EXHIBIT 46

IN THE UNITED STATES DISTRICT COURT
FOR THE MIDDLE DISTRICT OF FLORIDA
ORLANDO DIVISION

MDL DOCKET NUMBER: 1769

IN RE: SEROQUEL PRODUCTS LIABILITY
LITIGATION

DEPOSITION OF:
DONNA K. ARNETT, M.S.P.H
VOLUME II
**** HIGHLY CONFIDENTIAL ****

S T I P U L A T I O N S

IT IS STIPULATED AND AGREED, by and between the parties through their respective counsel, that the deposition of:

DONNA ARNETT, M.S.P.H.

may be taken before Lisa Bailey, Notary Public, State at Large, at University of Alabama at Birmingham, 1655 University Boulevard, Birmingham, Alabama, on October 7, 2008 commencing at approximately 8:30 a.m.

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1 **in Table A2 when you look at diabetes and you look**
2 **at quetiapine and placebo? And you can use the**
3 **calculator.**
4 A. So you want the relative risk?
5 **Q. Yes.**
6 A. Can I borrow your pen? The relative
7 risk, also known as the risk ratio, is 2.02.
8 **Q. If you look at page 10 of your report,**
9 **the top paragraph, you see the FDA analyzed all of**
10 **Study 126 and 127. Your conclusion at the bottom**
11 **says, "Not unexpectedly given these differences in**
12 **glucose and insulin resistance, the risk for**
13 **diabetes was 2.02"?**
14 A. Yes.
15 **Q. And the source for that is that table,**
16 **isn't it, Doctor? And by "that table," the table**
17 **we just marked and you just analyzed, Exhibit 24.**
18 A. Yes.
19 **Q. Now, that's not a relative risk that's**
20 **based on incidence density, is it?**
21 A. No. It's the number of events.
22 **Q. If you look at incidence density instead**
23 **of number of events, what is the relative risk when**
24 **you look at quetiapine versus placebo in Table A2?**
25 **Did you calculate it, Doctor?**

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1 A. I'm still trying to understand where the
2 numbers from this table -- what they actually mean
3 when they say "density."
4 **Q. When you calculate the relative risk in**
5 **Table A2 of diabetes melitis and you look at**
6 **incidence density, .4 for quetiapine and .6 for**
7 **placebo, what is the relative risk, Doctor?**
8 A. For -- this does not make sense to me as
9 an epidemiologist. The rate ratio is almost
10 identical to the incidence -- cumulative incidence
11 ratio. But the incidence density ratio is .46
12 divided by -- .4 divided by .6.
13 **Q. And what is that?**
14 A Point --
15 MR. BLIZZARD: Are you just asking for
16 the mathematical calculation?
17 A. -- 67.
18 **Q. Doctor, the relative risk, if you look**
19 **at incidence density in Table A2 for diabetes**
20 **melitis when you look at quetiapine versus placebo,**
21 **.4 to .6 is a relative risk of .67, correct?**
22 A. Yes.
23 **Q. Now --**
24 A. But it's unusual -- I've never seen in
25 all of my 25 years of epidemiologic experience a

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1 rate ratio and an incidence density ratio come on
2 opposite sides of 1. So there's something I don't
3 understand about their calculation of density. So
4 I can't say with accuracy that that's a correct
5 ratio.
6 **Q. You can't say with accuracy that it's**
7 **not either --**
8 A. No.
9 **Q. -- because you haven't analyzed it,**
10 **right?**
11 A. I'd have to see how these are
12 calculated. It's fishy.
13 **Q. The opinion that you gave yesterday that**
14 **Seroquel is unsafe, do you remember that?**
15 A. Yes.
16 **Q. Your opinion that Seroquel is unsafe, is**
17 **that -- withdrawn.**
18 **Is it your opinion that the chemical**
19 **composition of Seroquel is defective?**
20 A. I cannot comment with expertise about
21 the chemical composition.
22 **Q. Is there a safer alternative design for**
23 **Seroquel that you think AstraZeneca should have**
24 **used?**
25 A. From the totality of the data with

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1 respect to weight and metabolic abnormalities,
2 we've discussed the comparator drug Haloperidol
3 appeared safer with those indices. So I can't
4 comment on what AstraZeneca should have created or
5 in contrast to Seroquel. But there are other
6 alternatives out there that are metabolically
7 safer.
8 **Q. Is it your opinion that, according to**
9 **you, because Seroquel has a greater weight of --**
10 **risk of weight and metabolic abnormalities compared**
11 **to Haloperidol, that, therefore, Seroquel is**
12 **unsafe?**
13 A. In the absence of having -- let me
14 rephrase that.
15 In light of the fact that there were
16 other drugs without those metabolic abnormalities
17 that could be used to treat psychoses, in that
18 respect, Seroquel was unsafe.
19 **Q. You haven't looked at any of the first-**
20 **generation antipsychotics or second-generation**
21 **antipsychotics to evaluate them for the risk of**
22 **metabolic abnormalities, have you, Doctor?**
23 A. With respect to the --
24 MR. BLIZZARD: Object to the form.
25 A. -- studies that I've evaluated, yes.

1 **Q. Doctor, I asked you whether or not**
2 **you've evaluated the risk of -- well, let's stick**
3 **with Haloperidol, for example.**
4 **Do you know for Haloperidol how that**
5 **compares to Seroquel with respect to the risk of**
6 **EPS?**
7 A. In the follow-up study from the CATIE
8 trial, it appears to be equivalent.
9 **Q. Is it your testimony that involved**
10 **Haldol?**
11 A. No.
12 **Q. Let me go back to my original question.**
13 **Is there a safer alternative design for Seroquel**
14 **that you claim AstraZeneca should have used?**
15 A. I don't -- I don't have an answer.
16 **Q. Did the vast majority of patients who**
17 **used Seroquel benefit from it?**
18 A. Could you be more specific by the term
19 "vast"?
20 **Q. Did the majority of the patients who**
21 **used Seroquel benefit from the medicine, ma'am?**
22 MR. BLIZZARD: Object to the form.
23 A. In my opinion, no. Because there were
24 such high dropout rates in all of the clinical
25 trials that I reviewed that it would indicate that

1 the vast majority had no benefit because they
2 dropped out.
3 **Q. Do you know how many patients have used**
4 **Seroquel since it's been brought to the market in**
5 **the U.S.?**
6 A. No.
7 **Q. Any idea what percentage of patients who**
8 **used it think it benefited and helped them?**
9 A. It's irrelevant in the aspect of the
10 question at hand regarding diabetes and metabolic
11 risk. Because in randomized clinical trials where
12 you're using a placebo control, you can evaluate
13 benefit versus harm better than observational
14 studies post marketing.
15 **Q. The FDA had all the information, Doctor,**
16 **to evaluate the risk of metabolic effects from**
17 **Seroquel when it approved Seroquel, did it not?**
18 A. I could not find all of the metabolic
19 risks that was in the FDA, so I can't answer for
20 the FDA. I couldn't find it.
21 **Q. Did the FDA conclude that the benefits**
22 **of Seroquel outweighed the risks when the drug was**
23 **brought to market?**
24 A. I'll make the assumption that they did.
25 I haven't reviewed their documentation.

1 **Q. Has the FDA repeatedly approved Seroquel**
2 **as safe and effective and that the benefits**
3 **outweigh the risks --**
4 MR. BLIZZARD: Object to the form.
5 **Q. -- since it's been brought on the**
6 **market?**
7 A. As I indicated earlier in my testimony,
8 I haven't extensively evaluated all of the FDA
9 documents with respect to Seroquel.
10 **Q. Do you know that Seroquel has been**
11 **approved for multiple indications since it's been**
12 **brought to the market in the United States?**
13 MR. BLIZZARD: Object to the form.
14 A. Yes.
15 **Q. And on each of those occasions, the FDA**
16 **concluded the benefits outweighed the risks,**
17 **correct?**
18 MR. BLIZZARD: Object to the form.
19 A. I can't define what the FDA decided.
20 **Q. You don't know what it means when the**
21 **FDA approves a medicine for an indication?**
22 A. Yes.
23 **Q. What does it mean?**
24 A. I'm making an assumption that it means
25 that -- actually, I'm not going to make any

1 assumptions.
2 **Q. So you don't know?**
3 A. I want to go and review their actual
4 criteria before I answer that question.
5 **Q. As you sit here today, you don't know**
6 **what it means when the FDA approves a medicine for**
7 **an indication?**
8 A. All I can do as a scientist is -- am I
9 bothering you by the way I'm answering your
10 question?
11 **Q. No. I'm asking do you know --**
12 A. You're just sighing and rolling your
13 eyes at me.
14 **Q. Doctor, I'm just asking you if you**
15 **know. You're answering and giving very long-winded**
16 **answers. And my question is very specific.**
17 MR. BLIZZARD: No, no, no. She was
18 giving an answer. Now you've used the
19 opportunity where she was asking you to please
20 stop rolling your eyes to formulate some new
21 question because you didn't like the answer
22 she was about to give. She's doing a very
23 good job of trying to be responsive to you.
24 BY MR. GOLDMAN:
25 **Q. Doctor, I'm only rolling my eyes because**