

**In The Matter Of:**

*Pledger v.*

*Janssen*

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*(Jury Trial-AM Session)*

*XII*

*February 10, 2015*

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*John J. Kurz, RMR-CRR, Official Court Reporter*

*City of Philadelphia*

*First Judicial District Of Pennsylvania*

*100 South Broad Street, 2nd Floor*

*Philadelphia, PA 19110*

**(Jury Trial-AM Session)XII - February 10, 2015**  
**Pledger v. Janssen**

<p>1 IN THE COURT OF COMMON PLEAS OF PHILADELPHIA COUNTY  2 FIRST JUDICIAL DISTRICT OF PENNSYLVANIA  3 CIVIL TRIAL DIVISION</p> <p>4 <b>IN RE: RISPERDAL® LITIGATION</b>  5 March Term, 2010, No. 296</p> <p>6 Phillip Pledger, et al.,  7 Plaintiffs, : APRIL TERM, 2012  8 v. NO. 01997</p> <p>9 Janssen Pharmaceuticals, Inc.,  10 Johnson &amp; Johnson Company  11 and Janssen Pharmaceutical  12 Research &amp; Development,  13 L.L.C.  14 Defendants.</p> <p>15 <b>COURTROOM 425</b>  16 <b>CITY HALL</b>  17 <b>PHILADELPHIA, PENNSYLVANIA</b></p> <p>18 <b>B E F O R E:</b> THE HONORABLE RAMY I. DJERASSI, J.,  19 and a Jury  20 - - -</p> <p>21 <b>JURY TRIAL - VOLUME XII</b>  22 - MORNING SESSION - (AMENDED)</p> <p>23 <b>REPORTED BY:</b>  24 JOHN J. KURZ, RMR, CRR  25 REGISTERED MERIT REPORTER  CERTIFIED REALTIME REPORTER  OFFICIAL COURT REPORTER</p>	<p>- PLEDGER, et al. -vs- JANSSEN, et al. -</p> <p>1 <b>APPEARANCES:</b> (Continued)</p> <p>2 WEIL, GOTSHAL &amp; MANGES, LLP  3 BY: DIANE P. SULLIVAN, ESQUIRE  4 ALLISON BROWN, ESQUIRE  5 (admitted pro hac vice)  6 301 Carnegie Center, Suite 303  Princeton, New Jersey 08540  7 T: 609-986-1100 F: 212-310-8007  E-mail: diane.sullivan@weil.com  8 E-mail: allison.brown@weil.com  9 Counsel for Defendant Janssen Pharma.,  J&amp;J, and Janssen Research &amp; Development</p> <p>10</p> <p>11 <b>Also Present:</b></p> <p>12 Priscilla M. Brandon, Esq., Sheller, P.C.  13 Marianne Mari, Tipstaff  14 Cory Smith, Video Technician  15 Ken Reed, Video Technician  16 Thomas F. Campion, Esquire  17 Benita Pledger</p> <p>18</p> <p>19</p> <p>20</p> <p>21</p> <p>22</p> <p>23</p> <p>24</p> <p>25</p> <p>- PLEDGER, et al. -vs- JANSSEN, et al. -</p> <p>1 <b>I N D E X</b></p> <p>2 <b>WITNESSES</b> DIRECT CROSS</p> <p>3 LODEWIJK IVO CAERS, Ph.D.</p> <p>4 By Ms. Sullivan 9 --</p> <p>5 By Mr. Kline -- --</p> <p>6</p> <p>7</p> <p>8</p> <p>9 <b>E X H I B I T S</b></p> <p>10 NO. PAGE NO.</p> <p>11 D-54 Demonstrative; timeline 14</p> <p>12 D-55 Demonstrative; DG6-1 31</p> <p>13 D-56 Approval letter 34</p> <p>14 D-57 Exhibit 213A 54</p> <p>15 D-58 List of clinical trials 76</p> <p>16 D-59 Chart on the easel 93</p> <p>17 D-60 Article, RIS in children 93</p> <p>18 D-61 FDA Label in approval letter 107</p> <p>19 D-62 Mark-up, D234.1 114</p>
<p>- PLEDGER, et al. -vs- JANSSEN, et al. -</p> <p>1 <b>APPEARANCES:</b></p> <p>2 <b>SHELLER, P.C.</b>  3 BY: STEPHEN A. SELLER, ESQUIRE  4 CHRISTOPHER A. GOMEZ, ESQUIRE  5 E-mail: Sasheller@sheller.com  6 E-mail: Cgomez@sheller.com  1528 Walnut Street, 4th Floor  5 Philadelphia, PA 19102  Phone: (215) 790-7300 Fax: (215) 546-0942  Counsel for Plaintiff(s)</p> <p>7</p> <p>8 <b>KLINER &amp; SPECTER, A Professional Corporation</b>  9 BY: THOMAS R. KLINE, ESQUIRE  10 KRISTEN LOERCH SIPALA, ESQUIRE  11 E-mail: tom.kline@klinespecter.com  12 E-mail: kristen.loerch@klinespecter.com  1525 Locust Street, 19th Floor  11 Philadelphia, PA 19102  Phone: (215) 772-1000 Fax: (215) 772-1359  12 Counsel for Plaintiff(s)</p> <p>13</p> <p>14 <b>ARNOLD &amp; ITKIN, LLP</b>  15 BY: JASON A. ITKIN, ESQUIRE  16 6009 Memorial Drive  17 Houston, Texas 77007  18 Phone: 713-222-3800 Fax: 713-222-3850  19 Counsel for Plaintiff(s)</p> <p>20 <b>Representing Defendants:</b></p> <p>21 DRINKER BIDDLE &amp; REATH, LLP  22 BY: KENNETH A. MURPHY, ESQUIRE  23 MELISSA A. GRAFF, ESQUIRE  24 One Logan Square, Suite 2000  25 Philadelphia, Pennsylvania 19103-6996  Phone: (215) 988-2700 F: (215) 988-2757  E-mail: kenneth.murphy@dbr.com  melissa.graff@dbr.com  Counsel for Defendant Janssen Pharma.,  J&amp;J, and Janssen Research &amp; Development</p>	<p>Page 2</p> <p>1 <b>I N D E X</b></p> <p>2 <b>WITNESSES</b> DIRECT CROSS</p> <p>3 LODEWIJK IVO CAERS, Ph.D.</p> <p>4 By Ms. Sullivan 9 --</p> <p>5 By Mr. Kline -- --</p> <p>6</p> <p>7</p> <p>8</p> <p>9 <b>E X H I B I T S</b></p> <p>10 NO. PAGE NO.</p> <p>11 D-54 Demonstrative; timeline 14</p> <p>12 D-55 Demonstrative; DG6-1 31</p> <p>13 D-56 Approval letter 34</p> <p>14 D-57 Exhibit 213A 54</p> <p>15 D-58 List of clinical trials 76</p> <p>16 D-59 Chart on the easel 93</p> <p>17 D-60 Article, RIS in children 93</p> <p>18 D-61 FDA Label in approval letter 107</p> <p>19 D-62 Mark-up, D234.1 114</p>

**(Jury Trial-AM Session)XII - February 10, 2015**  
**Pledger v. Janssen**

- PLEDGER, et al. -vs- JANSSEN, et al. -  1       (The following transpired in open 2       court outside the presence of the jury:) 3 <b>COURT CRIER:</b> All rise. 4       (Call to order at 9:37 a.m.) 5 <b>THE COURT:</b> Good morning, everybody. 6 <b>MR. KLINE:</b> Good morning. 7 <b>THE COURT:</b> Virtually bright and 8       early. 9       Okay. Yes, sir. 10      You can be seated, everybody. 11 <b>MR. MURPHY:</b> Your Honor, I just have 12      a brief motion before we begin as to 13      defendant Johnson & Johnson. 14 <b>THE COURT:</b> Yes. 15 <b>MR. MURPHY:</b> We move for a compulsory 16      nonsuit as to Johnson & Johnson. The 17      evidence presented by the plaintiff did not 18      in any way implicate Johnson & Johnson as a 19      manufacturer, distributor, or a marketer of 20      the drug in question, Risperdal. It's beyond 21      question that Johnson & Johnson is but a 22      holding company. There's no evidence that's 23      been presented by plaintiff that would allow 24      them to pierce the corporate veil, as it 25      were.	Page 5	- PLEDGER, et al. -vs- JANSSEN, et al. -  1       We're not granting a nonsuit on that basis. 2 <b>MR. MURPHY:</b> Understood. I 3       understand your ruling, Your Honor. 4 <b>THE COURT:</b> All right. Let's get the 5       jury in here. 6       All right. I don't know whether you 7       have the memorandum ready now or sometime 8       later in the day. 9       There were two issues that were held 10      under advisement on the directed verdict 11      motion. I don't plan on reading it on the 12      fly today, but if it's available sometime 13      today, I would be happy to read it. 14 <b>MR. KLINE:</b> I don't believe I've seen 15      it yet; is that correct? 16 <b>MS. SULLIVAN:</b> It's on its way, Your 17      Honor. 18 <b>THE COURT:</b> Okay. No rush. Take the 19      pressure off. 20      - - - 21      (Pause.) 22      - - - 23 <b>COURT CRIER:</b> All rise. 24      (Whereupon the jury entered the 25      courtroom at 9:42 a.m.)	Page 7
- PLEDGER, et al. -vs- JANSSEN, et al. -  1       The only evidence regarding Johnson & 2       Johnson that was provided to this Court was a 3       LinkedIn page by the sales representative, 4       Mr. Gilbreath, who in fact was employed by 5       Janssen. There being no evidence as to 6       Johnson & Johnson, we would move that -- 7 <b>THE COURT:</b> Well, is Johnson & 8       Johnson a different party from any of the 9       other parties, or are they the same? I'm 10      talking about Johnson & Johnson versus 11      Janssen Pharmaceutica. 12 <b>MR. MURPHY:</b> A different company 13      totally. It is a mere holding company. 14 <b>THE COURT:</b> Ah, I see. 15      Well, you know what, that's denied. 16      We will cross that bridge when we get to it 17      as far as the -- I mean, it's been pretty 18      clear that the label involved in this case 19      and the company that manufactured this was 20      either Johnson & Johnson and/or Janssen 21      Pharmaceutica. That was testified to by 22      multiple witnesses in this case, ranging from 23      Dr. Gilbreath to Dr. Mathisen to Dr. 24      Kessler. 25      So the record will speak for itself.	Page 6	- PLEDGER, et al. -vs- JANSSEN, et al. -  1       (The following transpired in open 2       court in the presence of the jury:) 3       - - - 4 <b>THE COURT:</b> All right. Good morning. 5       Please be seated. 6 <b>JURY PANEL:</b> Good morning. 7 <b>THE COURT:</b> Good morning, everybody. 8       All right. Now, members of the jury, 9       as I told you yesterday, the plaintiff's side 10      has rested and so now we are going to begin 11      the testimony and evidence of the defense in 12      this case, and for that purpose, I ask 13      Ms. Sullivan to call your first witness when 14      you're ready. 15 <b>MS. SULLIVAN:</b> Thank you, Your Honor. 16      Good morning. 17 <b>THE COURT:</b> Good morning. 18 <b>MS. SULLIVAN:</b> The defense calls as 19      their first witness Dr. Ivo Caers. 20      Dr. Caers, if you could take the 21      witness stand. 22      (Witness took the stand.) 23 <b>COURT CRIER:</b> Just remain standing. 24      Please state your name for the record and 25      spell it.	Page 8

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1 <b>THE WITNESS:</b> My name is Lodewijk Ivo 2       Caers, but my call name is "Ivo." 3 <b>COURT CRIER:</b> Can you spell that, 4       please. 5 <b>THE WITNESS:</b> L-O-D-E-W-I-J-K, I-V-O, 6       C-A-E-R-S. I'm a Ph.D. 7 <b>COURT CRIER:</b> And raising your right 8       hand. 9       - - - 10      ... LODEWIJK IVO CAERS, Ph.D., after 11     having been first duly sworn, was examined 12     and testified as follows: 13     - - - 14 <b>DEFENDANT'S EVIDENCE</b> 15     - - - 16 <b>DIRECT EXAMINATION</b> 17     - - - 18 <b>BY MS. SULLIVAN:</b> 19 <b>Q.</b> <b>Good morning, Dr. Caers.</b> 20      A. Good morning. 21 <b>Q.</b> <b>Good morning, everyone.</b> 22 <b>Dr. Caers, could you introduce</b> 23 <b>yourself to our jurors; tell them who you are and</b> 24 <b>where you work.</b> 25      A. Well, as I told, I'm Ivo Caers. I'm a		1 <b>your career there, briefly.</b> 2      A. Sure. 3       In May 1979, I actually started in a 4       local operating company, Janssen the Netherlands. 5       So the Netherlands are just north of Belgium. And I 6       was there in a product development position and 7       product management position for three years, up to 8       1982. 9       In 1982 -- always based in Beerse, 10      Belgium. And in 1982, I switched to the clinical 11     research group and did clinical studies in various 12     domains: neurology, oncology, cardiovascular. I did 13     that for five years about. Then later in 1987, 14     about, I switched to what we called at that moment 15     global studies in marketing, which is a commercial 16     position, but more on strategic directions for drug 17     development and line extension, so additional 18     formulation development. 19       And during that time I also became 20     available for the psychiatry products, including 21     Risperdal. So me and my team, we did the global 22     launch of Risperdal back in 1992, '93. And we are 23     driving strategic directions for the compound up 24     to -- and I've been doing that for up to 1999, when 25     I switched again to the Janssen R & D organization.	
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1       scientist working with Janssen Research and 2       Development. I'm actually living -- I was born in 3       Belgium. I'm actually living in Belgium with my 4       family in a small town, Beerse, somewhere in the 5       north of Belgium, in Europe, middle Europe. And I'm 6       still working there daily, on a daily basis. 7 <b>Q.</b> <b>I think our jurors could tell it wasn't a</b> 8 <b>Philadelphia accent.</b> 9      A. I'm afraid not, no. But I'll improve on that 10     during the day. 11 <b>Q.</b> <b>And, Dr. Caers, for how long have you been at</b> 12 <b>Janssen Pharmaceuticals?</b> 13      A. More than 35 years. I've been working for 14     Janssen R & D for more than 35 years now. 15 <b>Q.</b> <b>And can you tell us a little bit about your</b> 16 <b>educational background.</b> 17      A. I studied -- I have a Master degree in 18     biology, which I did at the University of Leuven in 19     central Belgium. And the after that I did doctoral 20     work, Ph.D., as we call it, in biochemistry, which 21     I've terminated and completed in, I think, 22     April 1979. 23 <b>Q.</b> <b>And can you just walk us briefly through your</b> 24 <b>career experience at Janssen. What did you do when</b> 25 <b>you started back in 1979? And take our way through</b>		1 <b>Q.</b> <b>And R &amp; D, Dr. Caers -- I'm sorry to</b> 2 <b>interrupt -- is research and development?</b> 3      A. Yes. Janssen R & D, yes, Research and 4      Development. 5       So back in mid-1999, I was asked to 6      become the team leader for Janssen R & D for 7      Risperdal. And I have been doing that from 1999 up 8      to 2009. After which, since then, I'm doing all the 9      developments within Janssen R & D in other 10     psychiatry products. 11 <b>Q.</b> <b>And, Dr. Caers, we're going to talk about</b> 12 <b>Risperdal and its development by Janssen. But</b> 13 <b>first, can you give our jurors some background about</b> 14 <b>your experience in drug development, in the</b> 15 <b>discovery and development of medicines.</b> 16      A. Well, you will understand in 35 years I've 17     gone several times through the whole life cycle of 18     the product. I've most -- I'm most familiar with 19     Risperdal from the early days on up to 2009, as I 20     said earlier. But I also been involved in 21     developments in psychiatry, in the compounds for 22     attention deficit hyperactivity disorders. I've 23     been dealing with compounds in depression. I'm 24     actually now still a compound development team 25     leader for the depression compound. But as I said	

<p>- IVO CAERS, Ph.D. - DIRECT -</p> <p>1 earlier as well, I've started up new compounds that 2 first we didn't make it because of efficacy or 3 safety issues. So I'm pretty familiar with the 4 first step, up to launch and beyond.</p> <p>5 <b>Q. And, Dr. Caers, Janssen Pharmaceuticals, when</b> 6 <b>did that company become part of the Johnson &amp;</b> 7 <b>Johnson family of companies?</b></p> <p>8 A. It was back in 1962, even before my time, that 9 the company which was at that time also already 10 based in Beerse, so it was north of Belgium where it 11 still is, where that company was bought by Johnson &amp; 12 Johnson. And since then, Janssen Pharmaceutica is a 13 member of the companies of Johnson &amp; Johnson.</p> <p>14 <b>Q. And is Janssen named after somebody?</b></p> <p>15 A. Yes, indeed. The company, the Janssen company 16 was founded by Dr. Paul Janssen. Dr. Paul Janssen 17 was a scientist in Belgium, grew up in Belgium, is 18 from the region. And back in the early '50s, 1953, 19 I guess, he started up his own lab looking and 20 trying to invent new and better medicines; and he 21 had been very successful, by the way. <b>He has -- all</b> 22 <b>of his career, he is the inventor of up to 80,</b> 23 <b>eight-zero, new drugs for different areas of</b> 24 <b>medicine. And that's why obviously, as I told</b> 25 <b>earlier, back in 1962, that this company came under</b></p>	<p>Page 13</p>	<p>- IVO CAERS, Ph.D. - DIRECT -</p> <p>1 <b>THE COURT:</b> D-54. 2 (Whereupon Exhibit D-54 was marked 3 for identification.)</p> <p>4 <b>MR. KLINE:</b> I haven't seen this. 5 (Handing document to the witness.)</p> <p>6 <b>THE COURT:</b> Counsel, I still -- I am 7 going to ask that we follow the --</p> <p>8 <b>MS. SULLIVAN:</b> Oh, you can take it 9 down.</p> <p>10 Yeah. I'm sorry. I didn't realize 11 that they put it up, Judge.</p> <p>12 <b>THE COURT:</b> D-54.</p> <p>13 <b>MR. KLINE:</b> I've never seen it, Your 14 Honor. And it was not produced.</p> <p>15 <b>THE COURT:</b> Okay.</p> <p>16 <b>MS. SULLIVAN:</b> It's a demonstrative. 17 It's a timeline. I don't think it's 18 controversial.</p> <p>19 <b>MR. KLINE:</b> I have to see it first.</p> <p>20 <b>MS. SULLIVAN:</b> I'll give them 21 Dr. Caers' copy.</p> <p>22 <b>COURT CRIER:</b> Let me run that off.</p> <p>23 <b>MS. SULLIVAN:</b> That's okay.</p> <p>24 <b>COURT CRIER:</b> The Judge needs one and 25 counsel. Thank you.</p>	<p>Page 15</p>
<p>- IVO CAERS, Ph.D. - DIRECT -</p> <p>1 the attention of Johnson &amp; Johnson as a very 2 productive laboratory and very successful laboratory 3 and as an interesting company to join Johnson &amp; 4 Johnson.</p> <p>5 <b>Q. And, Dr. Caers, did you personally have the</b> 6 <b>opportunity to work with Dr. Paul Janssen?</b></p> <p>7 A. Oh, yes, very, very closely. I was actually 8 sitting on the same floor when I was in clinical 9 research; and my boss reported directly to Dr. Paul 10 Janssen.</p> <p>11 <b>Q. And, Dr. Caers, we're going to talk a little</b> 12 <b>bit about how to develop a medicine and then talk</b> 13 <b>about Risperdal. And you've been involved in</b> 14 <b>discovery and development of medicines including</b> 15 <b>Risperdal?</b></p> <p>16 A. Yes, indeed, yeah.</p> <p>17 <b>Q. And we have just as a demonstrative Defense</b> 18 <b>Exhibit -- Ms. Brown, can tell me?</b></p> <p>19 <b>MS. BROWN:</b> Yes; 54.</p> <p>20 <b>MS. SULLIVAN:</b> And, Lamia, it's 21 DG10.3.</p> <p>22 <b>MR. KLINE:</b> I'll need to see it.</p> <p>23 <b>THE COURT:</b> What is this now?</p> <p>24 <b>COURT CRIER:</b> This would be D-54,</p> <p>25 Your Honor.</p>	<p>Page 14</p>	<p>- IVO CAERS, Ph.D. - DIRECT -</p> <p>1 <b>MR. KLINE:</b> Whether controversial or 2 not, Your Honor, I object to the procedure.</p> <p>3 <b>THE COURT:</b> All right. Mr. Kline, 4 I'm going to ask you to speak into the 5 microphone.</p> <p>6 <b>MR. KLINE:</b> Yes. I object to the 7 procedure. I'll look at the document, but we 8 had an agreement to exchange all documents.</p> <p>9 Now it's, quote, just a 10 demonstrative.</p> <p>11 <b>THE COURT:</b> Well, right now we're on 12 court time here.</p> <p>13 <b>MR. KLINE:</b> I understand.</p> <p>14 <b>THE COURT:</b> We're going to proceed 15 with this document one at a time.</p> <p>16 <b>MR. KLINE:</b> I understand. I need to 17 see it. I still haven't seen it.</p> <p>18 <b>THE COURT:</b> Any objection?</p> <p>19 <b>MR. KLINE:</b> Other than the one I 20 raised, no, Your Honor.</p> <p>21 <b>THE COURT:</b> No. It's all right. 22 This is a demonstrative piece -- something to 23 help explain something to the jury. It's 24 okay.</p> <p>25 Go ahead.</p>	<p>Page 16</p>

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1 <b>MS. SULLIVAN:</b> Thank you, Your Honor. 2 <b>COURT CRIER:</b> D-54 to the witness. 3 <b>MS. SULLIVAN:</b> Ken, can we put it up? 4                   (Document D-54 displayed.) 5 <b>BY MS. SULLIVAN:</b> 6 <b>Q.</b> And, Dr. Caers, can you walk our jurors 7   through the process of discovery and developing a 8   medicine in accordance with the FDA -- by the way, 9   Dr. Caers, are you familiar with the FDA regulatory 10   scheme as it relates to the development and labeling 11   of medicines? 12   A. Yes, very much so, yeah. 13 <b>Q.</b> And is that something you deal with regularly 14   in your job? 15 <b>THE COURT:</b> You know what, before we 16   proceed, are we proceeding as an expert 17   witness here or a fact witness? What is 18   this? 19 <b>MS. SULLIVAN:</b> He's a fact witness, 20   Your Honor, but he certainly has expertise in 21   these areas. 22 <b>THE COURT:</b> Well, is he going to be 23   offering an opinion of some sort? 24 <b>MS. SULLIVAN:</b> He's -- no. Factual 25   testimony, Your Honor.	1                   select a couple, 10, 15, and you test them, and the 2                   next step is in animal models. You have a model 3                   where you can check whether indeed in living animals 4                   this molecule does what we hope to do; and, 5                   secondly, you check whether the safety, at least in 6                   animals, is good enough to go to the next step. 7 <b>Q.</b> And so, Dr. Caers, so that test tube, that 8   relates to just trying to test and discover 9   molecules in the laboratory? 10   A. That is correct. 11 <b>Q.</b> And is it true that most medicines never get 12   approved by the FDA? 13   A. Well, as you can see, we start with a couple 14   of hundreds. We selected a few tens, maximum, if 15   not less, for testing in animals. Very few make it 16   to the next step. And the next step is what we call 17   Phase I studies. And that's the first time we give 18   the molecule to a human subject. 19 <b>Q.</b> And do you need FDA approval before you can 20   start testing a medicine in people? 21   A. If you want to do this in the US, you need to 22   have an FDA approval. If you want to do it in other 23   countries, you need to have other regulatory 24   agencies' approval. Not an approval, an agreement. 25   We talked -- well, don't mix it up with the final		
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1 <b>THE COURT:</b> All right. Go ahead. 2 <b>BY MS. SULLIVAN:</b> 3 <b>Q.</b> And, Dr. Caers, can you walk us through -- 4   just to back up. 5 <b>Dr. Caers, how hard is it to get a 6   medicine approved by the FDA?</b> 7   A. Well, in all fairness, it's pretty hard, and I 8   will explain to you why. 9                   The whole process starts on the 10   left-hand side. So the start is, you need to have 11   an ID. So you have an ID that if you have a 12   molecule that acts -- 13 <b>Q.</b> Is that "idea"?" 14   A. Say again. 15 <b>Q.</b> Did you say you need an "idea"?" 16   A. You need an "ID," a hypothesis. And that 17   tells you if I would have a molecule that has a 18   certain activity, that may well be active in a 19   certain disease area. So what you need on the 20   left-hand side is a test and you need molecules. 21   And we start making hundreds of molecules and we 22   test them all in the lab to see whether this 23   molecule may have had some activity that we want and 24   that it is sufficiently powerful, this activity. 25                   Out of a couple hundred, you may	1                   approval at the end of the whole development. 2 <b>Q.</b> Yes. In other words, you need permission from 3   the FDA before you can even test it? 4 <b>MR. KLINE:</b> No. Objection. That is 5   not what he said. Objection; and she's 6   leading. 7 <b>THE COURT:</b> All right. Sustained. 8 <b>BY MS. SULLIVAN:</b> 9 <b>Q.</b> Dr. Caers, do you need permission from the FDA 10   before you can test in patients? 11 <b>MR. KLINE:</b> Objection; asked and 12   answered. 13 <b>THE COURT:</b> All right. That has been 14   answered. 15                   So in the interest of time, you know, 16   if you got your answer, let's get another new 17   subject or new -- you know. We don't have to 18   repeat everything. 19 <b>BY MS. SULLIVAN:</b> 20 <b>Q.</b> Dr. Caers, can you walk us through what the 21   company looks for -- and, by the way, when companies 22   test their medicines in patients, how is that done? 23   Is that done by outside doctors? 24   A. Yes. So once we are beyond the human 25   volunteers in Phase I and we still have a molecule		

<p>- IVO CAERS, Ph.D. - DIRECT -</p> <p>1 that shows safety and is pretty well-tolerated in      2 non-ill subjects, you go to the next phase, which we      3 call Phase II, where you do your first evaluation of      4 efficacy. And here you use -- you need patients and      5 you need investigators, clinical centers that have      6 those patients, because we don't have patients.      7 Patients don't come to us. They come to doctors.      8 And we ask the doctors to do a certain study. And      9 in this case we are in Phase II. The objective of      10 that study is how is that efficacy as we hope that      11 to be and is it pretty well-tolerated in the limited      12 number of patients that we include in Phase II      13 studies.</p> <p><b>14 Q. And do these outside doctors and the company      15 need informed consent from patients to participate      16 in these studies?</b></p> <p>17 A. Yes, absolutely. There is -- first of all,      18 there's a protocol and the protocol describes from A      19 to Z what the study is, what is the objective of the      20 study, how it will be done, what type of patients      21 you need, what type of patients you should not      22 include, what should you assess for efficacy and      23 safety. And there's always an informed consent.      24       And what is an informed consent?      25 That is a short description in language that every</p>	<p>Page 21</p>	<p>- IVO CAERS, Ph.D. - DIRECT -</p> <p>1 <b>Q. And, Dr. Caers, this testing in patients, do      2 you look at the impact the medicine has on various      3 systems in the body, blood, heart, lungs?</b></p> <p>4 A. Yes, indeed, yes.</p> <p><b>5 Q. And, in other words, are you examining, as      6 you're doing these clinical trials, how the medicine      7 affects the body?</b></p> <p>8 A. To a certain extent, to a certain extent that      9 it is possible to do so, yeah.</p> <p><b>10 Q. And as you're going through these clinical      11 trials, Dr. Caers, is the company collecting data,      12 collecting information about side effects?</b></p> <p>13 A. Collecting -- we are collecting information on      14 all adverse events, side effects, safety assessment      15 and efficacy assessments, yes.</p> <p><b>16 Q. And is that side effect information that's      17 being collected by the company from these outside      18 doctors, does the company report that information to      19 the FDA?</b></p> <p>20       <b>MR. KLINE:</b> Your Honor, objection;      21 leading. He's just saying "yes" or "no."      22 And this isn't testimony.</p> <p><b>23 THE COURT:</b> Yes. I'll sustain that.      24       Also, you know, again, unless it's a      25 very important aspect of this entire case,</p>	<p>Page 23</p>
<p>- IVO CAERS, Ph.D. - DIRECT -</p> <p>1 patient can understand that explains what the study      2 is all about; what are the potential risks; what is      3 known about the product. And only once the patient      4 has signed and agreed that he has understood it and      5 he agrees to enter the study, the physician and the      6 investigator can enter that patient in the study.</p> <p><b>7 Q. And what sort -- and so in these clinical      8 trials -- and is that what they call clinical trials      9 when you're testing it in patients?</b></p> <p>10 A. That is correct.</p> <p><b>11 Q. And in these clinical trials, what are the      12 kinds of things the company and these outside      13 doctors are looking for in terms of safety issues in      14 patients?</b></p> <p>15 A. Oh, always in clinical studies you have a      16 range of safety assessments. You have blood level      17 assessments. You have EKGs to test the safety on      18 the heart. You also collect adverse events. Every      19 adverse event reported or noticed with the patient      20 is written down by the investigator. You may also      21 have certain assessment skills that you follow a      22 certain structured interview to assess certain      23 particular elements for safety. And that is all      24 written down per the individual patient in a patient      25 record form.</p>	<p>Page 22</p>	<p>- IVO CAERS, Ph.D. - DIRECT -</p> <p>1 these things can be summarized in a few      2 minutes.</p> <p><b>3 MS. SULLIVAN:</b> Yeah.</p> <p><b>4 BY MS. SULLIVAN:</b></p> <p><b>5 Q. And, Dr. Caers, why don't you talk to our      6 jurors about what information the FDA has given      7 along the way in terms of the clinical trials.</b></p> <p>8 A. Okay. Of every single study, once the study      9 is complete, the last patient has completed the      10 study, then all the data are collected and brought      11 together in one single database. And at a certain      12 moment when we have all the information available,      13 then we close the database. That means all of the      14 information as provided by the investigators is      15 brought together. We analyze the study so that we      16 know that whether the study shows efficacy and/or      17 safety. This is written down in an extensive      18 report.</p> <p>19       Initially we go to a topline result      20 report, but that's only 10, 20 pages for internal      21 use. But the eventual result of every study is what      22 we call a Clinical Study Report. And that's a 100-      23 to 150-page document, plus an additional couple of      24 thousand pages of tables and individual data. That      25 is basically what we call the Clinical Study Report.</p>	<p>Page 24</p>

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<p>1 Q. And what kind of side effect information is 2 the FDA provided by the companies as a result of 3 these clinical trials?</p> <p>4 A. Everything related to safety and efficacy is 5 written down by the investigators and is included in 6 the database and eventually described in the 7 Clinical Study Report. And it's a full Clinical 8 Study Report that is eventually shared with the FDA.</p> <p>9 Q. And so, Dr. Caers, as it relates to Risperdal, 10 for example, did the company conduct clinical trials 11 as part of the FDA approval process for Risperdal?</p> <p>12 A. Yes, of course.</p> <p>13 Q. And as part of that process, did the company 14 report side effect information to the FDA?</p> <p>15 A. Yes, indeed.</p> <p>16 Q. Including all the information about any 17 patients that might have developed gynecomastia?</p> <p>18 MR. KLINE: Objection; leading. It's 19 all leading, including the information about 20 the things. And he just has to say "yes" or 21 "no." This is a direct witness, Your Honor. 22 I object.</p> <p>23 MS. SULLIVAN: I'll rephrase it, Your 24 Honor.</p> <p>25 MR. KLINE: I object to the</p>		<p>1 report. And that's all part of what we call the New 2 Drug Application.</p> <p>3 Q. And, Dr. Caers, would that include any side 4 effects the company saw about gynecomastia?</p> <p>5 MR. KLINE: Objection; leading.</p> <p>6 BY MS. SULLIVAN:</p> <p>7 Q. Would that have been reported?</p> <p>8 THE COURT: Sustained.</p> <p>9 BY MS. SULLIVAN:</p> <p>10 Q. Did the company report side effects including 11 any prolactin-related side effects?</p> <p>12 A. Yes, indeed.</p> <p>13 Q. And what were some of those?</p> <p>14 A. Well, there were cases of gynecomastia, 15 galactorrhea and amenorrhea, so disturbance of the 16 menstrual cycle in females, that was part of the 17 adverse events that were in the data package 18 submitted for the New Drug Application back in 1992.</p> <p>19 Q. And was the FDA provided all of that 20 information about those side effects?</p> <p>21 A. Yes.</p> <p>22 MR. KLINE: Objection, Your Honor.</p> <p>23 THE COURT: Yes. Yes. Sustained.</p> <p>24 MR. KLINE: The whole --</p> <p>25 THE COURT: Was the FDA provided</p>	
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<p>1 continuation of it.</p> <p>2 THE COURT: That's sustained.</p> <p>3 Sustained. I mean --</p> <p>4 BY MS. SULLIVAN:</p> <p>5 Q. Dr. Caers, did the company provide side effect 6 information to the FDA as it related to Risperdal as 7 part of the clinical trials?</p> <p>8 A. Yes.</p> <p>9 Q. And what kind of side effect information was 10 the FDA provided?</p> <p>11 A. Well, all the side effects, all adverse events 12 reported during the studies were summarized and 13 described in the Clinical Study Report. But 14 obviously, an NDA, a New Drug Application, there's 15 more than one study. There might be 20 to 30 16 studies in such NDA. And every study has its own 17 Clinical Study Report and with all the efficacy and 18 safety information, including all adverse events, in 19 your New Drug Application. That is the total 20 package that you send to the FDA. You also have a 21 summary on efficacy which summarizes the results of 22 all the studies combined. And you do the same for 23 safety information. All the adverse events reported 24 and all the different study reports and studies done 25 with the compound are summarized in an overview</p>		<p>1 with something, that's a leading question. 2 Maybe we can just do this: Kind of 3 ask him what the story is or whatever.</p> <p>4 MS. SULLIVAN: I was trying to move 5 it along, Judge; but okay.</p> <p>6 BY MS. SULLIVAN:</p> <p>7 Q. The --</p> <p>8 MR. KLINE: Your Honor, my other 9 objection is that none of this that relates 10 to the approval in 1992 has anything to do 11 with children. And this drug was off-label 12 from '02 to '06.</p> <p>13 MS. SULLIVAN: Your Honor, this is 14 not proper.</p> <p>15 THE COURT: All right. Mr. Kline, I 16 appreciate that.</p> <p>17 MR. KLINE: That's my objection.</p> <p>18 THE COURT: But, you know, this is a 19 defense, and they're permitted to approach it 20 any way they see fit, as long as it's 21 admissible.</p> <p>22 BY MS. SULLIVAN:</p> <p>23 Q. And, Dr. Caers, can you talk about -- how 24 long, Dr. Caers, for the first -- when was the first 25 FDA approval for Risperdal?</p>	

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1 A. The first approval for Risperdal was back in 2 December 1993, and it was for the manifestations of 3 psychotic disorders.		1 counsel, I really am not. I don't think the 2 jury is either.	
4 <b>Q. And that was in adults, correct?</b>		3 Well, you know what, I'll permit you 4 to use this after you've gone through these, 5 you know, after all of these different points 6 have been either stipulated to or testified 7 to by your client. You may certainly use 8 this as a summary of the points that you're 9 making. But it is in the fashion of leading 10 to put this particular document up there and 11 then just have your witness kind of reply 12 what's already in the document.	
13 <b>Q. Nine years of study before FDA approved it?</b>		13 <b>MS. SULLIVAN:</b> Okay.	
14 A. Yes, indeed.		14 - - -	
15 <b>Q. And I'm going to mark Defense Exhibit...</b>		15 (Whereupon Exhibit D-55 was marked 16 for identification.)	
16 <b>MS. BROWN:</b> 55.		17 - - -	
17 <b>MS. SULLIVAN:</b> And this is DG6-1, a 18 demonstrative.		18 <b>BY MS. SULLIVAN:</b>	
19 <b>MR. KLINE:</b> Your Honor, again, we had 20 an agreement to produce documents that are 21 going to be used with the witness; and I 22 object.		19 <b>Q. Dr. Caers, has Risperdal been approved by the 20 FDA for many different indications?</b>	
23 <b>THE COURT:</b> Let me see the document.		21 A. Yes, indeed.	
24 <b>MR. KLINE:</b> Before I even see it, we 25 had a specific agreement.		22 After the first approval in 1993, 23 there were additional approvals for Risperdal with 24 different formulations, so with different ways of 25 administration, such as a liquid, an oral liquid, or	
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1 <b>THE COURT:</b> Well, it may be. But 2 right now I'm going to go one by one and then 3 we'll look at it at another time.		1 a fast dissolving tablet which makes it easier for 2 patients to take the pill; or in other indications 3 such as bipolar mania, which is another psychiatric 4 disease in which antipsychotics can be very 5 effective.	
4 <b>MR. KLINE:</b> At a break, may I have 5 whatever is being used?		6 It was also approved later, somewhere 7 in 2006, I think, in irritability associated with 8 autism, which is a primarily child psychiatric 9 disorder. It was later then also approved for 10 adolescents with schizophrenia and for children and 11 adolescents with bipolar mania. Again, this is 12 another age group as it was approved for in adults.	
6 <b>THE COURT:</b> Pardon me?		13 <b>Q. And, Dr. Caers, when the company submits its 14 New Drug Application for approval to the FDA after 15 all of this years of testing, how long typically 16 does it take the FDA to review all of the data and 17 decide whether the medicine gets approved?</b>	
7 <b>MS. SULLIVAN:</b> Your Honor --		18 A. At that time it took about 12 to 15 months for 19 the FDA to review all your data that you provided. 20 And be aware, we not only give the paper document, 21 they also get the database electronically. So they 22 can check the analysis we do in the studies, whether 23 they are appropriate and do justify, indeed, the 24 conclusions.	
8 <b>MR. KLINE:</b> All I ask is to be 9 provided the documents ahead of time.		25 After that review by the FDA, and the	
10 <b>THE COURT:</b> Well, nothing's going up 11 on the screen or anywhere until you've seen 12 it, until it's reviewed, until it's either 13 objected to or not; and if it is, then I'll 14 rule on it.			
15 Do you have, actually, copies of 16 these documents?			
17 <b>MS. SULLIVAN:</b> We thought we did, 18 Your Honor. I'm not sure what happened.			
19 Your Honor, Mr. Kline provided us a 20 whole bunch of documents the day his 21 witnesses --			
22 <b>THE COURT:</b> Well, I'm not really 23 interested in a --			
24 <b>MR. KLINE:</b> That's also not true.			
25 <b>THE COURT:</b> -- back-and-forth between			

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<p>1 whole file is distributed to different reviewers, 2 different specialists within the FDA, they all make 3 their assessment, bring it all together, and that 4 eventually leads to a reply, first reply, which is 5 usually an approvable letter that says, yes, okay, 6 it looks good, but this and this and this we still 7 want you to explore and justify.</p> <p>8 And eventually then when you give 9 your complete response and because you reply then, 10 then they review that once more and then they can 11 approve. And as part of the approval, they provide 12 you the final label which is what they want to be 13 said about this compound in the label to inform 14 physicians how to use and prescribe this compound.</p> <p>15 <b>Q. And, Dr. Caers, when a medicine is approved by</b> 16 <b>the FDA, do you get from the FDA an approval</b> 17 <b>package?</b></p> <p>18 A. Yes, indeed.</p> <p>19 <b>Q. And have you seen the FDA review memos that</b> 20 <b>are part of that approval package?</b></p> <p>21 A. Yeah. As I said earlier, so every -- the 22 different parts of the file of the New Drug 23 Application is reviewed by different specialists 24 within the FDA. You have chemical; you have 25 clinical; you have safety physicians; you have</p>		<p>1 <b>THE COURT:</b> I don't mind the 2 admission of this, but the contents of this 3 are problematic, especially such that you 4 highlighted that has the phrase, "safe and 5 effective," which I did rule on in motion in 6 limine. I don't want to get into the issue 7 of safety and effectiveness as approved by 8 the FDA.</p> <p>9 <b>MS. SULLIVAN:</b> Well, Your Honor, I'll 10 block it out here. I will not --</p> <p>11 <b>THE COURT:</b> I don't know why you need 12 all this. You have an approval. It's in the 13 document, and that's it. The contents of 14 this are problematic.</p> <p>15 <b>MS. SULLIVAN:</b> Your Honor, 16 Dr. Kessler said the drug's unsafe. That 17 opens the door to this. It goes to 18 negligence, Your Honor. This is the FDA 19 standard. We've met it. It's evidentiary.</p> <p>20 <b>THE COURT:</b> But it was unsafe perhaps 21 for children. His point is well taken. This 22 was an approval for adults. It's actually 23 irrelevant. But beyond that, I'm telling 24 you, we had a motion in limine ruling that 25 specifically --</p>	
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<p>1 pharmacokinetics; so they are experts on how the 2 drug behaves in a body, et cetera, et cetera. So 3 they all make their review, bring it all together in 4 assessment reports, and those are, shortly after 5 approval, available in the public domain on the FDA 6 website. So we do have access to these assessment 7 reports.</p> <p>8 <b>Q. And, Doctor, so you -- does the company see</b> 9 <b>then the various review memos from the different</b> 10 <b>doctors at the FDA on the medicine?</b></p> <p>11 A. That is correct.</p> <p>12 <b>Q. And, Dr. Caers, I am going to mark as Defense</b> 13 <b>Exhibit 56, DX207, the approval letter from the FDA</b> 14 <b>for Risperdal in 1993.</b></p> <p>15 <b>MR. KLINE:</b> Objection to FDA 16 document.</p> <p>17 <b>THE COURT:</b> Overruled.</p> <p>18 <b>MS. SULLIVAN:</b> Do we have a copy for 19 the Judge and for --</p> <p>20 <b>MS. BROWN:</b> We do, yes.</p> <p>21 <b>THE COURT:</b> Well, let me see you at 22 sidebar.</p> <p>23 Take that down, please.</p> <p>24 (The following discussion transpired 25 at sidebar out of the hearing of the jury:)</p>		<p>1 <b>MS. SULLIVAN:</b> I'll block out the 2 safe and effective, then.</p> <p>3 <b>THE COURT:</b> And I don't think the 4 contents of this are admissible. They're not 5 necessary.</p> <p>6 <b>MS. SULLIVAN:</b> Well, this is the 7 label, Judge.</p> <p>8 <b>THE COURT:</b> Well, you have some 9 testimony about the effectiveness and safety. 10 You have testimony about it, or an opinion.</p> <p>11 <b>MS. SULLIVAN:</b> I'll block it out.</p> <p>12 <b>THE COURT:</b> But we're not doing it 13 this way through the FDA.</p> <p>14 <b>MS. SULLIVAN:</b> Okay.</p> <p>15 <b>THE COURT:</b> We've ruled it out 16 before.</p> <p>17 <b>MS. SULLIVAN:</b> Okay. I'll block out 18 the "safe and effective."</p> <p>19 <b>MR. KLINE:</b> Well, no. 20 Your Honor, Your Honor, as I 21 understood, the Court just told her not to 22 display it; and her answer back on the way 23 out was "I will block it out." 24 There's no good reason why this has 25 to be displayed.</p>	

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1 <b>THE COURT:</b> No. No. This document 2 is not going up because the contents cannot 3 be -- I can't -- I cannot -- 4 <b>MS. SULLIVAN:</b> Your Honor, this is 5 the label. And the FDA is saying this is the 6 label you have to use. 7 <b>THE COURT:</b> I'm telling you, you have 8 the approval. It's in the record, and it's 9 admitted. But the fact of the matter is the 10 contents of that document is not admissible. 11 It's not subject to cross-examination. It's 12 using a phrase that I had forbidden, and it's 13 putting the FDA imprimatur of safe and 14 effectiveness on this drug when in fact the 15 issue has to do with children. And this 16 particular label didn't have anything to do 17 with children. 18 <b>MS. SULLIVAN:</b> And, Your Honor, 19 just -- 20 <b>THE COURT:</b> That's my ruling. 21 <b>MS. SULLIVAN:</b> I understand. But for 22 the record, Judge, you initially ruled that 23 the FDA defense is part of the case. This is 24 the approval from the FDA. 25 <b>THE COURT:</b> Well, it has to be		1 <b>THE COURT:</b> Your defense is that in 2 1993 the thing was approved. You have an 3 official document to prove it. 4 <b>MS. SULLIVAN:</b> And the FDA says say 5 this. The FDA says you have to say this 6 verbatim. 7 <b>THE COURT:</b> You can use that. 8 <b>MS. SULLIVAN:</b> Thank you. 9 <b>MR. KLINE:</b> That would actually be 10 misleading because -- 11 <b>MS. SULLIVAN:</b> That's what it says. 12 <b>MR. KLINE:</b> Of course that's what it 13 says, after a negotiation with them and 14 having nothing to do with children. 15 <b>MS. SULLIVAN:</b> That's cross-exam. 16 <b>MR. MURPHY:</b> Your Honor, if I might. 17 <b>THE COURT:</b> The objection is 18 sustained. I'm not going down that route. 19 <b>MS. SULLIVAN:</b> I can't show that the 20 FDA says use this verbatim? 21 <b>THE COURT:</b> No, no. You can get that 22 from your witness. 23 <b>MR. MURPHY:</b> Your Honor, just so -- 24 <b>THE COURT:</b> Or get a stipulation. 25 It's a can of worms that injects the FDA's	
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1                   according to -- 2 <b>MS. SULLIVAN:</b> This is a business 3 record and a public record. 4 <b>THE COURT:</b> It is not -- the contents 5 of that document are not admissible in this 6 case -- 7 <b>MS. SULLIVAN:</b> This is the labeling. 8 <b>THE COURT:</b> -- for the purposes that 9 you are presenting it. This is not a 10 business record for whom the contents are 11 admissible. 12 <b>MR. KLINE:</b> I have no objection to 13 the label as a document being used. 14 <b>THE COURT:</b> That's already in 15 evidence. 16 <b>MR. KLINE:</b> I have an objection to -- 17 <b>MS. SULLIVAN:</b> But how about -- 18 <b>COURT REPORTER:</b> One at a time. 19 <b>MS. SULLIVAN:</b> How about the 20 statement from the FDA: This is the label 21 you have to use? 22 <b>THE COURT:</b> I don't think you really 23 need that. 24 <b>MS. SULLIVAN:</b> Well, Judge, that's 25 our defense.	1                   approval process as a -- without the FDA 2 people being here or an expert witness 3 testifying about these documents, just like 4 Kessler did. You cannot use this document to 5 speak for itself. You have to get an expert 6 in here to testify about these documents. 7 And that's my ruling. 8 <b>MR. MURPHY:</b> Your Honor -- 9 <b>THE COURT:</b> That's it. 10                   ----- 11                   (Sidebar discussion concluded.) 12                   ----- 13                   (The following transpired in open 14 court in the presence of the jury:) 15                   ----- 16 <b>THE COURT:</b> All right. The objection 17 is sustained, ladies and gentlemen. The 18 objection is sustained. 19                   This particular document here can be 20 used for a particular purpose; namely, that 21 an approval of the FDA took place in 1993, as 22 we already know. That's it. 23 <b>BY MS. SULLIVAN:</b> 24 <b>Q. And, Dr. Caers, as part of the FDA approval</b> 25 <b>process, did the FDA also review the labels?</b>		

<p>- IVO CAERS, Ph.D. - DIRECT -</p> <p>1 A. Well, part of the approval -- well, approval 2 is the label. And the label is -- this is the 3 document -- the FDA says this is the document that 4 will be the label for this compound which is part -- 5 an intrinsic part of the approval letter and 6 document.</p> <p>7 <b>Q. And, Dr. Caers, can you talk about your 8 experience with the FDA in terms of labeling for 9 medicines including Risperdal.</b></p> <p>10 A. Well, with every NDA, New Drug Application, 11 you propose a certain label, but you write this 12 label in line with the guidelines. There are FDA 13 guidelines on how to structure a label and what 14 should be in a label and what should not be in a 15 label, and that's a proposal. Part of the review 16 process by the FDA is reviewing that label and 17 always they will make recommended changes and 18 adaptations. They may delete certain things. They 19 may add certain things. And at the end, with the 20 approval, they say this is in our opinion what 21 should be in your label and this is part of your 22 formal approval, which means that basically this 23 product is safe and effective for the use as 24 described in that label and for the patients as 25 described in that label. That's a very strict</p>	<p>Page 41</p>	<p>- IVO CAERS, Ph.D. - DIRECT -</p> <p>1 <b>BY MS. SULLIVAN:</b> 2 <b>Q. -- in the label?</b></p> <p>3 <b>THE COURT:</b> Sustained. Sustained. 4 What we're looking for as admissible 5 as a fact witness is about this individual's 6 own experience with the Risperdal approval 7 process.</p> <p>8 <b>BY MS. SULLIVAN:</b> 9 <b>Q. And, Dr. Caers --</b></p> <p>10 <b>MR. KLINE:</b> I move to strike. 11 <b>THE COURT:</b> And we are going to 12 strike anything that this witness has to say 13 that has been objected to, any answers that's 14 been -- please do not consider that. 15 He is not qualified here as an expert 16 on pharmaceutical regulations. 17 If he were, I'd let you know.</p> <p>18 <b>BY MS. SULLIVAN:</b> 19 <b>Q. And, Dr. Caers, based on your experience with 20 the FDA, do they have final say in what goes in your 21 label?</b></p> <p>22 <b>MR. KLINE:</b> Objection. 23 <b>THE COURT:</b> That's sustained. 24 Sustained.</p> <p>25 <b>BY MS. SULLIVAN:</b></p>	<p>Page 43</p>
<p>- IVO CAERS, Ph.D. - DIRECT -</p> <p>1 process that is followed in that respect.</p> <p>2 <b>Q. And who, Dr. Caers, at the approval stage for 3 a medicine, has the final say as to what goes in the 4 label? The FDA or the company?</b></p> <p>5 A. That's the FDA.</p> <p>6 <b>Q. And will the FDA permit you to market your 7 medicine if you don't say what they tell you to say?</b></p> <p>8 <b>MR. KLINE:</b> Objection. <b>THE COURT:</b> All right. Sustained.</p> <p>9 Is this an expert witness on 10 pharmaceutical regulation, Counsel?</p> <p>11 <b>MS. SULLIVAN:</b> Your Honor -- <b>THE COURT:</b> I'm going to ask you at 12 this point to get into what this witness can 13 testify as a fact witness about his 14 involvement with the Risperdal approval 15 process.</p> <p>16 <b>BY MS. SULLIVAN:</b></p> <p>17 <b>Q. And, Dr. Caers, do you have a significant 18 amount of experience dealing with the FDA on 19 labeling issues?</b></p> <p>20 A. Yes, I do.</p> <p>21 <b>Q. And can you tell us whether a company can say 22 something different from what the FDA dictates --</b></p> <p>23 <b>MR. KLINE:</b> Objection.</p>	<p>Page 42</p>	<p>- IVO CAERS, Ph.D. - DIRECT -</p> <p>1 <b>Q. When you get an approval letter from the FDA, 2 what does it say about the label?</b></p> <p>3 A. It has the label as it is approved by the FDA 4 and as it will be used for the marketing of the 5 product in this country.</p> <p>6 <b>Q. And what does that mean?</b></p> <p>7 A. It means that the approved label as approved 8 by the FDA describes, in the opinion of the FDA, all 9 the relevant information that the physician needs to 10 know in order to appropriately prescribe this 11 medicine for his or her patients.</p> <p>12 <b>Q. And let's show our jurors the initial FDA 13 approved label for Risperdal. Defense Exhibit 24, 14 please.</b></p> <p>15 <b>COURT CRIER:</b> D-57. <b>MR. KLINE:</b> Your Honor, may we look 16 at it first? <b>THE COURT:</b> Of course. <b>MR. KLINE:</b> Rather than to display, 17 as per the Court's -- <b>THE COURT:</b> I thought I had made 18 myself clear about that.</p> <p>19 <b>MS. SULLIVAN:</b> Your Honor, this has 20 already been admitted. <b>THE COURT:</b> I don't care.</p>	<p>Page 44</p>

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<p>1                   <b>MS. SULLIVAN:</b> Okay.</p> <p>2                   <b>COURT CRIER:</b> Previously marked as</p> <p>3                   D-24, Your Honor.</p> <p>4                   <b>THE COURT:</b> Isn't that the same</p> <p>5                   document as some other document we've had,</p> <p>6                   plaintiff something?</p> <p>7                   <b>MR. KLINE:</b> No. It's the same as</p> <p>8                   D-24. Now it's marked D-57.</p> <p>9                   <b>MS. SULLIVAN:</b> No. It's D-24.</p> <p>10                  <b>THE COURT:</b> D-24. Fine.</p> <p>11                  All right. That's been previously</p> <p>12                  marked.</p> <p>13                  Go ahead.</p> <p>14                  <b>BY MS. SULLIVAN:</b></p> <p>15                  <b>Q.</b> Dr. Caers, let's take a look at the initial</p> <p>16                  FDA approved label back in 1993 for Risperdal.</p> <p>17                  And if we could go to the Precautions</p> <p>18                  section, Ken.</p> <p>19                  (Technician complied.)</p> <p>20                  <b>BY MS. SULLIVAN:</b></p> <p>21                  <b>Q.</b> And, Dr. Caers, can you talk about what was in</p> <p>22                  the initial FDA approved label in terms of</p> <p>23                  information about hyperprolactinemia or elevated</p> <p>24                  prolactin and gynecomastia?</p> <p>25                  <b>MR. KLINE:</b> Objection; misleading. I</p>		<p>1                   amenorrhea, gynecomastia, have been reported with</p> <p>2                   this type of drugs.</p> <p>3                  <b>Q.</b> And, Doctor, our jurors have heard the term</p> <p>4                  "association" and "causation." Is there a</p> <p>5                  difference between association --</p> <p>6                  <b>MR. KLINE:</b> Objection.</p> <p>7                  <b>BY MS. SULLIVAN:</b></p> <p>8                  <b>Q.</b> -- and causation?</p> <p>9                  <b>MR. KLINE:</b> Objection.</p> <p>10                 <b>THE COURT:</b> Overruled.</p> <p>11                 <b>THE WITNESS:</b> Well, association means</p> <p>12                 that these type of observations have been</p> <p>13                 made while patients were treated with</p> <p>14                 risperidone.</p> <p>15                 A causation means that the</p> <p>16                 observations have been induced and caused by</p> <p>17                 risperidone. And there is indeed a major</p> <p>18                 differentiation, because it's not because</p> <p>19                 it's associated that it is caused by it.</p> <p>20                  <b>BY MS. SULLIVAN:</b></p> <p>21                  <b>Q.</b> And can you explain why something associated</p> <p>22                  with something doesn't necessarily mean caused by</p> <p>23                  it, based on your experience?</p> <p>24                  <b>MR. KLINE:</b> Same objection; expert</p> <p>25                  testimony.</p>	
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<p>1                  will not object if the word "adult" is used.</p> <p>2                  <b>MS. SULLIVAN:</b> Your Honor, I just</p> <p>3                  asked him what was in the label. This is,</p> <p>4                  you know --</p> <p>5                  <b>THE COURT:</b> Well --</p> <p>6                  <b>MS. SULLIVAN:</b> Everybody knows --</p> <p>7                  <b>THE COURT:</b> -- I'm not sure why we're</p> <p>8                  going through this exercise.</p> <p>9                  I mean, the jury can read it for</p> <p>10                 themselves or what. I mean, is there a</p> <p>11                 question based on this label?</p> <p>12                 <b>MS. SULLIVAN:</b> Yeah.</p> <p>13                 <b>THE COURT:</b> All right. Then ask the</p> <p>14                 question.</p> <p>15                 <b>BY MS. SULLIVAN:</b></p> <p>16                 <b>Q.</b> And, Dr. Caers, in the FDA approved label, was</p> <p>17                 there information for physicians about the fact that</p> <p>18                 Risperdal could increase prolactin levels?</p> <p>19                 A. Yes, indeed. As you can see here, under the</p> <p>20                 title "hyperprolactinemia," it says that as other</p> <p>21                 products interfering with dopamine, and those are</p> <p>22                 receptors, somewhere in the brain, also risperidone</p> <p>23                 elevates prolactin in the blood, and that products</p> <p>24                 that can increase prolactin in the blood; that</p> <p>25                 certain adverse events such as galactorrhea,</p>		<p>1                  <b>THE COURT:</b> Sustained. Sustained.</p> <p>2                  You're -- again, this is like expert</p> <p>3                  testimony. If you want to qualify him as an</p> <p>4                  expert, I mean, I don't understand what --</p> <p>5                  let me see -- what are we trying to -- he's a</p> <p>6                  fact witness about what?</p> <p>7                  <b>MS. SULLIVAN:</b> He's a fact witness</p> <p>8                  who's a Ph.D., and has significant expertise</p> <p>9                  in drug development and drug labeling and is</p> <p>10                 familiar with these concepts for over 30</p> <p>11                 years, Your Honor.</p> <p>12                 <b>THE COURT:</b> That's an expert.</p> <p>13                 <b>MS. SULLIVAN:</b> He's both.</p> <p>14                 <b>THE COURT:</b> Well, then, qualify him</p> <p>15                 as an expert.</p> <p>16                 <b>BY MS. SULLIVAN:</b></p> <p>17                 <b>Q.</b> Dr. Caers --</p> <p>18                 <b>MR. KLINE:</b> There's no report, Your</p> <p>19                 Honor.</p> <p>20                 <b>THE COURT:</b> That's right. You can't</p> <p>21                 qualify him as an expert, I guess, because we</p> <p>22                 don't have an expert report.</p> <p>23                 <b>MS. SULLIVAN:</b> Your Honor --</p> <p>24                 <b>THE COURT:</b> So then the objection is</p> <p>25                 sustained. This is not the right witness for</p>	

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<p>- IVO CAERS, Ph.D. - DIRECT -</p> <p>1 that.</p> <p>2 <b>MS. SULLIVAN:</b> Your Honor, they've</p> <p>3 had extensive depositions of this witness.</p> <p>4 <b>THE COURT:</b> Not the right witness.</p> <p>5 There's no expert report.</p> <p>6 There are some Rules of Civil</p> <p>7 Procedure involved in Pennsylvania, and so,</p> <p>8 therefore, we're going to follow them.</p> <p>9 I'm sure you have some other expert</p> <p>10 witnesses who are going to testify and they</p> <p>11 may do so properly. But this is a fact</p> <p>12 witness, I presume, about his own experience</p> <p>13 with this particular medication.</p> <p>14 <b>MS. SULLIVAN:</b> And, yes, Your Honor,</p> <p>15 the concept of association and causation is</p> <p>16 in this label.</p> <p>17 <b>THE COURT:</b> Well, ask him as relates</p> <p>18 to Risperdal.</p> <p>19 <b>MS. SULLIVAN:</b> Okay. Fair enough.</p> <p>20 <b>BY MS. SULLIVAN:</b></p> <p>21 <b>Q.</b> Dr. Caers, can you talk to our jurors about</p> <p>22 this label and Risperdal as it relates to these</p> <p>23 concepts "association and causation"?</p> <p>24 <b>A.</b> Well, what this label reads is that the use of</p> <p>25 risperidone can be associated with the occurrence of</p>	Page 49	<p>- IVO CAERS, Ph.D. - DIRECT -</p> <p>1 <b>BY MS. SULLIVAN:</b></p> <p>2 <b>Q.</b> Dr. Caers, because gynecomastia is listed in</p> <p>3 the label as a potential side effect, does that mean</p> <p>4 it causes it?</p> <p>5 <b>A.</b> No.</p> <p>6 <b>Q.</b> And can you explain that.</p> <p>7 <b>A.</b> It is that it is observed in patients who are</p> <p>8 being treated with risperidone, but that does not</p> <p>9 necessarily mean that it is caused by it.</p> <p>10 <b>MR. KLINE:</b> Your Honor, move to</p> <p>11 strike.</p> <p>12 <b>THE COURT:</b> Well, it's --</p> <p>13 <b>MR. KLINE:</b> I just couldn't be on my</p> <p>14 toes like on every question.</p> <p>15 It's just every question.</p> <p>16 <b>THE COURT:</b> That is stricken. That</p> <p>17 is as an expert -- that is the testimony of</p> <p>18 an expert.</p> <p>19 He may be an expert, but you didn't</p> <p>20 follow the rules, so I can't help you on</p> <p>21 that. You have other experts, I'm sure, to</p> <p>22 get that particular testimony in if you have</p> <p>23 it.</p> <p>24 <b>Sustained.</b></p> <p>25 Excuse me. Members of the jury, that</p>	Page 51
<p>- IVO CAERS, Ph.D. - DIRECT -</p> <p>1 certain adverse events, such as galactorrhea,</p> <p>2 amenorrhea, gynecomastia.</p> <p>3 <b>Q.</b> And, Dr. Caers, in your experience, if the FDA</p> <p>4 concluded Risperdal caused gynecomastia, have you</p> <p>5 seen labeling where they say the word "caused"?</p> <p>6 <b>MR. KLINE:</b> Objection, Your Honor.</p> <p>7 <b>THE COURT:</b> Sustained.</p> <p>8 <b>MR. KLINE:</b> For many reasons.</p> <p>9 <b>THE COURT:</b> Sustained.</p> <p>10 <b>BY MS. SULLIVAN:</b></p> <p>11 <b>Q.</b> Has the FDA, Dr. Caers, in your experience</p> <p>12 with Risperdal, ever concluded that Risperdal causes</p> <p>13 gynecomastia?</p> <p>14 <b>MR. KLINE:</b> Objection.</p> <p>15 <b>THE COURT:</b> Sustained. Just not --</p> <p>16 he's not qualified.</p> <p>17 <b>MS. SULLIVAN:</b> That's not an expert.</p> <p>18 I said has the FDA ever concluded that.</p> <p>19 <b>THE COURT:</b> I don't have a basis for</p> <p>20 his testimony on that from this witness.</p> <p>21 <b>MR. KLINE:</b> That would be hearsay.</p> <p>22 <b>THE COURT:</b> I mean, the labels speak</p> <p>23 for themselves. We don't need this witness</p> <p>24 to read the label to the jury. This jury has</p> <p>25 seen this label about three times already.</p>	Page 50	<p>- IVO CAERS, Ph.D. - DIRECT -</p> <p>1 last question and that last answer is</p> <p>2 stricken. Just not the right person for</p> <p>3 that.</p> <p>4 <b>MS. SULLIVAN:</b> And --</p> <p>5 <b>THE COURT:</b> About the causation of --</p> <p>6 this particular causation issue as to whether</p> <p>7 or not Risperdal causes this. He's not the</p> <p>8 right guy for that.</p> <p>9 <b>MS. SULLIVAN:</b> And, Your Honor, the</p> <p>10 question related to labeling and what the</p> <p>11 FDA --</p> <p>12 <b>THE COURT:</b> I'm sorry, Ms. Sullivan,</p> <p>13 sustained. You're going to have to play by</p> <p>14 the rules.</p> <p>15 <b>MS. SULLIVAN:</b> Just trying to get a</p> <p>16 fair trial, Judge.</p> <p>17 <b>THE COURT:</b> Well, you have to play by</p> <p>18 the rules to get a fair trial.</p> <p>19 <b>MS. SULLIVAN:</b> The --</p> <p>20 <b>THE COURT:</b> There are two sides to</p> <p>21 the coin. That's why we have Rules of Civil</p> <p>22 Procedure.</p> <p>23 <b>BY MS. SULLIVAN:</b></p> <p>24 <b>Q.</b> And, Dr. Caers --</p> <p>25 <b>MS. SULLIVAN:</b> Can we look, Jed, at</p>	Page 52

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1 the safe and effective for children section?		1 whether the FDA noted that Risperdal could elevate	
2 <b>BY MS. SULLIVAN:</b>		2 prolactin in their review memos?	
3 <b>Q. And, Dr. Caers, in the adult label from 1993,</b>		3 <b>MR. KLINE:</b> Objection, Your Honor.	
4 <b>is there a section that tells doctors about safety</b>		4 <b>THE COURT:</b> Sustained as to what the	
5 <b>for children?</b>		5 FDA noted. This is -- you got a witness from	
6 A. The only reference to children in the label of		6 Janssen. What did he know?	
7 '93 is a statement that the efficacy and safety of		7 <b>MS. SULLIVAN:</b> Well, Your Honor, he	
8 Risperdal in children has not been established.		8 just testified that this is part of what the	
9 <b>Q. Okay. And that was in the adult label from</b>		9 company keeps as their business --	
10 <b>the beginning?</b>		10 <b>THE COURT:</b> But you have other	
11 A. That is correct. Well, it's in the Risperdal		11 witnesses who are properly permitted to	
12 label, full stop.		12 testify to these kind of things. This is not	
13 Q. Yeah. Okay.		13 the right one. You didn't qualify him. He's	
14 <b>And, Dr. Caers, when the company got</b>		14 not an expert on FDA pharmaceutical	
15 <b>the FDA approval for Risperdal, was there review</b>		15 regulations or any of those kind of issues,	
16 <b>memos from the FDA as part of the approval package?</b>		16 Ms. Sullivan.	
17 A. There are review memos, obviously, yes, we		17 I really -- I feel that in the end,	
18 discussed earlier. Because the FDA experts		18 we have to enforce at some point the Rules of	
19 summarize their findings in a review document, and		19 Civil Procedure.	
20 those documents are available to the companies once		20 <b>MS. SULLIVAN:</b> And, Your Honor, I'm	
21 your product is approved.		21 just asking what FDA told Janssen.	
22 <b>Q. And, Dr. Caers, is that information kept by</b>		22 <b>THE COURT:</b> What FDA told Janssen,	
23 <b>the company as part of their regular and ordinary</b>		23 why is that relevant to this man's testimony?	
24 <b>course of business?</b>		24 <b>MS. SULLIVAN:</b> Because he's Janssen.	
25 A. Yes. Obviously we keep all the documents from		25 <b>THE COURT:</b> I don't understand that.	
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1 the FDA after we receive --		1 <b>MS. SULLIVAN:</b> He's the doctor at	
2 <b>Q. And have you seen the review memos from the</b>		2 Janssen that got this information.	
3 <b>FDA for the 1993 approval?</b>		3 <b>THE COURT:</b> If you establish some	
4 A. Back in the early '90s, yes, yes.		4 foundation for something, yeah.	
5 <b>Q. And I'm going to show you what's been marked</b>		5 <b>MS. SULLIVAN:</b> Yes.	
6 <b>for identification as Defense Exhibit 213.</b>		6 <b>THE COURT:</b> But if you're just	
7 <b>MS. BROWN:</b> It will be 57.		7 throwing documents out there for him to read	
8 <b>MS. SULLIVAN:</b> 213A.		8 them for the jury, that's not permitted.	
9 <b>MR. KLINE:</b> The same thing we went to		9 <b>MS. SULLIVAN:</b> Well --	
10 sidebar on, Your Honor. I object.		10 <b>THE COURT:</b> We went through that	
11 <b>THE COURT:</b> I can't hear you.		11 before the trial.	
12 <b>MR. KLINE:</b> This would be the same		12 <b>BY MS. SULLIVAN:</b>	
13 thing we went to sidebar on already. I would		13 <b>Q. Dr. Caers, you received the FDA review memos</b>	
14 object. It's just another version of it, of		14 <b>on Risperdal?</b>	
15 an FDA document.		15 A. Yes, indeed.	
16 <b>THE COURT:</b> Is this an FDA document?		16 <b>Q. And --</b>	
17 <b>MR. KLINE:</b> Yes.		17 <b>THE COURT:</b> When did he receive them?	
18 <b>MS. SULLIVAN:</b> And also a business		18 <b>THE WITNESS:</b> Well, they were	
19 record.		19 available from shortly after the --	
20 <b>THE COURT:</b> We had a motion in limine		20 <b>THE COURT:</b> Well, were you involved	
21 about this entire subject. That is		21 in this 1993 application?	
22 sustained, at least through this witness in		22 <b>THE WITNESS:</b> I was involved in	
23 this manner.		23 Risperdal -- in all Risperdal issues from	
24 <b>BY MS. SULLIVAN:</b>		24 1991 on, yeah.	
25 <b>Q. Dr. Caers, are you -- are you -- do you know</b>		25 <b>THE COURT:</b> Well, if you establish	

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1 the foundation... 2 <b>MS. SULLIVAN:</b> May I show the 3 document to the jury? 4 <b>THE COURT:</b> No. You have to 5 establish a foundation as to how this witness 6 can share something about this document 7 that's meaningful for us. 8 <b>MS. SULLIVAN:</b> Okay. 9 <b>BY MS. SULLIVAN:</b>		1 leading. 2 <b>THE COURT:</b> Yeah. Sustained. 3 <b>MR. KLINE:</b> She's just asking for a 4 "yes" or "no." 5 <b>THE COURT:</b> Sustained. 6 I'd take a break right now except for 7 the fact that I do have this meeting, and 8 it's scheduled for 11 o'clock. I was trying 9 to use our court time. 10 But these questions, as you're 11 phrasing them, are impermissible. 12 <b>MS. SULLIVAN:</b> I understand the 13 Court's position, Your Honor. 14 <b>THE COURT:</b> It is my position. And I 15 hope you follow my position. 16 <b>BY MS. SULLIVAN:</b> 17 <b>Q.</b> Dr. Caers, did the FDA -- you already told our 18 jurors you provide a comparative data as part of the 19 initial approval process showing how Risperdal 20 faired against other medicines on the issue of 21 prolactin, right? 22 A. That is correct. 23 <b>Q.</b> And so, Dr. Caers, are you aware as to whether 24 the FDA commented back in 1993 that they knew that 25 Risperdal could elevate prolactin more than other	
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1 violation. 2 <b>THE COURT:</b> Sustained. Sustained. 3 Unless you lay a foundation as to this 4 doctor's personal knowledge of the issues in 5 play here and you set that up for us, we're 6 not going to just be flinging documents out 7 there. We've been here two and a half weeks. 8 We cannot just fling documents. 9 <b>MS. SULLIVAN:</b> I wasn't flinging, 10 Your Honor. 11 <b>THE COURT:</b> I think you are. 12 <b>BY MS. SULLIVAN:</b> 13 <b>Q.</b> Dr. Caers, did the company provide the FDA -- 14 and you were involved in the approval process for 15 Risperdal, right? 16 A. Yes. 17 <b>Q.</b> And did the company provide the FDA with 18 information on comparative trials, Risperdal 19 compared to other medicines? 20 A. Yes. 21 <b>Q.</b> And did the FDA -- and in those comparative 22 trials that you gave to the FDA, did it show that 23 Risperdal could elevate prolactin more than a first 24 generation antipsychotic? 25 <b>MR. KLINE:</b> Objection. This is all	1 <b>medicines?</b> 2 <b>MR. KLINE:</b> Objection. 3 <b>THE COURT:</b> All right. That's 4 another -- that's sustained. 5 That's, ladies and gentlemen, 6 hearsay. That's a statement that's made 7 outside of this courtroom not subject to 8 cross-examination. It's forbidden by our 9 rules of evidence except for certain 10 exceptions. I'm finding that there are no 11 exceptions at the moment. We cannot have 12 testimony about from the FDA through this 13 witness when that witness is not either here 14 or some exception. That's what's going on 15 here. And, you know, I just gave you an 16 education on hearsay. 17 <b>BY MS. SULLIVAN:</b> 18 <b>Q.</b> Dr. Caers, did you provide the FDA with 19 information that showed that Risperdal elevated 20 prolactin more than Haldol? 21 <b>MR. KLINE:</b> Objection. 22 <b>THE COURT:</b> No. As to what he 23 provided the FDA, absolutely permissible. 24 <b>MR. KLINE:</b> Why can't the question 25 be: What did you show to the FDA, rather		

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1 than her giving him the answer? 2 <b>THE COURT:</b> I agree with that. But 3 anything that he provided to the FDA or he 4 knows the company provided to the FDA, that's 5 fair game, absolutely. 6 <b>THE WITNESS:</b> Well, in our studies, 7 we had Risperdal patients and we had patients 8 on a reference compound, for example, 9 haloperidol, also other first generation 10 antipsychotics; and we had efficacy, safety, 11 including prolactin levels, in all these 12 different patients treated with different 13 agents, including Risperdal and Haldol, yes. 14 <b>BY MS. SULLIVAN:</b> 15 <b>Q. And did you review the FDA memos back when</b> 16 <b>they were provided?</b> 17 A. Well, we obviously had to look at them after 18 the approval. But as I said earlier, we only had 19 them available after the approval, so not during the 20 approval. 21 <b>Q. Yes. Did you review the FDA memos after the</b> 22 <b>approval?</b> 23 A. I did some of them, yes. 24 <b>Q. For what purpose, Dr. Caers, would you look at</b> 25 <b>the FDA approval?</b>		1 <b>Q. And, Doctor -- and did you note that, based on</b> 2 <b>your review of the FDA memos, that the FDA was aware</b> 3 <b>of that?</b> 4 A. Yeah, sure. 5 <b>MR. KLINE:</b> Object. 6 <b>BY MS. SULLIVAN:</b> 7 <b>Q. And, Dr. Caers --</b> 8 <b>THE COURT:</b> Overruled. 9 <b>BY MS. SULLIVAN:</b> 10 <b>Q. And, Dr. Caers, did you -- did the company,</b> 11 <b>after FDA approved Risperdal in 1993, continue to</b> 12 <b>study the medicine?</b> 13 A. Yes, very much so. We did additional studies 14 on schizophrenia but also in other psychiatric 15 disorders in order to further have approvals later 16 on, as we already reviewed. 17 <b>Q. And, Dr. Caers, once the FDA approved</b> 18 <b>Risperdal, can you talk to our jury about the kinds</b> 19 <b>of other studies the company did and the kinds of</b> 20 <b>other indications the company saw, from the FDA?</b> 21 A. From the early to mid-'90s we started 22 exploring Risperdal also in children with conduct 23 disorders or disruptive behavioral disorders. We 24 studied Risperdal in patients with bipolar mania, 25 again, another psychotic disorder where	
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1 A. Well, it's always interesting to see what the 2 opinion of the FDA expert is after they have seen 3 our full data set so that you understand their 4 position and how they came to the label text. 5 <b>Q. And what did you learn, Dr. Caers, about the</b> 6 <b>FDA findings in the review memos on prolactin</b> 7 <b>elevation and how Risperdal compared and what the</b> 8 <b>FDA knew about that?</b> 9 <b>MR. KLINE:</b> Objection, based on the 10 Court's prior rulings. 11 <b>THE COURT:</b> Well, that's -- now we're 12 getting closer to a permissible exception. 13 You know, if you ask him what did he know 14 that he then did on another test or 15 something, fine. 16 <b>THE WITNESS:</b> Well, our data showed 17 that the effective doses of Risperdal, there 18 was prolactin increase in the Risperdal 19 patients, but also in the haloperidol 20 patients. So if you just compared one versus 21 the other, it was not too much of a 22 difference in the degree of prolactin 23 increase compared to first generation 24 antipsychotics such as haloperidol. 25 <b>BY MS. SULLIVAN:</b>		1 antipsychotics can be very effective in. We started 2 studying psychosis in the elderly with Risperdal. 3 We started also studying Risperdal in adolescents 4 with schizophrenia because schizophrenia can start 5 up at the age of 12, 14, 16. 6 We also studied Risperdal in children 7 and adolescents with bipolar mania. As I said 8 earlier, we did additional studies in schizophrenia. 9 And we also studied different types of 10 administration in different psychotic disorders. 11 <b>MS. SULLIVAN:</b> And, Your Honor, I'm 12 sorry, what time does the Court want to 13 break? 14 <b>THE COURT:</b> In about five minutes. 15 <b>BY MS. SULLIVAN:</b> 16 <b>Q. And, Dr. Cares, as Janssen continued to study</b> 17 <b>the medicine -- and Risperdal is still on the market</b> 18 <b>today, sir?</b> 19 A. Yes, it is. 20 <b>Q. Still being prescribed today?</b> 21 A. Yes. Yes. 22 <b>Q. And so it's been on the market for how many</b> 23 <b>years, Dr. Caers?</b> 24 A. It's about 20 -- 21, 22 years now, about. 25 <b>Q. And can you give our jurors a sense of how</b>	

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<p>1 <b>much safety data there is on Risperdal as of today?</b></p> <p>2 A. Well, then you need to differentiate it in two</p> <p>3 databases. When I stopped working for Risperdal</p> <p>4 back in 2009, we had more than 16,000 patients</p> <p>5 documented in clinical studies with Risperdal. But</p> <p>6 apart from that, there's also another database that</p> <p>7 is based on spontaneous reporting. Physicians when</p> <p>8 they see an adverse event that is a particular</p> <p>9 concern of interest, they report it to the</p> <p>10 authorities. And that's another type of very huge</p> <p>11 database with thousands and thousands, even hundred</p> <p>12 thousands of patients of whom some are reported to</p> <p>13 have a certain adverse event on Risperdal, for</p> <p>14 example.</p> <p>15 So that's a very -- thousands and</p> <p>16 thousands of patients safety database, apart from</p> <p>17 the clinical studies we had in our 16,000 patients.</p> <p>18 <b>Q. And, Dr. Caers, are you familiar, as part of</b></p> <p>19 <b>your work in medicine development, with the FDA</b></p> <p>20 <b>standards in terms of how many studies and how many</b></p> <p>21 <b>patients you have to have to get FDA approval?</b></p> <p>22 A. Yes. The minimum for an approval, but that's</p> <p>23 the absolute minimum, is you need to have 1,500</p> <p>24 patients exposed to the product, different subjects</p> <p>25 exposed to the products. You need at least 3- to</p>		<p>1 <b>Q. Dr. Caers, do you know by how much Janssen</b></p> <p>2 <b>exceeded the FDA standards?</b></p> <p>3 <b>MR. KLINE:</b> Your Honor, objection.</p> <p>4 <b>THE COURT:</b> Sustained. You are</p> <p>5 asking for some kind of evaluation,</p> <p>6 quantitative evaluation that only an expert</p> <p>7 can make. You know, you can ask him what he</p> <p>8 did, what he didn't do. But that's a fact</p> <p>9 witness. But to ask him for his opinion on</p> <p>10 whether he did enough, that's what the</p> <p>11 subject of this trial is about. Sustained.</p> <p>12 We're going to take a recess right</p> <p>13 here till about 11:30, all right? I do have</p> <p>14 a meeting that I'm going to attend very</p> <p>15 briefly and then come back. So we're going</p> <p>16 to take a recess here till 10:30.</p> <p>17 No. Then what's going to happen is</p> <p>18 we're going to return -- I mean 11:30. And</p> <p>19 then what we're going to do, we will return</p> <p>20 for another hour and then we'll take a recess</p> <p>21 for lunch is what we're going to do. I</p> <p>22 apologize at my end. But that way we didn't</p> <p>23 lose a whole morning for this meeting for us,</p> <p>24 all right? So we'll see you in about, I</p> <p>25 guess, at 11:30 I'll be here.</p>	
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<p>1 600 patients exposed for six months. And you need</p> <p>2 at least 100 patients exposed for one year or more</p> <p>3 in order to have an approval package for one single</p> <p>4 indication.</p> <p>5 <b>Q. And, Dr. Caers, as it stands, how does what</b></p> <p>6 <b>Janssen did in terms of safety testing on Risperdal</b></p> <p>7 <b>compare with the FDA standards?</b></p> <p>8 <b>MR. KLINE:</b> I have an objection, Your</p> <p>9 Honor.</p> <p>10 <b>THE COURT:</b> That's sustained. That's</p> <p>11 sustained.</p> <p>12 <b>BY MS. SULLIVAN:</b></p> <p>13 <b>Q. Dr. Caers, did Janssen meet or exceed the FDA</b></p> <p>14 <b>standards?</b></p> <p>15 <b>MR. KLINE:</b> Objection. It's just a</p> <p>16 back door. Same question.</p> <p>17 <b>THE COURT:</b> You're asking his</p> <p>18 opinion?</p> <p>19 <b>MS. SULLIVAN:</b> Well, he's a fact</p> <p>20 witness, Your Honor. He knows.</p> <p>21 <b>THE COURT:</b> All right. That's</p> <p>22 sustained.</p> <p>23 <b>MR. KLINE:</b> That's an opinion</p> <p>24 question.</p> <p>25 <b>BY MS. SULLIVAN:</b></p>		<p>1 <b>COURT CRIER:</b> All rise.</p> <p>2 <b>THE COURT:</b> You may go outside, of</p> <p>3 course, if you want to. You know, you don't</p> <p>4 have to stay here. Same rules apply.</p> <p>5 - - -</p> <p>6 (Whereupon the jury exited the</p> <p>7 courtroom at 10:42 a.m.)</p> <p>8 - - -</p> <p>9 <b>THE COURT:</b> Sir, you are excused till</p> <p>10 11:30. But please do not discuss your</p> <p>11 testimony now with your lawyers.</p> <p>12 <b>THE WITNESS:</b> I understand, Judge.</p> <p>13 <b>THE COURT:</b> Yes, sir.</p> <p>14 <b>MR. KLINE:</b> May I have whatever</p> <p>15 demonstratives are going to be used with this</p> <p>16 witness?</p> <p>17 <b>MS. SULLIVAN:</b> Sure.</p> <p>18 <b>THE COURT:</b> I guess that would be</p> <p>19 efficient for everybody.</p> <p>20 <b>MS. SULLIVAN:</b> Yeah.</p> <p>21 <b>MS. BROWN:</b> Yeah.</p> <p>22 <b>THE COURT:</b> I do urge counsel to</p> <p>23 review the motions in limine. We spent a lot</p> <p>24 of time on them. And I hope that they're a</p> <p>25 guide to what this Court's rulings will be</p>	

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<p>- PLEDGER -vs- JANSSEN -</p> <p>1 here in court in front of the jury.  2 <b>MS. SULLIVAN:</b> And, Your Honor, other  3 than safe and effective, Your Honor, I  4 thought that Judge New ruled that the FDA  5 issues could come into this case.</p> <p>6 <b>THE COURT:</b> Well, the safe and  7 effective, that particular language was  8 forbidden. But I'm not, you know, going to  9 jump over heels on it, because it was used  10 just now by a witness and there was no  11 objection.</p> <p>12 But the reality of the matter is that  13 the FDA documents were precluded for reasons  14 that were stated on the record before. These  15 are documents that fundamentally can be used  16 if they are introduced through a proper  17 foundation the proper way. But not in order  18 to -- we went through the same thing with  19 Mr. Kline when he had Dr. Kessler here, and  20 we did not permit all of these documents to  21 be admissible. Only certain ones came in.</p> <p>22 If you want to run them by us ahead  23 of time before the trial or before a witness,  24 by all means. But it's at your peril if  25 you're going to go against rulings that have</p>	<p>Page 69</p>	<p>- IVO CAERS, Ph.D. - DIRECT -</p> <p>1 You may proceed when you're ready.  2 <b>MS. SULLIVAN:</b> Thank you, Your Honor.  3 Welcome back, everyone.</p> <p>4 - - -</p> <p>5 <b>E X A M I N A T I O N</b></p> <p>6 - - -</p> <p>7 <b>BY MS. SULLIVAN:</b>  8 <b>Q.</b> Welcome back, Dr. Caers. Let me just get  9 moving here.</p> <p>10 <b>Dr. Caers, I wanted to talk some more</b>  11 <b>about Janssen's study of Risperdal on children and</b>  12 <b>adolescents; and you were involved with that,</b>  13 <b>Dr. Caers?</b></p> <p>14 A. Yes, I was.</p> <p>15 <b>Q. Can you tell our jury the nature of your</b>  16 <b>involvement in Janssen's studying the medicine on</b>  17 <b>children and adolescents?</b></p> <p>18 A. Well, my team actually developed the study,  19 the study protocols and actually run it by  20 investigators, and also managed the analysis and the  21 reporting of the study in the Clinical Study  22 Reports, and eventually also managed and dealt with  23 the composition of the New Drug Application -- in  24 this case a Supplemental New Drug Application, which  25 concluded -- which had all the information we have</p>	<p>Page 71</p>
<p>- IVO CAERS, Ph.D. - DIRECT -</p> <p>1 already been made on these subjects.  2 All right. We're at recess till  3 11:30.</p> <p>4 - - -</p> <p>5 (Whereupon a recess was taken.)</p> <p>6 - - -</p> <p>7 <b>COURT CRIER:</b> Come to order, please.  8 <b>THE COURT:</b> All right. Please be  9 seated.</p> <p>10 - - -</p> <p>11 (Time noted: 11:36 a.m.)</p> <p>12 - - -</p> <p>13 (Witness resumed the stand.)</p> <p>14 - - -</p> <p>15 <b>COURT CRIER:</b> All rise as the jury  16 enters the courtroom.</p> <p>17 - - -</p> <p>18 (Whereupon the jury entered the  19 courtroom at 11:38 a.m.)</p> <p>20 - - -</p> <p>21 <b>THE COURT:</b> All right. Please be  22 seated, everybody.  23 All right. Thank you for your  24 indulgence, everybody. It was good. Thank  25 you.</p>	<p>Page 70</p>	<p>- IVO CAERS, Ph.D. - DIRECT -</p> <p>1 collected in the different studies in a big file,  2 which was eventually submitted to the FDA at  3 different occasions.</p> <p>4 <b>Q. And, Dr. Caers, after the medicine was</b>  5 <b>approved in 1993, did the company become aware that</b>  6 <b>it was being prescribed off-label by physicians to</b>  7 <b>children and adolescents?</b></p> <p>8 A. Well, we had information, indeed, that in this  9 country there were physicians that prescribed  10 Risperdal for children or adolescents at that time.</p> <p>11 <b>Q. And so if the company was already selling the</b>  12 <b>medicine for off-label prescriptions, can you tell</b>  13 <b>us what the reason was the company continued to</b>  14 <b>study the medicine in children and get towards</b>  15 <b>getting additional approvals?</b></p> <p>16 A. Well, for the company it's very important that  17 there's appropriate information on appropriate use  18 of this medicine in different populations, such as  19 in this case pediatric population, such as children  20 and adolescents. And although it was used in the  21 marketplace, which we call off-label, it is  22 important to document efficacy and safety, have that  23 reviewed by the FDA, so that you have appropriate  24 guidance in the label on how to use this medicine in  25 this population and for which type of population</p>	<p>Page 72</p>

<p>- IVO CAERS, Ph.D. - DIRECT -</p> <p>1 within this pediatric population.</p> <p>2 <b>Q. And, Dr. Caers, are there issues or challenges</b></p> <p>3 <b>when companies try to study medicines in children?</b></p> <p>4 A. Well, yeah. If you can understand, patients</p> <p>5 are requested and expected to give informed consent,</p> <p>6 as we discussed before the break, and particularly</p> <p>7 for children, this is not easy. I have three</p> <p>8 children as well. I have seven grandchildren. So</p> <p>9 you would think twice before you would conclude that</p> <p>10 you would allow your child or your grandchild to</p> <p>11 enter a study. Nevertheless, without the goodwill</p> <p>12 and the preparedness of these parents and children,</p> <p>13 we wouldn't be able to do these in clinical studies,</p> <p>14 and we would never be able to advise physicians on</p> <p>15 how to appropriately use this medicine in this</p> <p>16 population.</p> <p>17 Q. And, Dr. Caers, while you were supervising</p> <p>18 some of these clinical trials on children and</p> <p>19 adolescents, can you tell us whether the FDA had any</p> <p>20 involvement in encouraging companies to study</p> <p>21 medicines?</p> <p>22 MR. KLINE: Objection.</p> <p>23 THE COURT: Overruled.</p> <p>24 THE WITNESS: There are two ways that</p> <p>25 the FDA is involved. First of all, as we</p>	Page 73	<p>- IVO CAERS, Ph.D. - DIRECT -</p> <p>1 studies, the way the FDA asked you to do it</p> <p>2 and you complete the studies, you make the</p> <p>3 Clinical Study Report and you submit this</p> <p>4 information to the FDA, and if this is, along</p> <p>5 with the written request, what the FDA asked</p> <p>6 you to do, then companies get an additional</p> <p>7 six months exclusivity, which basically means</p> <p>8 that you have six months more exclusivity on</p> <p>9 your product than without these pediatric</p> <p>10 studies. So that genetic companies can only</p> <p>11 come six months later on the market with a</p> <p>12 genetic compound. That's basically the</p> <p>13 benefit for companies first that they ask you</p> <p>14 to do.</p> <p>15 <b>BY MS. SULLIVAN:</b></p> <p>16 Q. So the FDA and government provided incentives</p> <p>17 for companies to study the medicine in children?</p> <p>18 A. Within the --</p> <p>19 MR. KLINE: Objection. Objection.</p> <p>20 THE COURT: All right. That's</p> <p>21 sustained. Sustained.</p> <p>22 <b>BY MS. SULLIVAN:</b></p> <p>23 Q. And did you have meetings with the FDA,</p> <p>24 Dr. Caers, to get permission to study the medicine</p> <p>25 in children and adolescents?</p>	Page 75
<p>- IVO CAERS, Ph.D. - DIRECT -</p> <p>1 said earlier, for every study you want to do</p> <p>2 in this country, you need to have at least</p> <p>3 permission by the FDA to run the study. But</p> <p>4 there is a particular legislation as well</p> <p>5 that came into effect by the late '90s, and</p> <p>6 that has to do with pediatric exclusivity.</p> <p>7 What does pediatric exclusivity mean?</p> <p>8 Congress has voted legislation back</p> <p>9 in the late 1990s that said and that wanted</p> <p>10 to stimulate clinical research in children,</p> <p>11 because before actually we started in this</p> <p>12 area, there was no -- there was no research</p> <p>13 ongoing, not at all.</p> <p>14 So Congress and the FDA wanted to</p> <p>15 stimulate the companies to study drugs more</p> <p>16 in children and adolescents. And that's how</p> <p>17 the legislation of pediatric exclusivity came</p> <p>18 into account.</p> <p>19 And that legislation allowed and gave</p> <p>20 even the mandate to the FDA to tell companies</p> <p>21 this is the type of studies in this type of</p> <p>22 population that we want you to do. And if --</p> <p>23 on the other hand, there's a benefit for</p> <p>24 companies as well in the same legislation by</p> <p>25 Congress. If you actually do them, these</p>	Page 74	<p>- IVO CAERS, Ph.D. - DIRECT -</p> <p>1 A. We had meetings with the FDA on how to run</p> <p>2 these studies and how these studies would need to</p> <p>3 look like and what type of patients, et cetera, yes,</p> <p>4 we had several meetings of this kind.</p> <p>5 Q. And, Dr. Caers, I'm going to put up an exhibit</p> <p>6 that has been up before. And this is DG6-3. And</p> <p>7 Ms. Brown can tell me what is the --</p> <p>8 MS. BROWN: Yes. 58.</p> <p>9 MS. SULLIVAN: Defense Exhibit 58.</p> <p>10 (Exhibit D-58 marked for</p> <p>11 identification.)</p> <p>12 COURT CRIER: Counsel have it?</p> <p>13 MS. BROWN: Yeah, they have it.</p> <p>14 MR. KLINE: This is the</p> <p>15 demonstrative. I have no objection.</p> <p>16 <b>BY MS. SULLIVAN:</b></p> <p>17 Q. And, Dr. Caers, we're looking at Defense</p> <p>18 Exhibit 58. And can you tell the jury how many</p> <p>19 clinical trials Janssen did to support the approval</p> <p>20 of Risperdal in children and adolescents?</p> <p>21 A. Well, in total, we did at least 18 studies in</p> <p>22 different populations of children and adolescents</p> <p>23 ranging from autism, disruptive behavior disorders,</p> <p>24 adolescent schizophrenia, children and adolescent</p> <p>25 bipolar mania. And they're, more or less, a little</p>	Page 76

<p>- IVO CAERS, Ph.D. - DIRECT -</p> <p>1 bit listed here on this list.  2 And just for your information, on the  3 left-hand side, Clinical Trial, the NED-9 is a study  4 done in the Netherlands. The BEL is a study done in  5 Belgium. International is an international study in  6 different countries. USA is a USA study, and so on,  7 Canada, Canada, and so on.</p> <p><b>8 Q. Dr. Caers, what kind of safety information did  9 Janssen collect in the course of these clinical  10 trials in children and adolescents?</b></p> <p>11 A. Well, similar to the adults, you collect  12 basically all safety information. You do regular  13 blood analysis. You also systematically measure  14 prolactin in this population. We collected adverse  15 events as reported by patients and by the  16 investigator, which are written down by the  17 investigators in the file. And all this  18 information, apart from obviously the efficacy  19 assessments, was all collected together in the  20 database and eventually in the Clinical Study  21 Report, just similar to what we discussed before the  22 break on adult patients.</p> <p><b>23 Q. And did Janssen provide all of the side effect  24 information from these clinical trials to the FDA?</b></p> <p>25 A. Yes, indeed.</p>	Page 77	<p>- IVO CAERS, Ph.D. - DIRECT -</p> <p>1 authors up and down and different versions. Then at  2 the end you have a final manuscript which is  3 submitted to a medical journal with requested  4 publishes.</p> <p>5 Peer review means that experts in the  6 field review your paper, very often have comments,  7 recommendations to -- can you say this differently,  8 we don't think this is an appropriate phrase. Can  9 you do that additional analysis? So the next step  10 is you do, again, your additional things. You adapt  11 your manuscript. You resubmit it and then very  12 often it is either accepted for publication and it  13 goes in the waiting list for the final publication,  14 which may take another six to nine months. So  15 overall, this period can take a few years even,  16 usually.</p> <p><b>17 Q. And, Dr. Caers, how did the company decide  18 what kind of indications or reasons the company  19 should study Risperdal for as far as children and  20 adolescents?</b></p> <p>21 A. Well, there are two sources to make that  22 decisions. First of all, we had experts in the  23 field and we did advisory panels because we knew --</p> <p><b>24 Q. Is that advisory panels?</b></p> <p>25 A. Yeah, advisory panels, yes. So that's a group</p>	Page 79
<p>- IVO CAERS, Ph.D. - DIRECT -</p> <p><b>1 Q. And, Dr. Caers, did Janssen also publish these  2 studies for the world to see?</b></p> <p>3 A. Yes. The different studies were, indeed,  4 published in medical journals so that also the  5 medical community and doctors could read about the  6 experience and the findings in particular studies,  7 both on efficacy and safety.</p> <p><b>8 Q. And, Doctor, at this time was there any  9 requirement for Janssen to publish their studies?</b></p> <p>10 A. At that moment I don't think there was a  11 requirement to publish the studies, but that was  12 usually done.</p> <p><b>13 Q. And, Dr. Caers, can you describe -- so there's  14 been some discussion about the time lag between when  15 a study is done and when it's published. Can you  16 talk about the peer-review process?</b></p> <p>17 A. Yeah. It's a -- there are different steps,  18 obviously. Once you have your database closed and  19 your analysis, the first thing you do is making sure  20 you have the Clinical Study Report. And that's a  21 hell of a job, as I said earlier. That's a 100- to  22 150-page document with thousands of pages of tables.  23 And then the next step is you consider to publish  24 the findings of the study in a peer-review journal.  25 So you develop a manuscript, have it reviewed by</p>	Page 78	<p>- IVO CAERS, Ph.D. - DIRECT -</p> <p>1 of experts in the field that you bring together and  2 that you raise questions and you hear on their  3 opinion. And they said -- because we knew there was  4 widespread use in pediatrics of Risperdal -- and  5 they said, well, where is this used most prominent?  6 And consequently, that is where you have the most  7 prominent, pronounced medical need.</p> <p>8 On the other hand -- and also the  9 FDA -- and remember the pediatric exclusivity law --  10 there, the FDA said we want you to do clinical  11 studies in pediatrics in this indication, which was,  12 in our case, schizophrenia and bipolar mania,  13 because those are the two indications for which the  14 product was approved in adults. And they said once  15 this indication can also occur in pediatrics, we  16 want you to study that field. So there are two  17 different sources in making that selection.</p> <p><b>18 Q. So outside experts, outside doctors would  19 suggest ways that Risperdal may be helpful and then  20 the FDA also gave you some information about what  21 they wanted?</b></p> <p>22 <b>MR. KLINE:</b> Objection; asked and  23 answered; and simply repeating his testimony  24 as she's inclined to do, so I object.</p> <p><b>THE COURT:</b> How about leading?</p>	Page 80

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<p>1                   <b>MR. KLINE:</b> And leading, too.  2                   <b>THE COURT:</b> Sustained. Sustained.  3   <b>BY MS. SULLIVAN:</b>  4   <b>Q.</b> And, Dr. Caers, I want to show you a document  5   that was marked by the plaintiffs. It was  6   Plaintiff's Exhibit 16, if I may.  7                   <b>MS. SULLIVAN:</b> Okay. Is there any  8   objection?  9                   <b>THE COURT:</b> I don't know. What is  10   this document?  11                   <b>MR. KLINE:</b> I need to get the  12   document in front of me.  13                   <b>MS. SULLIVAN:</b> It's your Exhibit  14   Plaintiff's 16.  15                   <b>MR. KLINE:</b> I understand that. And  16   there was a pile this high.  17                   <b>THE COURT:</b> Okay. This is D-16?  18                   <b>MS. SULLIVAN:</b> Plaintiff's 16.  19                   <b>MS. BROWN:</b> P-16.  20                   <b>COURT CRIER:</b> It was a plaintiff's  21   exhibit.  22                   <b>THE COURT:</b> P-16.  23                   <b>MR. KLINE:</b> Your Honor, it's an FDA  24   contact document, and it's a Janssen  25   document. I just need to know what the</p>	<p>1                   the whole development program to study Risperdal in,  2   the umbrella term, "conduct disorder," or with other  3   words also, disruptive behavioral disorders. And we  4   did several double-blind studies.  5                   First, there's placebo. That means  6   you give one group the active compound and the other  7   group you give a sugar pill, but that looks the same  8   and you don't know which one of the two has the  9   active and which one has the placebo, the sugar  10   pill. And then you see whether you find a  11   difference between the active and the placebo, which  12   is the documentation of your efficacy, and obviously  13   also document all safety. So this is the efficacy  14   study.  15                   On top of that, we did long-term  16   safety studies where you have patients exposed to  17   the compound over a long period and you document all  18   safety aspects related to the product.  19   <b>Q.</b> And, Dr. Caers, you said it was already being  20   used in conduct disorder. What do you mean, sir?  21   A. Well, as was mentioned earlier today, there  22   was also in the '90s, there was a certain off-label  23   use in the US of Risperdal in pediatrics. And based  24   on the feedback we got from these experts, this was  25   one of the areas where there was substantial</p>		
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<p>1                   question is before the display.  2                   <b>THE COURT:</b> Yeah, I agree.  3                   <b>MR. KLINE:</b> Certainly every document  4   doesn't need to be displayed.  5                   <b>THE COURT:</b> All right. Why don't you  6   ask your questions and see how you're going  7   to use this document.  8                   <b>MS. SULLIVAN:</b> Sure.  9   <b>BY MS. SULLIVAN:</b>  10   <b>Q.</b> Dr. Caers, were you involved with interactions  11   with FDA and interactions with people in your group  12   who interacted with FDA about what indications  13   Janssen should seek approval for?  14   A. Yes, I was.  15   <b>Q.</b> And there are also meetings with the FDA on  16   that issue?  17   A. Yes, there were.  18   <b>Q.</b> And, Dr. Caers, you're familiar with -- well,  19   tell us about the conduct disorder issue.  20   A. Well, conduct disorder, that was back in the  21   mid-'90s when the advisors, as I referred to  22   earlier, advisors that this was one of the areas in  23   pediatrics where there was a major medical need and  24   where there was a substantial use already at that  25   moment. And that's why in the mid-'90s we started</p>	<p>1                   off-label use; but also that in their experience,  2   there was a very substantial benefit. But obviously  3   that had to be documented in well-designed studies.  4   <b>Q.</b> And, Dr. Caers, did the FDA have any concerns  5   about Janssen seeking approval for the indication  6   conduct disorder for children and adolescents?  7   A. Well, yeah. We consulted with the FDA to  8   which extent the FDA thought that this would be a  9   valid indication for Risperdal and they raised their  10   concerns. They thought that this product, and  11   particularly its use would be targeted towards  12   aggression and agitation in conduct disorders'  13   patients, and they didn't feel that aggression on  14   itself was an appropriate indication for label --  15   <b>MR. KLINE:</b> Your Honor, please.  16   <b>THE COURT:</b> I'm going to permit him  17   to finish his answer.  18   <b>MR. KLINE:</b> Yes.  19   <b>THE WITNESS:</b> They did not say it  20   didn't exist, because there's a big book -- a  21   thick book, the DSM-IV, which lists all the  22   psychiatry disorders by the American  23   Psychiatry Association. They said, yes, we  24   recognize it's in that thick book, but,  25   nevertheless, we don't think this is an</p>		

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- IVO CAERS, Ph.D. - DIRECT - <p>1 appropriate indication for label. 2 <b>MR. KLINE:</b> Move -- 3 <b>MS. SULLIVAN:</b> And -- 4 <b>MR. KLINE:</b> May I, please? 5 Move to strike. It's all hearsay 6 based on what he says the FDA says. 7 <b>THE COURT:</b> Well, I am going to deny 8 that motion at this time. I'm going to deny 9 it. 10 But, again -- 11 <b>MS. SULLIVAN:</b> May I use the 12 document, Your Honor? 13 <b>THE COURT:</b> I don't know. You have 14 to use that for a legitimate purpose. I 15 mean, to refresh memory, some kind of 16 reference, you know, something that has to be 17 legitimate as far as being flashed up on 18 evidence. 19 <b>MS. SULLIVAN:</b> Well, they've put it 20 up. This is their document. They put it up. 21 <b>THE COURT:</b> It doesn't matter whether 22 it's their document. They used it for a 23 particular purpose. 24 <b>BY MS. SULLIVAN:</b> 25 <b>Q.</b> And, Dr. Caers, are you familiar -- the jury</p>	Page 85	- IVO CAERS, Ph.D. - DIRECT - <p>1 <b>our jurors what role you had in the overall</b> 2 <b>Risperdal approval process?</b> 3 A. Well, not only in the approval process, my 4 team, as I said earlier, which was managed by me, so 5 headed by me, was dealing with all clinical studies 6 done with Risperdal worldwide. We were dealing with 7 all submissions. We were dealing with all the 8 consultations with regulatory bodies, including the 9 FDA, but not limited to the FDA. My team was 10 dealing with all the studies with it, reporting 11 them, putting the files together, submitting the 12 files, negotiating and having meetings with the FDA 13 before submission, if necessary after submission, 14 and eventually dealing with the final label as 15 approved by the FDA. 16 <b>Q.</b> And, Dr. Caers, as part of that process, would 17 you review minutes of meetings with the FDA? 18 A. Yes. 19 <b>THE COURT:</b> And also, Counsel, would 20 you ask him what the timetable of his 21 involvement in this -- what he just 22 described, what are we talking about? So I 23 can understand for relevancy sake, once and 24 for all -- 25 <b>MS. SULLIVAN:</b> Sure.</p>	Page 87
- IVO CAERS, Ph.D. - DIRECT - <p>1 <b>has seen the term -- and Mr. Kline showed</b> 2 <b>Dr. Kessler -- the term as it related to conduct</b> 3 <b>disorder, the FDA's concern about, quote-unquote, a</b> 4 <b>"chemical straitjacket."</b> Are you familiar with that</p> <p>5 <b>document?</b> 6 A. Well, yes. Because that was in the minutes, I 7 think, of that actual meeting. 8 <b>Q.</b> Yeah. 9 A. And that has exactly to do with the treatment 10 of aggression. That's -- that's a delicate issue. 11 Why do you treat aggression? Is it in order to help 12 the patient or is it in order to help the 13 environment? 14 <b>Q.</b> And, Doctor -- 15 <b>MR. KLINE:</b> Your Honor, move to 16 strike. He's not a physician. He's not even 17 a physician. 18 <b>THE COURT:</b> Well, no. Overruled. 19 Overruled. 20 It's still unclear to me, Counsel, 21 exactly what role this witness had in all of 22 this. 23 <b>MS. SULLIVAN:</b> Fair enough, Judge. 24 <b>BY MS. SULLIVAN:</b> 25 <b>Q.</b> Dr. Caers, can you describe -- can you tell</p>	Page 86	- IVO CAERS, Ph.D. - DIRECT - <p>1 <b>THE COURT:</b> -- what we're talking 2 about. 3 <b>THE WITNESS:</b> If I may. 4 <b>THE COURT:</b> Yeah. Go ahead. 5 <b>THE WITNESS:</b> I played this role as a 6 team development leader since 1999, mid-1999, 7 but also before I was involved in the 8 Risperdal strategy, but less so in dealing 9 with the FDA meetings. But from 1999 up to 10 2009, I was involved with basically all these 11 meetings. 12 <b>MS. SULLIVAN:</b> And so can I now 13 display Plaintiff's Exhibit 16? 14 <b>MR. KLINE:</b> No. It's just full of 15 FDA stuff, Your Honor. 16 I don't object to the "chemical 17 straitjacket" part. 18 <b>THE COURT:</b> Pardon me? 19 Well, as far as I'm concerned, is 20 this a document he's familiar with? 21 <b>MS. SULLIVAN:</b> Yes. 22 <b>THE COURT:</b> Why don't you just 23 authenticate it in the usual way. 24 <b>MS. SULLIVAN:</b> Yeah. 25 <b>THE COURT:</b> And then we'll go for it.</p>	Page 88

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<p>1 <b>BY MS. SULLIVAN:</b></p> <p>2 <b>Q. And, Dr. Caers, is this a document that you're</b></p> <p>3 <b>familiar with; that you've seen?</b></p> <p>4 A. Yeah, sure. Because Al Derivan is one of the</p> <p>5 gentlemen -- he was my clinical leader on my team as</p> <p>6 a child psychiatrist; Goedele DeSmedt. So, yes, all</p> <p>7 these people were a member of my team. And</p> <p>8 obviously I was involved from A to Z in preparing</p> <p>9 for this meeting. I was not actually at that</p> <p>10 meeting, but I was also involved in reviewing the</p> <p>11 minutes and the next steps.</p> <p>12 <b>MS. SULLIVAN:</b> And, Your Honor, may I</p> <p>13 display the --</p> <p>14 <b>THE COURT:</b> For what purpose?</p> <p>15 <b>MS. SULLIVAN:</b> I wanted to talk about</p> <p>16 their -- in response to Mr. Kline's argument</p> <p>17 about chemical straitjacket, what was really</p> <p>18 going on here.</p> <p>19 <b>THE COURT:</b> Well, why don't you have</p> <p>20 him review this document, look at the bullet</p> <p>21 point and ask him. You don't need to put the</p> <p>22 whole document up there because I don't</p> <p>23 believe this whole document was admitted</p> <p>24 before in its entirety, unless there's a</p> <p>25 reason for it.</p>		<p>1 no, because they don't -- they just raised a</p> <p>2 concern and referred to the term</p> <p>3 "straitjacket." But they also said, look,</p> <p>4 before we decide on this, you can go ahead,</p> <p>5 but we will bring it before a public advisory</p> <p>6 board. And a public advisory board is part</p> <p>7 of the review process with the FDA in which</p> <p>8 they ask, again, experts in the field,</p> <p>9 whether the experts support an approval, yes</p> <p>10 or no. So it's not you can't do it, but they</p> <p>11 said we are not convinced.</p> <p>12 <b>BY MS. SULLIVAN:</b></p> <p>13 <b>Q. And so what did Janssen do in response to</b></p> <p>14 <b>that?</b></p> <p>15 A. Well, we did two things, because, again, this</p> <p>16 is within the pediatric exclusivity legislation.</p> <p>17 Part of this meeting was as well. Our question to</p> <p>18 the FDA, this is the studies we have already done in</p> <p>19 pediatrics. Can this be used for submitting for the</p> <p>20 pediatric exclusivity?</p> <p>21 And there, the FDA said, no, we don't</p> <p>22 think so because we -- we -- and this legislation</p> <p>23 was very new at that moment. The position by the</p> <p>24 FDA was we want you, first of all, to study,</p> <p>25 according to the pediatric exclusivity legislation,</p>	
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<p>1 <b>MS. SULLIVAN:</b> They had it up with</p> <p>2 Dr. Kessler, Your Honor.</p> <p>3 <b>THE COURT:</b> Again, whatever -- I have</p> <p>4 to go through my notes as to what the reason</p> <p>5 was.</p> <p>6 For the purpose that you're telling</p> <p>7 me now, you can have him comment on what was</p> <p>8 going on with that chemical straitjacket</p> <p>9 bullet point by refreshing his memory about</p> <p>10 that point without putting the whole document</p> <p>11 in there.</p> <p>12 <b>BY MS. SULLIVAN:</b></p> <p>13 <b>Q. So, Dr. Caers, can you talk about the FDA's</b></p> <p>14 <b>concern on this chemical straitjacket statement that</b></p> <p>15 <b>Mr. Kline referred to in his case and what the</b></p> <p>16 <b>company's response was?</b></p> <p>17 <b>MR. KLINE:</b> Object to the hearsay.</p> <p>18 No objection to the company --</p> <p>19 <b>THE COURT:</b> No. As to his concern,</p> <p>20 FDA, or Janssen's response to that whole</p> <p>21 issue, absolutely.</p> <p>22 You may proceed.</p> <p>23 <b>THE WITNESS:</b> So as I said earlier,</p> <p>24 the FDA had concerns about treating</p> <p>25 aggression as a target, and they didn't say</p>		<p>1 we want you to study Risperdal in this case in</p> <p>2 schizophrenia and bipolar mania, because those are</p> <p>3 the two indications the product was also approved</p> <p>4 for in adults. And this indication, this disease</p> <p>5 can occur in children and adolescents, at least for</p> <p>6 schizophrenia in adolescents.</p> <p>7 <b>Q. And, Dr. Caers, did Janssen pursue those</b></p> <p>8 <b>indications in children, schizophrenia and bipolar?</b></p> <p>9 A. So as a consequence of this meeting, we</p> <p>10 definitely pursued and did studies in both</p> <p>11 adolescents with schizophrenia and in children and</p> <p>12 adolescents with bipolar mania, and we eventually</p> <p>13 got pediatric exclusivity approved.</p> <p>14 <b>Q. And was Risperdal approved for children with</b></p> <p>15 <b>schizophrenia?</b></p> <p>16 A. Not for children, but for only adolescents.</p> <p>17 <b>Q. Adolescents.</b></p> <p>18 A. Schizophrenia doesn't occur before the age of</p> <p>19 adolescents. So it was adolescents with</p> <p>20 schizophrenia and children of 10 years and older and</p> <p>21 adolescents in bipolar mania.</p> <p>22 <b>Q. And can you talk to our jurors about how</b></p> <p>23 <b>Janssen's decision to pursue FDA approval for kids</b></p> <p>24 <b>with autism came about?</b></p> <p>25 A. That's a whole different story.</p>	

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<p>1 It all started with a study and a 2 consortium of US academic centers. And there they 3 had to combine themselves -- organize themselves under 4 what they call the RUPP consortium. And RUPP stands 5 for Research Unit for Pediatric Psychotherapy, or 6 Psychopharmacology. And they concluded, with the 7 sponsorship of the National Institute of Mental 8 Health, which is a government organization that 9 sponsors and that stimulates research in mental 10 health, this consortium run what is called the RUPP 11 study, or the USA-150, totally without really 12 contacts and input from our side in the study design 13 and the study conduct.</p> <p>14 <b>Q. And, Dr. Caers, you were familiar with the</b> 15 <b>RUPP study?</b></p> <p>16 A. Yes, I am.</p> <p>17 <b>Q. And can we -- and did Janssen -- well, can we</b> 18 <b>mark -- I think it's already been used. Defense</b> 19 <b>Exhibit...</b></p> <p>20 <b>MS. BROWN:</b> It would be -- we're 21 going to mark the flip chart as 59. So it 22 would be 60, if we have not already used it. 23 (Exhibits D-59 and D-60 marked for 24 identification.)</p> <p>25 <b>MS. SULLIVAN:</b> Any objection?</p>		<p>1 <b>Q. And what did this government-funded study find</b> 2 <b>on the issue of Risperdal and whether it worked for</b> 3 <b>kids with autism?</b></p> <p>4 A. Well, the results which were published in 5 2002, I think, they showed that there was clear 6 efficacy of Risperdal in the children compared to 7 placebo. Remember, the sugar pill. It was a 8 double-blind study. And there was very robust 9 efficacy, particularly on what they call the 10 irritability associated with autism, which are 11 symptoms of agitation, aggression, restlessness and 12 things like that. And they also obviously 13 documented the safety in this study as described in 14 the paper.</p> <p>15 <b>Q. And can you tell us whether the RUPP study got</b> 16 <b>any press?</b></p> <p>17 <b>MR. KLINE:</b> Objection, Your Honor. 18 Whether it got press is irrelevant.</p> <p>19 <b>THE COURT:</b> Whether it got press, 20 sustained.</p> <p>21 <b>BY MS. SULLIVAN:</b></p> <p>22 <b>Q. How, Dr. Caers, if at all, did the findings of</b> 23 <b>the RUPP study impact Janssen in terms of their</b> 24 <b>research?</b></p> <p>25 A. Well, the data were published in the New</p>	
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<p>1 <b>MR. KLINE:</b> Yes. Your Honor, the 2 learned -- if it's learned treatise, it falls 3 under Aldridge. And to the extent he 4 testifies he knows it and the like, that's 5 fine. To the extent it's going to be read, 6 displayed, parroted, then I object, under 7 Aldridge, specifically under the Aldridge 8 case, which doesn't allow that.</p> <p>9 <b>MR. MURPHY:</b> He's not an expert.</p> <p>10 <b>MR. KLINE:</b> With an expert or a 11 nonexpert.</p> <p>12 <b>THE COURT:</b> Yes. Sustained.</p> <p>13 <b>BY MS. SULLIVAN:</b></p> <p>14 <b>Q. Dr. Caers, the study that you talked about,</b> 15 <b>who funded that study, the RUPP study?</b></p> <p>16 A. The RUPP study was funded by the National 17 Institute of Mental Health.</p> <p>18 <b>Q. And that's the government?</b></p> <p>19 A. That's a government-sponsored institute to 20 stimulate research in mental health in the United 21 States of America.</p> <p>22 <b>Q. And can you tell me -- and so Janssen -- did</b> 23 <b>Janssen have anything to do with the RUPP study?</b></p> <p>24 A. No. We were not involved in the design and 25 the execution of the study.</p>		<p>1 <b>England Journal of Medicine</b>, by the way, which is 2 one of the most famous medical journals here in this 3 country and worldwide, by the way. But also we were 4 contacted actually by the RUPP investigators, and 5 they said look --</p> <p>6 <b>MR. KLINE:</b> Objection to the hearsay. 7 <b>THE COURT:</b> Well, I'm really more 8 interested --</p> <p>9 <b>MR. KLINE:</b> "They said." 10 <b>THE COURT:</b> -- in what this witness 11 did. So if you can -- you know, if it was in 12 response to something --</p> <p>13 <b>MS. SULLIVAN:</b> Yeah. It's offered 14 for a non-hearsay purpose, Your Honor.</p> <p>15 <b>BY MS. SULLIVAN:</b></p> <p>16 <b>Q. So did the RUPP investigators communicate to</b> 17 <b>you information that led Janssen to research this</b> 18 <b>medicine in children with autism?</b></p> <p>19 A. Well, as I was trying to say, the RUPP 20 investigators contacted us and actually said, hey, 21 you should really look at those data because we 22 really think these are unique findings.</p> <p>23 <b>MR. KLINE:</b> Objection to the hearsay, 24 Your Honor. I can't cross-examine them.</p> <p>25 <b>THE COURT:</b> You know what, so we're</p>	

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<p>1 really clear, what is easy to tell the jury  2 about from a legal point of view is what you  3 did in response to what you were told by the  4 FDA. But you're really not allowed under the  5 general rules to tell us what the FDA told  6 you. So what you need to do is to say, I  7 heard from the FDA and I did this.</p> <p>8 <b>THE WITNESS:</b> I'm not referring to  9 what the FDA told us.</p> <p>10 <b>MS. SULLIVAN:</b> These are the --</p> <p>11 <b>THE WITNESS:</b> I'm referring to what  12 the RUPP investigators told us.</p> <p>13 <b>MS. SULLIVAN:</b> These are the folks on  14 the government study.</p> <p>15 <b>THE COURT:</b> But that's still the same  16 thing from a hearsay. That's still somebody  17 else. That somebody else is not here to  18 testify.</p> <p>19 <b>THE WITNESS:</b> Bottom line is: Those  20 RUPP investigators suggested to us to talk to  21 the FDA regarding this data, and they  22 suggested us to see what the FDA -- whether  23 this data might be suitable for including  24 this information in the label because they  25 were convinced that this was very important</p>		<p>1 And the outcome of that meeting was  2 that the FDA was prepared to accept such an SNDA, a  3 Supplemental New Drug Application, for use of  4 Risperdal in children and adolescents with  5 irritability associated with autism. And that's  6 important from the safety point of view with the  7 much larger database we had collected in children  8 and adolescents with conduct disorder.</p> <p>9 <b>Q. And, Dr. Caers, as part of the approval</b>  10 <b>process for Risperdal for autistic kids, did the</b>  11 <b>company do some of their own studies?</b></p> <p>12 A. We had -- apart from the RUPP study, we had  13 also a Canadian study which was company organized,  14 which was also a double-blind study with active and  15 the sugar pill, which the results of which were very  16 much in line with the findings of the RUPP study.  17 And that obviously was added to the weight of  18 evidence in the SNDA. And, by the way, it was all  19 information we had on the safety of Risperdal in  20 children and adolescents.</p> <p>21 <b>Q. So, Dr. Caers, the safety data -- did the</b>  22 <b>safety data that supported the autism approval with</b>  23 <b>FDA include the safety data from this</b>  24 <b>government-funded study, the RUPP study?</b></p> <p>25 A. That is correct.</p>	
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<p>1 and relevant for the medical field.</p> <p>2 <b>BY MS. SULLIVAN:</b></p> <p>3 <b>Q. And the RUPP investigators, can you, Dr.</b>  4 <b>Caers, based on your experience with them, describe</b>  5 <b>for our jurors who they were and what RUPP was</b>  6 <b>about.</b></p> <p>7 A. Well, RUPP was, as I said, a consortium of  8 academic child psychiatric centers all over the  9 country, and so these investigators were prominent  10 child psychiatrists linked to different universities  11 in this country.</p> <p>12 <b>Q. And, Dr. Caers, can you tell us what the</b>  13 <b>company did next as a result of this RUPP study and</b>  14 <b>your communications with these outside</b>  15 <b>investigators.</b></p> <p>16 A. Well, then we had a consultancy meeting with  17 the FDA on the database, on the data from the RUPP  18 study, but also because, as I had told earlier, we  19 had done substantial research already in disruptive  20 behavior disturbance in children and adolescents.  21 So we went to the FDA and said, look, this is valid  22 data on the use of Risperdal in children with autism  23 and beyond that. We have very substantial and large  24 database on Risperdal in children and adolescents,  25 more particularly in conduct disorder.</p>		<p>1 <b>Q. And also some studies done by Janssen?</b></p> <p>2 A. Yes.</p> <p>3 <b>Q. And, Dr. Caers, the plaintiffs in their case</b>  4 <b>allege that the autism approval was pushed</b>  5 <b>through --</b></p> <p>6 <b>MR. KLINE:</b> Objection to the form.  7 <b>THE COURT:</b> The plaintiff's claim?  8 <b>MR. KLINE:</b> Yeah.  9 <b>THE COURT:</b> No; sustained.</p> <p>10 <b>BY MS. SULLIVAN:</b></p> <p>11 <b>Q. Dr. Caers, was the autism approval pushed</b>  12 <b>through by Janssen or the FDA?</b></p> <p>13 A. I'm afraid it's very difficult to push  14 something through to the FDA. They are a fully  15 autonomous body and they make up their own mind  16 based on their own assessment by experts in the  17 field within the FDA.</p> <p>18 <b>Q. How long, Dr. Caers, did it take between the</b>  19 <b>time Janssen submitted the new drug approval package</b>  20 <b>for autism to the FDA to the time the FDA ultimately</b>  21 <b>approved the medicine for kids with autism?</b></p> <p>22 <b>MR. KLINE:</b> Your Honor, objection.  23 <b>THE COURT:</b> Basis?  24 <b>MR. KLINE:</b> Basis is that the entire  25 case here is '02 to '06. This is all about</p>	

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1 getting approval in '06. 2 <b>THE COURT:</b> All right. I realize 3 that. 4 <b>MR. KLINE:</b> We admit that, and 5 everyone in the case agrees -- 6 <b>THE COURT:</b> All right. I realize 7 that. That's overruled. 8 I mean, in case we forgot, why don't 9 you have him answer. just in case we forgot.		1 adolescents with autism. 2 <b>Q. Did the --</b> 3 <b>MR. KLINE:</b> Your Honor, we weren't 4 told the year. 5 <b>THE COURT:</b> Well, again, there's an 6 objection? 7 <b>MR. KLINE:</b> Yes. There's no 8 objection if we're told the year of this. 9 <b>THE COURT:</b> I mean, if you want to, 10 we can go back through all of that and give 11 the relevant time periods, if you want. 12 <b>THE WITNESS:</b> Well, as I said, the 13 first submission was in mid -- 14 <b>MR. KLINE:</b> My objection was only to 15 the year that it was approved. 16 <b>THE WITNESS:</b> The approval was in -- 17 <b>THE COURT:</b> No. Counsel, that's 18 overruled. Otherwise I would permit just 19 putting the document up there that 20 Ms. Sullivan wanted at the very beginning. 21 We need to get through this. 22 <b>THE WITNESS:</b> Yeah. Once again, we 23 did submit the SNDA in mid-2003, about, and 24 then the different steps, which I don't know 25 by heart the actual dates, but I do know I	
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1 means it looks okay, guys, but you need to provide 2 more information. Do you have more safety 3 information? Do you have more dose information? 4 Because that was a critical issue in this 5 submission. 6 We consequently brought additional 7 data together and submitted them in what we call a 8 complete response. Then the FDA once more reviews 9 this additional information and then comes back with 10 the next feedback and judgment, and that was an 11 unapprovable letter. They said we still have decent 12 questions about your dose recommendation, and 13 that's -- that has technical reasons. I can 14 elaborate upon, if you wish. 15 Then we had a meeting with the FDA, a 16 face-to-face meeting on what we could do next in 17 order to come up to their concerns, and particularly 18 the dosing recommendations. And eventually they 19 accepted that with some additional specific analysis 20 of the data and the existing data. They accepted an 21 approval with what we call a Phase IV commitment; 22 that the FDA said, yes, we approve, but that means 23 that you're going to need one additional study after 24 we approve, which is a Phase IV commitment, on 25 studying the lowest effective dose in children and	1 think we had the final approval in 2 October 2006. 3 <b>BY MS. SULLIVAN:</b> 4 <b>Q. So, Dr. Caers, can you tell us whether the</b> 5 <b>company satisfied the FDA's request for additional</b> 6 <b>safety data, additional information, as part of the</b> 7 <b>approval process?</b> 8 A. Yes. Of course we did, because otherwise the 9 FDA would not have approved the indication back in 10 October 2006. 11 <b>Q. And, Dr. Caers, I want to show you, and with</b> 12 <b>permission from the Court, I want to show the jury</b> 13 <b>the FDA October 23, 2006 approval letter for the</b> 14 <b>autism indication.</b> 15 <b>MR. KLINE:</b> Objection, based on the 16 Court's rulings. 17 <b>THE COURT:</b> That's sustained. That's 18 the same thing. 19 <b>MR. KLINE:</b> And she knows it. 20 <b>THE COURT:</b> We have a label in 21 evidence. And we know that this document 22 exists. The letter is -- you can mark it, 23 put it into the record. But there's no 24 reason to -- there is just no reason to put 25 that up on the board. We know that.		
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1 <b>MS. SULLIVAN:</b> Well, Your Honor, at 2 sidebar you said I could show the children 3 and adolescent label. 4 <b>THE COURT:</b> I didn't say anything of 5 the sort. 6 <b>MS. SULLIVAN:</b> I mean the approval 7 letter. 8 <b>THE COURT:</b> I didn't say anything of 9 the sort. We have the 2006 label. That's in 10 evidence. 11 <b>MS. SULLIVAN:</b> I can't show that 12 there was the approval letter from the FDA? 13 <b>THE COURT:</b> Was your application for 14 autism in children approved by the FDA? 15 <b>THE WITNESS:</b> Yes. 16 <b>THE COURT:</b> All right. So much so. 17 <b>BY MS. SULLIVAN:</b> 18 <b>Q.</b> And, Dr. Caers, as part of the approval 19 process, does the FDA send you an approval letter? 20 <b>A.</b> Yes, of course. 21 <b>Q.</b> And does the FDA communicate -- did the FDA 22 communicate to Janssen what they could say on the 23 FDA approved label? 24 <b>MR. KLINE:</b> Objection; violative of 25 the Court's direction.	1 <b>MS. SULLIVAN:</b> 61. 2 <b>MS. BROWN:</b> You're showing the label 3 from the approval, right? 4 <b>MS. SULLIVAN:</b> Just the label. 5                   It's DX210. Now it's 61. 6 <b>MS. BROWN:</b> From the approval letter, 7 the 2006 approval letter. 8                   - - - 9                   (Whereupon Exhibit D-61 was marked 10 for identification.) 11 <b>BY MS. SULLIVAN:</b> 12 <b>Q.</b> And, Dr. Caers, in order to get FDA approval 13 for children with autism, what did you have to 14 establish with the FDA? 15 <b>A.</b> In order to get the approval, you need to 16 submit your complete data set, obviously, as we did 17 in different steps. 18 <b>Q.</b> And the FDA concluded it was appropriate for 19 children? 20 <b>A.</b> Well, the FDA back in October 2006 concluded 21 that Risperdal is safe and effective in the 22 management of irritability associated with autism, 23 which is basically the meaning of an approval. 24 <b>Q.</b> And if we look at the 2006 label, Dr. Caers,		
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1 <b>THE COURT:</b> No. I mean, again, 2 you're permitted to ask that, sure. 3 <b>THE WITNESS:</b> Well, as every approval 4 letter, that gives you the label that the FDA 5 wants us to use from the day one, which is 6 obviously an updated label, because now it 7 covers all the relevant information that is 8 relevant for the appropriate use of Risperdal 9 in children and adolescents with irritability 10 and autism. 11 <b>BY MS. SULLIVAN:</b> 12 <b>Q.</b> And let's show -- and, Dr. Caers, were you 13 involved in the 2006 autism approval process with 14 the FDA? 15 <b>A.</b> Yes, I was. 16 <b>Q.</b> And can you tell the jury who made the final 17 decision on what should be said in the label? 18 <b>A.</b> Well, that's obviously the FDA, as we alluded 19 to earlier. 20 <b>Q.</b> And, Dr. Caers, I'm going to put up the FDA 21 approved label for autism in 2006. It's attached to 22 the approval letter, which I won't show per the 23 Court's instruction. 24                  Defense Exhibit... 25 <b>MS. BROWN:</b> 61.	1 <b>you have it on your screen?</b> 2 <b>A.</b> Yes, I do. 3 <b>Q.</b> Okay. And this -- 4 <b>MR. KLINE:</b> Your Honor, this is -- 5                  oh. It's the label. Okay. No objection. 6 <b>THE COURT:</b> Okay. 7 <b>BY MS. SULLIVAN:</b> 8 <b>Q.</b> And, Dr. Caers, if we look at Page 11, it 9 talks about the fact that it's now approved for 10 irritability associated with autism, right? 11 <b>A.</b> That is correct. 12 <b>Q.</b> And it describes the symptoms. And if you 13 could just read them for the jurors. 14 <b>A.</b> Yes. 15                  As you can see here, these basically 16 include symptoms of aggression towards others, 17 deliberate self-injuriousness, temper tantrums, and 18 quickly changing moods. 19 <b>Q.</b> And so the FDA specifically at this juncture 20 approved Risperdal for this purpose -- 21 <b>A.</b> That is correct. 22 <b>Q.</b> -- in children and adolescents? 23 <b>A.</b> That is correct. 24 <b>Q.</b> And is this the same -- so there's been 25 discussion -- and you mentioned there was off-label		

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1 <b>prescribing of Risperdal before it was approved in</b> 2 <b>autism, right?</b>		1    A.   Well, as has been in the label since 1993, 2    reference is made to the occurrence of 3    hyperprolactinemia in drugs such as Risperdal who 4    interact, as I said earlier, with the receptors in 5    the brain, the dopamine 2 receptors, and that in 6    patients treated with drugs, that can increase 7    prolactin; that certain adverse events, such as 8    galactorrhea, amenorrhea, gynecomastia, and 9    impotence, have been reported.	
4 <b>Q. Is this the same compound, in other words, did</b> 5 <b>the medicine change in terms of its compound or</b> 6 <b>chemical make-up in 2006 as compared to what was</b> 7 <b>being prescribed in '93, '94, 2002?</b>	8    A.   It's the same compound.	10 <b>Q. And, Dr. Caers, in the label there's also a</b> 11 <b>pediatric section?</b>	
9 <b>Q. So the same compound that was being prescribed</b> 10 <b>off-label now had on-label?</b>	11 <b>MR. KLINE:</b> Objection; asked and 12   answered. She just repeated.	12    A.   Yes, there is, yes.	13 <b>Q. And there is separate information about the</b> 14 <b>data in children and adolescents in the 2006 label,</b> 15 <b>right?</b>
11 <b>THE COURT:</b> Yes. Sustained. That is 14   sustained.	15 <b>BY MS. SULLIVAN:</b>	16 <b>Q. And can you talk to our jurors a little bit</b> 17 <b>about what was in the October 2006 label on children</b> 18 <b>and adolescents and elevated prolactin and</b> 19 <b>gynecomastia.</b>	20    A.   First of all, it is repeated in this section 21   that risperidone increases prolactin. And this was 22   also the case in the studies we provided. And that 23   in the clinical trials we provided up to 1,885 24   children and adolescents treated with Risperdal,
16 <b>Q. And, Dr. Caers, if we look further in the</b> 17 <b>label, there was a Precautions section in the label.</b>	18    A.   Yes.	25 <b>Q. And does the FDA dictate the sections and the</b>	
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1 <b>type and things like that?</b>	2    A.   Yes.	3 <b>Q. And, Doctor, to get the 2.3 percent, did you</b> 4 <b>look at all of the data in children and adolescents?</b>	
3 <b>MR. KLINE:</b> Your Honor, this goes --	4    this goes to whether he's an FDA expert or	5    A.   Yes. It takes --	
5    not. And I just can't be on my toes all the	6    time.	6 <b>Q. Go ahead.</b>	
7 <b>THE COURT:</b> Again, that's true.	8    Sustained.	8    A.   It takes all the studies that were done with	
9    You're going to have experts on this,	10   aren't you?	9    risperidone, Risperdal in children and adolescents	
11 <b>MS. SULLIVAN:</b> Well, Your Honor, this	12   gentleman --	10   together, and then you come to the overall incidence	
13 <b>THE COURT:</b> He doesn't know. He's	14   not a member of the FDA, nor has been	11   of, in this case, gynecomastia, in this total	
14   not a member of the FDA, nor has been	15   qualified as an expert. He knows from his	12   population of 1,885 patients.	
15   qualified as an expert. He knows from his	16   own experience what he did and what kind of,	13 <b>Q. And, Doctor, there's been some criticism in</b> 17   you know, things that he had to do to get	
16   own experience what he did and what kind of,	18   this thing approved for children.	18 <b>this case about --</b>	
17 <b>THE COURT:</b> He doesn't know. He's	19 <b>MR. KLINE:</b> Objection. I don't		
18   this thing approved for children.	20   object to straight questions.	20 <b>THE COURT:</b> Sustained. Sustained. I	
19 <b>BY MS. SULLIVAN:</b>	21   don't know what you're referring to. By	21   whom?	
20 <b>Q. And, Dr. Caers, going further in the</b> 21 <b>Precautions section, there's a section about</b>	22 <b>BY MS. SULLIVAN:</b>	22 <b>Q. Dr. Caers, the jury has heard Dr. Kessler</b> 23 <b>criticize --</b>	
22 <b>elevated prolactin.</b>	23 <b>MR. KLINE:</b> Objection. It's not a	23   proper way to start a question.	
23   A.   Yes, indeed.			
24 <b>Q. And can you talk to our jurors about what's in</b> 25 <b>that section and why.</b>			

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1 <b>THE COURT:</b> Why don't you rephrase 2                   it, Counsel.		1                   the mark-up of the label? 2 <b>MR. KLINE:</b> I have no objection to 3                   what I believe is the mark-up of the label.	
3 <b>BY MS. SULLIVAN:</b>		4 <b>MS. SULLIVAN:</b> And how about the 5                   e-mail from the FDA?	
4 <b>Q. Dr. Caers, whose idea was it to pool, to 5                   include data on all of the children to get the 6                   2.3 percent?</b>		6 <b>THE COURT:</b> Who's this made out to, 7                   by the way?	
7    A. That comes from the FDA. That's common 8                   practice. That's the only way they systematically 9                   document incidences in labels, incidences of adverse 0                   events. They take all of the patients exposed for a 1                   couple of days, up to a couple of years, take all 2                   together and take one single database in which they 3                   calculate the incidences. And that's how it is 4                   reflected in the label.		8 <b>MS. SULLIVAN:</b> This is to -- this is 9                   from the FDA to Janssen.	
5 <b>Q. And, Dr. Caers, I want to show you what's been 6                   marked -- what will be marked as Defense Exhibit...</b>		10 <b>MR. KLINE:</b> Yes; that I do. It 11                  just -- it doesn't say anything. But I don't 12                  believe they come in under the rules.	
7 <b>MS. BROWN:</b> 62.		13                  But I don't object to the document 14                  you want to show.	
8 <b>MS. SULLIVAN:</b> 62.		15 <b>THE COURT:</b> The front page?	
9 <b>BY MS. SULLIVAN:</b>		16 <b>MR. KLINE:</b> I do for the front page 17                  because it's the FDA document. But the going 18                  back and forth, which I think is what she 19                  wants to show, I don't object to.	
0 <b>Q. And it's a mark-up from the FDA of this 2006 1                   label. And I'm going to ask you about it, if the 2                   Court permits.</b>		20 <b>MS. SULLIVAN:</b> It's to Janssen, Your 21                  Honor. It's in their files. It's a business 22                  record, from their regulator.	
3 <b>It's D234.1.</b>		23 <b>THE COURT:</b> Let me see counsel here 24                  at sidebar quickly.	
4 <b>MS. SULLIVAN:</b> Do you have a copy, 5                   Dr. Cares?		25	-----
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1 <b>THE WITNESS:</b> I don't think so.		1                   (The following discussion transpired 2                   at sidebar out of the hearing of the jury:)	
2 <b>COURT CRIER:</b> Not yet.		2	-----
3                   Mr. Kline.		3	
4 <b>THE COURT:</b> It's been marked?		4 <b>THE COURT:</b> First of all, this is now 5                   going to be marked as what? D something?	
5 <b>COURT CRIER:</b> 62.		6 <b>MS. SULLIVAN:</b> 62.	
6 <b>MS. BROWN:</b> 62.		7 <b>THE COURT:</b> This discovery has been 8                   provided. There's no discovery issue here, 9                   correct?	
7                   (Exhibit D-62 marked for 8                   identification.)		10 <b>MR. KLINE:</b> No.	
9 <b>MR. KLINE:</b> This is just the FDA 0                   track labeling?		11 <b>MS. SULLIVAN:</b> No. We provided it.	
1 <b>MS. SULLIVAN:</b> It's an e-mail from 2                   FDA to Janssen about the label.		12 <b>THE COURT:</b> Okay. So where is the 13                  section on gynecomastia?	
3 <b>MR. KLINE:</b> I have no objection to 4                   the document.		14 <b>MS. SULLIVAN:</b> The section I want to 15                  show him is marked up by the FDA.	
5 <b>THE COURT:</b> It's now marked as P-62.		16 <b>THE COURT:</b> What page is that?	
6 <b>COURT CRIER:</b> D-62.		17 <b>MS. SULLIVAN:</b> It's Bates No. 752; 18                  and Page 24 of the document.	
7 <b>THE COURT:</b> D-62.		19 <b>MR. KLINE:</b> 752. Bear with me.	
8 <b>MR. KLINE:</b> The document itself, not 9                   the e-mail. I have no objection to the 0                   mark-up of the label.		20 <b>THE COURT:</b> I don't have the mark-up. 21                  There's a mark-up there or something?	
1 <b>MS. SULLIVAN:</b> I'm sorry, I didn't 2                   hear you.		22 <b>MS. SULLIVAN:</b> It's 752, Your Honor.	
3 <b>MR. KLINE:</b> I have no objection to 4                   the --		23 <b>THE COURT:</b> So who's in the marking 24                  up here?	
5 <b>THE COURT:</b> He has an objection to		25 <b>MS. SULLIVAN:</b> This is from the FDA;	

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1 and he can talk about how they marked it up 2 and what they told him to do. That's part of 3 the discussions with the FDA. 4 <b>MR. KLINE:</b> My understanding from -- 5 <b>MS. SULLIVAN:</b> And he can say he saw 6 it; he knew it. 7 <b>THE COURT:</b> All right. Well, this 8 is -- 9 <b>MR. KLINE:</b> Well, he might have seen 10 it, but he wasn't involved at all in this 11 mark-up. 12 <b>THE COURT:</b> Yeah. 13 <b>MS. SULLIVAN:</b> Sure, he was. 14 <b>MR. KLINE:</b> He may have been the 15 boss, but he wasn't involved in this mark-up, 16 as I understand it. 17 <b>THE COURT:</b> The problem here is, is 18 that unless this individual was the person 19 who's involved in the FDA -- from Janssen in 20 this correspondence, there's nothing to 21 cross-examine this fella on. 22 <b>MS. SULLIVAN:</b> He was -- he was 23 provided it at the time, Your Honor. He was 24 the boss. 25 <b>THE COURT:</b> No. No. If he was the		1 to be able to refer to two pages of this 2 document, if the proper foundation has been 3 laid. 4 <b>BY MS. SULLIVAN:</b> 5 <b>Q.</b> <b>And, Dr. Caers, are you familiar with this</b> 6 <b>document?</b> 7 A. Yes. 8 <b>Q.</b> <b>And were you involved at the time in the</b> 9 <b>labeling decisions and discussions with the FDA?</b> 10 A. Yes, I was. 11 <b>Q.</b> <b>And I want to just show our jurors what's been</b> 12 <b>marked as D-62.</b> 13 <b>And, Dr. Caers, this is an e-mail</b> 14 <b>from the FDA, right?</b> 15 A. Yes, indeed. 16 <b>MR. KLINE:</b> Your Honor, that's the 17 exact document we didn't agree to at sidebar. 18 But as long as I don't waive an inconsistency 19 objection, she can show it. 20 <b>THE COURT:</b> Well, this appears -- no. 21 I don't really have a problem. This is an 22 e-mail to Janssen saying that we are 23 negotiating and discussing this label; is 24 that right? 25 <b>MR. KLINE:</b> It's a transmittal.	
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1 one -- okay. If you lay the foundation that 2 he was personally involved in it -- 3 <b>MS. SULLIVAN:</b> Okay. Yeah. I'll do 4 that. 5 <b>THE COURT:</b> And then he's subject to 6 Mr. Kline's cross-examination, I'm fine with 7 it. 8 <b>MS. SULLIVAN:</b> I'll do that, Judge. 9 - - - 10 (Sidebar discussion concluded.) 11 - - - 12 (The following transpired in open 13 court in the presence of the jury:) 14 - - - 15 <b>BY MS. SULLIVAN:</b> 16 <b>Q.</b> <b>Last point, Dr. Caers, before I think the</b> 17 <b>Court wants to take a lunch break.</b> 18 <b>THE COURT:</b> First of all, we're now 19 on the record as to P-62. 20 <b>COURT CRIER:</b> "D." 21 <b>MR. MURPHY:</b> "D." 22 <b>COURT CRIER:</b> Defense Exhibit 62. 23 <b>THE COURT:</b> All right. This document 24 is admitted for the purposes of its 25 existence, and I think we are perhaps going		1 <b>MS. SULLIVAN:</b> This is a -- 2 <b>THE COURT:</b> So we can now go to the 3 actual points in question. 4 <b>MS. SULLIVAN:</b> Sure. 5 <b>THE COURT:</b> This witness was not on 6 this e-mail, correct? 7 <b>BY MS. SULLIVAN:</b> 8 <b>Q.</b> <b>But, Dr. Caers, you would have seen this</b> 9 <b>document?</b> 10 A. Yes. 11 <b>THE COURT:</b> So I'm interested in 12 laying a foundation for the other questions 13 involving the contents that are part of this 14 document. 15 <b>MS. SULLIVAN:</b> Sure. 16 <b>THE COURT:</b> Of the attachment. And I 17 don't need this particular document on the 18 screen. 19 <b>BY MS. SULLIVAN:</b> 20 <b>Q.</b> <b>Dr. Caers, did the FDA provide a mark-up to</b> 21 <b>Janssen before approval -- this is a month before --</b> 22 <b>the September 28th date is a month before the FDA</b> 23 <b>approves the medicine for autism?</b> 24 A. Yes, indeed. 25 <b>MR. KLINE:</b> Objection; leading;	

**(Jury Trial-AM Session)XII - February 10, 2015**  
**Pledger v. Janssen**

- IVO CAERS, Ph.D. - DIRECT - <p>1 simply leading. It's asking to confirm. 2 <b>THE COURT:</b> All right. Well, she's 3 attempting to lay a foundation, so that's 4 permitted. 5 Overruled. 6 <b>BY MS. SULLIVAN:</b> 7 <b>Q. And, Dr. Caers, did the FDA actually mark up</b> 8 <b>the label and tell Janssen what it wanted?</b> 9 A. Yes. 10 So what this is, is they identify 11 track changes. So you can see what they delete. 12 You can see what they add by underlining the 13 letters. So you can see what changes the FDA 14 proposes to the label in order to come to a final 15 approved label for Risperdal in irritability 16 associated with autism. 17 <b>Q. And as part of the proposed label that the FDA</b> 18 <b>marked up, did they make -- did the FDA comment on</b> 19 <b>how Janssen should disclose the data about</b> 20 <b>gynecomastia in the 2006 label, as it related to</b> 21 <b>children?</b> 22 A. Well, here it refers to, indeed, to the latest 23 number of patients that we eventually had in the 24 total file and consequently through the total 25 incidence, in these 1,923, about patients that have</p>	Page 121	- IVO CAERS, Ph.D. - DIRECT - <p>1 here? 2 <b>MS. SULLIVAN:</b> Yeah. That's good. 3 <b>THE COURT:</b> All right. Members of 4 the jury, we are going to recess for lunch 5 right here. Please come back around 1:30, 6 and we will continue. 7 To our juror from McDonald's, all I 8 can tell you is that I'm working on it, and 9 I'm very surprised by the reaction of 10 McDonald's, okay? We're working on it. 11 We will take a break here. Please do 12 not discuss this matter with each other, and 13 wear your yellow badges. And please do not 14 refer to any outside source for any 15 information about this case, all right? 16 Thank you. 17 See you at 1:30. 18 <b>COURT CRIER:</b> All rise as the jury 19 exits. 20 - - - 21 (Whereupon the jury exited the 22 courtroom at 12:36 p.m.) 23 - - - 24 <b>THE COURT:</b> All right. Then we're in 25 recess till 1:30.</p>	Page 123
- IVO CAERS, Ph.D. - DIRECT - <p>1 been documented with Risperdal. 2 <b>Q. And did the FDA ask Janssen to pool all the</b> 3 <b>data?</b> 4 A. Oh, yes. That's common practice. 5 <b>MS. SULLIVAN:</b> Okay. It's a good 6 time, Your Honor, if that makes sense for the 7 Court. 8 <b>THE COURT:</b> Sure. 9 Pages 24 and 25; is that what we're 10 talking about? Well, actually -- 11 <b>MS. SULLIVAN:</b> That was Page 24, Your 12 Honor, and also the first -- the document, 13 the e-mail from the FDA. 14 <b>THE COURT:</b> All right. For the 15 record, this is at JJRP00824751 and 4752. 16 You want to take a break now, 17 Ms. Sullivan? 18 <b>MS. SULLIVAN:</b> Oh, I'm sorry, I 19 thought we were. 20 <b>THE COURT:</b> No. We can take a break 21 anytime. 22 <b>MS. SULLIVAN:</b> Okay. I thought it 23 was a good spot, Your Honor. 24 Thank you. 25 <b>THE COURT:</b> You want to take a break</p>	Page 122	- IVO CAERS, Ph.D. - DIRECT - <p>1 (Morning Session concluded.) 2 - - - 3 (Whereupon the Afternoon Session was 4 reported and transcribed by Judith Ann 5 Romano, CRR, Official Court Reporter.) 6 - - - 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25</p>	Page 124

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2

3 I hereby certify that the proceedings  
4 and evidence are contained fully and  
5 accurately in the notes taken by me on the  
6 trial of the above cause, and that this copy  
7 is a correct transcript of the same.

8 I further certify that I am not a  
9 relative or employee of any attorney or  
10 counsel employed in this case.

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