now hypothetically, if it turned out that the
10 rate of success or failure was the same for resistant
11 cases as in susceptible cases, then what would happen
12 to the health impact --

13 MR. SPILLER: Object. I understand you can
14 ask a hypothetical, but the hypothetical needs a basis.
15 I've not heard the basis laid for that particular
16 hypothetical.

17 BY MR. BATES:

18 Q Now I have Exhibits G-354 --

19 JUDGE DAVIDSON: Is this the basis for the
20 hypothetical?

21 MR. BATES: Yes.

22 JUDGE DAVIDSON: Thank you. Witness got a

1 copy of it?

2 MR. BATES: Excuse me, Your Honor?

3 JUDGE DAVIDSON: Does the witness have a copy
4 of Exhibit 354? G-354? Are we referring to a page and
5 line?

6 MR. BATES: Yes, I'm just trying to find
7 the -- this is going to require a couple of steps here.

8 BY MR. BATES:

9 Q Will you look, please, at page 3, the section
10 entitled, "Clinical Outcome." And if you look at the
11 top of the second column on that page, this indicates
12 that there were two patients with campylobacter who
13 were prescribed ^{ciprofloxacin} ~~Ciprofloxacin~~ and failed treatment. Is
14 that correct?

15 A I will need to take a time to read this
16 because I have not read it from -- if I read it at all,
17 I haven't read it for a long time.

18 Is this a set of patients, all of whom had
19 resistant campylobacter? I didn't see that in that
20 passage.

21 Q We look at -- let me direct your attention to
22 the section in the first column on that page. It says,

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1 "Bacteriological outcome."

2 And as you go up to Table 2, it says "number of
3 patients in the treatment group that indicated -- of
4 Ciprofloxacin -- ³⁷~~27~~; and it says campylobacter
5 species -- 21. Is that the first -- the number of
6 isolates?

7 A Number of people with campylobacter.

8 Q Then if you look at page 3, right-hand column,
9 it says that we had -- ^{among} ~~one of the~~ patients who had only
10 campylobacter; seven were susceptible -- seven were
11 resistant isolates. Do you see that?

12 A You say the top of the right-hand column?

13 Q Right-hand column about midway down, page 3.

14 A Okay.

15 Q So we've got seven patients with susceptible,
16 seven with resistant.

17 JUDGE DAVIDSON: Two resistant.

18 MR. BATES: Seven patients with susceptible,
19 and seven with resistant, okay?

20 JUDGE DAVIDSON: Where are you reading this?

21 MR. BATES: The sentence begins: "^{Among} ~~of the~~
22 patients affected with campylobacter species

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1 isolate" --

2 JUDGE DAVIDSON: Yes.

3 MR. BATES: -- "and were treated with
4 *ciprofloxacin*
~~Ciprofloxacin~~" --

5 JUDGE DAVIDSON: Go ahead.

6 MR. BATES: -- "four of seven were
7 susceptible, and two of seven were resistant."

8 JUDGE DAVIDSON: That's what I thought, but
9 you kept saying seven resistant, seven --

10 MR. BATES: Seven patients with --

11 JUDGE DAVIDSON: I understand what it says,
12 but your question, I believe, left out the two of seven
13 when you got to the second part.

14 MR. BATES: I want to go back to the -- of
15 this paragraph where it says that there were two
16 people -- there were two clinical failures: one was
17 susceptible, one was resistant.

18 JUDGE DAVIDSON: Okay.

19 THE WITNESS: I don't see any -- you're
20 pointing me to something that talked about duration of
21 illness.

22