

# EXHIBIT 2

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

MDL DOCKET NUMBER: 1769

IN RE: SEROQUEL PRODUCTS LIABILITY  
LITIGATION

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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.

1           A.       Yes.  But you have to look at different  
2 levels of evidence.  So in evidence-based medicine,  
3 we evaluate different designs of studies to carry  
4 more weight than other designs.  So if your  
5 question is the totality of all data, the answer  
6 would be no, I would not look at the totality of  
7 all data.  I would look at the data with the best  
8 design that carries the most evidence.

9           Q.       Have you looked at the data that you  
10 consider to have the best design concerning  
11 Seroquel and diabetes?  That's a bad question.  
12 Withdrawn.

13                   In forming your opinions here,  
14 Dr. Arnett, did you look at all the relevant  
15 clinical trials for Seroquel and diabetes?

16           A.       To form my opinion, I looked at the  
17 studies in the NDA application, Studies 125, 126  
18 and 127 from the AstraZeneca Web site, and several  
19 other studies that were published in the Web site  
20 and are included in my report.

21           Q.       Am I right that the studies concerning  
22 Seroquel that you reviewed were the NDA studies and  
23 then whatever was on the AstraZeneca Web site for  
24 Study 125, 126, 127 and the other clinical studies  
25 that you mentioned in your report?

1 mechanistically might cause weight gain or  
2 diabetes?

3 A. I know more than the average  
4 epidemiologist.

5 Q. That doesn't make you an expert, though?

6 MR. BLIZZARD: Object to the form.

7 A. I don't know what you qualify as an  
8 expert.

9 Q. I don't know what you qualify as an  
10 average epidemiologist. Okay. So we're on the  
11 same page with that. All right?

12 A. All right.

13 Q. The fact that you say you know more than  
14 the average epidemiologist about how antipsychotics  
15 may cause weight gain or diabetes, does that make  
16 you an expert in how antipsychotics may cause those  
17 things?

18 MR. BLIZZARD: Object to the form.

19 A. Because of my pharmacogenetics  
20 expertise, I have to understand how drugs work.

21 Q. I'm being more specific than that.  
22 Okay?

23 A. Uh-huh.

24 Q. Yes?

25 MR. BLIZZARD: Object to the form. Just

1 ask the question.

2 Q. Dr. Arnett --

3 MR. BLIZZARD: You don't have to make  
4 the commentary or testimony yourself.

5 Q. Dr. Arnett, given that you're not --

6 MR. BLIZZARD: Please, please don't  
7 interrupt me. Okay?

8 Q. Dr. Arnett, given that you are not a  
9 pharmacologist and have never studied how  
10 antipsychotics may contribute to weight gain or  
11 diabetes, do you consider yourself an expert in how  
12 antipsychotics including Seroquel might cause  
13 weight gain or diabetes?

14 MR. BLIZZARD: Object to the form.  
15 Argumentative.

16 A. I have reviewed the literature and  
17 understand how drugs work --

18 Q. Generally?

19 A. -- and how Seroquel works specifically.

20 Q. As a --

21 A. Have I conducted my own research at the  
22 bench to evaluate the effect? The answer is no.

23 Q. Would you, Dr. Arnett, hold yourself out  
24 to the medical community as an expert in how  
25 antipsychotics cause weight gain and may cause

1 diabetes mechanistically?

2 A. No. But I have evaluated literature and  
3 have an understanding pharmacologically of how it  
4 causes weight gain and diabetes.

5 Q. That understanding came in the course of  
6 you serving as a plaintiff's expert in the Seroquel  
7 litigation, true?

8 A. Not entirely. I had a student who got  
9 her Ph.D. dissertation looking at weight gain and  
10 antipsychotics, and I served on her Ph.D.  
11 committee.

12 Q. Have you ever held yourself out to the  
13 medical community as an expert in how  
14 antipsychotics cause weight gain and diabetes?

15 A. No.

16 Q. Are you an expert in the area of obesity  
17 or the causes of obesity?

18 A. I have several publications on risk  
19 factors for obesity. We're evaluating genetic  
20 predictors of obesity. So in that context, I have  
21 expertise.

22 Q. Are you talking about the article you  
23 wrote on overweight children and adolescents? Is  
24 that the one?

25 A. Well, there's that. I also have a

1 Dr. Arnett.

2 MR. BLIZZARD: Wait a minute. She's not  
3 finished going through this exhibit.

4 Q. Yeah. I don't need to know all the  
5 specifics about it. I think I've got the gist of  
6 it.

7 Dr. Arnett, you were also sent two hard  
8 drives: One called Clinical Trials and one called  
9 NDA Documents that had over 28,000 documents. Did  
10 you review all those?

11 A. No.

12 Q. Do you know exactly what documents you  
13 considered in forming your opinions as you reviewed  
14 those hard drives?

15 A. In the -- the large hard drive, I didn't  
16 get to. The smaller hard drive, I reviewed. As I  
17 said, about the first 500 files, I opened and  
18 scanned and then found the integrated safety report  
19 and efficacy report. And those are the two I  
20 primarily relied on.

21 Q. So you accessed some of the documents in  
22 the NDA hard drive, but not the larger clinical  
23 trials hard drive?

24 A. I didn't get to them.

25 Q. Did you review any clinical study

1 reports for any of the clinical trials for  
2 Seroquel?

3 A. Yes, but I can't remember which ones.

4 Q. You mentioned the -- in your report that  
5 you reviewed some depositions, right?

6 A. No, sir.

7 Q. Did you review any depositions?

8 A. No, sir.

9 Q. Did you review any internal AstraZeneca  
10 documents?

11 A. Yes.

12 Q. Are the AstraZeneca documents that you  
13 are relying on reflected in your report?

14 A. Yes.

15 Q. Do you normally rely on internal company  
16 documents when forming opinions as an  
17 epidemiologist?

18 A. Yes.

19 Q. And I'm talking about not as a  
20 plaintiff's expert, but in your normal practice.

21 A. Well, in my normal practice, I don't  
22 have access to them.

23 Q. In your normal practice as an  
24 epidemiologist, do you rely on internal company  
25 documents in forming your epidemiologic opinions?

1           A.     I really didn't focus on this as a major  
2 part of my report because to me, in addressing  
3 issues of causation, placebo-controlled trials are  
4 the gold standard.

5           Q.     Well, you included it in your report,  
6 Doctor.

7           A.     I included it.

8           Q.     And you included it and you made a  
9 statement about weight gain with Seroquel being  
10 greater than that of another atypical  
11 antipsychotic, is your statement, right?

12                   MR. BLIZZARD: I object to your previous  
13 question because you misstated the statement.

14           Q.     Doctor, do you write that Seroquel's  
15 weight gain was greater than that of another  
16 atypical antipsychotic when you're referring to  
17 Study 7?

18           A.     I stated, "This active comparator study  
19 indicated that Seroquel's weight gain was greater  
20 than that of another atypical antipsychotic."

21           Q.     And you're referring to Study 7, right?

22           A.     Yes.

23                                 (Defendant's Exhibit No. 17  
24                                 was marked for identification.)

25           Q.     If you look at what I handed you as

1 indication. From the timing of '01 to '02 when the  
2 trial was conducted, my guess is it wasn't  
3 schizophrenia.

4 Q. So you're relying on a non-schizophrenia  
5 trial and the relative risk of weight gain in that  
6 trial to calculate an attributable risk of weight  
7 gain in patients who have schizophrenia?

8 A. I can't comment on it because, as I  
9 said, I didn't write down and I don't recall the  
10 patient population in that one trial, 105.

11 Q. Is it an appropriate methodology,  
12 Doctor, to take a relative risk from a study not  
13 involving schizophrenia patients for weight gain  
14 and applying that to calculate an attributable risk  
15 for a different patient population?

16 A. I don't know because I haven't evaluated  
17 the data systematically for bipolar. But certainly  
18 there's consistency in the relative risk estimates.

19 Q. Your weight chart here, Table 1, you  
20 created this based on the clinical trial summaries,  
21 right, that were on the Web site?

22 A. Yes.

23 Q. Am I right that there were many more  
24 than just 11 clinical trial synopses on the  
25 AstraZeneca Web site?

1           A.     Yeah.  I took them in sequential order  
2 from top to Number 11 until I ran out of time.

3           Q.     Did you review any of the clinical trial  
4 summary reports that were on the Web site from  
5 Numbers 12 on the list thereafter?

6           A.     I went systematically from the first  
7 listed.

8           Q.     So when you reviewed the clinical trial  
9 summaries on AstraZeneca's Web site, you started at  
10 the first entry study number, and then you reviewed  
11 the first 11 trials and stopped?

12          A.     Yes.

13          Q.     Doctor, you don't include any statements  
14 about glucose in this chart except for Study 43.  
15 Do you see that?

16          A.     They weren't provided.  Well, 43 I state  
17 specifically, "Both weight and glucose  
18 significantly increased, but no data was provided  
19 in this study synopsis."

20          Q.     When you reviewed the clinical trial  
21 summaries for the rest of these studies, you didn't  
22 find any comments about glucose on there?  Because  
23 I assume if you did, that you would have included  
24 it.

25          A.     I don't recall.

1 more based on body weight. There are changes in  
2 triglycerides, thyroid level, waist circumference.  
3 All of these are markers of diabetic risks.

4 Q. Can you name, Doctor, any clinical trial  
5 that shows a correlation between Seroquel weight  
6 gain and diabetes?

7 MR. BLIZZARD: Object to the form.

8 Asked and answered.

9 A. AstraZeneca has not evaluated the data  
10 in that way.

11 Q. You said yesterday there's a dose  
12 response between Seroquel and weight gain; is that  
13 your testimony?

14 A. Yes.

15 Q. Is there a dose response relationship  
16 between Seroquel and diabetes?

17 A. Can we take a break?

18 Q. After you answer my question because  
19 there's a question pending.

20 A. You'll have to restate the question.  
21 And let me just state before you restate it, there  
22 are going to be people opening and closing the door  
23 because we have to vacate the room potentially at  
24 9:00.

25 Q. Is there a dose response relationship

1 between Seroquel and diabetes?

2 A. From the observational studies that I've  
3 evaluated, there are some observational studies  
4 that suggest that.

5 Q. My question is, is there --

6 MR. BLIZZARD: Don't start another  
7 question if we have to --

8 Q. Go ahead.

9 A. Let me evaluate when we have to vacate  
10 the room.

11 (Break held, 09:06 a.m.)

12 Q. Can you say to a reasonable degree of  
13 scientific certainty, Dr. Arnett, that there is a  
14 dose response relationship between Seroquel and  
15 diabetes?

16 A. There's a dose response relationship  
17 with all of the metabolic parameters that are a  
18 part of the diabetic -- Type II diabetes. There's  
19 some indication from the observational studies that  
20 there is a dose response between diabetes incidence  
21 and dose of Seroquel.

22 Q. Are you testifying to a reasonable  
23 degree of scientific certainty that there's a dose  
24 response relationship between Seroquel and  
25 diabetes?

1 A. Yes.

2 Q. Is there a dose threshold above which  
3 that risk of diabetes exists with Seroquel?

4 A. I haven't evaluated the DNF with respect  
5 to that question. And I may before trial, but I  
6 haven't evaluated in that way yet.

7 Q. In your report, Doctor, for Studies 126  
8 and 127, you say that they were conducted with  
9 secondary aims to evaluate more detailed measures  
10 of glucose homeostasis. Do you see that?

11 A. Yes.

12 Q. You agree that generally if you're  
13 looking at the effects of a drug on a particular  
14 endpoint, say X, a clinical trial that has endpoint  
15 X as the primary endpoint is more reliable than a  
16 trial with endpoint X as a secondary endpoint?

17 A. It depends. So I can't agree with that  
18 statement.

19 Q. Are you aware of any Seroquel clinical  
20 trials where glucose metabolism was a primary  
21 endpoint?

22 A. They may exist. They weren't included  
23 in my review to date.

24 Q. You haven't reviewed any clinical  
25 studies with Seroquel where glucose metabolism was

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 excess of 300 milligrams.

2 Q. Do you know what the relative risk is of  
3 diabetes or hyperglycemia and what the confidence  
4 intervals are if the dose is 400 milligrams of  
5 Seroquel?

6 A. I haven't reviewed the data with respect  
7 to dose for hyperglycemia other than the NDAs,  
8 which were primarily 300 or more milligrams.

9 Q. So is the answer to that you don't know  
10 what the relative risk is of diabetes or  
11 hyperglycemia or what the confidence levels are for  
12 a dose of 400 milligrams of Seroquel?

13 MR. BLIZZARD: Object to the form.

14 A. I said I haven't reviewed it yet.

15 Q. What is the relative risk of Seroquel  
16 that you say exists for the risk of diabetes?

17 A. In the studies that have compared  
18 Seroquel to general population, specifically  
19 observational studies, the estimated relative risk  
20 of diabetes, the relative risk ranges from a low of  
21 1.7 to a high of 33.

22 In the aggregate of the studies that I  
23 cited in this report from the clinical trials  
24 conducted by AstraZeneca, the relative risk was  
25 just over 2.

1 Q. 2.02, you're talking about?

2 A. Yes.

3 Q. When you look at the observational  
4 studies, are you going to tell the jury that the  
5 relative risk for Seroquel is somewhere between 1.7  
6 and 33 based on the observational studies?

7 A. Yes, compared to a general population.

8 Q. Can you be any more specific about what  
9 the relative risk is that you say applies to  
10 patients who use Seroquel compared to those who  
11 don't?

12 A. Not at this point.

13 Q. And when I'm talking about relative  
14 risk, we're talking about hyperglycemia and  
15 diabetes, right?

16 A. No. You specifically asked me about  
17 diabetes.

18 Q. Okay.

19 A. And I qualified it by saying in the  
20 observational studies, this was observed, and in  
21 the clinical trials --

22 Q. Yes.

23 A. -- the 2.02 was observed.

24 Q. On observational studies for diabetes,  
25 just so I'm clear. Okay?