1   A   If I may answer a little informally, for

2   everything that mattered they did, but there are some

3   sensitivity analyses involving log exponential

4   distribution in which I believe they varied microbial

5   load distribution.

6   Q   Thank you for both parts of that answer. In

7   your model -- and this time when I'm referring to your

8   model, I'm referring to Exhibit A-17. And I don't

9   believe I've given you a copy today, have I?

10   A   I don't think you have.

11   Q   I'm handing you now Exhibit A-17, a dynamic

12   simulation model of campylobacter illness, final

13   report, prepared for the Animal Health Institute.

14   MR. SPILLER: Excuse me, your Honor. I gave

15   you a copy yesterday. I believe I asked you if you

16   would save it for today.

17   MR. NICHOLAS: I don't believe I got a copy

18   yesterday.

19   MR. SPILLER: I'm looking now to see if we

20   have an extra copy.

21   MR. NICHOLAS: I have together all the

22   documents I believe we received.

1   MR. SPILLER: Handing counsel for Bayer a copy

2 of Exhibit A-17.

3   MR. NICHOLAS: Thank you.

4   BY MR. SPILLER:

5   Q   On page 29 of that, Dr. Cox --

6   A   Hold on. I'm looking for it.

7   Q   I apologize. I've given you a bad page

8 number. In the exhibit, do you have page 111?

9   A   I do.

10   Q   And does that correspond to page 29 at the

11 bottom?

12   A   Yes, it does.

13   Q   Am I correct that your model assumes that any

14 dosage below -- and we're talking here a dosage of

15 campylobacter -- below 500 CFU has a zero probability

16 of producing an illness?

17   A   Not really.

18   Q   I'm sorry. I'll quote. In your model, does

19 the phrase occur, and I quote, our model assumes that

20 any dosage below 500 CFU has a zero probability of

21 producing an illness, close quote?

22   A   Yes. The report said so at that time. As I

1   say, but not really.

2   Q   And in -- I'm sorry. Did you say that's not

3   really the case? That's what the report says but

4   that's not really the case?

5   A   Yes. Subsequent sensitivity analysis showed

6   that assumption was unnecessary.

7   Q   But you still represent that it's true.

8   A   Let me say yes to make things easy. As I say,

9   there are multiple runs of the model, there are

10   multiple versions, and there are extensive sensitivity

11   analyses. In some of those sensitivity analyses, that

12   simplification was relaxed. It didn't make any

13   substantial difference, but it was relaxed. So at this

14   time, those sensitivity analyses hadn't been run.

15   Q   However many times you ran it, did you cite

16   for that 500 CFU minimal infected dose, Robinson 1981?

17   A   Yes, I did.

18   MR. SPILLER: I'm sorry, your Honor. I'm lost

19   in my paper. I'm looking for a copy of that paper.

20   JUDGE DAVIDSON: All right. Off the record.

21   (Off the record.)

22   JUDGE DAVIDSON: Back on the record.

1   MR. SPILLER: Thank you, your Honor. I

2 apologize for my delay.

3   BY MR. SPILLER:

4   Q   Do you know, Dr. Cox, how many test subjects

5 were involved in the research that led you to use that

6 figure?

7   A   I see that as being a compound question.

8 First, I don't remember how many test subjects were

9 used in Robinson. Secondly, I don't agree that I used

10 that figure and I would cite in the exhibit that you

11 handed me, B-1629, my statement that "sensitivity

12 analysis provides a partial solution to the problem of

13 unknown and variable dose response relations."

14   MR. NICHOLAS: Excuse me, your Honor. We seem

15 to have G-1816. I'm not sure we have the same exhibit

16 as the witness is referring to.

17   JUDGE DAVIDSON: All right. We'll straighten

18 it out.

19   MR. NICHOLAS: Is this the --

20   MR. SPILLER: You have an advance copy of an

21 exhibit that the witness doesn't have now.

22   MR. NICHOLAS: Okay.

1   MR. SPILLER: The pending question is whether

2   or not he recognizes -- excuse me -- whether or not he

3   knows how many study subjects were in the Robinson

4   study on which he relied.

5   THE WITNESS: And I'm telling you --

6   MR. NICHOLAS: Excuse me, I'm still --

7   THE WITNESS: I'm sorry.

8   MR. NICHOLAS: The Robinson study is what

9   exhibit? I was just handed G-1816.

10   MR. SPILLER: And it was a great mistake of

11   mine to hand it to you because I was only giving you an

12   advance copy of something that I was about to hand the

13   witness.

14   MR. NICHOLAS: But as I understood, you handed

15   the witness Robinson?

16   MR. SPILLER: I have not handed the witness

17   the Robinson paper.

18   MR. NICHOLAS: Okay. Sorry.

19   JUDGE DAVIDSON: All right. Come on. Let's

20   move on.

21   MR. SPILLER: Okay.

22   THE WITNESS: Did he say anything to me?

1　　　　　JUDGE DAVIDSON:　I don't think so, but I'm not

2　sure.　Do you have a question pending, Mr. Spiller?

3　　　　　MR. SPILLER:　The question pending included,

4　as he pointed out, two parts, one, that you don't have

5　any subjects.　I believe he's indicated that he

6　doesn't.

7　　　　　BY MR. SPILLER:

8　　　Q　And the second part, that I thought was

9　routine, that you relied upon -- and am I correct, Dr.

10　Cox, you're explaining to us why you didn't rely on it?

11　　　A　I'm reading my previous written description on

12　that subject, yes.

13　　　Q　The description that we're inquiring about is

14　the description in Exhibit A-17.

15　　　A　Yes.

16　　　Q　And the paragraph that begins on page 111 of

17　that exhibit, that begins the minimum infective dose.

18　And you say in the second sentence, other research has

19　shown that the minimum dosage may be as low as 500 CFU

20　(Robinson, 1981).　I thought that meant you were citing

21　Robinson for that.　No?

22　　　A　Of course it means I was citing Robinson.

1 What I was not relying on as I have clearly written is

2 any assumption that there can't be any risk below 500

3 CFUs. And as I've written in Exhibit B-1629 on page

4 36, any dose response relation with these qualitative

5 features that are discussed tends to produce similar

6 expected number of CB cases from given population

7 frequency distribution microbial loads.

8 I'm not relying, in any way, on that 500

9 number.

10 Q   But you said it in the model that you did for

11 AHI --

12 A   That's what I'm explaining. That's an early

13 model.

14 Q   And you've identified that model in your

15 testimony here as a model you were relying on.

16 A   Oh?

17 Q   Excuse me. That's a question. Did you?

18 A   No. Not to my knowledge.

19 MR. SPILLER: Now, your Honor, I'll hand the

20 witness what has been marked, and counsel has a copy

21 of, G-1816.

22 BY MR. SPILLER:

1   Q   Dr. Cox, looking at that one-page exhibit in

2   the lower left-hand corner, does it identify the author

3   of that article as D.A. Robinson?

4   A   Yes, it does.

5   Q   And is that article about 8 inches tall in one

6   column?

7   A   Let's say it is. Yes.

8   Q   A short article. How many study subjects got

9   the dose of -- got any dose in that study?

10   A   This is one guy administering to himself.

11   JUDGE DAVIDSON: Say that again? I didn't --

12   THE WITNESS: He gave himself the dose. This

13   is one subject.

14   JUDGE DAVIDSON: Okay.

15   BY MR. SPILLER:

16   Q   So in this study, one subject got one dose one

17   time. Am I right?

18   A   Yes.

19   Q   And that dose was 500 CFUs.

20   A   Uh-huh.

21   Q   And he got sick. He got abdominal cramps and

22   mild diarrhea, didn't he?

1   A   Yes.

2   Q   And this is the paper that in A-17 you relied

3 on to establish the minimal dosage as low as 500 CFUs.

4   A   Yes. This is the paper that I relied on for

5 that 500 CFU number. Yes.

6   Q   Now, a moment ago, were you reading to me from

7 G-629?

8   A   I'm sorry. Can you tell me --

9   Q   A moment ago, I was taking you back. You

10 picked up another exhibit and you said something else.

11 Was that 629?

12   A   No, I think it's 1629. I'm reading from my

13 book.

14   Q   Okay. Let me give you Exhibit G-629.

15   A   629. Okay.

16   MR. SPILLER: I believe this is in evidence,

17 your Honor.

18   BY MR. SPILLER:

19   Q   You relied on this in you're A-17?

20   A   A-17 being --

21   Q   I'm sorry. The AHI report. It's labeled

22 final report.

1   A   I cited it.

2   Q   Okay. Thank you. That's satisfactory for the

3   present purpose. Are you aware that this *Teunis* ~~Tunis~~ article

4   that you cited, the beta-Poisson dose response model

5   that you use for the probability of infection, assumes

6   that one can get infected from just one bacterium?

7   A   I realize that from the model, yes.

8   Q   And are you aware that that dose response

9   model that you used for the probability of illness

10   given infection assumes that one can become ill from

11   just one bacterium, not just that you get infected but

12   that you can get ill?

13   A   Yes, I'm familiar with that assumption.

14   Q   Isn't your arbitrary threshold in A-17 of 500

15   CFU therefore inconsistent with using the *Teunis* ~~Tunis~~ model?

16   A   It is not. As I -- should I elaborate?

17   Q   Only if you need to to be responsive to the

18   question. I understand you to have said you don't

19   believe it's inconsistent. Is that right?

20   A   That's correct. And for the reasons

21   previously cited.

22   Q   Have you ever seen the combined *Teunis* ~~Tunis~~ dose

1   response model described in G-629 at page 7, figure

2   2(c) -- I should let you find that.

3   A   G-629.

4   Q   G-629, page 7, figure 2(c).

5   A   Yes.

6   Q   Have you ever seen that combined model being

7   used in any other microbial risk assessment?

8   A   Have I seen -- I'm hung up on the word "used."

9   I've seen it cited in other mi -- may have to say

10 microbial risk assessments or antimicrobial risk

11 assessments.

12   Q   Yes. I'll refine the question. In other

13 study in this record, is there any indication that you

        Teunis

14 know of that the ~~Tunis~~ model has been used to prepare a

15 risk assessment for a microbial or antimicrobial?

16   A   Well, hold on, please. This is going to take

17 me a minute.

18   JUDGE DAVIDSON: Off the record.

19   (Off the record.)

20   THE WITNESS: I am not aware of this -- hold

21 on a second. The Rosenquist, et al. paper does not

        Teunis

22 cite this paper of ~~Tunis~~, et al. Now, I can't quickly

1 tell whether it cites the same combined model to which

2 you refer. So it's definitely beta-Poisson model.

3 Whether it's the identical model would take me a little

4 more work.

5   In addition, I don't remember -- and I think

6 you asked whether anywhere in the record has this been

7 used, if I'm remembering your question correctly. I

8 believe that the record somewhere discusses the WHO

9 groups -- oh, yes.

10   In Curtis Travis' -- that's where it comes

11 out. It talks about the use of the WHO, made in its

12 model and its valuation. But that's all I can do while

13 I sit here.

14   BY MR. SPILLER:

15   Q   So we can find that in, it's your

16 recollection, the testimony of Curtis Travis in this

17 record.

18   A   Yes. He cites the WHO discussion and says

19 that the beta-Poisson model is a good model and is

20 adequate.

21   Q   And is it your testimony that whatever that is

22 that we'll find in Dr. Travis' testimony applies to the

Teunis
1   combined ~~Tunis~~ model as depicted on page 7 of G-29 in

2   figure 2(c) like Charlie?

3   A   No. It's my testimony that I don't remember

4   whether it was the combined model.

5   MR. SPILLER: Your Honor, I am about to lapse

6   into statistics, which will take me a while.

7   Would it be appropriate to begin lunch recess

8   now so that I could be more efficient?

9   JUDGE DAVIDSON: Any objection?

10   MR. NICHOLAS: Do we have any indication how

11   long we're going to --

12   JUDGE DAVIDSON: We haven't gotten into that.

13   MR. SPILLER: In connection with my commitment

14   yesterday to let us finish today, your Honor, I'm very

15   hopeful of finishing by 2:00 to enable any direct to be

16   completed during the day.

17   JUDGE DAVIDSON: You mean you think you have

18   about an hour, hour and 15 minutes more altogether?

19   MR. SPILLER: Yes, your Honor.

20   JUDGE DAVIDSON: Okay. We'll adjourn until 10

21   minutes to 1:00.

22   (Whereupon, a luncheon recess was taken.)

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

2   (12:45 p.m.)

3   JUDGE DAVIDSON: On the record.

4   Counsel for Bayer and the witness are not back

5   yet, so we'll wait for them. The record will reflect

6   it is a quarter to 1:00.

7   Off the record.

8   (A brief recess was taken.)

9   JUDGE DAVIDSON: On the record.

10   It has come to my attention that I may have

11 gone on the record five minutes early, but all I said

12 was we'll wait, so there's nothing for you to worry

13 about.

14   MR. NICHOLAS: I apologize, your Honor.

15   JUDGE DAVIDSON: No, you weren't late. I

16 think it's me. I was five minutes early.

17   MR. NICHOLAS: Thank you, your Honor.

18   JUDGE DAVIDSON: Mr. Spiller? Let the record

19 reflect that the witness is still under oath and Dr.

20 Cox is still available for your brief cross-examination

21 on statistics.

22   MR. SPILLER: Thank you, your Honor.

1   BY MR. SPILLER:

2   Q   Dr. Cox, you have your final report, Exhibit

3   A-17, in front of you?

4   A   Yes, I do.

5   Q   Would you look at page 111 and 112, please?

6   I'm sorry. Look at page 112 first.

7   A   Okay.

8   Q   And your figure 2.5 is your dose response

9   probability curves by age group. Taking, if I may,

10 just focus on the bottom one, that would be a plot

11 using the ~~Tunis~~ *Teunis* combined model as we described before,

12 right?

13 A   I believe that's correct.

14 Q   And the ~~Tunis~~ *Teunis* paper you also have in front of

15 you, Exhibit G-29, page 7. You have that before you?

16 I'm referring to the page number on the little exhibit

17 stamp in the upper right-hand corner.

18 A   And which page number do you refer to?

19 Q   Page 7.

20 A   Yes, I do.

21 Q   And just for illustrative purposes and not to

22 introduce, I have a blowup here. You should refer to

1 the official exhibit. I'm going to be tracking along

2 here because those figures are small for my eyes.

3   Am I right that his combined model is depicted

4 in figure 2(c)?

5   A   Yes.

6   Q   And if I understand the description of that

7 figure correctly, it looks like there are three curves,

8 a solid -- I'll call it a smooth hill with sloping

9 edges as the middle curve and quite a jagged dotted

10 line above it, and a much smaller dotted line below it.

11   Do those dotted lines represent the fifth and

12 ninety-fifth percentile confidence intervals above that

13 plotted line?

14   A   I don't know offhand. I can read the --

15   Q   All right. I should let you have a chance to

16 do that. Read the legend at the bottom of figure 2 of

17 ~~Tunis~~ *Teunis* page 7.

18   A   Yes. These are confidence intervals for

19 bootstrap replicates. Yes.

20   Q   And I don't know the statistical term. To me,

21 that looks like a whopper of an upper confidence limit.

22 Dr. Cox, is it the case that at approximately 10 to the

Corrected as per OR 46 6/13/03

1   second -- that would be 100, right?

2   A   Uh-huh.

3   Q   At 100 CFU, the confidence intervals for that

4   value on this plot would range roughly from zero to 60

5   percent probability of illness, right?

6   A   The bootstrap replicate confidence intervals,

7   yes.

8   Q   And it's good, careful science to define the

9   confidence intervals about data.   Is that right?   Or

10   about plots.

11   A   Depending on how you do it, confidence

12   intervals often don't indicate model uncertainty so

13   they may not be useful in the context where the model

14   was uncertain.

15   Q   Is it a good thing in both models and

16   statistics to be explicit about depicting and

17   describing uncertainty?

18   A   Yes.   Extremely important.

19   Q   And he did that here?

20   A   Well, he was explicit about the resampling the

21   bootstrap replicate variability.   He's not really

22   characterizing model uncertainty.   As you can see,

1   example.

2   A   Okay.

3   Q   And so the 500 CFU cutoff would be a vertical

4   line, I'm indicating with red just for illustration

5   purposes, at about log 2.7, here. So the actual --

6   when I say here, I'm indicating a vertical line

7   extending from the ~~Tunis~~ *Teunis* plot down to the X axis of

8   about log 2.7.

9   So your model, because it includes the 500 CFU

10   cutoff, actually includes a cliff on the side of the

11   hill, doesn't it?

12   A   Well, no. My model states -- or my

13   description and discussion of exactly this issue in my

14   model states that risks are low or zero. They don't

15   have to be zero, they can be low for sufficiently small

16   doses, e.g., less than 500 CFUs, doesn't have to be 500

17   CFUs, and illness probability increases rapidly as a

18   function of dose reaching an approximate plateau --

19   this is now describing why I deal with this model in my

20   model -- it reaches an approximate plateau of about .2

21   for CFU levels of about a thousand to 10,000 CFUs.

22   What I've said is by doing sensitivity

1 analyses, I've found that any dose response model that

2 captures the rough qualitative features of the data

3 will suffice. So I'm not -- I forget the exact word

4 that you used but I'm not assuming a cliff and I'm not

5 assuming anything that's strange behavior outside the

6 range of the data in terms of declining risk.

7   Q   On page 111 of Exhibit A-17, Dr. Cox, right

8 about the paragraph response rate by age, there's a

9 smaller paragraph and in that smaller paragraph a

10 sentence that begins our model.

11   A   Uh-huh.

12   Q   That's your model and your ~~partner~~ *partner's*, Douglas

13 ~~Popkin~~ *Popken*, right? Your associate?

14   A   Yes. That is our February 20, 2001 version of

15 the model, before the sensitivity analyses in the final

16 form were published.

17   Q   And that model -- excuse me -- that statement

18 says our model assumes that any dosage below 500 CFU

19 has a zero probability of producing an illness, doesn't

20 it?

21   A   Yes.

22   Q   And a zero probability of producing an illness

Teunis

1 on the ~~Tunis~~ plot, figure 2(c), would be along the X

2 axis, wouldn't it?

3   A   Yes, it would.

4   Q   And it would continue flat with zero

5 probability on the X axis from the origin to the point

6 that corresponds to 500 CFU and then it would ascend

7 vertically to join the rest of the curve, right?

8   A   Yes, that's correct.

9   Q   So that would indicate that for all doses

10 between zero and 498, the zero probability of illness,

11 zero at 498, zero at 499 and at 500 CFU suddenly the

12 response would be 20 percent of the population, right?

13   A   Yes. That would be the approximation.

14   Q   In this record, do you know of any observed

15 database where either humans or chickens were observed

16 to have responded in that way to a series of doses such

17 that there was no response at 498, 499 and 20 percent

18 response at 500?

19   MR. NICHOLAS: Your Honor, if I may, I object.

20 Chickens don't respond. The question is compound and

21 improper.

22   MR. SPILLER: I volunteer to rephrase my

1   question, your Honor.

2   JUDGE DAVIDSON: Go right ahead.

3   BY MR. SPILLER:

4   Q   Dr. Cox, in this record, is there any data set

5   that indicates that humans respond in such a way that

6   the dose response would be plotted as no probability of

7   illness up to 498 or 499 CFUs and a 20 percent response

8   in humans to campylobacter at a dose of 500 CFU?

9   A   Can you remove the front exhibit to show the

10 poster with number 1257 on it?   Thank you.

11   If you look at those data, you'll see that

12 assuming that there's zero response to zero dose, the

13 pattern as far as we know is that not much happens and

14 I don't believe that there are data for humans below

15 about 500 CFUs.   Well, not in this experiment.

16   Basically, not much happens until you get up

17 to a few hundred CFUs, then about 20 percent of people

18 get sick.   So I think that these data from one feeding

19 study -- it's hard to know what to make of them but

20 they're consistent with the idea that there's a higher

21 response probability when you have several hundred,

22 several thousand CFUs.   And we don't really know what

1   happens in the low dose range.

2   JUDGE DAVIDSON: Let the record reflect the

3   witness is referring to Exhibit G-629 page 7, the

4   figure thereon, when he said 1257, which happens to be

5   the page number in the actual publication as opposed to

6   our exhibit number.

7   THE WITNESS: Thank you, your Honor.

8   BY MR. SPILLER:

9   Q   Dr. Cox, my question was whether or not you

10   could indicate in this record a human dose-response at

11   data ~~plot~~ *plot?* Did you indicate that you believe that

12   ~~Tunis~~ *Teunis* at the reference just cited is such a plot that

13   shows a sudden change at 499 where there's no response

14   to 500 where there's a 20 percent response?

15   A   No, he didn't look at 499 so no, I don't think

16   he shows what happened below 500.

17   Q   So we agree that he did not show but I haven't

18   gotten an answer to my question about whether there is

19   anything in this record that indicates there is any

20   human dose response curve to campylobacter plotted that

21   would show a sharp break in the dose response curve

22   such that there is no response at 498, and none at 499,

1   but a 20 percent response at 500?

2   A   I'm not aware of any data that contains 498

3   and 499 and I believe that these data -- well, I think

4   these data support the usefulness of the approximation

5   that I made.

6   Q   And your assumption about the -- your

7   assumption in A-17 at page 111 that any dosage below

8   500 CFU has a zero probability is based on Robinson.

9   What is the statistical significance of such a

10 determination based on a single dose single human

11 study?

12   A   Well, first I disagree with the premise

13 embedded in your question.   I've tried to be really

14 clear that I did not assume that 500 CFUs is a magic

15 threshold.

16   Q   I stand corrected.   You did not assume.   Your

17 exhibit says that our model assumes, and I thought we

18 had established previously that our included Dr. Cox.

19   A   Of course it includes me.   It does not in any

20 way depend upon the assumption.   At the time of this

21 early exhibit I had not yet done the sensitivity

22 analyses that I've reported and published subsequently.

1   Q   And in A-17, where do you describe the

2 uncertainty about this value?

3   A   In A-17, I had not yet done the sensitivity

4 uncertainty analysis so they are not yet described.

5 That came subsequently.

6   Q   They're not described in A-17. Is that right?

7   A   Right. They're in B-1029.

8   Q   In your final model report to AHI, Exhibit A-

9 17 at page 110, near the top of the page, a

10 subparagraph numbered 3, you have an assumption one

11 chicken provides four servings, the CFU count per

12 simulated chicken is divided by the number of servings.

13 The dose response model is then applied to each

14 serving.

15   Did I read that right?

16   A   Yes, you did.

17   Q   Then for a serving to have at least 500 colony

18 forming units in your model the carcass from which it

19 was derived would have to have had 2,000 CFUs, right?

20   A   Let me first correct something that you said

21 in asking your question and then answer your question.

22 You referred to this report as a final model report. I

1   want to again state that this was the final report of

2   an initial modeling project that has subsequently led

3   to additional runs, additional sensitivity analyses,

4   additional data, and there has subsequently been peer

5   review to published. So I wouldn't want this to go on

6   the record as being the final model report. It's the

7   final report of a preliminary model.

8   Within that context, yes. To get 500 CFUs on

9   one serving, you would need 2,000 CFUs on one chicken.

10   Q   And 2,000 CFUs or 2,000 of anything is about

11 3.3 log to base 10, is that right?

12   A   That sounds right.

13   Q   So referring in A-17 to your figure 1.5, and

14 that's on page 104, 3.3 logs would be very near the

15 tiny skinny toe at the right-hand side of that curve.

16 Is that correct?

17   A   Yes, it would be in the right-hand tail of

18 this distribution.

19   Q   So if this distribution of microbial load on a

20 carcass is even slightly wrong, it would probably have

21 an enormous effect on your model's accuracy, wouldn't

22 it?

1   A   No.

2   Q   Well, let's say --

3   A   Not on the accuracy of the conclusions which,

4   as demonstrated in the subsequent sensitivity and

5   uncertainty analyses are extremely robust, the

6   assumptions.

7   Q   If that plot in that exhibit, we compare the

8   value at log 3.3 and if it were shifted only to log 4

9   so it would go from 2,000 to 10,000, there would be a

10   change from a very small amount to none, is that

11   correct, in this plot?

12   A   I think you're misinterpreting the plot.

13   Q   I'll withdraw the question then. I don't want

14   to misinterpret.

15   In your testimony at page 23, in the first

16   paragraph -- let me know when you have that.

17   A   Okay. I'm there.

18   Q   You testified that CVM, by assuming its model

19   form is correct, despite overwhelming evidence to the

20   contrary --

21   A   Yes.

22   Q   Is this overwhelming evidence to the contrary

1 that the risk increases disproportionately with

2 microbial loads above 500 CFU, simply the dose response

3 model that we've been talking about?

4   A   No, it is not. It's the observation that most

5 people eat a lot of chicken and most people don't get

6 sick.

7   Q   On page 10 of your testimony, Dr. Cox, you

8 mention the traditional risk assessment steps and you

9 note there in the sixth numbered paragraph that

10 uncertainty characterization is one of the steps. Am I

11 correct that you agree that that's important?

12   A   Yes, I do.

13   Q   And in your final report to AHI, dynamic

14 simulation model of campylobacter illnesses, Exhibit A-

15 17, page 14 -- excuse me -- page 96, for the first

16 parameter, you did provide a characterization of

17 uncertainty. Am I right?

18   A   A partial characterization, yes.

19   Q   And for all the others you did not, right?

20   A   That's incorrect. For example, if you look at

21 the colonization index, a ~~bilinear~~ *binomial* probability equal to

22 .90, that number specifies an entire probability

1 distribution.

binomial
2 For the next one down, another ~~bilinear~~

3 distribution, the one number specifies entire

4 distribution. For the surface microbial load which

5 starts to get exciting from a cause and effect point of

6 view, as specified, a triangular distribution for the

7 lot of 10 of the values.

8 For the one beneath that, transportation

9 factor -- and so forth.

10 Q   In the triangular distribution that you

11 mentioned as significant, is that a description of

12 variability or a description of uncertainty?

13 A   Yes.

14 Q   You've answered assuming that I was asking if

15 it was one or the other. Are you indicating that it is

16 both?

17 A   For a full explanation of the interpretation

18 of these distributions, I would refer to Exhibit B-1029

19 starting on page 36.

20 MR. NICHOLAS: Excuse me. I believe the

21 reference is 1020, not 1029.

22 THE WITNESS: Thank.

1   JUDGE DAVIDSON: Thank you.

2   THE WITNESS: Thank you.

3   BY MR. SPILLER:

4   Q   Is that description, Dr. Cox, a description of

5   variability?

6   A   There's a false dichotomy here. These

7   distributions are used in the simulation model to

8   approximate both uncertainty about model parameters and

9   variability in the microbial load that will reach

10   individuals.

11   And there's a substantial framework that these

12   piece by piece steps get into to justify that dual role

13   and that is the framework outlined in the exhibit that

14   I just referred to, the B-1020 -- in my book.

15   Q   And in your risk model for campylobacter

16   described in the book, and I think you have an excerpt

17   of the book there that you've been referring us to, B-

18   1260, and in the A-17 report, you used data, didn't

19   you, from studies by Stern, et al. to arrive at your

20   estimate of initial microbial loads? Matter of fact,

21   that's the source of the triangular distribution that

22   you just cited me to, isn't it?

1 A   It's a source of the data.

2 MR. NICHOLAS: Your Honor, I'd just like to

3 clarify which exhibit we're talking about. I know Dr.

4 Cox's book is B-1020, so it doesn't --

5 JUDGE DAVIDSON: It's B-1020. You said B-

6 1260, Mr. Spiller.

7 MR. SPILLER: I did say that. I acknowledge

8 the correction. I believe both of those refer to it

9 but counsel is correct that the version in front of the

10 witness is 1020. I'll settle for A-17 at the page we

11 were discussing, page 96.

12 BY MR. SPILLER:

13 Q   And, Dr. Cox, you referred me to the surface

14 microbial load, triangular distribution, Stern, et al.

15 That's one of the papers you relied on, right?

16 A   I again want to stipulate that reliance is too

17 strong a term because of the sensitivity and

18 uncertainty analyses but Stern is the data source for

19 this distribution of the model, yes.

20 Q   And it's the only source that you cited for

21 that particular --

22 A   In this row of the table, yes.

1   Q   I'm handing you now Exhibit B-712, which I

2 believe is in the record.

3   A   Thank you.

4   Q   Dr. Cox, is B-712 the Stern paper to which you

5 refer?

6   JUDGE DAVIDSON: Excuse me again. In the

7 record as what -- with what number?

8   MR. SPILLER: The only number I have is B-712,

9 your Honor.

10   JUDGE DAVIDSON: Well, based on my records

11 here, B-712 has not been moved into evidence.

12   MR. SPILLER: I move Bayer's Exhibit B-712 --

13   JUDGE DAVIDSON: Wait a minute. It may be

14 that it has another number.

15   MR. SPILLER: It may be, and I apologize, your

16 Honor. I don't have a conversion table with me. I

17 think for purposes of discussion, even if it were not

18 an exhibit, we can cover the point.

19   JUDGE DAVIDSON: All right. If it's not in

20 otherwise, we'll deal with it subsequently but right

21 now you can refer to it as B-712.

22   MR. SPILLER: Thank you, your Honor.

1   BY MR. SPILLER:

2   Q   If you look in B-712, Dr. Cox, at page 3,

3   table 2, and page 4, table 3, are those the sources of

4   the data that you used for the parameter described that

5   we just discussed in A-17, page 96?

6   A   Sorry. Oh, for the surface microbial load?

7   Q   Yes.

8   A   Okay. Which two tables again, please?

9   Q   Table 2 on page 3 and table 3 on page 4.

10   A   Yes.

11   Q   And you know how those levels were determined.

12   A   Not in detail.

13   Q   It's described in the paper.

14   A   Uh-huh.

15   Q   On page 2, the right-hand column under

16   sampling and microbiological analysis --

17   A   Yes.

18   Q   I'm sorry. When I said paper I'm referring to

19   B-712. I'll let you read it quietly. Let me offer a

20   description and you see if I've got it fairly.

21   You put the bird carcass in a bag and you

22   massage the dead bird carcass so that some of the

bacteria are rinsed off the carcass. You put the ~~rinse~~ *rinsate*

~~aid~~ in a centrifuge, you spin it down, you plate the

resulting materials, you grow it out and you count the

colonies.

   Is that a crudely fair description?

  A That pretty much matches my understanding,

yes.

  Q So to know how many bacteria were really on

the bird, you couldn't call the result of that plating

the surface microbial content unless you knew what your

percent recovery was from that rinsing, right?

  A When you say the bird, which bird are you

referring to?

  Q The birds that are subjected to this process

to determine -- to get the values recorded. I assume

that there are a number of birds.

  A I assume so, too, and I think there's a

distribution of measured values as a result of this

process for those birds. Bearing that in mind, could

you re-ask your question, please?

  Q Don't the values recorded from such a carcass

rinse procedure necessarily and persistently understate

1   the actual bacteria counts on the bird because the

2   rinsing process cannot recover 100 percent of the

3   bacteria on the bird?

4   A   This is a matter of what the operational

5   definition of the numbers mean. My operational, I mean

6   what measurement procedures are we using.

7   I agree with you that if you mean -- if you

8   count the CFUs on the bird using a different procedure,

9   would you get a different or possibly greater answer, I

10   would agree with you.

11   Q   You fitted triangular probability

12   distributions to these data, did you not, Dr. Cox?

13   A   Fit is a little bit strong but we approximated

14   a mean and variance by triangular distributions in this

15   case.

16   Q   So for instance, in Exhibit A-17 on page 99

17   under the paragraph with the heading initial level of

18   exterior infection microbial load, in the second

19   sentence --

20   A   I'm sorry. I'm not finding it.

21   Q   We're in Exhibit A-17, page 99, near the

22   middle of the page, you see a paragraph headed initial

1 level of exterior infection?

2   A   Oh. The heading. Yes. Yes, I do.

3   Q   And then in that paragraph, I think the third

4 sentence is a triangular distribution for the log to

5 the base 10 of the value captures these three points.

6 You have a T in parentheses zero, 298 and 638. Is that

7 correct?

8   A   With one --

9   Q   I'm sorry; 2.98.

10   A   That's right. That is correct.

11   Q   And you state just above that the distribution

12 there ranges from zero to ten to the 6.38 in the

13 preceding sentence.

14   A   Correct.

15   Q   Where in Stern's paper does it say -- I'm

16 sorry. The first of your triangular values there, in

17 the parentheses you have a zero. Is that a minimum in

18 the triangular distribution?

19   A   Yes. That's the minimum of the three

20 parameters shown.

21   Q   Where in the Stern paper does it say that a

22 minimum of zero CFUs were observed?

1   A   I'm not sure that it does.

2   Q   So if you only cited Stern for this

3   distribution and he didn't say zero, how can you put a

4   zero in?

5   A   Well, the way a triangular distribution works,

6   as discussed more fully in the uncertainty and

7   sensitivity analyses as I've referred to several times,

8   is that one has a plausible lower bound, a plausible

9   upper bound and a plausible central estimate.

10 The distribution is not intended to be

11 completely physically accurate. The distribution is

12 intended to capture the approximate mean and

13 variability for use in something called the central

14 limit theorem that comes in later. That's the

15 substantial framework that I referred you to earlier.

16 And in this case, zero would be a plausible lower

17 bound.

18 Q   And 6.38 logs is the highest level Stern

19 observed, correct?

20 A   That sounds right. Uh-huh.

21 Q   And by using that triangular distribution with

22 that maximum value you exclude the possibility of any

1   higher value like 7 or 8 load?

2   A   I do not. That point is specifically

3   addressed in the uncertainty and sensitivity analysis

4   that I've referred you to many times. The --

5   Q   I'm sorry. Is that the analysis that's not in

6   A-17, it's somewhere else, it's in your book?

7   A   It's the analysis in my book and in other

8   publications, yes.

9   Q   Thank you.

10   A   The point there is that mean variance for each

11   step in a process where a number of factors are being

12   multiplied is sufficient when there are a large number

13   of steps, as there are here, fully characterize the

14   distribution, the meaning of the variance for the

15   overall process.

16   Q   Thank you.

17   A   Uh-huh.

18   Q   The center number in that triangular

19   distribution, the 2.98, is that a calculated value?

20   A   I believe that it is. It's been a few years

21   since I've done this but I believe that reads like a

22   geometric ~~medium~~ *median* and -- data points.

1   Q   And for a triangular distribution, it's

2 supposed to be the geometric median, not the average?

3   A   As I've explained, a plausible upper bound,

4 plausible lower bound and something that's about right

5 as a measure of central -- whether it's the median, .6

6 mode, makes no difference because at the end I'm going

7 to use the central limit there.

8   Q   In you're a-17, did you provide any visual

9 demonstration of the degree of fit of these triangular

10 distributions?

11   A   You mean --

12   Q   The goodness of fit.

13   A   Goodness of fit of the triangular

14 distributions to?

15   Q   The data.

16   A   No, not for each individual step. And again

17 you understand that to be irrelevant in the context of

18 this.

19   Q   You mentioned a moment ago the central limit

20 theorem.

21   A   I did.

22   Q   Did I understand you, that's the distribution

1   of -- does that include the fact that a distribution of

2   the mean of a random sample from a population has a

3   standard deviation that is proportional to one over the

4   square root of the sample size?

5   A   No, that's got nothing to do with it.

6   Q   That has nothing to do with the central limit

7   theorem?

8   A   No.

9   JUDGE DAVIDSON: Need some time?

10   MR. SPILLER: Yes, your Honor.

11   JUDGE DAVIDSON: Okay. Off the record.

12   (Off the record.)

13   JUDGE DAVIDSON: Back on the record.

14   MR. SPILLER: Thank you, your Honor.

15   JUDGE DAVIDSON: Okay. Let's go.

16   BY MR. SPILLER:

17   Q   Dr. Cox, I'm passing you what's been marked G-

18 1817. Dr. Cox, G-1817, does that appear to be a

19 partial copy of Fundamentals of Biostatistics by

20 Bernard or edited by Bernard Rosner?

21   A   It looks that way, yes.

22   Q   And would you refer within that to the book's

1   page 158?

2   A   I'm looking at it.

3   Q   At the top is there a boxed definition or a

4   description of the central limit theorem?

5   A   Yes, I would say a central limit theorem.

6   Yes, there is.

7   Q   Do you agree with that definition?

8   A   It leaves out some technically necessary

9   conditions, so it's an approximate statement to the

10 central limit theorem. For example, this would be

11 incorrect if the population had a ~~certain~~ *Cauchy* distribution,

12 but it's an approximation to it, yes.

13   Q   The -- using the central limit theorem, isn't

14 it true that a mean of a random sample of 25

15 measurements would have one-fifth the standard

16 deviation of the population's distributions?

17   A   I'm sorry. Would you repeat the question?

18   Q   Isn't it correct, then, that if one took a

19 mean of a random sample of 25 measurements, the mean

20 would have one-fifth of the standard deviation of the

21 population's distribution?

22   A   You mean the sample mean?

1   Q   Yes.

2   A   Well, actually, for 25, a rough rule of thumb

3   is -- you chose a bad example. You would use the T

4   distribution for 25. But I take your point. It's a

5   square root relationship.

6   Q   The data you used from Stern's paper, and

7   we're now looking at B-712, are geometric means of

8   samples sized 10 and 25, right, referring to those same

9   two tables, table 2 and table 3?

10   A   Yeah.

11   Q   And those are geometric means, right?

12   A   Uh-huh.

13   Q   So for the sample size 10, the square root is

14   about 3 and the samples of size 25, the square root is

15   5. So fitting the triangular distributions to these

16   mean data and using those fitted distributions as if

17   they represent individual carcasses, you would actually

18   have underestimated the standard deviation of the

19   carcass load by a factor of somewhere between 3 and 5,

20   wouldn't you?

21   A   No. No. Not at all. That's not how it

22   works. I mean, you're talking --

1   Q   If -- I'm sorry. Finish your answer.

2   A   Keep on going. But no, we're not talking

3 about sample standard deviation and sample mean of the

4 components of the overall process. The sample limit

5 theorem that I referred to deals with the composition

6 of multiple multiplicative steps. We're not even

7 approximately in the same ballpark here.

8   Q   Dr. Cox, in your testimony at page 7 --

9   JUDGE DAVIDSON: Getting tired, Mr. Spiller?

10   MR. SPILLER: Yes, your Honor, and I'm hoping

11 to finish soon.

12   BY MR. SPILLER:

13   Q   On that page, Dr. Cox, at line 15 of your

14 paragraph 7, you note your opinion that banning Baytril

15 will greatly increase human health risks and you expect

16 the ban to cause more than 25 additional days for each

17 hypothetical day of Fluoroquinolone-resistant

18 campylobacter illness prevented.

19   A   Yes. That's my opinion.

20   Q   That conclusion arises from your risk

21 assessment model, doesn't it?

22   A   In part, yes.

1   Q   So if the model is unreliable, the conclusion

2   is also?

3   A   No. It's only partially derived but there's a

4   much simpler argument to getting there that's much more

5   data driven.

6   Q   In your testimony at page 37, there's a chart

7   there, linear --

8   A   Yes.

9   Q   You plot the total chicken ~~concerned~~ *consumed* -- I

10   think you call that totchick on the X axis.

11   A   Total chick, yes.

12   Q   Against the case rate on the Y axis.

13   A   Yes, that's correct, although the

14   interpretation -- it's not exact because I don't have

15   measurement for these seven FoodNet areas of the actual

16   chicken consumed. I had to construct a proxy from

17   survey data that I had.

18   Q   Nonetheless you fit a ~~layer of direction~~ *linear regression*

19   through them to show that the slope was negative,

20   right?

21   A   I fit a simple linear regression to see what

22   the slope would be.

1   Q   And that's one of your bases for calling CVM's

2 assumption that cases are proportional to chickens

3 consumed incorrect, the fact that you got --

4   A   No. This particular diagram is what's called

5 an ecological study. No, I didn't rely on this one.

6 It shows --

7   Q   You didn't rely on this but you include it in

8 your testimony?

9   A   Yes, that's correct. It shows the point

10 without going through nearly as much detail as the full

11 broad data analysis.

12   Q   And even though you don't rely on it and you

13 say in the first bullet on that page plotting CP case

14 rates against the summary of self-reported and per

15 capita chicken consumption for FoodNet catchment area

16 reveals a negative association -- that's your italics

17 -- negative association between them, consistent with

18 the results from the CDC and case control studies? Am

19 I not correct in saying that that you did rely on that

20 plot?

21   A   Yes, you are incorrect. No, I didn't rely on

22 it because you might be able to remove one or two

1   points and change the answer in something that only has

2   7 data points. What I relied on was the underlying

3   data, which is a lot richer but this is the simplest

4   way of showing the results.

5   Q   You picked the regression equation for this?

6   A   The statistics package that I was using in the

7   upper not clearly legible margin of the picture.

8   Q   And according to your testimony, that's the

9   relationship.

10   A   Was that the end of the question?

11   Q   Yes.

12   A   I'm sorry. If that's what relationship?

13   Q   That's what you intended to indicate CVM's

14   incorrectness by depicting that negative association?

15   A   Again, the really convincing evidence here is

16   from the individual data analysis. This is aggregated

17   analysis by, I think, seven FoodNet sites. So I don't

18   consider this by itself to be -- this isn't the

19   overwhelming evidence that I'm speaking about. This is

20   like shadow analysis.

21   Q   And did you show your statistical analysis for

22   this plotted line -- for instance, did you show the

1　confidence interval?

2　　A　No.　This is just exploratory.

3　　Q　Did you show the R square values?

4　　A　No.

5　　Q　It's only exploratory but you have it in your

6　testimony for us.

7　　A　Sure.　What I'm saying is if you take the

8　simplest possible look at the data, you'll see it

9　doesn't look anything like straight line sloping upward

10　to the right.　That's my point.　That's what CVM

11　assumes; it's not even proximately true.

12　　Q　And if you plotted 7 completely random points

13　in a two-dimensional space like a chart, isn't there a

14　42 percent probability that you'd get a higher R square

15　value than your analysis revealed for these points?

16　　A　That sounds plausible to me.

17　　Q　Doesn't that demonstrate the fragility of the

18　point you've made here and therefore that we'd need to

19　show some measure of confidence about the data you

20　portray?

21　　A　No.　I keep saying this is an exploratory

22　analysis that is designed to show the simplest possible

1 way of looking at the data. I already showed that what

2 I referred to as the K model doesn't come close to

3 fitting the data. I see no reason to calculate R

4 squareds or to calculate confidence intervals to make

5 this point. I do see a need to do those things when we

6 do the serious data analysis.

7   Q   So if it's serious you would explain that this

8 is exploratory but for your testimony you didn't

9 identify this as exploratory.

10   A   I don't think I used the jargon exploratory

11 data analysis. I think I have indicated in multiple

12 places that the simplest way of looking at the data

13 that the hypothesis, that it's a cluster around a

14 straight line leaning from the lower left corner

15 upwards has no relation to the real data even when you

16 look at it in the simplest possible way.

17   Q   You called this I think just now in your

18 testimony today an ecological --

19   A   This is an ecological presentation, not

20 because it has anything to do with the ecology but

21 because the data is collected at the FoodNet area

22 level.

1   Q   So in your analysis, as depicted in your

2 testimony, did you include the ecological confounders?

3   A   I did mention -- I believe I mentioned that

4 there were several risk factors that were significant

5 at this ecological level and several suggested

6 confounders. So I think I did mention that probably --

7 yes, I think I mentioned it but I couldn't swear to it.

8   Q   Are they mentioned close enough to this part

9 of your testimony so that you could point me to it on

10 this or the nearby page?

11   A   Well, this testimony was written with

12 hyperlink in it and they were very close based on

13 hyperlink but I'm not sure how close they are in terms

14 of pages.

15   Q   The cite in your book to your model was a

16 hyperlink also, wasn't it, Dr. Cox?

17   A   That was a URL.

18   Q   Are both of those ways of referring from a

19 computer document to a web site, for instance.

20   A   No. The hyperlink within this document are to

21 locations within the document.

22   Q   Are you suggesting that the printed version of

1 your testimony that the Court and that the Center have

2 enable us to jump from one point of your document to

3 another?

4 A   No. I'm not. I'm just saying that the way I

5 wrote this and intended for it to be used, there are

6 hyperlinks all over it to get from point to point. But

7 we can't do that in the version --

8 Q   Intended for who to be able to use it that

9 way?

10 A   First and foremost, me.

11 Q   And the rest of the world who didn't have your

12 document in electronic format didn't have that ability.

13 A   CVM had my document in an electronic format.

14 Q   The version filed in this record --

15 A   To my sorrow, PDF translation lost the links

16 so what we have is less convenient than what I wrote.

17 Same words.

18   Now, I'm sorry. What was it --

19 Q   Whether there was something on the adjacent

20 pages of the version that is before you now of your

21 testimony includes a description of ecological

22 confounders for this ecological depiction?

1   A   Oh. I don't remember where confounders -- I'm

2   sorry. I don't know.

3   Q   Each of the seven points that you've plotted

4   there represents a different FoodNet catchment area,

5   right?

6   A   I would be very -- no, I don't think these

7   points would represent FoodNet data -- represent

8   FoodNet areas at all.

9   Q   I'm sorry. I was misreading, I suppose, in

10   your testimony at page 37, right above the chart.   I

11   thought it said linear ~~aggression~~ *regression* case rate against

12   total chicken consumption in seven FoodNet catchment

13   areas. What did I miss there?

14   A   I thought you had used the word "represent" to

15   imply that FoodNet data represents the states from

16   which they're taken or represent the larger population.

17   Q   So do we now agree that each of the points

18   plotted on your testimony, page 37 in that plot, you

19   meant to refer to 7 different FoodNet catchment areas?

20   A   That's correct. Or actually the samples that

21   are taken from those areas.

22   Q   Surely those different areas reflect areas

1 with different eating habits, environmental factors,

2 different localized poultry sources. There would be

3 substantial differences from the areas from which that

4 data derived.

5   A   I think there are huge differences in all of

6 those respects, yes.

7   Q   And where on this or adjacent pages have you

8 explained to the readers ~~or~~ of your testimony that factor?

9   A   Which factor?

10   Q   The factor that these data points are derived

11 from different areas with different unidentified

12 ecological confounders?

13   A   Give me a minute, please. Oh, well, here.

14 First, I don't believe that I give any additional

15 discussion of this figure beyond what we've covered. I

16 may have referred to it elsewhere.

17   Right in this bullet point it says plotting CP

18 case rates against a summary of per capita chicken

19 consumption for FoodNet catchment areas. The plot is

20 self-explanatory in terms of there being wide

21 differences in the case rates. You can see they go up

22 almost as high as 34 and they go down about as low as

1 5.

2   I don't think I have a written discussion of

3 what the data show beyond what's already discussed.

4   Q   And did you extend this analysis, Dr. Cox, in

5 your 2002 publication to do multiple linear regressions

6 on just 7 points?

7   A   Yes. Yes, I did.

8   Q   Again, in that circumstance, without

9 uncertainty analysis, right?

10   A   Well, you know, I would say that --

11   MR. NICHOLAS: Your Honor, could I know what

12 document counsel is referring to, please?

13   MR. SPILLER: I'm referring to, as I indicated

14 in the question, his 2002 model. I believe that's

15 Exhibit B-1252.

16   MR. NICHOLAS: Is that in evidence, B-1252?

17   MR. SPILLER: It's a Bayer exhibit. I don't

18 know.

19   MR. KRAUSS: Yes, it is.

20   MR. SPILLER: I apologize, Dr. Cox. The

21 lawyers have interrupted your answer.

22

1   BY MR. SPILLER:

2   Q   I think the pending question was in that one

3   -- and I can hand it to you if you want, but am I

4   correct, there is no uncertainty analysis on this one

5   either in this plot?

6   A   I'm a little slow to go along with either. I

7   think uncertainty in this ecological analysis is fairly

8   well expressed in the scatter plot. You can see that

9   the points do not fall on a straight line. There is

10   some scatter in the scatter plot.

11   Moreover, I note right underneath it that

12   while these data suggest that aggregate chicken

13   consumption is not positively associated with the risk

14   of CP illness unless one forces -- use CVM's model, for

15   example, several other factors do appear to be

16   significantly associated.

17   That immediately antecedes the article that

18   you're now referring to where which specific factors

19   that vary from site to site are significantly

20   associated are listed.

21   Q   So the analyses, both in your testimony and in

22   B-1252, you would agree is reflective of the quality of

1   your analyses of the CDC data set.

2   A   Oh, by no means.   This is an exploratory

3   analysis.

4   It's just a picture saying hey, let's take a

5   look at the data.   And that's -- what I was taught when

6   I took statistics is you should always start by looking

7   at the data.

8   But that's hardly where you end.   That's just

9   the beginning.

10   MR. SPILLER: I think the beginning is a good

11 place for me to end, your Honor.

12   I have no further questions on cross-

13 examination of Dr. Cox.

14   JUDGE DAVIDSON: Okay.   We'll take a short

15 break while you change positions.   I assume you have

16 some redirect?

17   MR. NICHOLAS: Yes, your Honor.

18   JUDGE DAVIDSON: Okay.   And when we come back

19 on, the first thing we'll take care of is the rest of

20 these exhibits, because I think I've got them in a

21 little bit of a mess here.

22   We're off the record.

1   (A brief recess was taken.)

2   JUDGE DAVIDSON: Back on the record.

3   REDIRECT EXAMINATION

4   BY MR. NICHOLAS:

5   Q   Good afternoon, Dr. Cox.

6   A   Good afternoon.

7   Q   I'd just like to clear up the record. Would

8   you tell us how your Ph.D. degree reads, what it says

9   on it, the degree?

10   A   It says Louis Anthony Cox, Jr. is awarded the

11   Doctor of Philosophy in risk analysis. And I believe

12   it also gives the name of the department, Department of

13   Electrical Engineering and Computers.

14   Q   Is there any doubt in your mind or does

15   anybody else have that question, whether you have a

16   doctoral degree in risk analysis?

17   A   None. I have a doctoral degree in risk

18   analysis.

19   Q   There was testimony yesterday with respect to

20   a meeting. I believe it was described as the Boston

21   meeting, and you were presented with what I believe was

22   an abstract from that meeting that -- and this is

1 Exhibit -- I think it's G-1811. It's a little hard to

2 read. Entitled "International Journal of Infective

3 Diseases."

4   MR. SPILLER: You're right, Mr. Nicholas. G-

5 1811.

6   BY MR. NICHOLAS:

7   Q   Dr. Cox, would you open that and tell me if it

8 describes the participants of that meeting? Mr.

9 Spiller, if I recall correctly, asked you whether there

10 were any people who were basically government people,

11 or he seemed to imply non-affiliated people with this

12 case.

13   A   I don't see a list of participants.

14   MR. NICHOLAS: Your Honor, if I could mark for

15 exhibit the actual journal this came from, which would

16 be, I believe, 1948, I believe, your Honor.

17   JUDGE DAVIDSON: Okay.

18   MR. NICHOLAS: And I'm going to show this to

19 counsel if I may because I don't have an additional

20 copy, your Honor.

21   JUDGE DAVIDSON: Well, then, you better not

22 mark it. I mean, show it to counsel -- if it has to be

1 put in the record, we'll put it in but right now you

2 can't put it in. You don't have enough copies.

3   MR. NICHOLAS: Your Honor, this is the only

4 one I have.

5   JUDGE DAVIDSON: What am I looking at?

6   MR. NICHOLAS: The page on the left, your

7 Honor.

8   JUDGE DAVIDSON: All right.

9   MR. NICHOLAS: Thank you, your Honor.

10   BY MR. NICHOLAS:

11   Q   Dr. Cox, I am going to give you this, which

12 I'd like to mark 1948 --

13   JUDGE DAVIDSON: You can't mark it.

14   MR. NICHOLAS: I'm sorry.

15   BY MR. NICHOLAS:

16   Q   Dr. Cox, let me give you this journal article

17 -- journal, rather --

18   JUDGE DAVIDSON: Excuse me. I don't mean to

19 interrupt you but what's the purpose of this, so he can

20 read the names of the people that are there?

21   MR. NICHOLAS: No, I'd just like to refresh

22 his recollection, your Honor.

1   JUDGE DAVIDSON: I understand, but for what

2 purposes?

3   MR. NICHOLAS: For that purpose --

4   JUDGE DAVIDSON: Well, then he can read those

5 names into the record. Mr. Spiller has looked at it,

6 he can look at it again to make sure it's accurate. We

7 don't need the document, particularly because you don't

8 have copies for everybody, and you leave me at a

9 disadvantage if I'm going to move it in or mark it.

10   MR. NICHOLAS: I'm sorry, your Honor.

11   THE WITNESS: I see I blew my reply yesterday.

12   BY MR. NICHOLAS:

13   Q   And, Dr. Cox, does this refresh your

14 recollection as to who were participants at the

15 meeting?

16   A   It does. And I had forgotten -- I think I

17 said no government people showed up, and I was wrong

18 about that. Of course Dr. Fedorka-Cray was there,

19 and --

20   Q   Was someone from the American Veterinary

21 Medical Association there?

22   A   Uh-huh.

Corrected as per OR 46 6/13/03

1   Q   And to your knowledge was that person a

2 witness in this case?

3   A   No.

4   Q   And to your knowledge is that person employed

5 or otherwise affiliated with Bayer?

6   A   No.

7   MR. SPILLER: I apologize for interrupting,

8 Mr. Nicholas.   Since I don't have that in front of me,

9 could we name the person being described at the AVMA?

10   THE WITNESS: Lyle Vogle.   And then Paula

11 Fedorka-Cray, from the ~~FDA~~ *USDA*.

12   BY MR. NICHOLAS:

13   Q   And are there other people, to your knowledge,

14 who were at that meeting whose names appear on the

15 participant list who are also not witnesses in this

16 matter, if you know?   Just tell us who they are.

17   A   There's my friend and colleague Kim Thompson

18 from Harvard University.   You just want folks who are

19 not witnesses?

20   Q   That's correct.

21   A   Well, let me embarrass myself here.   There are

22 a fair number of names here I don't recognize as being

1   witnesses.

2   Q   Would you pick up exhibit -- tell me what

3   number is on there, please?

4   A   It's Exhibit G-1811.

5   Q   And you have there -- is the list of

6   participants included in that exhibit?

7   A   I still do not see a list of participants

8   here, no.

9   Q   Thank you, Dr. Cox. Now, Dr. Cox, Mr. Spiller

10 asked you about whether you provided advice to Dr. Vose

11 and whether you were paid as a consultant for that and

12 whether you provided advice to the FDA with respect to

13 risk assessment and whether you were paid with respect

14 to that, and then I believe he went on to question you

15 specifically about whether in your 1999 appearance

16 before the -- at the workshop on risk assessment hosted

17 by CVM and whether in your correspondence with Dr.

18 Vose, whether in those instances you had specifically

19 used the word dose response. And I'm referring now to

20 G-1810 and G-1809.

21   MR. SPILLER: Object to the form of the

22 question. I don't believe I asked about the

1   correspondence with Vose. I know that I did ask about

2   the transcript reflecting the December '99 meeting.

3   JUDGE DAVIDSON: That's my recollection.

4   That's all right. When he asked the question, you

5   brought up and said it referred to the question and he

6   said -- answering you out of position because he's not

7   supposed to talk to you, Mr. Spiller said your counsel

8   will take care of that on redirect.

9   But he only talked about 1810.

10   MR. NICHOLAS: I'm sorry, your Honor. I stand

11   corrected. Dr. Cox did in fact, I believe, respond to

12   G-1809, the correspondence, as well, and I'd like to

13   give the witness copies of G-1809 and G-1810, unless he

14   has copies there.

15   THE WITNESS: I have a copy of G-1810, but not

16   G-1809.

17   BY MR. NICHOLAS:

18   Q   Now, Dr. Cox, would you review those, and is

19   it true that you did not use the term "dose response"

20   in either of those documents?

21   A   Based on a quick review, I think I did not use

22   the words, although I did use the concept.

1   Q   And could you explain why you did not use the

2   words?

3   JUDGE DAVIDSON: I think he's already done

4   that.

5   THE WITNESS: Well --

6   JUDGE DAVIDSON: Excuse me.   He was asked the

7   same question by Mr. Spiller and he said I didn't use

8   the words, but what I said was the same as using the

9   words.   He went into great detail about which portion

10   of which word and he said -- I forget the exact word he

11   said, but in even reading the quote, he said something

12   to the effect "that means."

13   If you're going to add something to that,

14   that's fine.   If you're going to have him repeat it, I

15   don't want to hear it.

16   MR. NICHOLAS: No, your Honor, my intent was

17   not to have him repeat that.

18   JUDGE DAVIDSON: Okay.

19   MR. NICHOLAS: Thank you, your Honor.

20   BY MR. NICHOLAS:

21   Q   Dr. Cox, would you please explain why you did

22   not use those words?

1   A   I will. I initially thought that the

2   assumption that I now like to call the big K

3   assumption, which is the human health risk, is directly

4   proportional to pounds of contaminated chicken

5   consumed. That originally sounded plausible to me, and

6   my colleague, David Vose, suggested that's how he was

7   looking at it based on his understanding of physics and

8   the situation or the physical situation.

9   And I later became very full of talk about the

10 dose response relation, because as I recommended to CVM

11 in a 1999 document, the G-1810, I went to try to

12 validate the assumption that the big K framework is

13 essentially correct -- not correct in every detail, but

14 the basic, risk, increases in proportion to exposure.

15   And I quickly found out, as soon as I got some

16 real data, that that big assumption -- what I called

17 the big assumption or the key assumption, excuse me --

18 it just doesn't fit the data.

19   So then I thought, well, why not? I mean,

20 intuitively, what is it that we're missing? Then I

21 started to talk to CVM and anyone who would listen

22 about microbial load, dose response, the fact that

1   people who have exceptionally high exposures, the

2   people with exceptionally high microbial loads in their

3   food, those are the ones who are getting sick.

4   And that's when I started to say things like

5   the average has got nothing to do with it. We've got

6   to look at dose response. And at that time, I began to

7   use dose response very explicitly, because this comes

8   down to a dose response and microbial load exposure

9   issue and I didn't understand that back in 1999, so I

10   only raised it in a theoretical possibility and went on

11   record to say that I expected that when CVM validated

12   it, it would find that it was no big deal.

13   I was very much mistaken in that.

14   Q   I believe I'm correct that when Mr. Spiller

15   was questioning you he made -- a fair number of times

16   he emphasized your final risk assessment, your final

17   report, document A-17. And then he went to some length

18   to ask you questions about it and whether it accurately

19   portrayed various aspects of the risk assessment,

20   whether some exceptions were explicit or implicit and

21   whether you had various qualifications.

22   Can you tell us what this document represents,

1   whether it was your final -- I believe you testified it

2   wasn't your final risk assessment, but could you

3   explain what this document is and whether it evolved or

4   not?

5   MR. SPILLER: Object to the question. It's

6   already been asked and answered.

7   JUDGE DAVIDSON: The witness has already

8   explained it was not his final. He said what it was.

9   I mean, the last time I gave you an opportunity to put

10 something on the record that you hadn't put on before,

11 you went way beyond the scope of the questioning on

12 cross and I don't want that to happen again.

13   MR. NICHOLAS: Yes, your Honor.

14   JUDGE DAVIDSON: In other words, he's already

15 explained it's not his final, that it was -- he

16 explained what it was.

17   MR. NICHOLAS: Your Honor, if I may, I'm

18 asking him to explain the evolution of this because the

19 way it was presented is even though it's not his final,

20 he was questioned about the details of this and this is

21 an early document and I think it's important for him to

22 be able to explain how this document evolved into

Corrected as per OR 46 6/13/03

1 something that --

2   JUDGE DAVIDSON: I'm sorry. I sustain the

3 objection. It's been asked and answered.

4   BY MR. NICHOLAS:

5   Q Dr. Cox, did you confirm the models other than

6 this model?

7   A Yes, I did. As I tested different

8 assumptions, and sought to validate modeling functions

9 that seemed reasonable to me initially, I found that

10 several didn't fit the data and needed to be changed.

11   So, for example, it's not just the big K

12 framework, but I eventually noticed that the

13 attributable number of cases formula was the wrong

14 formula. It actually doesn't calculate anything that's

15 useful for ~~predictable~~ *predicting* attributable number of cases.

16 So that led to a revision in my model formulas.

17   I noticed that ruling and appendix

18 inappropriately overwrote the data with prior opinion,

19 that a certain fraction could be .5 even though the

20 data set was .06 and that that was done over and over

21 again. And so I published a series of corrections and

22 versions of the model as I came to understand better

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

1   the limitations in the initial model.

2   Q   Have your further models been published?

3   A   They have. Not all of them -- one of them

4   went through a review process at the Society of Risk

5   Analysis and was presented with a Best Paper Award last

6   December. The process now moves into a journal review,

7   and that takes a while. It has not yet been published.

8   Q   And during the course of your various

9   revisions, did you have discussions with CVM, with CDC,

10   with other parties, or was this something you did

11   totally private?

12   A   I had initially some discussions with CVM. We

13   had a lot of casual conversations about we should get

14   together for a day and really take a look at the data

15   and try to work things out and come to a shared

16   understanding.

17   And once David and I got together for at least

18   part of the day, I think, under the joint auspices of

19   AHI and CVM. But then CVM pretty much stopped

20   responding, and then I started drafting comments and

21   sending those in and never got any response to those.

22   So for a while, yes, but no.

1   Q   Have you attempted to validate your model?

2   A   I have.

3   Q   And can you tell us what efforts you took to

4   validate your model and the results, please?

5   MR. SPILLER: Object. Not within the scope of

6   the cross.

7   JUDGE DAVIDSON: You're going beyond the cross

8   examination. Sustained.

9   BY MR. NICHOLAS:

10   Q   Let me turn now to page 30 of your testimony.

11   I believe yesterday with respect to bullet 2 on page 30

12   of B-1901, Mr. Spiller questioned you fairly

13   extensively on some of the references there, Effler,

14   Kassenborg and so forth and so on.

15   And I believe he was trying to draw a

16   distinction between what the papers said and what your

17   conclusions were. Did you rely on anything else in

18   reaching your conclusions with respect to this

19   paragraph, this bullet point?

20   A   The major conclusion in this paragraph is

21   restaurant dining that we spent so long on yesterday.

22   Yes. As stated here -- actually all it states is it's

1   consistent with. What I relied on was the raw data.

2   What I primarily relied on for my understanding is

3   analysis of the raw data of Effler and the individual

4   -- I'll just call it raw data -- the individual level

5   data from the CDC case control study, which I think is

6   the best source, that also underlies Kassenborg here.

7   Then I did go to the literature including

8   these sources and I looked to see -- well, look, if

9   it's a restaurant problem and not a chicken problem,

10   what are other people finding. And as I -- perhaps we

11   adequately covered yesterday, there are papers such as

12   that of Rodriguez which, if read in their entirety,

13   fairly show that other people are thinking along the

14   lines of the same things.

15   But I relied on the raw data and on my

16   analysis of that data as the primary basis for my

17   conclusion.

18   Q   Just so there's no confusion, when you say you

19   relied on the raw data, could you please explain what

20   you mean?

21   A   Well, that means I like to use an analytic

22   approach. Suppose we don't know anything about what

1   causes what? Suppose we don't know anything about

2   model form, whether it's exposure is proportional to

3   risk or something else? Is there some way to let the

4   data itself speak?

5   And there is such a way. There is a body of

6   methods known as non-parametric methods. I applied

7   these standard techniques in packages such as SAS that

8   anybody else can run, they're very verifiable, they're

9   very objective. And I used them to test certain

10 hypotheses.

11   Ones that are most interesting to me are what

12 causal hypotheses are consistent with the data? For

13 example, is the causal hypothesis that there are excess

14 days of diarrhea from Fluoroquinolone resistance? Is

15 that something that we can test with the data? And for

16 some data sets, for example, the CDC data set which is

17 a great data set, the answer is yes.

18   So in general, I rely on the raw data and then

19 I rely on canned statistical packages or commercial

20 packages that run analyses. And in the ideal world, I

21 just dump in the data, push the button and say what

22 does it show.

1   JUDGE DAVIDSON: And you got that from the

2   question of what data you relied on? That's the answer

3   to that?

4   THE WITNESS: No --

5   JUDGE DAVIDSON: Well, that's my problem with

6   you, Doctor. You -- the question was would you

7   describe what data you relied on, and you went on to a

8   lot of other things which may or may not be

9   interesting.

10   When you said that you relied on the data,

11   what did you mean?

12   THE WITNESS: I thought that was the question,

13   yes, and I assumed that question mean --

14   JUDGE DAVIDSON: Well, I would like to hear

15   what data you relied on as opposed to, you know, how

16   you went about it and all the other ramifications,

17   because I've got you -- you've referenced publications.

18   THE WITNESS: Now --

19   JUDGE DAVIDSON: Now, the publications I see,

20   some of it has a lot of data in it, some of it has very

21   little data in it. It makes it difficult for me to see

22   what you're talking about.

1   THE WITNESS: Your Honor, I apologize for

2   being not clear. To me, none of the publications we've

3   talked about has any data.

4   JUDGE DAVIDSON: Okay. So then you went

5   behind that?

6   THE WITNESS: Yes.

7   JUDGE DAVIDSON: In each one of those

8   publications and you looked at the raw data. How did

9   you get it?

10   THE WITNESS: Only three. I looked at the raw

11   data for the CDC publications, which are actually more

12   than three, the Friedman publication, Kassenborg --

13   JUDGE DAVIDSON: I'm talking about the

Rodrigues

14   ~~Rodriguez~~, the --

15   THE WITNESS: There I got the Effler raw data.

16   I originally sent an e-mail and asked for it, and he

17   wouldn't give it to me, and then it was gotten for me I

18   think under Freedom of Information.

19   So I got the Effler data. I got the Smith

20   data. And those three data sets are the primary basis

21   that I --

22   JUDGE DAVIDSON: That's what I wanted to hear.

1 Okay.

2   THE WITNESS: Okay.

3   JUDGE DAVIDSON: Proceed.

4   MR. NICHOLAS: Thank you.

5   BY MR. NICHOLAS:

6   Q   Now, there was a fair amount of questioning

7 this afternoon about a dose response model. Do you

8 believe that your risk assessment accurately portrays

9 the incorporation of appropriate dose response modeling

10 and have you validated that? And by risk assessment,

11 we can start with your 2001 draft report, A-17, and to

12 your latest risk assessment of the publication that I

13 believe you referenced as B-1262.

14   MR. SPILLER: Objection. Beyond the scope of

15 cross.

16   JUDGE DAVIDSON: You're asking him for an

17 awful lot of material just on the basis of the fact I

18 believe you were questioned about dose response. If

19 you're going to ask him questions to explain his

20 answers on cross, I'd be glad to let you do that but

21 you're giving him a platform for another 20-minute

22 lecture and I don't want that.

1   MR. NICHOLAS: Your Honor, that wasn't the

2   intent --

3   JUDGE DAVIDSON: I know that, but that would

4   be the result when you ask a question that has that

5   many things in it.

6   MR. NICHOLAS: Well, Mr. Spiller spent the

7   better part of an hour, I believe, asking Dr. Cox about

8   dose response.

9   JUDGE DAVIDSON: I understand.

10   MR. NICHOLAS: And I'm trying to narrow this

11   down, your Honor.

12   JUDGE DAVIDSON: Well, narrow it, otherwise

13   it's going to go all over the place.

14   BY MR. NICHOLAS:

15   Q   Dr. Cox, on page 29 -- I'm sorry -- on page 37

16   of B-1901, which is your testimony, Mr. Spiller asked

17   you a number of questions about the -- what I would

18   call a graph that appears on that page under the title

19   linear regression, et cetera, et cetera. Do you see

20   that?

21   A   Yes.

22   Q   Is there anything -- do you believe that this

1   is still an accurate presentation with respect to the

2   issues discussed on this subject -- under this title?

3   A   I do.

4   JUDGE DAVIDSON: That's enough. You already

5   said that before on cross.

6   BY MR. NICHOLAS:

7   Q   How does your final model deal with dose

8   response?

9   MR. SPILLER: Objection, your Honor. I

10 believe that's beyond the scope. I don't think we ever

11 got into the final model, although we dealt with the

12 models that we had in the testimony.

13   JUDGE DAVIDSON: My recollection is the

14 witness referred to it himself but it wasn't part of

15 any of your questions, so I'll sustain the objection.

16   BY MR. NICHOLAS:

17   Q   Dr. Cox, could you explain how the model in

18 your textbook, B-1020, deals with dose response?

19   A   Yes. The issue of dose response modeling and

20 of uncertainty about the dose response relation was

21 dealt with explicitly there by saying we don't know

22 what the true dose response relation is. Can we try a

1   bunch of different dose response models that are all

2   passing through the data, so the only thing they have

3   in common is they're consistent with the data; does

4   that change the results?

5   And that technique, called sensitivity

6   analysis, is what allowed me to reach robust

7   conclusions despite uncertainty about the details of

8   dose response model. And there's a fuller discussion,

9   of course, in that reference.

10   Q   Now, with respect to Exhibit A-17, which is a

11   -- referred to by Mr. Spiller as your final report

12   about two years ago, do you rely on that document for

13   your testimony?

14   A   No. No, I don't. My testimony is mainly

15   about the CVM model.

16   Q   And to the extent you're discussing your own

17   model in your testimony, do you rely on that -- on the

18   discussion in A-17?

19   A   No. As I've stated, that was an early model

20   before I understood that the attributable risk form was

21   wrong and that other things were wrong. So I do not

22   rely on that.

1   Q   How critical -- I'm sorry. Strike that. And

2   I believe you testified that you had attempted to

3   validate the CVM model?

4   A   Yes, I tried to fit key assumptions to the

5   data, yes.

6   Q   And can you tell us briefly how you tried to

7   do that and what the results were?

8   A   Yes. I obtained three what I refer to as raw

9   data sets, the three I referred to a few minutes ago,

10 so the CDC case ~~controlled~~ *Control* data, the Smith data and the

11 Effler data. And first thing I noticed is that those

12 sources raised the apparent anomaly of chicken

13 consumption at home being associated with reduction in

14 risk and chicken consumption in restaurants no.

15   So that made me think well, big K -- there

16 probably needs to be more than one K in there and the

17 algebraic form that risk is proportional to exposure

18 can't be right for all the different groups that were

19 exposed. It certainly can't be right for groups who

20 were exposed at home.

21   So then I set out to say, okay, that big

22 simplifying assumption isn't right, what can we do

1 instead. And I used a non-parametric method based on

2 what's called causal graph analysis to figure out how

3 different factors relate to each other and how to back

4 out confounding effects.

5 Finally, I adjusted for non-causal relations

6 between exposure and risk. What I mean by that is just

7 the point that males, for example, turn out to be --

8 whether or not they eat chicken, they're at greater

9 risk of campylobacteriosis than females, so that you

10 might want to have a different K for males and females.

11 What I did was to form an analysis that said

12 is this a direct causal -- is the data consistent with

13 this being a direct causal relation or is it just

14 because males eat out in restaurants more often.

15 And one can objectively discriminate between

16 those alternative causal hypotheses that being male is

17 a direct driver of susceptibility versus being male is

18 an indirect driver because it means you're more likely

19 to have insurance coverage, eat out in restaurants and

20 so forth.

21 So applying those standard techniques I was

22 able to determine what was causal and what was not

1   within the ability of the data to resolve. And that's

2   the basis for my published opinions and also for my

3   testimony.

4   Q   Now, if I recall correctly, Mr. Spiller asked

5   if your opinion that the use of Baytril provides 25

6   more cases than it might caused was based on your model

7   and I believe you said there is a much simpler way to

8   get to these. What did you mean when you said that?

9   A   I said it was based in part on my model but

10   the basic facts -- the basic -- here's what's going on.

11   If you use Baytril, you reduce the incidence of

12   ~~Erisycolitis~~ *air sacculitis* in chicken flocks. ~~Erisycolitis~~ *air sacculitis* is a

13   condition that leads to underweight chickens.

14   Underweight chickens, when they show up at

15   processing plants, are out of tolerance for the

16   machines there and they spray fecal matter here and

17   there and the net result is the consumers see more

18   microbial load coming at them.

19   Because I developed a model that tracks

20   microbial loads on chickens I was able to quantify what

21   is the expected health impact of the additional

22   contamination that could be caused by the loss of

1   Baytril.   So that was the -- that's the argument

2   without the model.   The model then adds number around

3   that, and the essence of it is just to realize high

4   microbial loads are the source of risk and ~~Erisycolitis~~ *air sacculitis*

5   chickens have high microbial loads.

6   Q   So you did not rely on A-17 for your opinion?

7   A   No.   A-17 was just an old -- that's just the

8   starting point.

9   Q   Dr. Cox, I don't want to mischaracterize Mr.

10 Spiller's question, but if I were to sum it up, I would

11 say that in terms of the questions Mr. Spiller has

12 tried to question you and create the impression that

13 you are the only one who has this opinion and that

14 somehow your opinion is at odds with the community, and

15 I believe yesterday he asked you about today's

16 standards, could you please tell me whether you believe

17 that your opinion is outside the mainstream on risk

18 assessment in this issue?

19   MR. SPILLER: Object to the form of the

20 question as it incorporates counsel's characterization.

21 It sounds like the actual question may have been the

22 last part.

1   JUDGE DAVIDSON: Sustained.   Do you want to

2 ask it again?

3   MR. NICHOLAS: I will, your Honor.   Thank you.

4   JUDGE DAVIDSON: And I'm cautioning the

5 witness not to repeat what you've already said on the

6 record.   I recall one of the first questions that was

7 asked you.   This is -- along the vein of this is Cox as

8 opposed to the world and you explained that that wasn't

9 the case, there are other people who hold it, so I

10 don't want hear the same thing over again.

11   THE WITNESS: Got you.   Thank you, your Honor.

12   BY MR. NICHOLAS:

13   Q   Dr. Cox, do you believe your opinion is

14 outside the mainstream of people who have looked at

15 this issue and looked at risk assessment with respect

16 to the question of whether the use of Baytril or

17 antibiotics in veterinary medicine has an impact on

18 human health?

19   A   Being mindful of his Honor's direction, I'll

20 answer that I believe the mainstream is becoming

21 redefined.   I think that five years ago and ten years

22 ago, common knowledge in the mainstream -- common

1   belief was that chicken was the primary source.

2   Now I look at papers like Rosenquist's. I

3   look at the ~~Rodrigues~~ Rodrigues paper and other papers from the

4   United Kingdom, where I see a lot of support. People

5   are ~~saying it~~ saying: "it doesn't seem to be chickens, what could

6   it ~~be;~~ be? why didn't things go down when we got rid of a

7   ~~drug.~~ drug?

8   So no, I don't think that my opinion is

9   outside the changing paradigm of what would be

10 mainstream.

11   Q   I believe, as well, you were questioned about

12 restaurant dining, and the question was whether it

13 isn't the chicken in the restaurant that's causing

14 campylobacteriosis.

15   Do you believe it's chicken in the restaurant

16 that's causing campylobacteriosis?

17   A   I like to derive all of my assertions off of

18 data. In the data, I do not see evidence for that

19 hypothesis, and I do see evidence against it. Also,

20 once I've done my own analysis, I like to look at what

21 other people have said and here, the ~~Rodriguez~~ Rodrigues and

22 other papers explicitly address that issue and the big

1 thing is it doesn't look like it could be chickens

2 because those same chickens, by and large, go home and

3 people roll around in them, basically. I mean, there's

4 chicken juice, raw chickens.

5   No, I don't -- based on that evidence and

6 based on the literature, no, I don't think that it's

7 really chickens that are doing it.

8   MR. NICHOLAS: Thank you. I have no further

9 questions, your Honor.

10   JUDGE DAVIDSON: Recross?

11   MR. SPILLER: Yes, your Honor, very few.

12   RECROSS EXAMINATION

13   BY MR. SPILLER:

14   Q   The last question might be freshest in your

15 mind, Dr. Cox. I understand you don't believe it's

16 chicken in the restaurant. Do you believe it's

17 campylobacter in the restaurant?

18   A   That --

19   Q   Causes campylobacteriosis in the humans who

20 dine there.

21   A   Again, I hate to get out in front of the data

22 but yes, campylobacteriosis causes campylobacter -- or

1   the other way around.   Excuse me.   Wrong way.

2   Q   And apart from chicken, in this record, in

3   your testimony, how do you suppose the campylobacter

4   got into the restaurant?

5   A   Did you say we could include all the stuff

6   like drinking water -- I'm sorry -- ground water or

7   streams contaminated, so forth?

8   JUDGE DAVIDSON: He just asked you what you

9   got.

10   THE WITNESS: Thank you.   First, I haven't

11 found any useful data to study it, but water on

12 lettuce, the hands of the restaurant workers, as we've

13 seen in some outbreak studies, non-poultry meats and

14 vegetables.   If you go to a salad bar you'll find

15 campylobacter.

16   The key question for me is always do you get

17 enough of it to cause illness with high probability,

18 and I think the consensus now is well, once in a while

19 you do, whether it's people shedding, what it is I

20 don't think can be unambiguously identified from the

21 data, but it doesn't look like chicken is the primary

22 or predominant source.

1   BY MR. SPILLER:

2   Q   And you mentioned in that answer do you get

3   enough of it.   I believe on redirect you indicated it

4   was the exceptionally high loads that are the ones that

5   cause people to get sick.

6   A   Disproportionately so, yes.

7   Q   In this record, thinking of the one person who

8   got the lowest known dose tested in this record, did he

9   get sick?

10   A   Are you referring to Robinson?

11   Q   I'm referring to Dr. Robinson.

12   A   The lowest reported infectious level of which

13   I'm aware is Robinson's.

14   Q   And did he get sick?

15   A   He did.

16   Q   Was that an exceptionally high dose?

17   A   500 CFUs, compared to what most people get?   I

18   think it's many times the average.

19   Q   You mentioned also that you preferred to use a

20   causal analysis and you have some causal anal -- I

21   think you said causal graphic analysis --

22   A   Causal graph analysis.

1   Q   Causal graph analysis. Is that exemplified,

2   for instance, in Exhibit G-1811 that you still have up

3   there?

4   A   Can you tell me which G-1811 it is?

5   Q   That's the International Journal of Infectious

6   Diseases.

7   A   You know, I don't -- can you --

8   Q   I think your counsel left the copy for you.

9   He certainly asked you questions about it.

10   A   Hold on. I'm getting buried here. Okay. I

11   found the paper.

12   Q   So if you look, for instance, at page 3S30 of

13   that, is that a causal graph analysis?

14   A   This is a -- you mean the figure, right?

15   Q   I mean figure 3.

16   A   Thank you. No. This is a classification tree

17   that reveals what are called conditional independence

18   relations. Conditional independence just means, look,

19   if you see people going into restaurants and getting

20   sick, is it because they went into the restaurants or

21   is it because males go into restaurants and males get

22   sick?

1   If going into restaurants is conditionally

2   independent of getting sick, given that ~~your~~ *you're* male --

3   meaning males get sick at the same rate whether or not

4   they go into restaurants, then we can say no, the data

5   aren't really consistent with it being the restaurant.

6   So this kind of tree looks for conditional

7   independence relations. It's very useful for saying

8   are people getting excess days of diarrhea because of

9   Fluoroquinolone resistance and the answer is very

10 strongly no. But this would then get assembled into a

11 causal graph model along the lines outlined in my book.

12   Q   And these trees are grown using the commercial

13 software that you described in your redirect, right?

14   A   These trees were prepared using something

15 called Knowledge Seeker which is commercial software.

16 What I described in my redirect, I referred to SAS, S-

17 Plus. The distinction between these is that the ideal

18 form of analysis is the SAS analysis where you pour the

19 data in, push a button, get the result.

20   In Knowledge Seeker, there's some flexibility

21 about the order in which the factors are listed so

22 there's -- it doesn't happen to be one of the ones that

1   I mentioned but it is a commercial package useful for

2   getting at conditional independence relations as a

3   prelude to causal analysis.

4   Q   And referring to figure 4 in that paper, in

5   this commercial software generated document, am I

6   correct that in the grid analysis there the multiple

7   question marks mean missing data?

8   A   Missing data, no answer, yes.

9   Q   Was it the machine or you who determined at

10   each level of the classification whether to put the

11   unsures or the no answers with the yeses or the nos?

12   A   The machine.

13   Q   And sometimes the machine puts the unsures

14   with the yeses and sometimes it puts the no answers

15   with the nos?

16   A   That's correct. It tries to ask the most

17   informative questions at each stage. Oh. And a key

18   correction to the testimony I just gave is that at the

19   bottom level of these trees, on the right-hand side you

20   see there's a variable called eight chick. This is a

21   reanalysis of the Smith, et al data set. "~~Eight~~ *Ate* chick",

22   as explained in the text, does not enter into the tree

1   by itself.

2   What that means is there's no statistical

3   association between recently eating chicken and

4   Fluoroquinolone resistance. Therefore, I forced that

5   variable in and that would be an exception. I said no,

6   yes and other. That was my choice, not the machine's

7   choice.

8   Q   So you can force this classification tree

9   analysis.

10   A   You can force -- you can split on a variable.

11 You can't force non-significant variables to come into

12 the tree analysis but you can take any one variable.

13   Q   And in your figure 3 in that paper, the very

14 top item, the first branch in the classification tree

15 is Vis Farm, that's for whether or not the person

16 visited a farm?

17   A   I think recent farm visit was the longer name

18 of that variable, yes.

19   Q   And is the reason that that variable came off

20 first because you got a very strong signal between the

21 cases and controls, 99 and a half percent versus a half

22 a percent?

1   A   Let's see. Why this came out -- the answer

2 may be yes but the salient point is I let these

3 identified risk factors take themselves out of the

4 analysis. They all showed up as lick and splits. I

5 didn't want to analyze cases where we thought we knew

6 what the explanation was going to be.

7   So as explained in more detail in the article,

8 you'll see we take out foreign travel. I took out pet

9 08, which is having a puppy. Drinking boiled water.

10 And this gets us down to sex. Not the end of the tree

11 but the beginning of the expanded tree.

12   Now we get into stuff that I'm not just taking

13 out. So, for example, if sex is really relevant, it

14 makes a difference between 44 percent and the -- this

15 is now autodiscovery, if you will.

16   Q   And confining your answer, if you will, to my

17 question, in the top classification, "vis farm," you got

18 a very strong signal between the cases in the controls

19 there. They split 99 and a half percent one way and a

20 half a percent the other, didn't you?

21   A   On the right-most branch.

22   Q   Yes.

1   A   Yes.

2   Q   And tell the record why we pulled out 211

3 cases for that.

4   A   For two reasons. The first I've alluded to,

5 which is I didn't want to look at things where visiting

6 a farm or foreign travel, both of these might be the

7 issue. And secondly, because we didn't have data on

8 those people. 7 is the code for not applicable or

9 didn't answer. Question mark is the default code for

10 missing data.

11   Q   Did it not seem remarkable to you as a

12 professional analyst of data that not having data would

13 so strongly be correlated with the distinction between

14 cases and controls? Why would cases versus controls be

15 lacking data?

16   A   Oh. This gets back to the fact that it's

17 survey data. You have a bunch of recall biases, people

18 are more willing to think about 101 chicken questions

19 under some conditions, like they're -- you plant the

20 idea it's chicken that's the problem, they may be more

21 willing to put up with a long questionnaire. And I see

22 this kind of thing in data from telephone companies and

1   -- it's not all initial.

2   Q   Do you know, Dr. Cox, whether that elimination

3   was actually based on whether they were a secondary or

4   a primary case in the family?

5   A   No.

6   Q   So you don't actually know why your commercial

7   software no human hands-on classification tree lost out

8   on 211 of the data points in the study?

9   A   Well, I know that I sent out the visit farm

10   cases or allowed to select themselves out -- the visit

11   farm cases and I stuck with the 1,104 who said no, I've

12   not visited a farm. I'm trying to eliminate competing

13   explanations.

14   Q   Dr. Cox, you mentioned on redirect your recent

15   model was not yet published, it was in the peer review

16   process?

17   A   That's correct.

18   Q   And I think you mentioned that one of those

19   papers that's in review was currently -- had won you a

20   best paper award from SRA.

21   A   Yes, it did.

22   Q   Congratulations.

1   A   Thank you.

2   Q   What peer review process is involved in the

3 choice of who gets the best paper award at the Society

4 for Risk Analysis?

5   A   I don't know the details. The chair of the

6 committee is also the president of the Society and

7 there's a ladder where you start off just submitting

8 abstracts, maybe 600, a thousand -- some large number

9 of abstracts are submitted. And then the committee

10 says well, this looks interesting. Can you draft three

11 or five pages, which is kind of the second round.

12   And based on those so-called extended

13 abstracts, you may then be invited to submit a whole

14 paper. That's the -- now you're getting close to the

15 end of the process.

16   Then those who are I believe officers of the

17 Society -- the high and mighty of the Society for Risk

18 Analysis then ultimately winnow down perhaps 350 fully

19 developed abstracts to last year 7 finalists and then

20 they notify you of that.

21   Personally I wouldn't consider that a peer

22 review. I mean, yeah, your peers look at it, but

1   that's the prelude to then submission and peer review.

2   So that's what I know of the process.

3   Q   Thank you, and I appreciate the answer there

4   at the end.

5   MR. SPILLER: Your Honor, I have no further

6   questions on recess.

7   JUDGE DAVIDSON: Mr. Nicholas, do you need

8   anything else?

9   MR. NICHOLAS: No further questions, your

10 Honor.

11   JUDGE DAVIDSON: You're excused, Dr. Cox.

12   THE WITNESS: Thank you.

13   (The witness was excused.)

14   JUDGE DAVIDSON: Ms. Steinberg, what have you

15 got for me?

16   MS. STEINBERG: Yes, your Honor. During the

17 lunch break I did look at the documents that you asked

18 about and I do have an answer. I believe that all the

19 documents are different. The one that might be the

20 same is G-1806 and B-1946. For clarity I would ask

21 that all of this be put in the record and marked with

22 exhibit numbers.

1   JUDGE DAVIDSON: Okay. I had asked Ms.

2 Steinberg to check because my records show that 1806,

3 1807, and 1808 that I had ruled out and then when you

4 put in 1946 and 47, I let them in. I figured it should

5 all be in or it should all be out. I didn't think that

6 -- because they're somewhat the same, they're slightly

7 different.

8   They all deal with the same issue. I didn't

9 think it qualified as evidence, to tell you the truth.

10 I think they should all be out. But you moved 1946 and

11 47 into the record to offset stuff that I didn't put

12 into the evidentiary record. This is dealing with his

13 qualifications, with his degrees, with the letters from

14 the --

15   MR. NICHOLAS: Your Honor --

16   JUDGE DAVIDSON: I understand what happened.

17 It's not your fault. So I still say I'd just as soon

18 not have them in but if you want them in, I'll leave

19 them all in.

20   MR. NICHOLAS: We're happy to just withdraw

21 those.

22   JUDGE DAVIDSON: Okay. So none of them will

1   be in the evidentiary record.

2   (Respondent Exhibits 1946 and

3   1947 were withdrawn.)

4   JUDGE DAVIDSON: Now, we have 1936. I don't

5   think I've ruled on that. B-1936. Looks like a one-

6   page document dealing with PubMed Chemotherapy Agents

7   campylobacter.

8   MR. NICHOLAS: That's the Hollander article,

9   your Honor. It's an abstract with respect to --

10   JUDGE DAVIDSON: Right. Abstract. I just

11   want to clean up my paper here.

12   MR. SPILLER: Could we see it, your Honor? In

13   our confusion, we don't have a collective recollection

14   of what it is.

15   JUDGE DAVIDSON: You don't remember it?

16   MS. STEINBERG: No objection, your Honor.

17   JUDGE DAVIDSON: Okay. B-1936 is received.

18   (Respondent Exhibit 1936 was

19   marked for identification and

20   received in evidence.)

21   JUDGE DAVIDSON: Now, I have G-1809, 1811,

22   1816 and 1817, which were introduced by the CVM during

1   the cross-examination of Dr. Cox.

2   I don't even think -- I don't know if you

3   moved them into evidence or you just want to leave them

4   there.

5   It's okay with me, whatever you choose.

6   MR. SPILLER: Your Honor, 1811 is the

7   International Journal of Infectious Diseases and if I

8   did not previously make explicit, we do not need this

9   as an exhibit, your Honor. If it can be subject to

10 discussion, that's fine. If counsel needs it for

11 clarification --

12   MR. NICHOLAS: Your Honor, we would like to

13 have that in the record, provided we could use the

14 full-blown report. I believe parts of this report are

15 already in the record, your Honor, but since the

16 issue --

17   JUDGE DAVIDSON: Well, we handled the page

18 with the names on it already. He read the ones in the

19 record.

20   Is there something else in there you think is

21 missing?

22   MR. NICHOLAS: I believe all the rest of the

1   papers that are discussed in here are in the record,

2   your Honor.

3   I don't believe there are discussions with

4   respect to --

5   JUDGE DAVIDSON: I'm sorry; what discussion?

6   MR. NICHOLAS: These are the proceedings

7   that --

8   JUDGE DAVIDSON: I understand what they are --

9   MR. NICHOLAS: And the proceedings contained

10 both authored papers as well as discussion.

11   JUDGE DAVIDSON: And the discussions, you say,

12 are not here?

13   MR. NICHOLAS: I don't believe so, your Honor.

14   JUDGE DAVIDSON: I'm not trying to say you're

15 wrong, but there's a section entitled "discussion." Is

16 that not the same thing?

17   Well, it won't be received in evidence and if

18 you think it's important to get the whole thing in, you

19 can try again. But as I said before, it's got to end

20 sometime. So 1911 is not received in evidence. Excuse

21 me, G-1811.

22   MR. SPILLER: And your Honor, G-1816 is the

1   Robinson study. If I did not previously, I now move G-

2   1816 in evidence.

3   JUDGE DAVIDSON: Any objection?

4   MR. NICHOLAS: No, your Honor.

5   JUDGE DAVIDSON: It's received in evidence,

6   1816.

7   (Government Exhibit 1816 was

8   marked for identification and

9   received in evidence.)

10   JUDGE DAVIDSON: Now 1817.

11   MR. SPILLER: 1817 is a copy of a portion of a

12 Rosner textbook and includes the disputed definition of

13 the central limit theorem, I believe, and if I did not

14 previously, I do now move 1817 in evidence.

15   MR. NICHOLAS: We have no objection, your

16 Honor.

17   JUDGE DAVIDSON: All right. 1817 is received

18 in evidence.

19   (Government Exhibit 1817 was

20   marked for identification and

21   received in evidence.)

22   MR. SPILLER: Your Honor, I believe the last

1 one on the list is G-1809, which is the collection of

2 e-mail correspondence between the witness, Dr. Cox, and

3 Mr. David Vose, which has been discussed at several

4 points both in cross and on redirect. And if I did not

5 previously, I do now move that exhibit in evidence.

6   MR. NICHOLAS: We have no objection.

7   JUDGE DAVIDSON: Okay. It's received in

8 evidence.

9   (Government Exhibit 1809 was received

10   in evidence.)

11   JUDGE DAVIDSON: Any others I missed? I hope

12 not.

13   MR. NICHOLAS: No, your Honor.

14   JUDGE DAVIDSON: Okay. You can sit down, Dr.

15 Cox. Find a chair.

16   Okay. I think we're finished. We just have

17 to take care of some minor things like transcripts.

18 Does anybody know how long it's going to take to get

19 the transcript?

20   THE COURT REPORTER: I don't know.

21   JUDGE DAVIDSON: Okay. I just wanted to know

22 if either of the parties had contacted your agency to