

EXPERT WITNESS REPORT

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I.

This expert witness report is authored by David J. Rothman. I am the Bernard Schoenberg Professor of Social Medicine at the Columbia College of Physicians & Surgeons, the medical school of Columbia University. I am also the director of the Center on Medicine as a Profession at the Columbia College & Surgeons. In addition, I am president of the Institute on Medicine as a Profession.

My qualifications for undertaking this assignment include substantial research and leadership in the field of medicine-industry relationships, in particular the pharmaceutical industry and the medical device industry. My vita (appended as Exhibit 1) contains the list of my publications and activities relative to this area. Highlights include my serving as co-chair of a task force to define appropriate relationships with industry for academic medical centers, and co-chair of a task force to define appropriate relationships with industry for professional medical associations. Both of these reports were published in the Journal of the American Medical Association, one of the most prestigious journals in medicine, and are helping to establish standards for behavior among these centers and organizations. Over the past several years, I and my colleagues at the Center have published 8 articles in this area, all in peer reviewed and prominent journals. The most recent article that we published in this area appeared in the Archives of Internal Medicine (website prior to printed journal, September 13, 2010) and was discussed in a New York Times article of the same day, Wilson, "Medical Industry Ties Often Undisclosed in Journals." (B1) The impact of my work is also evidenced as well by the substantial grant support I receive from leading foundations.

In the past ten years, I have served once before as an expert witness. The case involved the ethics of human experimentation, prompted by the disclosure that investigators at a prominent medical school had fed radioactive iron to pregnant women in the late 1940s without informing them that they were receiving the substance or were subjects in a research project. (*Craft v. Vanderbilt*).

I have been hired as an expert witness in this case by the Texas Attorney General's office, and I submit this report for the Plaintiffs.

II.

I was asked to address the following questions:

- 1) Are appropriate safeguards necessary to guard against conflict of interest in relationships of medicine with the pharmaceutical industry? Was Johnson & Johnson (hereinafter J&J, which includes Janssen and other subsidiaries named as defendants in this lawsuit) aware of the need for such safeguards?
- 2) In the relationship between J&J and medical and state personnel, were there appropriate safeguards in place to prevent opportunities for undue influence in the activities of the Texas Medical Algorithm Project (TMAP)?
- 3) Were appropriate safeguards in place to prevent opportunities for undue influence in other marketing efforts for Risperdal?
- 4) Did Dr. Shon have any relationships with any Defendants that created conflicts of interest in his role as medical director of TDMHMR?
If so, was disclosure sufficient to resolve the problem?
- 5) Did Dr. Crismon have any relationships with any Defendants that created conflicts of interest in his role as a leading member of TMAP?
If so, was disclosure sufficient to resolve the problem?
- 6) Did Dr. Miller have any relationships with any Defendants that created conflicts of interest in his role as a leading member of TMAP?
If so, was disclosure sufficient to resolve the problem?
- 7) Is the ghostwriting of scientific research articles appropriate, and if not, why not?
- 8) Did Defendants engage in ghostwriting of scientific research articles?
- 9) Did Defendants disguise promotion of Risperdal through the use of advocacy and third party organizations?

To answer these questions, I drew on my substantial knowledge of the norms and ethical standards for the field, the literature in the field, and the standards set by medical and government bodies. I explored the documentary evidence in the case; I had access to all depositions, exhibits, and documents. I conducted my own searches of the online materials, assisted by Columbia Professor of Public Health, Sheila M. Rothman and by a research assistant. In addition, I reviewed the materials and the documents cited in my report.

My work is still ongoing and as discovery continues, I will supplement my report. The documents cited here to support my opinions are further supplemented by an extensive scholarly literature that addresses conflicts of interest and appropriate measures to reduce or eliminate them. Additional references may be used in support of my opinions.

1) Are appropriate safeguards necessary to guard against conflict of interest in relationships of medicine with the pharmaceutical industry? Was J&J aware of the need for such safeguards?

Yes. Appropriate safeguards are necessary to guard against conflicts of interest. Conflicts of interest in the relationships between physicians and industry arise because financial ties have the potential to subvert scientific integrity. Although some physicians and researchers think that they are not affected by industry, many studies have demonstrated that even gratuities as insignificant as drug samples and small gifts can compromise judgment about scientific evidence and influence prescribing practices. The power of the gift to prejudice decision-making, whether consciously or unconsciously, was and is fully appreciated.

The explicit need for appropriate standards to govern medical-pharmaceutical industry relationships were both fully appreciated and well established by the time Risperdal was introduced in 1994. (Here and below, references to "industry" are specific to the pharmaceutical industry.) Then and now, there is general recognition on the part of the leaders of academic medical centers, medical organizations, medical journals, foundations, government agencies, and within the industry itself that, unless properly managed, the marketing goals of industry pose both real and potential dangers to scientific and educational integrity.

Documents make clear that J&J was not only aware of and knowledgeable about compliance requirements, but also had enacted its own compliance policies that were consistent with general standards. The problems were that it was slow to do so and did not consistently live up to them in practice. Despite the widespread knowledge of the need for standards as detailed above, Janssen's then compliance officer (Mallegol) testified that Janssen did not have a formal compliance policy in place until 2000. The earliest regulatory guidelines that I could locate were those of J&J in late 1998.

Both the objective literature and J&J's own compliance documents show a widespread sensitivity among parties to the problems posed by conflicts of interest between medical researchers, authors, and practice guideline writers on the one hand, and drug companies on the other. Pharmaceutical influence is pervasive, but there are several distinct areas that are particularly troubling: 1) gifts, honoraria, and other types of financial support to those who prescribe drugs or who influence the prescribing behavior of others; 2) industry-funded continuing medical education courses (CME); and 3) biasing the medical literature through ghost-writing and strategic publication plans.

1. Gifts, honoraria, and other types of financial support to those who prescribe drugs or who influence the prescribing behavior of others.

It is well understood by all parties that honoraria, consulting agreements, travel, entertainment, and research grants provided by industry to medical professionals have the potential to bias research outcomes, educational materials, and practice guidelines. The power of the gift to prejudice decision-making, whether consciously or unconsciously, is fully recognized.

The medical literature reveals how influential the interactions between industry and physicians are. They affect:

1. Prescribing practices (See for example, A. Wazana, "Physicians and the Pharmaceutical Industry." JAMA (283) 2000, 373-380.)
2. Requests for addition of drugs to hospital formularies (See, for example, M. Chren et al., "Physicians' Behavior and their Interactions with Drug Companies..." JAMA (271) 1994, 684-689.)

3. The conclusions of industry sponsored research (See, for example,, J. Bekelman et al., "Scope and Impact of Financial Conflicts of Interest..." JAMA (289) 2003, 454-465.)
4. The recommendations of clinical practice guidelines (See, for example, N. Choudhry, "Relationships between Authors of Clinical Practice Guidelines and the Pharmaceutical Industry," JAMA (287) 2002, 612-617.)

Although the issues in conflict of interest are intricate, there is extraordinary unanimity about the principles that should govern industry relationships. Several groups have issued guidance, including a committee of the American Board of Internal Medicine Foundation and the Institute on Medicine as a Profession (See Brennan, Rothman, et al., Health industry practices that create conflicts of interest, JAMA, 2006; 295: 429-433; and Institute of Medicine report, "Conflict of Interest in Medical Research, Education, and Practice" (2209). They recommend that gifts to physicians be eliminated; that honoraria and consulting arrangements be closely monitored and fully disclosed; that transparency and management of conflict of interest is especially crucial when it comes to the formation of clinical practice guidelines and publishing research results.

The Office of the Inspector General of the Department of Health and Human Services has also issued relevant guidance for ethical behavior. (See "OIG Compliance Program Guidance for Pharmaceutical Manufacturers.") Addressing fraud, abuse, and the False Claims Act, it cites several practices especially relevant to the issues on gifts and other financial support. First, "kickbacks:" The OIG is particularly concerned with the relationship between a manufacturer and persons "in a position to generate federal health care business for the manufacturer," citing specifically purchasers, benefit managers, and formulary committee members. It asks: "Does an arrangement or practice have a potential to interfere with or skew clinical decision-making? In still more particular terms: does it have a potential to undermine clinical integrity of a formulary process?" It is also especially sensitive to the quality of the information provided to "decision makers, prescribers, or patients." (Federal Register, vol. 68, May 5, 2003, p. 23734) Second, the Guidance addresses company relationships with physicians. It notes that "gifts, entertainment and personal services compensation ...have a high potential for fraud and abuse." (23737) Third, the Guidance

emphasizes the need for prompt reporting by a company of misconduct to state and federal authorities. (23742)

In addition, not only physicians but also state employees in positions to influence prescribers must guard against conflicts of interest. The Texas Ethics Commission, in an advisory opinion issued in March 1996, declared that an honorarium is not permissible if the public servant's official status was a deciding factor in the payor's decision to hire him to perform services. It cited the Texas Penal Code provision prohibiting state employees from accepting honoraria in such circumstances. (Hunt Exhibit, 1636) Finally, the Texas Government Code stipulates that a state employee may not have a financial interest or engage in a business or "professional activity" that is in "substantial conflict with the proper discharge or...duties in the public interest." (Texas Gov't Code ANN. §572.001(a))

J&J was fully cognizant of these principles. In December 1998, it issued "Health Care Regulatory Documents for Promotional and Marketing Practices." Noting recent government enforcement efforts and fines to companies, it aimed to "provide guidance to J&J companies and their employees and to facilitate employee training in appropriate marketing practices." (J-TXCID1336536) The document included materials on kickbacks, warning that payments were not allowed to induce "referrals or product recommendations." (.....6541) So too, consulting and service arrangements were not to be used to promote the purchases of J&J products. (.....6547) It went on to declare that advisory board meetings "should generally not be held in resort locations." (.....6557). Finally, it stated that "J&J companies may not provide clinical grants to customers in exchange for or based on referrals, purchases, or recommendations for J&J products." (.....6573) As we shall see below, J&J practices did not consistently meet these standards.

In 2000, Janssen produced a formal compliance policy document. (Mallegol Deposition, 20-24) The Health Care Compliance manual issued to its sales staff included such directives as: "Janssen employees must not provide any gifts, gratuities, or payments for meals, travel, or lodging to federal, state or local government employees." (J-TX2163186) The company policy declared: "Government employees are bound and responsible for complying with the Government Code of Ethics." It immediately added: "Janssen employees must be aware of these standards and avoid creating situations that compromise them." (Mallegol Exhibit, 40,

27) It went on to note that "special circumstances may apply with the written authorization from the government supervisor." (28) As we shall see below with Dr. Steven Shon, the company failed to fulfill its own standard.

2) Industry-funded continuing medical education courses

To attend CME courses is required for physicians. CME attendance is the primary method by which physicians fulfill their obligation to carry out life-long-learning and maintain professional competence. Accordingly, it is vital the CME courses conform to the highest standards of scientific integrity and reflect best practices for patient care. They must be free of bias and not allow pharmaceutical marketing to affect the content of the presentation.

Professional guidelines reflect how CME should be conducted so as to limit industry influence. The Accreditation Council of Continuing Medical Education (ACCME) promulgated guidelines in 1992 that set standards regarding the independence of CME activities. CME activities "must be free of commercial bias for or against any product; if the activities are concerned with commercial products, they must present objective information about those products, based on scientific methods generally accepted in the medical community." To this end, "Commercial supporters of such activities shall not control the planning, content or execution of the activity." (Standards for Commercial Support of Continuing Medical Education, Approved by ACCME March 20, 1992).

The ACCME further elaborated its Standards for Commercial Support in 2004. Among its most relevant and significant stipulations were:

"Standard 1: Independence

1.1 A CME provider must ensure that the following decisions were made free of the control of a commercial interest..... (a) Identification of CME needs; (b) Determination of educational objectives; (c) Selection and presentation of content; (d) Selection of all persons and organizations that will be in a position to control the content of the CME.

Standard 2: Resolution of Personal Conflict of Interest

2.1 The provider must be able to show that everyone...has disclosed all relevant financial relationship with any commercial interest to the provider.

2.3 The provider must have implemented a mechanism to identify and resolve all conflicts of interests.

Standard 3: Appropriate Use of Commercial Support.

3.1 A provider cannot be required by a commercial interest to accept advice or services concerning teachers, authors, or participants or...content.

3.7 The provider must have written policies and procedures governing honoraria and reimbursement of out-of-pocket expenses for planners, teachers and authors.

Standard 5: Content and Format without Commercial Bias

5.1 The content...must promote improvement or quality in healthcare and not a specific proprietary business interest or a commercial interest.

5.2 Presentations must give a balanced view of therapeutic options. Use of generic names will contribute to this impartiality.

Standard 6: Disclosure Relevant to Potential Commercial Bias

6.1 An individual must disclose to learners any relevant financial relationship(s)"

Here, too, J&J demonstrated familiarity with existing standards. Its Health Care Regulatory Documents of 1998 made explicit reference to CME programs: "The sponsor must have complete discretion with respect to the use of funds" (J-TXCID1336544-45) and "J&J must remain largely 'hands off' with respect to influencing the content of the program." (.....6567)

3) Biasing the medical literature through ghostwriting and strategic publication plans.

Medical publications are at the heart of scientific progress and patient care. Investigators design their research projects based on prior findings. Physicians prescribe medications to their patients based on reports of

efficacy in medical journals. For these reasons, the integrity of publications is absolutely essential. Ghostwriting subverts this integrity by concealing information about who conducted the research, who authored the article, and who funded the research. It takes several guises: it omits the names of participants in the project, usually by omitting the names of industry employees. It includes the names of persons who had no role or a minimal role in the project, usually by including the names of key medical opinion leaders. It also omits the names of members of medical communication firms so as to further obfuscate the role of pharmaceutical companies. These companies through ghostwriting hide their role in defining the research project, in analyzing the data, and in editing and revising the manuscript. In all these ways, ghostwriting gives a veneer of objectivity to findings that may have been manipulated to serve the marketing interests of a drug company.

To counter such abuses of scientific integrity, medical journal requirements for publication and authorship set the appropriate standards. (See, "Uniform Requirements of the ICJMA," *New England Journal of Medicine*, January 23, 1997) The stipulations include:

Each author should have participated sufficiently in the work to take public responsibility for the content." (p. 311). The order of authorship should be a joint decision of the coauthors." (p. 311) Acknowledgments should include:

b) Acknowledgments of financial and material support which should specify the nature of the support; and (d) "Relationships that may pose a conflict of interest."

Although I saw no reference to ghostwriting standards in J&J documents prior to 2005, the company had to be aware of these principles, given the intensity of its involvement with the publication in medical journals of its in-house research. In August, 2005, in a "Guidance Document on the...Dissemination of Scientific Information," J&J stated that "J&J companies should not engage in or condone the 'ghost writing' of articles, i.e., omitting from a publication the name of an individual that contributed materially or giving a misleading impression of the contribution made by an individual." J&J does not state that this is a new policy or a departure from previous practice. (J-TXCID1826155-6)

In addition, the 2005 document goes on to declare: "J&J companies must be particularly mindful when developing a 'publication plan' for a product to insure that the above principles are complied with. Thus, while it is appropriate to anticipate and plan for potential publication venues and scientific themes, the scientific results of the J&J company's research must govern the publication outcome." (J-TXCID1826156) As we shall see, J&J and the medical writing companies that it hired frequently and indisputably violated these principles.

As in the case of financial conflicts of interest, there is a rich and relevant medical literature setting out the principles for publication. See for example: D Rennie, "When Authorship Fails," JAMA (278), 1997, 579-585; JS Ross et al., "Guest Authorship and Ghostwriting..." JAMA (299) 2008, 1800-1812; S Sismondo, "Ghost management..." PLOS (4) 2007, e286.

Other areas of concern in medicine-industry relationships and the problems beyond undue influence have been well documented and fully analyzed in the medical literature. This literature makes eminently clear just how problematic and worrisome payments from industry are to medicine, and how such payments bias medical decision making. These issues have been so emphasized in the medical literature (and not surprisingly by the media) that J&J periodically issued a variety of compliance guidelines and policies. As we shall see, however, they did not enforce the stipulations or use them to guide their own behavior as evidenced by several activities discussed below.

Thus, a J&J Healthcare Compliance Policy Update of September 23, 2004, declared: "Grants must not be used to support promotional activities." (J-TX2204305) A J&J Healthcare Compliance Contracting Handbook (October 2004) also declared: "These programs cannot principally benefit the Company directly." (J-TX2774170) But these standards, as evidence on J&J-TMAP activities makes clear, were not adhered to by J&J or by the communication firms that it hired.

J&J compliance manuals stated unambiguously: "Janssen will not place Educational, Advisory, Consultant or Training programs at 'Resorts.'" (TXJAN 0079965) It declared: "Education must be modest in value and location." (Mallegol Exhibit, 40) Nevertheless, violations of this policy were frequent, as witness the events discussed below at the Mansion at Turtle Creek (Texas) and Amelia Island (Florida).

Another Janssen manual "Questions and Answers for Health Care Compliance," responding to "conviction of individuals and organizations engaged in activities that defraud Federal Health Care programs," set forth in the period 2000-2002 standards that should govern company activities. However, the standards were not upheld. (Mallegol Exhibit, 36, preface-1) In particular, the manual declared that in terms of advisory boards, speakers, and other consulting services, "interactions should not be used as a selling opportunity to physician." (1-3) J&J practice differed. So too, the manual stipulated that CME programs must give the provider "full control over program content, planning and speaker selection." (1) Again, J&J practice departed from the standard. The focus of the program was to be "free from commercial bias," (2) and yet J&J used the programs for marketing purposes. In terms of educational grants, J&J's stated policy was that such grants should not be "promotional," but again, practice did not follow policy. (3-1) Grants were to go to the provider, not the speaker, but J&J frequently circumvented the policy. (3-2)

Finally, a J&J "Commercial Compliance" manual demonstrated the depth of the company's knowledge of compliance standards, including anti-kickback and safe harbor provisions in the guidance issued from the Office of the Inspector General of Health and Human Services. (J-TX2204015). The J&J manual showed familiarity with these stipulations. (See, for example,...4020) It closed with a check list of questions that a prosecutor might pose to create a "Perfect Storm." Included are: "Who did the sales force target? Are there budgets for unapproved use? CME-Independence of provider?" (4033) Nevertheless, as will be discussed, J&J ignored the guidance and sailed straight into the perfect storm.

2) In the relationship between J&J and state of Texas medical and official personnel, were there appropriate safeguards in place to prevent opportunities for undue influence in the activities of the Texas Medical Algorithm Project (TMAP)?

A review of the documentary record demonstrates that adequate safeguards were not in place. In promoting its drug, Risperdal, in its oral and injectable forms, J&J exerted improper influence over potential payors and prescribers. Activities that it funded in medical education, research, and publication were, in fact, thinly disguised marketing activities. J&J's funding of these activities created conflicts of interest that subverted

scientific objectivity and professional medical integrity. J&J dispensed gifts, honoraria, speaking fees and meeting attendance payments to win favors from payors and prescribers; these activities represented a deliberate effort by J&J to influence payors and prescribers to favor Risperdal. J&J carefully targeted its efforts at physicians who were Key Opinion Leaders (KOLs) or in positions to influence the purchase of J&J products, with the goal of establishing relationships that would advance marketing.

Even before Risperdal received FDA approval, J&J understood that the dominant market for the drug would be in the public sector—mental hospitals, outpatient clinics, nursing homes, jails, and prisons. Its efforts were aimed, therefore, at payors, physicians, and advocates in a position to affect public spending, especially Medicaid spending.

The strategy was set forth early in the history of Risperdal. Already in September 1992, a consulting firm (State and Federal Associates) gave J&J a blueprint that it would subsequently follow. (J-TXCID 1513719-3849) The firm advised J&J that between 60 and 80 percent of schizophrenia medications were paid for by state mental health and Medicaid programs, and should be the prime target of promotional activity. (p. 2) The firm also recommended devoting special attention to issues of cost, on the grounds that Risperdal would be more expensive than the generic alternatives, such as Haldol, but cheaper than the competing drug, Clozaril. (81) It particularly advised J&J to identify state mental health officials because they would be essential to Risperdal's marketing success, including marketing in Texas. J&J should meet with the key state officials and establish relationships with them; (96) the company should be certain to interact with mental health program directors, make its case to them, and use research findings from pharmoeconomics to buttress the argument. (83-84). So too, the firm urged J&J to work with such patient advocacy groups as the National Alliance on Mental Illness (NAMI) to expand mental health insurance benefits and thus gain more of a market for Risperdal. (95) Indeed, it recommended that J&J enlist support from NAMI to accompany the product launch. (97) J&J generally followed their advice, and undue influence frequently marked J&J's efforts to fulfill this agenda.

In 1993, GTFH Public Relations echoed what State and Federal Associates had recommended the year before. It, too, emphasized the need to cultivate state officials along with members of the psychiatric community. (J-TXCID1513850) GTFH also emphasized that J&J should be convening

Expert Task Force Meetings: "Formulate position and draft guidelines for consensus (J-TXCID 1513883) Use: "Personalized invitational campaign to maximize participation." (...1513885) Finally, it counseled J&J to "Form exclusive partnership with growing advocacy group," citing NAMI as one case in point. J&J should help establish chapters and co-sponsor educational programs on patient issues. (...892)

It is worth noting that J&J policies referred to physicians and other health care personnel (nurses, managed care employees) as "customers," defined as "any individual or company that has the ability to prescribe or influence the use of Janssen products." (Mallegol Exhibit, 40, J-TXCID0909360) Rather than conceptualize them as healers with responsibility to alleviate pain, suffering, and disease, they defined them as purchasers and customers. This mindset, as we will see, extended as well to advocacy groups, researchers, state officials and decision-makers. These, too, are all "customers." See Customer Interaction Strategic Plan November 6, 2003 J-TX4955228 which lists Shon, Crismon and others as customers. This orientation at once reflected and reinforced the priority of marketing over scientific integrity and medical professionalism.

As one of its first activities, and in disregard of professional medical ethics and principles of conflict of interest, in 1995 J&J funded a project led by three psychiatrists at three medical centers (Duke, Cornell, and Columbia) to formulate Schizophrenia Practice Guidelines. From the start, the project subverted scientific integrity, appearing to be a purely scientific venture when it was at its core, a marketing venture for Risperdal. In fact, the guidelines produced by this project would become the basis for the TMAP algorithms, giving a market edge to the J&J products in Texas.

Three psychiatrists, Dr. Allen Frances, Chairman of the Department of Psychiatry, Duke University, Dr. John P. Docherty, Professor and Vice Chairman of Psychiatry, Cornell University and Dr. David A. Kahn, Associate Clinical Professor of Psychiatry, Columbia University, took the lead in designing and developing the Tri-University guidelines. Dr. Frances negotiated the agreement with J&J (November 9, 1995), to set forth the Schizophrenia Practice Guidelines. (J-TXCID1722938-40) The project would employ three questionnaires to establish the guidelines: one went to academic experts, one to clinicians, and one to policy experts. Including the third group was in all likelihood J&J's idea as witness the fact that Frances

wrote J&J: "This is new to us and requires additional discussion. The panel members would include mental health commissioners, community mental health directors, state hospital directors, managed care medical directors, pharmacy directors, NAMI representatives, experts in pharmoeconomics, and so forth." These were precisely the constituencies that J&J was eager to influence. J&J was the exclusive supporter of the project, dividing an "unrestricted" grant of \$450,000 among the three schools. It further agreed to a \$65,000 bonus incentive payment if the team was timely with its product. The team met the requirement, requested the additional payment, and received it. (Anderson Deposition, 56)

The guideline team promised wide distribution of its product, including publication in a journal supplement. The team was prepared to have J&J participate in its work, not keeping the company even at arms length. With a disregard for conflict of interest and scientific integrity, the group shared its drafts with J&J. On June 21, 1996, Frances wrote Lloyd: "We are moving into the back stretch and thought you would be interested in seeing the latest draft of the guideline project.... *Please make comments and suggestions.* (Italics added) So too, the group was eager to cooperate with J&J in marketing activities. Frances wrote without embarrassment or equivocation: "We also need to get more specific on the size and composition of the target audience and *how to integrate the publication and conferences with other marketing efforts.*" (Italics added) (J-TXCID1722944) Indeed, from the start J&J had made it apparent to the team that this was a marketing venture. In a letter to Frances, Lloyd set forth what he called an "aggressive time line" for the project, and added: "There are a number of other Treatment and Practice Guidelines for schizophrenia being developed or published during this same period that may well serve our marketing and implementation needs at a substantial lesser cost." (J-TXCID 1722945)

Not only were Frances, Docherty and Kahn ready to violate standards of conflicts of interest in mixing guideline preparation with marketing for J&J, but also in publicizing the guidelines in coordination with J&J. The three men established Expert Knowledge Systems (EKS). The purpose of this organization was to use J&J money to market the guidelines and bring financial benefits to Frances, Docherty, and Kahn.

EKS wrote to Janssen on July 3, 1996 that it was pleased to respond to its request to "develop an information solution that will facilitate the

implementation of expert guidelines." (Anderson Exhibit 2247, p. 1) It assured the company: "We are also committed to helping Janssen succeed in its effort to increase its market share and visibility in the payor, provider, and consumer communities." Now that the "first phase" was completed, with the guidelines created, "EKS is now ready to move forward in a strategic partnership with Janssen." (p.2) The strategy will allow Janssen to "Influence state governments and providers.... Build brand loyalty and commitment with large groups of key providers around the country." (p.2) EKS also promised "rapid implementation," with particular attention to having an impact on Texas decision making. (p.3) "It is our intent to work with the State of Texas immediately in implementing this product in a select number of CMHC's with the assistance of A. John Rush, MD." (p.3) Again EKS emphasized: "It is essential for Janssen to distinguish Risperidone from other competitors in a timely and creditable way." (p.8) In its Summary of the document, EKS wrote: "Your investment in the development of state of the art practice guidelines for schizophrenia is already beginning to pay off in terms of positive exposure in the Texas implementation project." (p.9)

The costs for these various activities included: \$250,000 for "educational conferences;" and dissemination of publications at \$177,659. (Anderson Exhibit, 2244, 2245). J&J agreed to them. (Anderson Deposition, 56-67) So all told, J&J paid at least \$942,659 on the production and marketing of the Tri-University guidelines.

The framing of the inquiry, the sharing of the data, and the tie to marketing make it clear that J&J's use of the phrase "unrestricted educational grant" to describe its funding was misleading. Generally, the term "unrestricted" means that the company would exert no influence over any aspect of an educational program it supported (in keeping with ACCME Guidelines). In practice, J&J did not remain at arm's length from the choice of speakers or the content of the educational materials. Lloyd, J&J's lead contact with Frances, was "Director of Reimbursement Services." On July 18, 1996, as the project coming to a close, Lloyd wrote Frances to express his delight with the way the project had turned out: "How we work together as a team to insure their [guideline] delivery and implementation will be critical..." (J-TXCID1722936) Even more telling is the heading to the letter, which demonstrates how closely the company linked the Tri-University Guidelines to its product. It was entitled: "RE: RISPERDAL (risperidone) Treatment Guidelines." In official terminology, these were general guidelines supported by an unrestricted grant. In fact, to J&J, this was a

venture to help Risperdal expand its market. And so it was in all too many ways to the Tri-University leaders. As Frances wrote Lloyd: "We also need to get more specific on...how to integrate the publication and the conferences with other marketing efforts." (J-TXCID1722944)

J&J took great credit internally for the Tri-University guidelines. In the "Reimbursement 1996" report, the J&J team noted among its "Team Projects and Accomplishments:" "Tri-University Schizophrenia Guidelines, Design, development and implementation." (J-TXCID-1403148) So too, J&J's Reimbursement Team considered at length how it "can leverage the Expert Consensus Opinion to increase Risperdal sales by making atypical antipsychotics more widely available.... *We decided that a key would be presenting these at 'arms length' making sure that our customers realize that the protocols are not Janssen influenced but rather Janssen supported.*" (Italics added) Making this point suggests that J&J tried to conceal its true motives and active participation in the project. (J-TXCID1395263)

J&J turned the guidelines into a powerful marketing tool. The slides presented at a CNS National Sales Meeting in March 1997, instructed employees to use the guidelines to convince its "Primary customers: P & T members, Formulary Decision Makers and Psychopharmacologists"-- those who made purchasing and reimbursement decisions-- that they should use the guidelines to justify making Risperdal the drug of choice. (TXJAN0048073) J&J also wanted the guidelines to promote the product's use among "Secondary Customers," namely "Physicians who are not convinced of RISPERDAL's 1st line status." So although the front piece for the guidelines described them as "suggestions for clinical practice," from J&J's perspective, they provide "credibility; Reinforces RISPERDAL's 1st line status; Differentiates RISPERDAL from convention APS and other atypical APS." To make certain the customers got the message, the "Full Supplement [of the guideline publication] should be left behind." J&J also funded CME offerings to publicize the guidelines, including a "Free 1/2 Day Seminars, Earn Up to 8 Hours of CE/CME." The panel of experts included Frances, Doherty, and Kahn, and also John Rush (who would play a key role in TMAP). (web.archive.org/web/19961106071503/www.ibh.com/expert1.htm)

The guidelines were published in the Journal of Clinical Psychiatry (1996) 57 Supplement 12B. The Journal, in a preface, acknowledged that the supplement was supported by an unrestricted educational grant from J&J.

Dr. Alan J. Gelenberg, the editor-in chief of the Journal, however, was sufficiently troubled by what he knew that he took a highly unusual step. He warned readers of the possibility of undue pharmaceutical company influence. "Pharmaceutical companies devote enormous sums to academic departments and individual faculty members who consult, conduct research, and teach under the auspices of the company. There then are the experts who create consensus guidelines. While few of us sell our opinions to the highest bidder, fewer still are immune from financial influence." (Crismon Exhibit, 559)

Tri-University was the first of the guideline strategies that J&J deliberately, and at substantial expense, pursued. J&J next gave funding to the Texas Medical Algorithm Project (TMAP), again looking to increase the sales of Risperdal by getting it well placed in the recommended sequence for the use of pharmaceutical agents. One J&J employee, Rob Kraner, explained J&J's approach to colleagues: *"One of the reasons Janssen committed substantial funding was to develop treatment guidelines/algorithms for schizophrenia that positioned atypicals as the first line agents (at the time atypicals were usually positioned after conventionals) and test it in a real world setting. The rationale was to develop this approach in Texas, find out the most effective way to roll it out, and then other states could replicate TMAP with minimal investment."* (Italics added) (Kraner Deposition, p. 255, citing Snyder Exhibit 75.)

Just as Kraner noted, J&J effectively applied both the substance of Tri-University and the tactics that worked so well there to TMAP. Its "substantial funding" accomplished its goals. TMAP members adapted themselves all too readily to the opportunity. Rather than maintain appropriate distance, TMAP was willing to take industry money if it was "technically" unrestricted. (Crismon Exhibit, 556) The record contains TMAP Minutes from June 6, 1996 (with Drs Crismon and Shon among the five participants present). (Crismon Exhibit, 556) It noted under item 12: "New Policy discussed: No drug company money for conferences. Drug company money can be used if donated as an unrestricted educational or research grant to a foundation- companies will not be able to change protocol or algorithm nor state how the money will be used. May be able to get multiple grants from the same company if donating to different foundations. The money will be used to support the protocol in Phase I and II." These qualifications ignored both the reality of conflicts of interest (the

conscious or unconscious need to reciprocate to industry for gifts) and the appearance of conflicts of interest (developing algorithms that had crucial implications for drug companies with drug company money).

The record continues with Minutes from July 18, 1996 (with Crismon one of the 6 participants present and with Minutes distributed to Drs. Miller and Shon). (Crismon Exhibit, 448) Section XI declared: "At this point in the project it is time to bring the researchers on board. They will be helpful in reviewing the protocol and making revisions to the protocol. These individuals will also be asked to assist in seeking unrestricted grants from the pharmaceutical industry to fund the project."

In short order, even these qualifications were ignored. On September 5, 1996, Dr. John Rush, a TMAP member, wrote to J&J (at the suggestion of John Lloyd, who led the J&J Tri-University initiative) about TMAP and J&J support for Phase I activities to pilot the administration of the TMAP drug algorithm. (Dr. Shon was copied on the memorandum.) (TXJAN0018178) The expectation was that J&J would contribute \$75,000. (J_J_DSHS 0085247)

Moreover, to ask researchers in a position to revise the TMAP protocol to assist in soliciting grants from industry violates standards governing the reality and appearance of conflicts of interest. From the very beginning of TMAP, its leaders gave only lip service to conflict of interest considerations, ignoring principles in their search for industry funds.

Two additional points suggest how serious this lapse was. First, in the design of the schizophrenia algorithm, great weight was given to the recommendations of the Tri-University committee (led by faculty from Duke, Columbia and Cornell) that emphasized the benefits of the atypical antipsychotics. (Miller Deposition, p. 281) As discussed above, the work of the Tri-University group was funded by J&J. (Crismon Exhibit, 559) Second, the schizophrenia guidelines were being developed in this very period—and the algorithms used in TMAP placed atypicals such as Risperdal into the first level of use, while typicals went into the third or fourth tier. (Crismon Deposition, pp. 351-360) This change had obvious benefits for the manufacturers of atypicals in general and J&J in particular.

Thus, J&J fingerprints were all over the TMAP algorithms. As Dr. Miller declared in his deposition, the creators of TMAP adopted the guidelines of Tri-University "wholesale." (Miller Deposition, pp. 279-281)

The result was to transform the order of drug preference in the algorithm. In the "initial version" of the TMAP schizophrenia guidelines (1996), "conventional antipsychotic or risperidone" were both in Stage 1. (Crismon Exhibit, 519). The March 6, 1997 TMAP Meeting Minutes note the receipt of the \$75,000 expected from J&J along with contributions from Wyeth (\$75,000), Lilly (\$25,000), and promises of \$175,000 from three other companies. (Crismon Deposition, pp. 345-356) Then in the revised version (1998), the atypicals moved to Stage 1, and the "typical" or conventional antipsychotics moved down to Stage 4. (Crismon Exhibit 519, the 1999 publication of the Texas Medication Algorithm Project in Psychiatric Services, vol. 50, pp. 69-74) To be sure, Risperdal was not alone in Stage 1 but as we shall see, J&J through the exercise of undue influence with TMAP leaders, notably Drs. Shon, Crismon, Miller, and Chiles, was able to position its drug favorably. To cite one example, on June 6, 2000, a J&J employee, Yolanda Roman, outlined the "PHS&R Business Plan." The document emphasized the need for working with Medicaid officials and "ongoing interaction with Advocacy," as well as focusing on "price as a key element in the decision tree," in light of the extent of public funding for psychiatric drugs. The Plan also called for promoting Treatment Guidelines to the psychiatric community so as to make Risperdal the "standard of care." (Roman Exhibit, 129) In sum, J&J had its script and it proceeded to follow it closely.

J&J aimed its efforts directly at selected physicians and state mental health decision makers who were in the best position to advance its marketing interests and its particular aim to affect guideline development in the TMAP deliberations. Its activities and funding were not undertaken for the purpose of enhancing professional knowledge but for promoting the sale of its products. In its exercise of undue influence, J&J closely tracked TMAP physicians, in particular, Steven Shon, Lynn Crismon, and Alexander Miller. It also paid close attention to John Chiles, John Rush, and Kenneth Altshuler.

The attention that J&J gave to these physicians is evident from its internal memoranda (Leech Exhibit, 825). They include such observations as: Dr. Miller: "He is an investigator in the RIS-112 trial.... I will use the concept of this trial to support the idea that Risperdal is the better drug [than olanzapine]." Dr. Chiles: "My goal with Dr. Chiles is to keep him informed of advances with Risperdal research data and neutralize the influence of our competitors.... As we get new data and slides into his hands, I believe he

will use them. ... I will also include him in all advisory functions that we hold in the southwest part of the country." Dr. Rush: "It will be important to maintain a relationship with Dr. Rush as the TMAP project moves toward Phase III...."

In this same vein, J&J employees regularly performed what they called a SWOT (Strength, Weakness, Opportunities, Threats) analysis on the physicians whose status, marketing power, and influence over colleagues, interested them:

Dr. Crismon: track all his advisory board activities; his speaking development; information exchange; partnering activities. Strength: "nationally known; good podium skills;" Weakness: none; Opportunities: develop as a speaker for a new J&J drug; Threats: "Lynn is data driven, and as new information becomes available from other companies, Janssen products could move from favorable positions." (J-TXCIDrev 1449315-16)

Of particular importance to J&J was Dr. Steven Shon, the medical director of the Texas Department of Mental Health and Mental Retardation. J&J, for example, wanted Texas-based Magellan Health Care to give preference to Risperdal. The chief medical director of Magellan, however, wanted assurances that the state would agree. J&J's Evelyn Grasso-Sirface, in an internal email, noted that "Dr Shon has already given this his blessing." (Kraner Exhibit, 1161) Her email went on to suggest how to use Shon's assurances to open the market for Risperdal still further. She proposed a meeting for "national advocates with Magellan and J&J to address 'why Risperdal should be preferred (of course we will call it something like 'stretching the available financial resources for maximum patient care.')

Shon was also considered a pivotal figure by another J&J employee, Percy Coard. (Frank Exhibit, 224) After thanking his colleagues for attending a Shon presentation, he listed all the reasons why J&J wanted a "strategic alliance" with him. As Coard explained, Shon was a KOL, influential in the public sector, where "85 Percent of all anti-psychotic dollars come from;" he has influenced and supported the use of new drugs in TMAP, and a proactive approach to him "to support/partner with his current and future projects in the public sector arena will continue to position Janssen as a true partner in public mental health initiatives." (Gorsky Exhibit, 952)

Apart from TMAP, J&J also funded Visiting Faculty positions to recruit national and local speakers so as to win their allegiance. "Programs for our speakers will be directed toward solidifying their message" so as to "Own schizophrenia/OL [opinion leader] endorsement." (J-TXCID 1277436) "Tactics directed at the opinion leaders are aimed at enhancing our relationship, but more importantly ensuring their endorsement for RISPERDAL." (...439) Part of this strategy was carried out through Annual CNS summits as discussed below.

J&J made gifts of food and drink part of their business strategy to win over Texas providers and increase market share. Thus: "See Dr. Katz every Monday until end of quarter. Bring in Starbucks coffee once a week.... Take out to lunch once a month. Get Risperdal Consta available in clinic by March 15." (J-TX2551850)

The importance of TMAP to J&J was so great that it made extraordinary efforts to co-opt Drs. Crismon, Chiles, Miller, and Shon. Not only were their positions in Texas vital to J&J marketing efforts in Texas, but to its marketing efforts in other states. Its strategy took several forms.

First, the four were to be invited to attend regional meetings and gatherings, with accompanying honorariums. This approach was regularly adopted and successfully implemented. The number of meetings that the four attended is almost too many to count. (Hunt Exhibit, 1623, 1624, 1626, 1629) Crismon and Miller, for example, along with Chiles, were at the J&J Dallas Regional Advisory meeting October, 1997; then a few months later, they were in Palm Springs, Ca. for another J&J advisory meeting. (Miller Exhibits, 647, 648) Beginning in 1999, these TMAP principles were invited to J&J CNS summits which they almost always attended through 2003. (Hunt Exhibit, 1624)

Second, from the very start of the TMAP project, J&J used Crismon and Shon to advise other states on how to make use of similar guidelines. J&J sent the director of pharmacy services at Harrisburg (Pennsylvania) State Hospital a memorandum on TMAP, adding that Shon, Rush, and Crismon "are available for any questions you might have." (Snyder Exhibit, 93) They invoked the four again and in the same terms in writing to Stephan Karp, Medical Director of Pennsylvania's Office of Mental Health. (Snyder Exhibit, 94) So too, J&J told the Tennessee Care Pharmacy Director that if

he and some colleagues wanted to learn more about TMAP, it would arrange for them to go to a program in Texas. "Janssen will cover the cost of the program and your travel to and from Texas. We can also bring Dr. Chiles or Miller to Tennessee to speak about the program to a defined group." (TXJAN 0061917)

Third, J&J sent the four leaders of TMAP around the country to promote TMAP, and, in the process, Risperdal. (Hunt Exhibit, 1623) The exercise of undue influence both on the leaders themselves and their audiences is apparent. In preparation for the June 2002 meeting conducted by J&J at the Mansion at Turtle Creek, Yolanda Roman of J&J wrote her colleagues to tell them that "Key states dependent on TMAP" included Pennsylvania, Ohio, Virginia, Connecticut, Washington, and four others as well. "I'm wondering if most Janssen attendees understand how wide the net is relative to the impact of TMAP?" She also noted: "These 'state' visits have been in the form of influencing, implementing, monitoring and managing TMAP or TMAP-like initiatives. Shon and Miller are also on the CME Public Sector series faculty (2000, 2001, and 2002 series) specific to TMAP initiatives. We have a great opportunity to position this subject matter again in 2003." (Roman Exhibit, 145)

When J&J brought out Consta, a longer acting form of injectable Risperdal, it carefully coordinated its efforts to position the product favorably on the TMAP algorithm. "Alec Miller and Lynn Crismon will be the primary drivers on this decision," noted one J&J employee, Rob Kraner. Observing that Miller would soon be meeting with J&J, he also wanted a meeting arranged for Crismon. "I don't mean to underestimate Steve's [Shon] importance on this decision, it's just that Alec and Lynn play a more active role relating to algorithm modifications." (TXJAN 0057124) (Miller Exhibit, 656.) This approach was duplicated by another J&J employee (Sid Frank): "We should be actively communicating with our TMAP KOLs to lay the groundwork for adding Consta as a first line agent along with Risperdal oral." (Leech Exhibit, 828) When it was suggested that Consta would not be placed in "equal status with the other atypicals," J&J felt "it would be best to wait until the appropriate data is available before RC [Consta] is added specifically to the algorithm." (Scott Exhibit, 2212)

The J&J strategy won sustained cooperation from Shon, Crismon, and Miller. Although it certainly was a breach of responsibility on their part, they devoted an exceptional amount of attention to meeting J&J's needs. As

J&J's Roman informed her colleagues in an email of May 29, 2002: "During the last few months, Steve Shon, Miller and Crismon have spend (sic) a considerable amount of field time with most of the PHS&R Managers." (Roman Exhibit, 145) That the three devoted so much time to J&J, that although they were members of TMAP they allowed themselves to monitor and manage TMAP issues for J&J, and that they were involved with CME presentations despite their own biases and involvements, points to the improper influence exerted by J&J as well as to the failure of the three to manage their own conflicts of interest and maintain professional integrity. (J-TXCID1103181)

When J&J learned in 2001 that competitors "are NOT happy with Dr. Shon's influence over prescribing behaviors that favor RISPERDAL," and were mounting "a full court press" to move him away from J&J, the company responded with alacrity. It noted: "Dr. Shon can and is influencing not only the \$50m atypical dollars in Texas, but likewise in many other states." The bottom line: "WE WILL NOT LET LILLY OR PFIZER PREVAIL WITH OUR MOST IMPORTANT PUBLIC SECTOR THOUGHT LEADER." (Bursch-Smith Exhibit, 1801, 1800) When Yolanda Roman heard about competitors' efforts, she noted: "Steve I suppose is enjoying the vast attention and response he can command from Industry." Lilly was apparently flying him by corporate jet to a site visit. "Obviously Steve has the right to be served by all Industry, let's hope he remains fair balanced and remembers who PLACED HIM ON THE 'MAP' MAP." Bursch-Smith Exhibit, 1799) (Materials below address the special activities and relationships of these individuals in greater detail.)

3) Were appropriate safeguards in place to prevent opportunities for undue influence in other marketing efforts for Risperdal?

No. J&J utilized multiple channels to exert undue influence in marketing Risperdal, including: 1) meetings like the CNS Summit, Advisory Board, and other meetings; 2) research projects that were veiled attempts to promote marketing; 3) Continuing Medical Education events (CMEs) that violated ACCME guidelines; and 4) special pet projects that were funded for promotional reasons.

The undue influence exerted by J&J is manifested in its convening of annual CNS Summit meetings in order to win favor with Key Opinion Leaders (KOLs). Texas mental health leaders were frequently included,

both as a reward to them and as an opportunity to spread the TMAP approach to other states. J&J used the occasions to pay honoraria to KOLs (typical payments were \$3000), gifting them to win their favor. (Shon Exhibit, 317, 319-321, 673) The meetings were also the opportunity for J&J, in both formal and informal ways, to promote and market Risperdal. This is evidenced by the very heading on J&J's internal report on the 2nd Annual CNS Summit meeting in Tempe Arizona: "MARKETING." The report notes at the outset: "The objective of the meeting was attained in that we were able to further enhance our relationship and increase endorsement of RISPERDAL with our KOLs. The meeting was very well attended with over 150 of the top US KOLs and 40 international KOLs." (TXJAN 0048992) As one J&J sales representative explained, part of a sales rep's responsibility was to identify KOLs and arrange for them to be J&J speakers. As a Field Conference report declared: "Key Opinion Leaders have been utilized to influence other customers to positively impact their prescribing decisions." (Moake Exhibit 1957) One KOL, for example, citing the Expert Consensus Guidelines that made Risperdal the first choice in switching patients to a new drug, prompted four other physicians to agree this information was "beneficial." The Conference report concluded: "Great job utilizing a KOL to influence other physicians." (Moake Deposition, 93-97)

J&J expended large sums of money to influence the attitudes and prescribing behavior of KOLs. To cite one example, a CNS Summit in Phoenix Arizona brought together KOLs at a cost of nearly one million dollars. Among the attendees were several of the key decision makers in the TMAP project: Dr. Steven Shon (who received a check for \$3,000 made out to him, not his employer, the Texas Department of Mental Health) (Shon Exhibit, 317); Dr. Lynn Crismon (\$3000) (Crismon Exhibit, 516); and Dr. Alexander Miller (\$3000). The total cost of the honoraria distributed to physicians at the meeting \$564,500; hotel costs were \$187,701; and travel, \$135,527. Added to this was a cost of another \$47,547, to cover expenses incurred by J&J employees. (RIS 00052620)

J&J gave out invitations to these meetings so as to influence TMAP decision making. As one internal J&J memo noted, it wanted to schedule a get-together with TMAP leaders to discuss where on the TMAP algorithm Risperdal Consta would be placed. Not by accident did a J&J employee suggest that the meeting be held at an upcoming CNS Summit. "All the principles (sic) involved with TMAP are on the invitation list." (Miller

Exhibit, 656) When asked why he invited Dr. Shon to a CNS meeting, a J&J employee responded: "He was the medical director in the largest state in my geography." (Leech Deposition, 199) This statement is important because it indicates a clear violation of the Texas Penal Code Section 36.07. The Texas Ethics Commission states that a public servant may not accept an honorarium if their "official status" was a deciding factor. (Hunt Exhibit 1636) In his deposition, Dr. Shon acknowledged that he was aware of the penal code section. (Shon Deposition, 287)

J&J knew the value of using KOLs for marketing. When an article unfavorable to Risperdal appeared in a Florida newspaper, J&J brought in media experts to train KOLs to refute the story. KOLs were trained to be more effective communicators, through the use of videotaping and mock interviews. (Lin Deposition, 56-57) For example, at a meeting of KOLs held in New York in December 2002, Robert Findling, director of child and adolescent psychiatry at University Hospitals of Cleveland, spent an hour with a media expert "to work on specific on-camera interview and message techniques." (Lin Exhibit, 1072, J-TXCID1261521)

J&J also exerted undue influence in convening Advisory Board meetings to enhance its marketing activities, again paying out consulting fees to prescribers and presenting them with J&J data so as to win their prescribing allegiance. At one these meetings, for example, J&J presented findings on the research that it had conducted, organizing a round table "to discuss side effects of antipsychotics with particular emphasis on weight gain." (TXJAN 0048992) This format was designed to emphasize findings that J&J believed would give it an advantage of competitors' products. The goal was not a presentation of balanced and objective findings but an exercise in marketing.

At another advisory board meeting J&J assembled Medicaid officials to advance its marketing capacity. The purposes were laid out by Parexel, a medical marketing firm that organized the meeting. (Josephson Exhibit, 64, 65) It noted that with 50 percent of revenues for Risperdal coming from Medicaid payments, this market was of crucial importance to J&J. Bringing a select group of Medicaid officials together would give J&J knowledge of the barriers that limit access to its drug, and give it the opportunity to counter the threat of "restrictive utilization control mechanisms, such as prior authorization." The meetings would also enable Johnson and Johnson to "facilitate ownership" among Medicaid officials in "addressing barriers to

... atypical antipsychotic drug therapy." (Josephson Exhibit, 64, p. 2) Paraxel would identify those officials likely to "champion the idea of facilitating access to...psychotropic medications," and "solidify Janssen's profile among Medicaid officials." (Josephson Exhibit, 65, p. 7)

Importantly, J&J targeted Texas Medicaid decision-makers by sponsoring the Medicaid Mental Health Pharmacy Advisory Board which met April 14-16, 2000 in La Mansion del Rio in San Antonio. (JTXCID 0079013; Josephson Exhibit, 66) In attendance as a member of the Board was Martha McNeill, Director of Prescriber and Product Management in the Texas Department of Health; she was a key decision maker in the Texas Vendor Drug Program which administered reimbursement for drugs listed on the Texas Medicaid drug formulary. (J&J also brought her to the 2000 Advisory Board meeting in New Orleans.) The messages McNeill heard included Shon declaring that although physicians should use cost-effective drugs, "the problem," the J&J minutes report him saying, "is using a stage 4 drug [typicals] for stage 1 treatment [atypicals like Risperdal]" He added that Risperdal had now caught up to Zyprexa in sales—the two were "dead even." She also heard Joe Lovelace of NAMI speak to the theme of: "Cost of Medication: Being Penny Wise can Result in Pound Foolish." McNeill wrote J&J to say how grateful she was for being a member of the advisory group. (McNeill Exhibit, 1233) Her successor, Leslie Harper, attended the 2001 meeting, held at the Marriott in Miami Florida. (Vaughan Exhibit, 722)

So too, J&J convened a June 4, 2002 meeting at the luxurious, five star, Mansion at Turtle Creek for the Antipsychotic Algorithm Advisory Forum (at a cost of no less than \$114,000). (Hunt Exhibit, 1625, 001904; Chiles Exhibit, 1299; Roman Exhibit, 135, 136, 138, 145; Crismon Exhibit, 565; Trivedi Exhibit, 1333). At this Forum, speakers included J&J employees (Mahmoud), and TMAP member Miller (delivering an "Overview and Update on TMAP and Clinical Opportunities for Risperdal Consta"). (J-TX2243219) Shon was also in attendance as were Crismon, Chiles, Rush, Trivedi, and Suppes). The J&J goal, as an internal memo explained, was to: "Identify hurdles to [Consta] adoption;" to "Develop next steps to overcome hurdles;" and to "Develop next steps for roll out beyond Texas." (J-TXCID1476201) (For additional discussion of this meeting, see below.)

J&J also organized a series of meetings which were the occasion to have KOLs speak on behalf of J&J at a variety of settings, both spreading

the J&J message and giving the company the opportunity to reward them financially. Thus, J&J organized a Mental Health in the Millennium series on schizophrenia and used Texas TMAP personnel frequently: Shon spoke in Sacramento (travel paid and \$2000 honorarium), and in Chicago (\$2000); Miller in Tampa (\$2000), and in Nashville (\$2000); Crismon in Tampa (\$2000), in Buffalo (\$2000), in Madison (\$2000), in Nashville (\$2000), and in Richmond (\$2000). (TXJAN 0083033-11).

The choice of speakers at these events was carefully calculated to increase sales for Risperdal. As a September 21, 2002, J&J, internal memorandum stated: "It is critical that we support and maintain a strategic alliance with Dr. Shon...." (Frank Exhibit, 224) The J&J reasoning was that Shon was a KOL who was a prominent figure in the public sector, and the public sector represented the largest percentage of spending on anti-psychotic drugs.

In another example of the exercise of undue influence, **J&J coordinated its research projects to promote its business interests, merging sales and research to the detriment of scientific integrity.** As the CNS Monthly Status Report of July/August 2001 declared: "This trial *should demonstrate correction of olanzapinic-induced glucose dysregulation by risperidone and will provide data to advise on how to switch patients from olanzapine to risperidone.*" (Italics added: RIS-USA-250 Rescue Study, TXJAN 0038617).

Yet another example can be found in J&J material on RIS-OUT-090: The purpose of the research was "To document Risperdal's advantages in reduced hospitalization, weight gain, and employment/vocational training." (TXJAN 0068294) Each column listing the research project is headed by "Business Strategy." The goal was not to analyze whether Risperdone has such an effect but to document it. So too, the goal of RIS-OUT-097 was: "To Document Risperdal's cost advantages over Zyprexa in the setting of the VA." (TXJAN 0068300) Again, the conclusion is presented before the research is performed. Indeed, the funding given to Joseph Biederman, discussed below, is part of this same tactic of elevating market goals over scientific integrity.

The J&J exercise of undue influence is also found in medical education and its violations of ACCME guidelines. These guidelines, and J&J's own policies, prohibit company influence over educational programs.

Nevertheless, the company was deeply involved in the selection of CME speakers and in the content of their presentations. J&J conceived of CME as part of its marketing strategies. In an internal report of October 1996, under the heading: "Aggressive Direct Promotion," it listed, along with national symposia and speaker training, "CME half day symposia." (J-TXCID1378228)

As an example of undue influence, J&J organized a CME Symposium Project, "The Emerging Public Sector Dilemma," along with Excerpta Medica, a commercial organization that organized both CME presentations and oversaw the production of journal articles. (J-TXCID1132222) J&J made the objective of the Project for 2000 to "define therapeutic options," analyze pharmoeconomics, and identify guidelines to get newer treatments to patients. The Project audience was to include mental health administrators and mental health clinicians along with legislative staff and advocates. Ten meetings were set up by J&J to export TMAP to states across the country: Shon was scheduled to speak at 5 of them, Crismon at 3 of them, Csernansky (author of a key NEJM article on Risperdal) at 3 of them, and Chiles, another TMAP leader, at 2 of them. Materials specifically note "CME Accredited for Physicians" (...31). The final page declared: "Measuring Success." 1- Target Audience Attendance; 2- Feedback from Target Audience; 3. "*Risperdal preference as a result of meeting.*" (...2253, italics added) The document closed with FAQs: "How did you select faculty? Answer: "Based on recommendations from Janssen, our CME provider Excerpta Medica, selected faculty for the series." This company influence over the choice of speakers was a flagrant violation of ACCME guidelines.

Undue influence on CME was integral to J&J's 1999 Tactical Plan for Risperdal. It looked to establish "CME Case Study Programs" with the "Objective: Increase Risperdal share among HVP" (high volume prescribers). To this end, it looked to schedule an "Interactive CME discussion" in a small group setting in 8 cities, from Boston to Los Angeles. (J-TXCID 1277434)

Other examples of undue influence and violations of CME rules include:

An Arizona organization (Community Partnerships) asked J&J support for an educational grant whose stipulations included: "Specific

program content was not selected or controlled by Janssen." Companies were not to have influence over the selection of speakers. Nevertheless, the organization asked J&J for a grant specifically to bring Miller and Crismon to talk on TMAP. The \$2500, the organization notes, was to be applied to the honoraria for the two speakers. (J-TXCID 0079275)

Still another example is found in a memo by J&J employee, Laurie Snyder, referencing an upcoming schizophrenia guideline program: "What's in it for CNS sales?" "This program, funded by Reimbursement, will have two speakers that present favorably on Risperdal." One of the two presenters was Shon. "Physicians will hear a favorable Risperdal message and learn about guidelines that could possibly affect Risperdal share in the long run." A week after the meeting was held, Snyder was congratulated by J&J employee Sid Frank. "Great program Laurie!! Your 'next steps' are on target and should result in business growth.-Keep up the job!" (Snyder Exhibits, 97, 98)

J&J disregarded the fundamental conflict of interest that these practices engendered. It is no coincidence that in 1998, TDMHMR together with Texas Medicaid represented \$34.6 million in Risperdal sales, or 72% of the Texas total. (J-TXCID 0070899) From J&J's perspective the ends were clear and trumped the means: "It is incredibly important that we are the market leaders in schizophrenia and bipolar disorder." (...27) The goal is to be met through providers, influencers, and payers." (...27)

Finally, J&J's readiness to exercise undue influence and ignore principles of conflict of interest was standard company practice, not unique to Texas, and not the result of idiosyncratic relationships between J&J employees and TMAP officials. One of the most glaring examples was the funding that Johnson & Johnson gave Dr. Joseph Biederman of Harvard University and the Massachusetts General Hospital. The overt purpose of the agreement with Biederman was to give J&J access to a team which would carry out research on bipolar diseases in children and adolescents. The latent purpose, as set down in email strings and annual reports, was to have the Center's research promote the use of Risperdal for children and adolescents. J&J calculated that the fact that the research on the drug was conducted by a leading child psychiatry researcher at a very prestigious academic medical center would give the findings more authority.

The idea of a J&J Center for Pediatric Psychopathology originated with Dr. Biederman. On February 5, 2002, George Gharabawi, a J&J employee, informed his colleagues that Biederman had "approached Janssen multiple times to propose the creation of a Janssen-MGH center for C[hildren] & A[dolescent] Bipolar Disorders." Gharabawi described Biederman as "a pioneer in the area of C&A Bipolar Disorders." The purpose of the Center, Gharabawi explained, would be "to generate and disseminate data supporting the use of risperidone in this patient population." Biederman agreed that J&J support would lead to a focus on two topics, Diagnostics, and "Therapeutics including short and long-term outcomes on the management of C&A BPD with risperidone including the long-term prophylactic effect on drug abuse." (J-TX4695121)

J&J would commit \$500,000 a year to support the Center, the costs shared by several J&J companies: "In a number of meetings with McNeil and OMP, it was agreed that there was a need for all J&J companies to act as partners and share this research, data generation and dissemination opportunity." Further, it was agreed that "the 3 teams should meet and elaborate a plan that would ultimately include research initiatives on combination therapies." Biederman concurred. In response to J&J's request for deliverables, his team produced "A Risperdal Reanalysis, Reach and Publication grid." (J-TX4695121)

Biederman and his team consulted regularly with the company and were invited for a Home Office Visit. To give one example: "This meeting," noted Gharabawi, "will involve, in addition to Dr Biederman's research team, the Risperdal, Concerta, and Topamax team with the objective of elaborating a full research plan for the years 2002-2007." As Gharabawi saw it, the Center would position "Janssen as a major partner in the area of C&A psychopharmacology." (J-TX4695121-2) Biederman also received J&J funds for travel to conferences and funds to organize publications. (J-TX4693092) (J-TX4692727) (J-TX4691916)

For J&J, the MGH center was an opportunity to join together marketing and clinical research. Indeed, the funds that went to Biederman came from a J&J marketing division. (Lin Deposition, 77-78) In a slide set entitled, "New Initiative! J& J Pediatric Research Center at Mass General Hospital," developed by Gahan Pandina for the marketing team, the synergy that J&J so desired for research and marketing is spelled out. Biederman

was a "global expert" with a "large research team with multiple collaborations at MGH McClean (sic) Hospital, & Harvard University." The research at the center was to involve "specific extramural research with risperidone," and to review "specific scientific questions related to key business areas." The center would allow J&J to "Support a broader range of scientific activities than would be possible from JPI alone... Reinforce J&J image as a CNS company with a strong scientific commitment; Provide a model for J&J sister-company partnerships with key opinion leaders." (Pandina Exhibit, 1130)

The 2002 Annual Report of the J & J Center at MGH included references to its value for company marketing efforts. "An essential feature of the Center is its ability to conduct research satisfying three criteria: a) it will lead to findings that improve the psychiatric care of children; b) it will meet high levels of scientific quality and c) *it will move forward the commercial goals of J & J.*" (Italics added) So too, the Center's research agenda included work on J&J products, with no attention paid to the obvious conflict of interest. "The Center is poised to test the effectiveness and safety of RISPERDAL, CONCERTA, REMINYL, TOPAMAX and new products as they emerge from the pipeline." (Pandina Exhibit, 1129)

The J&J funding appeared to impact the *choice* of studies at the center. It was primarily examining the efficacy and safety of J&J products. Thus one report noted that the Center was "Using MGH open-label studies to assess the differential effectiveness and safety of RISPERDAL and ZYPREXA in the treatment of pediatric bipolar disorder (BPD). For example, we have already shown that ZYPREXA leads to twice the weight gain as RISPERDAL." Had objective parties been armed with full disclosure of J&J's relationship with the center, they would have viewed an outcome so favorable to J&J with great caution, if not dismissing it entirely. (Pandina Exhibit, 1129)

In sum, neither J&J nor Biederman ever raised the self-evident issues of conflict of interest inherent in the collaboration or the threats it posed to scientific integrity. The Center was investigating J&J products with J&J money; that support from a pharmaceutical company to a Center to study its own products created both the appearance and reality of bias did not deter J&J or the recipients of its funding.

4) Did Dr. Shon have any relationships with any defendants that created conflicts of interest in his role as medical director of TDMHMR? If so, was disclosure sufficient to resolve the problem?

Dr. Steven Shon did not adhere to appropriate professional standards on conflict of interest in responding to or soliciting personal and institutional support from J&J. Dr. Shon's conflicts of interest were acute, undermining the scientific integrity of his medical publications, lectures, and educational activities, and his responsibilities as a state official. (A more detailed discussion of the relationships between Dr. Shon and J&J are documented in Hunt Exhibit, 1619.) Disclosure is not sufficient to resolve such profound conflicts of interest. Rather J&J and Shon himself should have refrained from such activity.

Dr. Shon cultivated financial relationships with J&J, accepting checks made out to him of at least \$30,000 in fees and honoraria as well as soliciting research grants from the company. (Hunt Exhibit, 1623) Shon agreed to serve as a consultant to J&J to promote use of Risperdal. (Shon Exhibit, 315) Although these arrangements created very serious conflicts of interest, he neither curtailed nor eliminated them. Instead, Dr. Shon continued to solicit and accept favors from J&J, despite the fact that he was Medical Director of the Texas Department of Mental Health and Mental Retardation and had a significant role in the administration of TMAP. (Killion Exhibit, 1137)

Although he had significant influence over Texas drug purchases, formulary decisions, and the design as well as implementation of TMAP (and a subsequent children's medication algorithm project (CMAP), Dr. Shon often counseled J&J on how to best promote its products in Texas and many other states. (Exhibits 98, 834, 1345) His failure to consistently disclose, acknowledge or manage his conflicts of interest not only undercut his educational presentations, but also biased his official decision making capacity in the state and as a member of TMAP. Moreover, Dr. Shon accepted travel fees and honoraria from J&J so as to persuade other states to adopt TMAP-like structures. (Hunt Exhibit, 1623) He does not appear to have informed his many audiences in other states of his close financial ties to J&J. He also failed to disclose this relationship to journal readers when he served as an author. (Crismon Exhibit, 519)

The record indicates that Dr. Shon was a frequent speaker and consultant for J&J, accepting honoraria for these activities. (Hunt Exhibit, 1623) On several occasions, the payments were directed to him, not to the state of Texas, in violation of Texas law. (Hunt Exhibit, 1633) On at least one occasion he was "upset because the check was not made out to him" but rather to the Texas Department of Mental Health and Mental Retardation. J&J's medical communication firm then mailed him another check, made out to him. (Roman Exhibit, 160) Although Dr. Shon testified otherwise, he did not with any frequency consult with Department attorneys as to the propriety of his activities. (Shon Deposition, p.479) Counsel for the Department remembers having only one conversation with him, and notes "he infrequently asked me for my legal advice." (Campbell Deposition, p.138)

J&J did not move expeditiously or effectively to enforce their requirement that state employees submit an official letter from the government agency approving the arrangement. (Thompson Deposition, pp. 272-278) Not until June 10, 2003, several years after Shon had been consulting and speaking for the company, did J&J ask "for a letter from your Governmental Agency's supervisor or authorized representative, acknowledging the approval for you to speak at future programs.... This written approval must be attached to the enclosed signed agreement." (Shon Exhibit, 314; Roman Exhibit, 156, 159) When J&J official Gary Leech was asked whether in arranging payment for Shon in connection with earlier CNS Summits he had ever sought approval "from Dr. Shon's supervisor for him to receive any kind of honoraria or other monies," he replied no. (Leech Deposition, p. 199-200) Nevertheless, J&J did not report this failure despite its awareness of the relevant OIG requirements to do so. (Federal Register, vol. 68, May 5, 2003, p. 23734)

Several observations are in order. First, it took an inordinate amount of time for J&J to take note of the compliance failure. Second, even after it did take note, Shon failed to deliver such an authorization and J&J did not follow up on the failure by requiring such a submission or discontinuing using him. By admission from Defendant's counsel, no letter from state officials granting him permission to pursue these activities exists. (Newton Exhibit, 442, Defendants' response to State of Texas's first set of requests for admission No. 1) Third, even had authorization been forthcoming, it would not eliminate the clear conflict of interest.

The record is clear that despite his official position, Dr. Shon inappropriately and frequently served as a consultant to J&J. (Hunt Exhibit, 1623) The terms of the Consulting Agreement of September 10, 2002 highlight the extent of the conflict of interest created by this situation. (Shon Exhibit, 315) Notwithstanding Shon's state office, the Agreement declares: "Consultant represents that he/she is under no obligation, contractual or otherwise, to any other person, institution or entity that would interfere with the rendering of services called for in this agreement...." As consultant, Shon's 2002 duties included making two presentations to J&J senior management on TMAP "and its influence on public sector psychiatry." (Frank, Exhibit 224) That J&J had a direct interest in marketing to Texas and Dr. Shon was in the direct position to influence the use of J&J's product is a clear example of a conflict of interest, and one that a responsible public official was obliged to avoid. (See also Shon Exhibits, 295, 308, 309, 314, 322, J-TXCID 0068387, for other examples.)

Although Shon later denied participating in J&J Speaker Bureau activities, the record reveals otherwise. On July 11, 2001, Dr. Shon signed an agreement with J&J to participate as a speaker for a fee of \$1500. (Shon Exhibit, 308) As the company wrote: "We appreciate your interest in participating as a speaker on behalf of Janssen regarding Risperdal and Treatment Guidelines for Schizophrenia." (Shon Exhibit, 308) The contract stipulates that Dr. Shon disclose the relationship but even if he did so, for a medical director to promote a drug, when his office influences the purchasing of that drug, created an unacceptable conflict of interest. The medical director of the state's mental health agency should not be serving as an official spokesperson for a pharmaceutical company whose product state agencies are purchasing. (See discussion above and Texas Government Code Section 572.001(a).)

Another example of an acute conflict of interest involved Dr. Shon advising J&J regarding positioning of a form of Risperdal, Consta, in the TMAP algorithm. (Bursch-Smith Exhibit, 1802) As one J&J employee informed her colleagues after her meeting with Shon: "Steve suggested that we take the TMAP algorithm, change it to how we see Consta fitting in, and then asking the TMAP folks to respond." He advised J&J to focus its marketing efforts on state mental hospitals because these institutions had greater leeway with their budgets. (Stanislav Exhibit, 599) (Roman Exhibit, 153) It should be noted, too, that accompanying the advice was a request from Shon that J&J fund him so that he could go to Korea to present on

TMAP and fund a medical resident to accompany him. (Roman Exhibit, 153) Such a quid pro quo represents a gross violation of conflict of interest standards and professional integrity. Since Shon was at the same time serving as consultant and speaker for J&J, an untenable conflict of interest existed in which state interest gave way to personal advantage.

As noted above, J&J was advised by consultant firms to emphasize the comparative cost advantage of Risperdal as compared to competitors. Dr. Shon played an active role in implementing this strategy. (Shon Exhibit, 293) He emphasized cost comparisons frequently. However, Dr. Shon made his cost comparisons among atypical antipsychotic drugs, not against first generation typicals, which were considerably less expensive than Risperdal. TDMHMR sent a memorandum to state hospital and community clinic officials, with an exhibit showing that Risperdal was less expensive than another two atypicals (Olanzapine and Quetiapine). (Shon Exhibit, 293) It did give clinic officials room for choice among drugs, allowing that cost was only one consideration. Cost, the memorandum noted, should not "override clinical rationales." However, the memorandum immediately added: "If the clinical decision does not dictate the choice of a specific medication, then cost data should be a considered factor." To make certain that the point was not lost, the closing paragraph of the memorandum observed that "resources are extremely precious," and referred to a legislative directive to the Department to "employ strategies to limit medication costs." It is again highly relevant that none of this official advice mentioned first generation anti-psychotics which were far less expensive. If costs were so important, surely Shon should have discussed the possibility that for some patients, the first generation drugs would have been effective.

This same message on cost was delivered by Shon in a memo of July 27, 2000. (Shon Exhibit 294) When drugs in one stage of a drug algorithm had been found to be equivalent, he wrote, "it is reasonable to consider medication acquisition cost in medication selection within a stage." The memo goes to say that TDMHMR is "requiring" this approach. The memo did discuss the use of generics, but only in the case of Clozaril, and even there introduced a series of qualifications that undercut its use.

J&J was well aware that Shon followed its marketing line and very pleased with its positive impact. Sid Frank, a J&J employee, noted in an internal email, that Lilly had "strong objections" to the policy. Confident that J&J was winning the battle, he was comfortable declaring: "May the

butt kicking begin!!!” (Frank Exhibit, 229; Roman Exhibit, 140; J-TXCID1121994) So too, another employee, Laurie Snyder, wrote her J&J colleagues on November 30, 2000, referring to a lecture program in Pennsylvania that her division was funding, “Steve Shon, MD will present the Texas Medication Algorithm. Currently in Texas there is a memo that mandates that physicians use the most cost effective medication within a stage. *Physicians will hear a favorable Risperdal message and learn about guidelines that could possibly affect Risperdal share in the long run.*” (Italics added)

The gravity of Dr. Shon’s conflict of interest is apparent in the “Summary of the Medicaid Mental Health Pharmacy Advisory Board Meeting,” April 14-16, 2000, a meeting at which Martha McNeill, Director of Prescriber and Product Management in the Texas Department of Health, was in attendance. (Josephson Exhibit, 67) In the Q&A section, Shon is quoted making several comments that promote atypical antipsychotics in general and Risperdal in particular. He said: “The private sector is afraid of algorithms because they designate the new drugs as first-line therapy.” He noted that he had negotiated with a managed care company, Northstar, to use “the most effective first-line option.... Shon said Janssen’s Risperdal is preferred first-line treatment.” He also opposed a not uncommon practice of patients dividing their pills in half, a cost-saving measure that drug companies typically resist. Finally, asked about Lilly’s Zyprexa versus Risperdal, “Dr. Shon said that in Texas Zyprexa was once used 2:1 over Risperdal, but since cost became an issue, the two are dead even.” To make all these statements in light of his financial involvement with J&J is a striking example of how Dr. Shon ignored conflicts of interest. There is no record of disclosure by Dr. Shon at this meeting of his relationship with J&J.

Dr. Shon, despite his official position, freely advised J&J on TMAP deliberations, assisting the company to position Risperdal favorably and increase its sales. For example, a J&J employee wrote her colleagues to report on a meeting with Shon, in which Shon counseled J&J to become more aggressive in its marketing efforts for Consta. (Stanislav Exhibit, 599) “Steve suggested that we take the TMAP algorithm, change it to how we see Consta fitting in, and then asking TMAP folks to respond.” To these same ends, Shon “Suggests we hit the state hospitals and county hospitals hard.” That a medical director is dispensing this type of advice to a drug company and receiving payment for it is altogether inappropriate for a state official and a medical professional.

Dr. Shon's consulting sessions with J&J were frequent. Shon was brought to the J&J home office in order to debrief them on TMAP. (J-TXCID 01898962) So too, Shon frequently attended advisory meetings for J&J. A partial list includes: February 1999; Tempe, Arizona, February 2000; Scottsdale, February 2001; Scottsdale, March 2002; Amelia Island; September 2002; private meeting with J&J, February 2003, CNS Summit, Scottsdale. (Hunt Exhibit 1624, 1626) In effect, the ties between Shon and J&J were extensive, creating conflicts of interest that were left unmanaged and clearly violated professional standards.

Several of Shon's colleagues noted his frequent absence from the office. As one of them observed: "I found Steve to be somewhat loose with his job as medical director.... He was rarely there.... I think Steve liked to travel." (Rago Deposition, 45; see also, Vesowate Deposition, 541-555; Muse Deposition, 71; Killion Deposition, 81-87) He traveled around the country to promote TMAP, typically at J&J's expense and with personal remuneration. Examples include promoting TMAP on several occasions in Pennsylvania, California, Virginia, Missouri, Florida, Georgia, Michigan, Nevada, Louisiana, Illinois, Oregon, Washington D.C., and Washington State. (Snyder Exhibit, 96; Roman Exhibit, 147; Hunt Exhibit, 1626) J&J was pleased with this arrangement, eager to use his services, as well as those of one of his TMAP colleagues, John Chiles. In its Texas Business Plan, June 21, 2000, J&J noted regarding TMAP: "Goal: favorable positioning of Risperdal in treatment guidelines. Status: John Chiles and Steve Shon used extensively throughout Texas and nation as experts in guideline development and implementation." (Vaughan Exhibit, 718)

5) Did Dr. Crismon have any relationships with any defendants that created conflict of interest in his role as a leading member of TMAP? If so, was disclosure sufficient to resolve the problem?

Dr. Lynn Crismon was a key decision maker in TMAP as well as the director of CMAP, and was, therefore, in a position to influence Texas drug purchases, reimbursements, and prescriptions. He was under contract with MHMR Office of Medical Director, at 80 percent of his working time. (Crismon Exhibit, 543; Crismon Deposition 424-425) He was also a professor at UT College of Pharmacy. (Crismon Exhibit, 544) Thus, he was in positions to exert a powerful influence in favor of Risperdal. Nevertheless, Crismon cultivated a financial relationship

with J&J, accepting substantial fees and honoraria and soliciting research grants from the company. He agreed to serve as a member of the J&J Speakers' Bureau so as to promote the use of Risperdal. Although these arrangements created serious conflicts of interest, he did not curtail or eliminate them. Instead, he continued to solicit and accept favors from J&J. As a result, Dr. Crismon subverted the scientific integrity of his research and educational presentations, and biased his decision making capacity as a member of TMAP and CMAP. Disclosure is not sufficient to resolve such profound conflicts of interest. Rather, J&J and Crismon himself should have refrained from such activity. (For a detailed discussion of the relationships between Dr. Crismon and J&J see Hunt Exhibit, 1619.)

Dr. Crismon sought grants from J&J by suggesting that his research would benefit the use of its drug. (Crismon Exhibit, 549) Crismon courted J&J by telling the company that he was seeking to form a relationship with them and, therefore, he would accept a company grant that did not cover all the costs of the research project he was proposing. (Crismon Exhibit 550) Dr. Crismon sought grants from J&J with little regard for conflicts of interest or the company's stake in the outcome of the research. (Crismon Exhibit, 549) Thus, he submitted a grant to analyze medications for use in mental retardation, with the project specifically addressing "which drugs to prescribe, and at what doses." (page 2 of grant application, 5/12/99)

Although Dr. Crismon's decisions clearly had an important impact on Texas's use of Risperdal, he agreed to join the company's Speakers' Bureau. (Crismon Deposition, pp. 557-559) This activity is essentially a marketing activity, wherein speakers are trained carefully to promote a company product. The record reveals how close the link was between Crismon and J&J. He served on the J&J Speakers' Bureau, for example, in April 2001, June 2001, and May 2005. To be a member of a company speakers' bureau without recusing yourself from decision making about company products violates professional standards for managing conflicts of interest. Despite this activity, Crismon did not recuse himself from TMAP and CMAP deliberations.

Further, Dr. Crismon made visits to company headquarters in order to advise on "strategic decision making," again ignoring conflicts of interest. (Crismon Exhibit, 494) He attended the CNS advisory meeting in Amelia Island, Florida, receiving a check for \$3000 for his participation. (Crismon

Exhibit, 536) On June 20, 2002, he advised J&J on "clinical and marketing-related issues" in regard to Consta. (Crismon Exhibit, 494) Although TMAP evaluated where to place Consta on its algorithm, Crismon, as per his contract with J&J, was prepared to help "guide strategic-decision making." (Crismon Exhibit, 536) For consulting and assistance, Crismon earned at least \$60,000 from J&J. (Hunt Exhibit, 1623)

These conflicts notwithstanding, Crismon lectured frequently on issues related to Risperdal, including at CME presentations. The practice was to have the guest institution pay Crismon's honorarium, but the funds, as Crismon knew well, came from J&J. (See Sensabaugh, a J&J employee, writing to Crismon, March 23, 2003, to the effect that "Janssen will be providing a grant to Case Western Reserve to cover your expenses and honorarium. They will reimburse you directly." (J-TXCID 1136783) By the same token, Crismon was comfortable asking J&J for lecture slides on the cost and effectiveness of new antipsychotic drugs, treating company materials as though they were unbiased source. (Crismon Deposition, p. 273) Crismon also worked with Excerpta Medica (EM), a company that arranged meetings, lectures, and publications for J&J. Through EM he delivered lectures in Oregon, November 27 and 30, 2000, and received payment of \$4500. (Crismon Exhibit 529)

Crismon was prepared to accept a smaller research grant from J&J "in order to develop a pharmacoeconomics research relationship with Janssen." We would like to develop a long term relationship with your company." (Crismon Exhibit, 550) Not only was the research subject, as we have seen, directly relevant to J&J's marketing approach but Crismon was prepared to foster a relationship even when he would be evaluating the company's products. This insensitivity to conflicts of interest considerations clearly violated the professional standards outlined above.

This same disregard of standards is found in Crismon's grant request to J&J to study clinical and economic effects of anti-psychotics in prison populations. (Crismon Exhibit, 554) He told J&J that he had been persuaded that "atypicals may have even more potential benefiting this population than they do in schizophrenia." He would be certain to look at cognition "which may be the most beneficial effect of atypical agents as compared with traditional agents." To promote a grant application by suggesting to the company that its product's use would be enhanced goes against the core

principles of research integrity, as noted by the IOM. Not surprisingly, Crismon received the grant from J&J for \$20,000 (Crismon Exhibit, 518).

Dr. Crismon was so closely linked to J&J that the company tendered him a job offer. After consideration, he turned it down, on the grounds that it would require him to move from Texas to New Jersey. This negotiation itself was not only grounds for disclosure and recusal by Crismon from all decision making that affected a J&J product, but also for resignation from a decision making body that was central to J&J's commercial interests. (Crismon Exhibit 539)

In his early work as a member of TMAP, Dr. Crismon recognized the need to distance TMAP deliberations from industry funding. (Crismon Deposition, p. 97) Nevertheless, he and others (including Dr. Shon) almost immediately disregarded the principle. Rather than have TMAP remain independent of drug company funding, they proceeded to violate standards for managing conflicts of interest. Indeed, by failing to observe professional standards, they may well have encouraged J&J to dispense additional payments which personally benefited them.

6) Did Dr. Miller have any relationships with any defendants that created conflict of interest in his role as a leading member of TMAP? If so, was disclosure sufficient to resolve the problem?

Dr. Alexander Miller, professor at UT Health Science Center, cultivated financial relationships with J&J, accepting substantial fees and honoraria and soliciting research grants from the company. He also agreed to serve as a member of the J&J Speakers' Bureau. Although these arrangements created serious conflicts of interest, he neither managed nor eliminated them. Instead, he continued to solicit and accept favors from J&J, despite the fact that he was a key decision maker in TMAP and was in a position to influence Texas drug purchases. As a result, Dr. Miller subverted the scientific integrity of his research and educational presentations and biased his decision making as a member of TMAP. (A more detailed discussion of the relationships between Dr. Miller and J&J are documented in Hunt Exhibit, 1619.) Disclosure is not sufficient to resolve such profound conflicts of interest. Rather, J&J and Miller himself should have refrained from such activity.

Dr. Miller was a frequent speaker for J&J, receiving in excess of \$70,000 over the period of time with which he was involved with TMAP. (Hunt Exhibit, 1623) He joined J&J's Speakers' Bureau, undertaking activities which were directly involved in promoting company products. (Miller Deposition, p. 93) He was so closely connected to the company and so inattentive to considerations of conflict of interest that he engaged in multiple back-and-forth discussions with the company about where it wished to place one of its products (Consta) on the TMAP algorithm. (Miller Exhibit 665 and Miller Deposition, p.505) At no point did Dr. Miller recuse himself from participation in TMAP decision making because of his close ties to the company.

Dr. Miller agreed to join J&J's "Making Choices" program, not uncomfortable with J&J's active engagement. (Miller Exhibit, 655) "I will have our medical editor contact him and conduct a one-on-one training," one J&J employee wrote. (Miller Exhibit, 655). His services were in great demand by J&J, who put him at its highest honoraria level and regularly invited him to regional and national advisory boards. (Miller Exhibit, 651) Miller accepted these offers, not managing the ensuing conflicts of interest affecting his research, lecturing, and decision-making responsibilities.

Miller also cooperated with J&J to the point where he became a "guest author" for the company. (See below for a full discussion of ghostwriting and violations of professional integrity.) Miller was "nominated" by J&J to be a first author on an outcome study. (Miller Exhibit, 665) On June 9, 2006, Susan Serpico sent him on behalf of J&J an "Invitation to coauthor START study Manuscript." "The attached manuscript draft is based on the SCH-404-START study and the APA 2005 poster presentation of the results, and on feedback received from coauthors during the poster presentation development process....Please confirm your participation as a coauthor at your earliest convenience and provide any comments or suggestions from your review of the manuscript." Miller responded (June 12): "Yes, I am happy to be included as a co-author. I made a few minor edits and comments in the manuscript." That he was willing to serve as a co-author after making admittedly only minor edits and comments demonstrates Miller's readiness to serve J&J's interests rather than uphold professional standards. His claims that none of his activities with J&J biased him cannot substitute for active management or elimination of conflict of

interest and commitments to professional integrity. (Miller Deposition, pp. 90-94, 368, 480-481.)

Dr. Miller advised J&J about locating its new drug, Consta, in the TMAP algorithm, again in disregard of conflict of interest standards with regard to his other responsibilities to TMAP and to his professional obligations. (Miller Exhibit, 656) He attended a J&J advisory board meeting at a luxury hotel (Turtle Creek), and then asked J&J employees "where in the algorithm we [J&J] thought that Consta should be positioned." (Stanislav Exhibit, 599) The record is filled with evidence demonstrating how often Miller discussed the placement of Consta in the TMAP algorithm. (Miller Exhibit, 658) Apparently, he wanted it placed high; one J&J employee told another that Miller wanted it to be an "early choice," not just "another first choice." (Leech Exhibit, 832) In this way, J&J inserted itself into the TMAP algorithm development process, aided and abetted by Miller, as well as by Crismon. The company viewed both Miller and Crismon as "primary drivers." (Miller Exhibit, 656)

Miller, along with Shon and Crismon, gave J&J advice frequently not only on Consta but also on other issues as well. "During the last few months," wrote one J&J employee, "Steve Shon, Miller and Crismon have spent a considerable amount of field time with most of the PHS&R Managers. These 'state visits' have been in the form of influencing, implementing, monitoring, and managing TMAP or TMAP-like initiatives. Shon and Miller are also on the CME Public Sector series faculty (2000, 2001, and 2002 series)- specific to TMAP initiatives." (Roman Exhibit, 145) For a member of TMAP to be so involved with the major drug company affected by TMAP presents glaring violations of conflict of interest principles and professional medical standards.

7) Is the ghostwriting of scientific research articles appropriate, and if not, why not?

Scientific integrity requires that research papers present the most objective, accurate, and thorough report of all the evidence. Research design and findings must fully reflect the data gathered and the results analyzed. In the first instance, this standard requires that authors be responsible for the veracity of the material presented. If they have not participated in gathering and analyzing the material, if they allow their

names to be added to a paper in which they have had no or only minor involvement, they cannot fulfill this professional obligation. Indeed, they are committing deceit, giving journal editors, reviewers, and readers the erroneous impression that they vouch for the presentation of the data. At the same time, articles that omit the names and affiliations of those who have performed research, analysis, and writing are also misrepresentations. Editors, reviewers, and readers must be informed about who actually carried out the activities. In order to evaluate findings, they must know whether the authors were independent researchers or employees of a pharmaceutical company or consulting firm. If either of these two scientific and professional standards are violated, if there are sins of commission (adding names), or omission (not including names), then gross misconduct, what is labeled ghostwriting, has occurred. (See "Uniform Requirements of the ICJMA," NEJM January 23, 1997)

8) Did defendants engage in ghostwriting of scientific research articles?

Yes. These principles notwithstanding, J&J frequently assigned authors to articles that they had not researched or written or used authors whose participation was not acknowledged. J&J frequently hired medical communication companies to carry out research and writing; J&J employees (some of whom might eventually be listed as authors) reviewed the work. J&J or the communications company would "invite" one or more "external authors" or "guest authors" to lend their names to the publication. None of this process would be reported in the submitted or published article. Journal editors, reviewers, and readers had no way of knowing what role the company played in its production. The result of all these practices was to make ghostwriting systemic, subverting the scientific integrity of data.

It should also be noted that in J&J-supported research that involved ghost writing, the message of the article was consistently favorable to the J&J product. Ghostwriting helped market J&J products at the cost of violating scientific and professional standards.

J&J adopted a series of specific practices that violated scientific and professional standards. As I will document below, J&J stipulated that J&J employees should not be listed as first authors in an article. Second, J&J

wanted its marketing divisions to be extensively involved in setting out the research agenda and defining desired outcomes. J&J employees articulated this position. As an internal reviewer of a draft manuscript (Ris-USA-121 Inpatient) on Risperdal wrote his J&J key contact: "I think it [the manuscript] misses the mark a little bit. Although we like to think we develop these manuscripts for scientific purposes, the real value is when a sales rep can reference them, show them, present them, etc." He continued: "The data is something you cannot change, but I do think the commentary can be framed to help a rep argue that R/C should be started on the inpatient unit prior to discharge. I know this is not a review paper, but it is a subanalysis that allows us a little more flexibility to shape it as we like." (J-TX2247482-3)

Third, regardless of the actual work performed by the authors, it was J&J or a contracted medical communications firm, like Excerpta Medica (EM), who determined whether or not to "invite" "external authors." Decisions were often made after the manuscript had been drafted, reviewed internally, and revised. External authors were usually the first authors listed for the study. To enhance the reputation of the study and strengthen its marketing impact, J&J often made those it considered KOLs the first authors.

J&J organized and funded two types of research on efficacy and side effects of Risperdal. The first was an investigator-initiated research program. Researchers would propose a study which J&J would then fund or not fund. (As we have seen, researchers would suggest research outcomes that would please J&J.) The second was a J&J-initiated research program, conducted in-house by J&J employees, or in some cases, outsourced to a commercial research organization. To assist in writing and arranging for the publication of the results of its sponsored research, J&J hired medical communications companies. These organizations were given the task of managing a large number of the in-houses research projects. They reported to J&J on a regular basis so that the company's employees could track the writing and placement of the publications. These reports are very valuable in analyzing the record of J&J in ghostwriting, particularly the reports of EM, a Reed Elsevier Company that was frequently hired by J&J.

Two EM reports, "Risperidone Publication Program Status Reports," July 2003 and December 2003, demonstrate the pervasiveness of ghost writing. (J-TXCID127174 July 2003) Of the 80 articles listed in the July 2003 schedule, 16, or 20 percent, note "author TBD," or "author to be

confirmed." Of the 65 articles that EM was developing in December 2003, 14 or 22 percent had "Author TBD" or author "to be confirmed." These two EM reports, distributed to over 50 J&J employees in the United States, Europe, and Canada, reveal just how carefully EM and J&J managed the writing and presentation of articles, posters, and abstracts. J&J had to sign off before EM could begin writing or revising an article; before EM could invite external authors; or before EM could make submissions to medical journals. (J-TXCID rev 2127275 July 03 and Mahmoud Exhibit, 683).

Reports of meetings between EM and J&J reveal that employees of the two companies discussed how and when to use external authors in sponsored research. In a Minutes Update: August 11, 1999, EM noted: "Janssen authors cannot be 1st or 2nd. Immediate needs [for authors]: RIS 112, RIS 79, RIS 102." Precisely why this decision was made is not clear, but it appears to be a marketing decision to give the papers greater currency by obscuring the precise role of J&J. An article with a J&J employee as first author would have less marketing power than one in which the author was a KOL. In another section of the minutes labeled "Immediate needs: RIS-112, RIS-79, and RIS-102." EM queried J&J: "There appears to be a question whether J&J needs to also have external authors for its outcome studies: "Same policy for outcomes?" (J-TXCID1222079)

The frequent use of KOLs as assigned first authors of sponsored studies can be found in documents produced by J&J. For example, in September 2002, J&J staff listed as a priority for developing its Child and Adolescent segment, "to visit with select KOLs." Four of the ten KOLs on that list Lawrence Scahill, Robert Findling, Michael Aman, and Peter Jensen are first authors of studies that will be discussed below. (Lin Exhibit, 1074)

EM's July and December 2003 reports provide further documentation on the marginality of the external author. Even when the external author is selected early in the drafting of the article, he/she has only a limited role. The external author is kept informed, but it is EM that writes the article and the J&J team that reviews it. In the July 2003 report page 35, the proposed article and the possibility of Scahill becoming the external author is mentioned: "Use of atypical antipsychotics in managing severe behavioral problems in autistic children," (L. Scahill, to be confirmed)" EM notes that it had completed the outline for the article on February 12, 2003. EM then sent the outline to J&J on May 5, 2003. On June 13, 2003, EM followed up on the inquiries made by the J&J reviewers. Scahill had no part in these crucial

activities. (TXCIDrev2127213) The EM December 2003 report noted that in July 7, 2002, J&J employees Joseph Lin and Gahan Pandina approved the suggested author—Scahill. On August 11, 2003, EM sent the outline to Scahill, who had agreed to be the author a week before. EM reported that he responded positively to the outline. EM then began to draft the article. When EM completed the first draft, it updated Scahill on the status of the article. On September 23, 2003, EM sent the draft to J&J for review. EM then revised the article and on November 24, 2003, it again sent the article to J&J to review again. The author was not part of the process, although his name was to be attached to the article. (J-TXCIDrev1511827) The selection of Scahill may reflect his ongoing relationship with J&J. He was a J&J KOL, a member of its CNS Child and Adolescent Advisory Board during the years 2002-2003. For his participation J&J paid him honorarium and expenses in excess of \$31,171. 46. (Hunt Exhibit, 1628)

EM also developed manuscripts for Supplements to medical journals. EM paid for the Supplement and then passed the cost along to J&J. In the case of the American College of Clinical Pharmacy, it turned transcripts into articles, writing the introduction and discussion sections of the Supplement, and "trafficking the supplement." This process is enumerated in EM's invoice to J&J of January 13, 1998. EM billed J&J \$26,000 for preparing a supplement for the American College of Clinical Pharmacy—"The Changing Applications of Newer Antipsychotic Drugs"/O'Connor. The supplement contained three articles. EM charged \$8000 for preparing each article and \$2000 for Intro/Discussion. The invoice included pass-through costs of \$1,700—\$500 honoraria for each of the three authors (Litrell, O'Connor, Tugrul) and \$200 for permissions. In the case of Supplements, authors not only received academic credit but honoraria that EM paid on behalf of J&J. (J-TX2214886)

The posters that J&J presented at medical conferences also undermined scientific integrity. After J&J decided that a poster at a conference would be useful, it selected a presenter. If the data might have a negative impact on marketing, for example, a study showing evidence of high EPS side effects, then the poster was omitted. As a company employee noted to J&J staff after reviewing abstracts for an APA meeting: I "singled out the ones that appeared to me to be 1) potentially interesting to targeted media types; 2) important to the brand; and 3) doable from a regulatory point of view." Of one proposed abstract on the Impact of Weight Gain, she remarked: "Down side: Only J&J authors." On another: "My bias now is

not to publicize it, due to the study country [India] and the high EPS rate." On still another: "No recognized external author." (J-TXCID 1049756-7)

The posters demonstrate in yet other ways how J&J exercised undue influence over scientific research. External authors had to ask J&J's permission to present a poster based on J&J-sponsored research. When J&J was pleased with the presentation, it was prepared to fund the cost of travel. Thus, Steven Saklad (University of Texas, pharmacology faculty) wanted to present a poster at the APA meeting (October 1999) based on work funded by J&J; accordingly, he informed a J&J employee (Mahmoud), of his intention. Mahmoud reported to J&J: "We would be happiest, when possible (and I think Steve agreed) if we have the opportunity to see drafts before they are final and provide our comments to Steve." Another J&J employee (Leech) told Mahmoud: "Steve has agreed to let Excerpta submit the abstracts and format the poster. This gives us better control over the content of the poster.....I am sure Steve would be willing to change the slant of the presentation to meet the needs of his audiences. He is ready to share the data—have poster-will travel. Where do you want the data presented? ACCP ASHP? ACNP? He is willing and wants to do them all." (Mahmoud Ex. 685)

In this same spirit, Leech informed colleagues: "I have attached an abstract that was presented at NCDEU on work funded by Janssen. The data shows that Risperdal patients have a shorter length of stay in the State Hospital, long remission and lower cost. Steve Saklad is interested in presenting at ASHP (Dec 99) ACNP (Dec 99) and is being submitted for the psych Services Meeting in Oct 99 by Excerpta. What help can we give him?" (Mahmoud Exhibit, 685)

The section that follows provides many examples of J&J's ghostwriting practices. In all these examples, J&J worked closely with a medical communication firm, most often EM. J&J routinely hired EM and other such firms to provide assistance with writing and drafting articles for publication in medical journals. As J&J's Gahan Pandina declared in his deposition: "An author was "a scientific contributor, someone that participated in the generation, summarization and interpretation of the data." (Pandina Deposition, 198) By contrast, a medical writer was "a technical person who puts together the information and results per the guidelines and per the instructions of the authors." However, as we shall see, medical writers hired by J&J composed the first and additional drafts of a paper even

before authors were identified. Moreover, although the writers were performing as authors, J&J did not have their contributions acknowledged in published articles. Neither editors nor readers could know of their role in the preparation of the publication.

J&J also exerted very close oversight of forthcoming publications. Teams of J&J employees were assigned to review each manuscript during its drafting, before it was submitted for publication, and during the revise and resubmit process prior to final acceptance for publication. Having a team of reviewers read the manuscript and make substantive changes was company practice. (Pandina Deposition, 522) "Manuscripts that are based on company data would be reviewed by the compound development team. We have clinical reports that we write that are consistent and it is important for us to have the clinical conclusions from those clinical research reports correspond to our company interpretation of the data and the overall expert interpretation of that the data....be consistent with the primary data." Nevertheless, J&J did not disclose its employees' roles in the preparation of the manuscript either to the editors or to the readers of the journal. By not acknowledging that its employees' revisions and having it appear that the principal author had made the changes, J&J violated the principle that requires full disclosure about the funders' role in writing or editing of a manuscript.

1. RIS-USA-64

Madhusoodanan S, Brecher M, Brenner M, Kasckow J, Kunik M, Negron AE, Pomara N, "Risperidone in the Treatment of Elderly Patients with Psychotic Disorders," American Journal of Geriatric Psychiatry 1999; 7: 132-138.

Message: "Risperidone was well tolerated and efficacious in elderly patients with schizophrenia or schizoaffective disorders." (Abstract: 132)

"In conclusion, risperidone was a safe, well-tolerated, and effective antipsychotic in elderly patients with schizophrenia and schizoaffective disorders." (Conclusion, 137)

The EM billing to J&J for its work on this article reveals just how extensive the involvement of the medical communications company was in developing articles and how marginal the external author was. EM typically

billed J&J separately for each manuscript that it developed and the invoice set out in detail the various tasks that EM had performed to prepare the manuscripts for publication. On January 13, 1998, EM sent J&J an invoice for \$15,000 for Manuscript Development on RIS-USA-64—"Risperidone in Elderly Patients with Psychotic Disorders/Madhusoodanan."

[Madhusoodanan was a physician at St. John's Episcopal Hospital in New York.] EM enumerated its services: preparing 5 drafts and a final manuscript; coordinating all Janssen/Author reviews; securing all relevant information from a target journal; preparing the submission package (including redrawn figures); obtaining permissions for author(s); and managing the project through submission to the target journal. EM also billed for its consultation with the "designated author," Madhusoodanan. (J-TX2214881)

In a related document entitled "Primary Reports," EM discussed more about RIS-USA-64. It listed the authors as Madhusoodanan et al. It listed EM as the writer and set as the primary audience for the article, psychiatrists. EM noted (4/29/98) when the article was accepted for publication. It also noted that it had arranged for poster presentations of the findings of RIS-USA-64 at six professional meetings, including the American Psychiatric Association (APA), and the International Psychogeriatric Association (IPA). (J-TX2524103)

RIS-USA-64 appeared in the American Journal of Geriatric Psychiatry (Spring 1999, 7, 2: 132-138). Madhusoodanan was the first author. The second author was a J&J employee, Martin Brecher. **There is no disclosure in the article of the role of EM. No mention is made of the fact that it prepared five drafts as well as the final manuscript. Beyond noting that Brecher was a J&J employee, the article gave no indication of J&J's role as funder or organizer. There is no indication that Madhusoodanan was a "designated author," not actual author. Journal editors, reviewers, and readers would have incorrectly believed that the work was done by Madhusoodanan.** So too, there is no indication that the third author, Ronald Brenner, was a member of J&J's Certified Speakers Bureau Program. (Hunt Exhibit, 1628) Thus, it is not surprising that the article's conclusion reiterates a message J&J was eager to promulgate: Risperidone was "a safe, well-tolerated, and effective antipsychotic in elderly patients with schizophrenia and schizoaffective disorders." By using medical communications companies to draft articles based on J&J-sponsored research, and having J&J employees help develop the messages that were

presented to the public sector, J&J was undermining scientific integrity to promote marketing.

A second EM invoice was sent to J&J on February 13, 1998. It made clear that not only were there academic rewards for guest authors (publishing enhanced their reputations), but they also received such tangible benefits as expense-paid trips and honoraria to academic meetings and international conferences; these expenses and honoraria were paid for by EM on behalf of J&J. Noted on the EM invoice were "Pass-Through Costs" of \$4,331.92 for Madhusoodanan for presenting a poster related to RIS-USA-64 at the IPA meeting in Jerusalem. Madhusoodanan also received a \$1000 honorarium for the presentation. In addition, J&J, through EM, reimbursed Madhusoodanan \$784.77 for his hotel, \$1751.15 for his airfare, \$590.00 for conference registration, and \$200 for food, tips, and ground transportation. (J-TX2214878)

2. RIS-USA-251

Mittal D, Jimerson NA, Neely EP, Johnson WD, Kennedy RE, Torres RA, Nasrallah HA, "Risperidone in the Treatment of Delirium: Results from a Prospective Open-Label Trial," *Journal of Clinical Psychiatry* 2004; 65: 662-667.

Message:

"Low-dose risperidone can improve cognitive and behavioral symptoms of delirium in medically ill patients." (Abstract, 662)

"In conclusion, results of this open-label study indicate that risperidone is an effective and safe alternative to conventional antipsychotics and in the treatment of delirium." (Conclusion, 666)

The EM Report of July 2003, referring to RIS-USA-251, "Treatment of delirium with Risperidone," noted on October 23, 2002: "need Janssen approval to begin." It added: "Received approval from Janssen reviewers (4/18/03), and only then "completed and sent revisions to...[authors]" (J-TXCIDrev2127179) It was EM and J&J who were primarily responsible for drafting the findings and analysis, with the ostensible authors coming in at the end of the process.

The last author on RIS-USA-251 is Henry Nasrallah, a J&J KOL. Nasrallah participated in regional meetings, CNS Summits, and was a member of J&J's Speaker Bureau Program. From 2000 to 2004, Nasrallah received \$73,000 from J&J for participating in these activities. (Hunt Exhibit, 1628)

3. RIS-USA-209

Muslant BH, Gharabawi GM, Bossie CA, Mao L, Martinez RA, Tune LE, Greenspan AJ, Bastean JN, Pollock BG, "Correlates of Anticholinergic Activity in Patients with Dementia and Psychosis Treated with Risperidone or Olanzapine," Journal of Clinical Psychiatry 2004; 65: 1708-1714.

Message: "Efficacious doses of olanzapine increased Anticholinergic activity in older patients with dementia, while similarly efficacious doses of risperidone did not." (Abstract, 1708)

"Thus, these data indicate that one possible reason for the lack of efficacy of olanzapine at higher doses in dementia may be its potential for increased Anticholinergic activity. This possibility should be considered in other populations such as older patients with schizophrenia, as higher doses of olanzapine are being investigated as possible treatments for schizophrenia." (Conclusion, 1713)

On page 3, July 2003 the EM report discusses RIS-USA-209 "Impact of the Anticholinergic effect of atypical antipsychotics on safety in elderly patients." It notes a possible author (Tune), and then adds, TBD. Although EM notes that they are planning to publish RIS-USA-209 in the next 6 months, it is still waiting for J&J to assign external authors. (J-TXCIDrev2127279) The article was published in December 2004.

4. RIS-INT-57

Lasser RA, Bossie CA, Zhu Y, Gharabawi G, Eerdeken M, Davidson M, "Efficacy and Safety of Long-Acting Risperidone in Elderly Patients with Schizophrenia and Schizoaffective Disorder," International Journal of Geriatric Psychiatry 2004; 19: 898-905

Message:

"Long-acting risperidone was associated with significant symptom improvements in stable elderly patients with schizophrenia or schizoaffective disorder. Treatment was well tolerated." (Abstract, 898)

"Our data suggest that the long-acting formulation of risperidone will offer a new treatment option for elderly patients, eliminating the need for daily dosing and potentially improving outcomes." (Conclusion, 904)

EM notes of RIS-INT-57: "Risperidone microspheres for treatment of psychotic disorders in elderly patients (Davidson, Lasser, Bossie, Eerdekens, Zhu, Gharabawi; external authors to be confirmed)." The roster of names is composed in advance of confirmed participation. (p.13, July 2003) As of 7/22/03, EM reports on extensive comments from J&J employees, and notes that more internal reviews are needed. Its next step is "to incorporate comments" and send to "Janssen reviewers." It also plans to "ask C. Bossie [a J&J employee] when to send to aus [authors]." (J-TXCIDrev2127189)

5. RIS-IND-2

Khanna S, Vieta E, Lyons B, Grossman F, Eerdekens M, Kramer M, "Risperidone in the Treatment of Acute Mania: Double-blind, Placebo-Controlled Study," *British Journal of Psychiatry* 2005; 162: 229-234.

Message:

"In patients with severe manic symptoms, risperidone produced significant improvements in YMRS scores as early as week 1 and substantial changes at end-point. Treatment was well tolerated." (Abstract, 229)

"Results confirm those of other trials involving diverse patient populations in which risperidone was found to be effective and safe in patients with acute mania." (Conclusion, 234)

External authors played a minimal role in the design and development of the RIS-IND-2 manuscript, its revision, and the choice of journal for publication, and post-publication, a letter to the editor. IND-2 was a 3 week randomized, double-blind trial conducted at eight sites in India.

("Risperidone in the Treatment of Mania or mixed Episodes of Bipolar Disorder")

The "Publication kickoff meeting" for RIS-IND-2 was held July 23, 2002, with J&J team members and two representatives from EM present. (J-TX4311837) In the first instance the report notes: "Lengthy discussion ensued around the importance of authorship from internal and external perspectives, and from clinical vs. commercial perspectives." The group recommended "potential authors" and the order of authors, and then made assignments among themselves as to who would be contacting suggested authors. Authorship determination came from the team, not from work submitted or performed by authors— indicating that ghostwriting was a key element in IND-2. (J-TX4311838)

Further substantiation of this conclusion came be found in the report note that follows the discussion of authors. "M. Kramer [of J&J] reviewed IND-002 data with the team and a list of key messages were tentatively developed." The formulation of these messages by the J&J team in advance of the selection of authors makes clear is another indication of the role of ghostwriting in this protocol.(J-TX4311838)

EM started writing IND-2 in September 2002. It sent the first draft of the article to J&J's Mood Publication Review Team for comments. Also, in September, two physicians, one Indian and one Spanish, were named as first and second author. (J-TX3086311) Shortly thereafter, a J&J product director noted that investigator meetings for IND-2 would be taking place. He commented: "I am not concerned regarding the IND-002 investigator meetings because they are all Indian physicians and will have no impact in shaping perceptions of US prescribers." (J-TX3086308)

On January 14, 2003, EM sent a second draft, responding to comments by several J&J employees. There is no mention by EM of external authors or of the two men who will become the first and second authors. Between 5-28/03 and 6/11/03, EM "formatted & edited revised ms." "7-1-03: Completing edits & formatting." The first mention of authors in this draft review is 10/7/03, "authors reviewing mss. for approval." By then, J&J had already selected the The British Journal of Psychiatry for submission. (J-TXCIDrev2127198) In the December 2003 report, IND 2 has five authors: Khanna, Vieta, Grossman, Lyons, Kramer. The two first authors are external authors. Sumant Khanna is from New Delhi and Eduard Vieta, from

Barcelona. (J-TXCIDrev1511810) The article is published in 2005 in The British Journal of Psychiatry under a different title: "Risperidone in the Treatment of Acute Mania: Double-blind, Placebo-Controlled Study." It appeared with 6 authors: Khanna, Vieta, Lyons, Grossman, Eerdekens and Kramer. The last four were J&J employees, the company that supported the study. Despite the history, Khanna is the corresponding author. There is no statement on his precise role in the study. The same is true for Vieta. Once again, the active engagement of EM in the writing process is not acknowledged. And once again, J&J published data that was favorable to Risperdal. The findings included statements that patients given Risperdal "demonstrated significantly greater improvements than those given placebo on each of the efficacy measures." (at p. 233) More, Risperdal "was generally well tolerated, as evidenced by the low incidence of other adverse events and the high completion rate." (at p. 233)

Finally, the role of the authors was so minimal that on March 24, 2006, EM billed J&J \$5100 for composing a "Reply letter to the editor for RJS-IND-2." (EXCERPTA0005369) The EM tasks, as it reported it, included: "Development of a letter to the editor- includes research, phone calls, literature search, first draft (average 3 pages, sent to client and author for review). Reference articles, second draft (includes comments from client review and from each author sent to client and author for final review). final (sic) draft (includes finalizing from client review and from each author), copy editing, styling for journal, proofreading, and submission package. (EXCERPTA0005370)

6. RIS-USA-250

Ganguli R, Brar JS, Mahmoud R, Berry SA, Pandina GJ, "Assessment of Strategies for Switching Patients from Olanzapine to Risperidone: A Randomized, Open-Label, Rater-Blinded Study," BMC Medicine 2008; 6: 17.

Message:

"Switching via any strategy was associated with significant improvements in positive and anxiety symptoms and was generally well tolerated."

"Our study confirms that stable outpatients with schizophrenia or schizoaffective disorder who require an alternative treatment can be safely switched from olanzapine to risperidone and experience improvements in symptom control. Our results also suggest that the rapid initiation of the new medication and the very gradual withdrawal of the old medication may be more successful than more rapid withdrawal strategies."

Another example of how marginal a designated author was to a published article comes from RIS-USA-250. (J-TXCID1216826) To increase its sales, J&J decided to design a clinical trial whose outcome would persuade its "strategic customers" to switch patients from Olanzapine to Risperdal. The trial designed to implement this strategy was known as the Risperidone Rescue Study. Sally Berry was the Medical Director and Gahan Pandina the clinical Director, and Courtney Lonchena the project manager; all were J&J employees. The protocol was agreed upon in 2000. In November 2001, while the trial was underway, J&J's Updated Monthly Report stated that the goal of the trial was "Product Differentiation." So as to "Maximize cost and reimbursement opportunities, the trial should demonstrate correction of olanzapine-induced glucose dysregulation by Risperdal and will provide data to advise our strategic customers on how to switch patients from Zyprexa to Risperdal." As J&J was aware, "Competitors have published switching data." J&J's "Outcome Statement" stipulated: "Submission of one or more abstracts to one or more major psychiatry meetings on effective strategies by which patients with schizophrenia can be converted from olanzapine to risperidone treatments by January 2002 for a study cost of no more than \$2.8 M."

Rohan Ganguli, a J&J KOL, was the designated "external author," and he was sent materials for review. In 2002, he was asked by J&J to become first author on an abstract to be presented to a professional medical meeting and he agreed. (EXCERPTA 0031719 and....725) Ganguli only saw the manuscript after it was vetted, reviewed, and commented upon by the J&J team. (JTXCIDrev2127221, for details on manuscript review) In this case, the eventual publication did disclose some of the process. Acknowledgments included the fact that J&J "had a role in writing and decision to submit." Still, readers would not know just how extensive the J&J role actually was and the market-based reasons why the project was undertaken in the first place. (Ganguli et al., "Assessment of Strategies for switching patients...." BMC Medicine, 2008.) Again, it should come as no

surprise that the article's conclusion in 2008 faithfully mirrored the original aim: "Patients...who require an alternative treatment can be safely switched from olanzapine to risperidone and experience improvements in symptom control."

7. RIS-CAN-23

Shea S, Turgay A, Carroll A, Schulz M, Orlik H, Smith I, Dunbar F, "Risperidone in the Treatment of Disruptive Behavioral Symptoms in Children with Autistic and other Pervasive Developmental Disorders," *Pediatrics* 2004; 114: e634-e641.

Message:

"Risperidone was well tolerated and efficacious in treating behavioral symptoms associated with PDD in children." (e634)

"The encouraging efficacy outcomes achieved with this agent offer new hope for the management of behavioral symptoms exhibited by children with PDD." (e640)

The politics of author assignment is illuminated by the report of a Risperdal Data Rollout meeting held on April 21, 2004 by Johnson & Johnson. One item agenda was a discussion of RIS-Can-23-Subanalysis April 21, 2004 (J-TXCID1174074-5). The meeting notes declare: "Responsibilities were discussed and it was agreed that Gahan Pandina [of the company] would take primary responsibility for all the sub-analyses and publication." Although Pandina was in the US office and was responsible for data management and publication, authorship was to rest elsewhere. "JOI requested that whenever possible we include at least one of the Canadian investigators on subsequent publications. It was also noted that a European KOL...be included on a targeted publications (sic)." In keeping with this decision: "The list of Canadian investigators was reviewed." The RIS-CAN-23 Subanalysis was published in *Pediatrics* 2004 under the title: "Risperidone in the Treatment of Disruptive Behavioral Symptoms in Children with Autistic and Other Pervasive Developmental Disorders." The authors were those suggested at the April 24, 2004 meeting and a J&J Canada employee was the last author. In this case, there was no conflict of interest statement or a description of authors' contributions. The article

acknowledges J&J support but gives no information about J&J's role in the process and author selection, a failure which constitutes improper conduct.

8. RIS-USA-79

Csernansky JG, Mahmoud R, Brenner R, "A Comparison of Risperidone and Haloperidol for the Prevention of Relapse in Patients with Schizophrenia," New England Journal of Medicine 2002; 346: 16-22

Message:

"Adult outpatients with clinically stable schizophrenia and schizoaffective disorder have a lower risk of relapse if they are treated with risperidone than if they are treated with haloperidol" (Abstract, 16)

"Our results demonstrate that substantial reductions in the risk of relapse can be achieved in such patients with the use of risperidone, even in comparison with the use of an effective conventional antipsychotic." (Conclusion, 21)

J&J wanted an article that endorsed Risperdal published in the most prestigious medical journal, The New England Journal of Medicine (NEJM), believing it would benefit its sales. (J-TX2168744) On January 3, 2002 an article appeared in the NEJM authored by John G. Csernansky, Ramy Mahmoud, a J&J employee and Ronald Brenner: "A Comparison of Risperidone and Haloperidol...." The message was consistent with J&J's marketing message. "Adult outpatients with clinically stable schizophrenia or schizoaffective disorder have a lower risk of relapse if they are treated with risperidone than if they are treated with haloperidol." The article contains no information on authors' responsibilities and manuscript development; there is a conflict of interest statement that acknowledges J&J financial support and sources of industry support for Csernansky and Brenner. When an NEJM editor asked prior to publication about methods, it was J&J who supplied the content for the reply to the queries. More, the NEJM was told: "Drs. Csernansky and Brenner were never members of the clinical research team in charge of the study." (J-TX2260221) Publication proceeded, but it does not speak well for J&J or the NEJM that the lead author was not even a member of the clinical research team.

Indeed, as late as March 26, 2001, J&J was still discussing who would be the final authors of the manuscript. On June 26, 2001, while the manuscript was still undergoing revision at J&J, Mahmoud wrote colleagues at J&J: "One BIG question- I was under the impression (perhaps mistaken) that Brenner would NOT be an author... did we submit with him as an author?" In the manuscript, Brenner did become the third author. Clearly, then, authorship was a J&J negotiation, not a reflection of who actually conducted and wrote the manuscript.

Csernansky was not a member of the research team but he was member of a J&J Speaker Bureau program—he received \$1500 honorarium each time he spoke— and beginning in 2000, an attendee at its yearly CNS summits. He received between \$2500 and \$5000 for each meeting he attended. Between 2000 and 2003, J&J paid Csernansky at least \$61,731 for his activities promoting Risperdal. (Hunt, 1628)

An email string on the NEJM article also contains a message from a J&J employee and NEJM author Mahmoud to the J&J CNS team. (October 23, 2001) Mahmoud's language makes clear that this is J&J's publication. They own it despite the fact that the first and last authors are external authors. Mahmoud did not include the external authors on this email:

Great news! We have final acceptance on our NEJM paper!

This must have been a new world record for number of reviews and editorial exchanges...but we always had the answers. A great big thanks to all who contributed to this process (please pass along my thanks to anyone I may have missed!) This will help our business tremendously—none of our competitors have, or are likely to have, any long term relapse comparisons showing unequivocal superiority over an active treatment.

I will advise as soon as know the exact publication date, but we can immediately mark all materials related to this paper with "in press" and we can prepare plans on how to use this so we can act quickly when it hits. (J-TX2168744)

This same message was repeated by other J&J employees. One wrote: "The most important point here, however, is that CSERNANSKY CAN HELP US DRIVE BUSINESS!!!... If a doc says anyone can manipulate

numbers, ask them why Lilly hasn't done it." The memo ends with the phrase: "CRUSH THEM." (J-TX2614229) Another declared: "This is a great opportunity to 'Change the way our key customers Rx atypicals' and drive RISPERDAL market share. Let's take advantage of it." (J-TX2614230)

J&J did take advantage of it. Csernansky was funded to present the findings to consumers, including patient advocacy groups. (J-TXCID1131384) And J&J told staff in its 2003 Franchise Plan that the NEJM article "Supports Risperdal's long term efficacy advantage vs other antipsychotics with a unique study design and published in a premier medical journal for both primary care and specialists." As a result of the publication J&J was able to revise its sales aid and sales training workshop, as well as add new CME materials, and slide sets. (J-TX2165928)

Records that J&J sales representatives submitted to the company also indicate that they discussed the NEJM article when visiting physicians in Texas. For example, one rep reported during a visit to a physician in Texas City, Texas: "Focused on long term efficacy via Csernansky (sic) well tolerated and low side effect profile." (J-TX711191) Another, after visiting a physician in Big Spring Texas, notes: "Discussed Csernansky data for Relapse prevention. Doctor said he has always thought Ris was great for efficacy." (J-TX2720333) So too, a sales rep who visited a physician in Rosenberg, Texas commented: "Focus on Csernansky data reporting long-term efficacy and safety at correct doses." (J-TX2841053) These reports indicate that J&J sales reps used the NEJM article to persuade Texas physicians about the safety and efficacy of Risperdal. The Texas physicians who were encouraged by the sales representatives to use Risperdal based on the findings presented in the NEJM study were not informed about the role of the J&J employees in the study.

Even without being privy to all these details, an editorial accompanying the article raised the crucial question of whether research conducted by the pharmaceutical companies and the goals of the research were problematic: "In view of the fierce competition...these trials would benefit from being designed and conducted by researchers who are independent of the pharmaceutical manufacturers. Rather than being targeted primarily at meeting the demands of the regulatory authorities, the studies should aim to produce reliable, clinically useful estimates of the effects of treatment." (NEJM 2002; 346: 58)

9. [No Ris Number]

Jensen PS, Buitelaar J, Pandina GJ, Binder C, Haas M, "Management of Psychiatric Disorders in Children and Adolescents with Atypical Antipsychotics: A Systematic Review of Published Clinical Trials," European Journal of Child and Adolescent Psychiatry 2007; 16: 104-120.

Message:

"The review of published scientific data suggests that most of the atypical antipsychotics, excluding clozapine, have a favourable risk/benefit profile and effectively reduce disabling behaviours in paediatric psychiatric patients." (Abstract, 104)

"There is growing evidence of favourable risk/benefit profile of risperidone, olanzapine, and quetiapine in both short-and long-term studies." (Conclusion, 117)

The secondary role that J&J assigned external authors, to the clear detriment of scientific integrity, appears in the origins and publication of Risperdal in pediatric use. The J&J team wanted to produce a "pediatric positioning briefing document," which would position "Risperdal in all pediatric indications, pharmacological and non-pharmacological." (February 10, 2004)(J-TXCID1261508) EM carried out the assignment, with a proposed title: "Antipsychotics for the management of psychiatric disorders in children and adolescents: The current state of the art." Its "Strategic Objectives" were carefully defined and included:

Promote the concept that psychiatric disorders in children require treatment, non-pharmacological and pharmacological. Notes on quality of life and consequences of not treating this population.

Position Risperdal as the pharmacological treatment for severe behavioral symptoms that occur across disorders, i.e. autism and bipolar disorder...in children and adolescents.

To leverage data from clinical trials and open-label studies in DBDs, autism and bipolar, to underpin Risperdal key efficacy and safety messages.

Focus on positive outcomes (risk/benefit; costs; successful early treatment)

(J-TXCID1261509)

EM proposed that conclusions of the article include "the need for treatment and Risperdal being the most established treatment choice in children and adolescents." (J-TXCID1261512) The EM Publication Briefing Document also suggested several KOLs as possible authors: "KOL Pub team: Please advise: Stan Kutcher in Canada or Sandra Fisman? If European journal- Jorg Fegert in germany (sic), Peter Jenssen (sic)in US?" (J-TXCID1261509)

The marginality of the external authors was increasingly relevant as EM continued to develop this manuscript. Developing the manuscript was a joint effort by EM and J&J. On April 21, 2004 EM sent J&J a first draft of the "so-called pediatric positioning paper. "Could you please let us know your ideas and comments on this paper? As we currently do not have an author for this paper could you also give some suggestions for an opinion leader to author this paper." (J-TXCID1204312) On May 6, EM wrote again noting it had only a few comments: "We however prefer to have your thoughts on the scope of the paper including some suggestions for external authors and preferred journal." (As above....311) On May 13, EM wrote: "It would be very helpful to receive some guidance in relation to the flow, format and subject discussed in this paper and whether you think this is too marketing oriented or not, in order to prepare a next draft. Besides that we would like have some suggestions for external authors on this paper. Maybe an (sic) US and a European KOL? Your input will be much appreciated." (...311) J&J's concern was with the market impact of the article, not its substance. As one of them noted: "If we try to describe efficacy in multiple diagnoses, this will support the argument of pseudospecificity of the effects on symptoms, and be perceived negatively by clinicians even if it what they believe.... I think the message is too broad and the intent a bit transparent." (As above....310-311)

The article eventually appeared in the European Journal of Child and Adolescent Psychiatry in 2007. The authors were a US KOL, Peter S. Jensen, a European KOL, Jan Buitelaar, and 3 J&J authors, Pandina, Binder, and Haas. Jensen was the only proposed author from EM to be included. The published article did note funding from J&J and identified the three J&J authors. However, there is no conflict of interest statement, and no information on the contribution of the authors or mention of the fact that medical writers were involved. There is sufficient overlap of language and data from early EM draft to the published article to justify the conclusion that the authors had improperly put their names on and failed to credit EM's work.

It should be noted that the title on the first draft of the EM article and the title on the published article are the same. The published article included citations that EM used in the first draft. More, EM designed three tables for the first draft and they reappear in slightly revised form in the published article.

Examples of similar language:

First draft: "Common, disabling psychiatric disorders in children and adolescents, include disruptive behavioral disorders (DBD), pervasive developmental disorders (PDD), schizophrenia, and bipolar disorder. These disorders include disturbing and disruptive behavioral symptoms that significantly impact quality of life for both the patient and their caregivers." (J-TXCID1204317)

Page 104 Published article: "Common disabling psychiatric disorders in children and adolescents that have been targeted for treatment with atypical antipsychotics include disruptive behavioural disorders (DBDs), pervasive developmental disorders (PDDs), tic disorders, schizophrenia, and bipolar disorder. These disorders include disturbing and disruptive behavioural symptoms that have a significant and often long-lasting negative effect on the quality of life for both the patients and their caregivers."

First Draft: "DBD of childhood include conduct disorder (severe destructiveness and violence), oppositional defiant disorder (e.g. tantrums), and DBD not otherwise specified. DBD is the most common reason for psychiatric referral in children." (J-TXCID1204317)

Page 105 Published article:

Disruptive behavioral disorders (Table 1)

DBDs of childhood include conduct disorder (destructiveness and violence), oppositional defiant disorder (e.g. defiance of authority and rule-breaking behaviour), and DBD-not otherwise specified. These are among the most common reasons for psychiatric referral in children."

First Draft: "Short-term reduction of DBD symptoms has been demonstrated with both olanzapine and risperidone (Table 1). With both medications, significant behavioral improvement occurred within the first 1-2 weeks of treatment. Long-term maintenance of DBD has been demonstrated with risperidone in both open-label and double-blind studies, with children followed up to three years. (Croonenberghs (RIS-INT-41), Buitelaar (INT-79), Croonenberghs (INT-70), Olah HUN 4). (J-TXCID1204322)

Page 105 Published Article: "Short-term reductions in DBD symptoms have been demonstrated with both olanzapine and risperidone (Table 1).....In the double-blind and open-label risperidone (0.002-0.006,g/kg/day) trials and the one open-label trial with olanzapine (0.25-0.30 mg/kg day), significant behavioural improvement was seen within the first 1-2 weeks of treatment....Long-term maintenance of efficacy in treating DBD has been demonstrated with risperidone in open-label studies (Croonenberghs 2005, Findling 2004, Reyes 2006, Turgay 2002)

First Draft: "Schizophrenia is typically recognized in young adults rather than children. Childhood-onset schizophrenia occurs for about 0.01% of children <12 years old, with incidence increasing during the teenage years." (Remschmidt, 2002) (J-TXCIDD1204318)

Page 110 Published Article: "Schizophrenia and bipolar disorder are typically recognized in adolescents or young adults rather than children. Childhood-onset schizophrenia is reported in about 0.01% of children aged <12 years, with the incidence increasing during the teenage years "Remschmidt, 2002).

First Draft: Safety and tolerability of atypical antipsychotics in pediatrics "In general, atypical antipsychotics are better tolerated with improved compliance compared with conventional neuroleptics (Chakos, 2001).....The most frequent significant AEs reported with atypical antipsychotics are sedation and weight gain. (J-TXCID1204324-5)

Page 114 Published Article:**Safety and tolerability of atypical antipsychotics in paediatrics**

"In general, atypical antipsychotics are better tolerated and show improved medication compliance than typical antipsychotics." (Chakos 2001)....The most significant adverse events reported with these atypical antipsychotics in a paediatric population were sedation and weight gain."

First Draft: "Somnolence occurs frequently with atypical antipsychotics, although it is usually transient and mild to moderate in severity. The impact of somnolence can be reduced by switching from morning to evening dosing, using divided dosing, or reducing dosage (Soderstrom, 2002; Shea CAN 23 submitted). (J-TXCID1204325)

Page 114 Published Article: "Somnolence was frequently reported with atypical antipsychotics, although it was usually mild to moderate in severity and infrequently resulted in treatment discontinuation. The impact of somnolence was effectively reduced in studies with olanzapine and risperidone by switching from morning to evening dosing, using divided dosing, or reducing dosage." (Shea 2004, Soderstrom 2002)

First Draft: "Physical and sexual development must also be carefully studied in pediatric patients, especially when exposed to long-term therapy. Growth was assessed in 350 children and sexual maturation in 222 children who participated in long-term treatment with risperidone for DBD (Dunbar, 2004). After 12 months, mean height increase was 1.2 cm greater in children treated with risperidone compared with placebo. In addition, there was no delay in progression through Tanner staging with risperidone." (J-TXCID1204326)

Page 115 Published Article: "Physical and sexual development should also be carefully studied in paediatric patients, particularly when exposed to long-term therapy. A recent meta-analysis assessed growth in 350 children and sexual maturation in 222 children who participated in long-term treatment of DBD with risperidone. (Dunbar, 2004) After 12 months, there was no inhibition of the expected growth (National Health and Nutrition Examination Survey data and growth velocity charts), nor was there any delay in sexual maturation as assessed by Tanner staging, with risperidone."

First Draft: "Antipsychotic treatment has also been linked to hyperprolactinemia. A survey of prolactin levels at baseline and after 6 weeks of treatment in children and adolescents (mean age=14.1 years) showed elevations with both atypical and typical antipsychotics (Wudarsky, 1999). Prolactin increase was significantly higher with haloperidol (mean=47.8 ng/ml) compared with olanzapine (mean=23.7 ng/ml) or clozapine (mean=11.2 ng/ml; $P<0.001$). Prolactin levels with treatment exceeded the upper limit of normal for 90% of the patients treated with haloperidol, 70% treated with olanzapine, and none of those treated with clozapine. A post-hoc analysis of 592 children with DBD participating in long-term risperidone treatment showed elevation in serum prolactin within the first 4-8 weeks of treatment, followed by the steady decline to values within the normal range by 3-5 months (Findling, 2003). In addition, prolactin-mediated AEs occurred in 4.7% (most commonly gynecomastia, seen in 3.4%). Interestingly, prolactin elevation did not correlate with these AEs." (J-TXCID1204326-7)

Page 115 Published Article: "Antipsychotic treatment has also been linked hyperprolactinaemia. A survey of prolactin levels at baseline and after 6 weeks of treatment in children and adolescents (mean age 14.1 years) showed elevations with both atypical and typical antipsychotics. (Wudarsky,1999) Prolactin increase was significantly higher with haloperidol (mean: 47.8 ng/ml) compared with olanzapine (23.7 ng/ml) or clozapine (mean: 11.2 ng/ml; $P<0.001$). Prolactin levels with treatment exceeded the upper limit of normal in 90% of the patients treated with haloperidol, 70% treated with olanzapine, and in none treated with clozapine. Post-hoc analysis from five large prospective clinical trials including a total of 592 children with DBD and subaverage intelligence demonstrated that, despite hyperprolactinaemia associated with the first 4-8 weeks of risperidone treatment, prolactin levels tended to normalize by 1 year of treatment. (Findling, 2003) Adverse events potentially related to prolactin were reported in 4.9 % (most commonly gynaecomastia in males, seen in 3.7%)."

First Draft: "Cognitive AEs occur infrequently with atypical antipsychotics. In addition, although treatment of cognitive deficits is not improved by neuroleptics in adult schizophrenics, they are improved with atypical antipsychotics (Meltzer, 1999). Verbal learning and continuous performance tasks showed improvements with risperidone in two large, open-label studies of children with DBD (Findling 2004, Croonenberghs INT-70). Additional

studies measuring cognitive changes and academic performance in pediatric patients are needed." (J-TXCID1204327)

Page 116 Published Article: "Cognitive adverse events were infrequently reported with atypical antipsychotics. Although cognitive deficits do not improve in adult patients with schizophrenia receiving conventional antipsychotics, it has been reported that they can improve with atypical antipsychotics (Meltzer, 1999). Verbal learning and continuous performance tasks showed improvements with risperidone in two large open-label studies of children with DBD (Croonenberghs 2005, Findling 2004). Additional studies measuring cognitive changes and academic performance in paediatric patients are needed."

First Draft: "Atypical antipsychotics are recommended for children requiring antipsychotic medication, due to consistently documented efficacy and superior tolerability to neuroleptics. Numerous open-label and double-blind studies have demonstrated both rapid efficacy and good short-and long-term tolerability of atypical antipsychotics for treating a broad spectrum of psychiatric disorders in children and adolescence. Symptoms of DBD, PDD, schizophrenia, and mania are often reduced during the first 1-3 weeks of typical antipsychotic therapy." (J-TXCID1204327)

Page 116 Published Article: "Atypical antipsychotics might be considered because of their documented efficacy in both double-blind and open-label studies and low incidence of EPS. As noted above, a number of double-blind and open label studies have demonstrated rapid efficacy in combination with favourable short-and long-term tolerability of atypical antipsychotics for treating a broad spectrum of psychiatric disorders in children and adolescents."

First Draft: "In addition to measuring cognition development, future studies using atypical antipsychotics in pediatric patients should also measure long-term academic and social development in treated children. Longer-term studies may also help establish how long medication treatment of pediatric psychiatric symptoms needs to be continued to maintain symptom control. Pharmacoeconomic studies, measuring both treatment and societal costs from pediatric psychiatric diseases, should also be conducted." (J-TXCID120328-9)

Page 117 Published Article: "In addition to measuring cognitive development, future studies using atypical antipsychotics in paediatric patients should also measure long-term academic and social development in treated children, as well as the need for long-term maintenance therapy. Pharmacoeconomic studies, measuring both treatment and societal costs from paediatric psychiatric diseases, should also be conducted."

First Draft: "In summary, significant psychiatric illness occurs in about 20% of children. These psychiatric disorders lead to impaired academic and social development, as well as increased societal costs. Atypical antipsychotics offer effective management of a broad spectrum of common pediatric disorders, including DBD, PDD, schizophrenia, and mania." (J-TXCID1204329)

Page 117 Published Article: Conclusion "Significant psychiatric illness occurs in about 20% of children. These psychiatric disorders lead to impaired academic and social development, as well as increased societal costs. In patients with DBDs and PDD and moderate-to-severe symptoms who have not adequately responded to behavioural interventions or primary disease therapies, it is apparent that atypical antipsychotics can effectively reduce disabling behaviours across a broad spectrum of common paediatric psychiatric disorders, with a growing literature suggesting tolerability."

Jensen was a prominent J&J KOL. He was a member of its CNS Child and Adolescent Advisory Board between 2002 and 2004. Over these years, J&J paid him honoraria and expenses in excess of \$80,148.50. (Hunt, 1628)

10. RIS-USA-97

Findling RL, Aman MG, Eerdekens M, Derivan A, Lyons B, "Long-Term Open-Label Study of Risperidone in Children with Severe Disruptive Behaviors and Below-Average IQ," American Journal of Psychiatry 2004; 161: 677-684.

Message:

"Long-term risperidone appears to be generally safe, well tolerated, and effective for treating severely disruptive behaviors in children with subaverage intelligence." (Abstract, 677)

"This 48-week follow-up study suggests that risperidone is generally well tolerated at doses up to 0.06mg/kg/day and may have long-term effectiveness in children with severe disruptive behavior disorders and subaverage intelligence. Given these findings and the chronic nature of these conditions, further study is warranted to assess the safety and efficacy of risperidone in pediatric patients treated for more than 1 year." (Conclusion, 683)

This article provides an example of EM's and J&J's extensive involvement in manuscript developing and editing, an involvement that could not be known from a review of the eventual publication. The following detailed calendar makes the case.

On December 5, 2001 EM was writing the manuscript. (J-TX4696052) On March 29, 2002, EM sent the first draft to J&J. On June 26, 2002, EM sent the final copy to authors and J&J. On August 7, 2002, Robert Findling, an external author, submitted the manuscript for publication. On November 14, 2003, EM reported to J&J that the American Journal of Psychiatry had sent a revise and resubmit decision to Findling, the external author, and asked him to address the reviewers' comments. On December 3, 2003, EM addressed the reviewers' comments with assistance from one of the J&J authors, De Smedt. On January 28, 2003, EM sent the revised manuscript to the authors and to J&J. On February 27, 2003, EM sent the revised manuscript to M. Eerdeken, a J&J employee. She sent EM an email telling it to remove De Smedt as author and to substitute her. In his deposition, Gahan Pandina confirmed that De Smedt was removed from the author list, but he states that he did not know why she had been removed. (Pandina deposition, 546-547) Although he maintained that J&J had "authorship criteria" (548), both EM reports and Pandina's own statements demonstrate the fluid and self-serving nature of authorship on J&J sponsored publications.

On April 15, 2003, EM received Eerdeken's comments on the revised manuscript and incorporated the changes. On April 18, 2003, EM sent the revised manuscript to all the authors. On April 22, 2003, EM received the authors' responses and incorporated the changes. On April 23, 2003 EM sent the revised manuscript to Findling, Aman, and B. Lyons. On May 8, 2003, EM received additional data from Lyons. On May 12-14, 2003 EM incorporated the data and then reviewed and prepared the resubmission package. On May 20, 2003, EM sent the final manuscript to all the authors.

It then revised the cover letter per Findling's request, and on June 12, 2003 sent the package to Findling for submission. (J-TXCIDrev212721)

J&J conducted a separate review of the manuscript and made changes that would put Risperdal in a better light. (Pandina Exhibit 1248) Pandina reviewed the manuscript and made "comments both in the paper and in the summary form." (J-TXCID1051211) In the abstract, for example, Pandina changed "no negative effects" to "positive effects." (J-TXCID1051262), and in his deposition acknowledged making this change. (Pandina Deposition, 536) Only after J&J signed off was the external author allowed to resubmit the article to the journal. On June 26, 2002, Karen Zimmerman wrote to the J&J team: "Attached For your approval is the **final version** of the RIS-USA-97 manuscript.... After you've reviewed the manuscript, please send your approval to me at the address below. The manuscript has been sent simultaneously to the authors for their approval." She went on to note that this version of the paper had been reviewed by "all Janssen and external authors and reflects our efforts to incorporate multiple and sometimes conflicting reviewer comments... Once we have received approval from all authors, we will prepare and send to Dr. Findling a journal submission package." (J-TXCID1051613)

RIS-USA-97 appeared in the American Journal of Psychiatry in April, 2004. The authors were Robert Findling, Michael Aman, Marielle Eerdeken, Albert Derivan, and Ben Lyons. The first two authors were external authors; the other three were J&J employees. The paper acknowledged J&J Pharmaceutical Research and Development for support and for providing the study medications. However, there was no conflict of interest statement for the authors and no acknowledgement of the work of EM or its writers. Editors, reviewers, and readers could not know the extent of the roles that J&J and the communications company played.

The external author, Robert Findling, was a member of one of J&J's Speakers' Bureau Program, a member of its Risperdal Child and Adolescent National Advisory Board, an attendee at its CNS Summit meetings and a speaker at an American Academy of Child and Adolescent Psychiatry Symposium. From 2000 to 2004, Findling received at least \$28,260.48 for his participation in these Risperdal promotional activities. (Hunt 1628) Findling was also a member of J&J's KOL media program. J&J trained him on how to work with the media on how to effectively deliver the J&J messages that promoted the safety and efficacy of Risperdal. (J-TXCID1261521)

Michael Aman, the second external author, was a member of at least two J&J advisory boards, the Mental Retardation and Developmental Disabilities Board (MRDD) and the Risperdal Child and Adolescent National Advisory Board. During the years 2001 to 2004, Aman received at least \$16,337.68 for his participation in these Risperdal promoting activities. (Hunt 1628)

Records of J&J sales representatives submitted to the company indicate that they used the article to market Risperdal. For example, a sales representative visiting a physician in San Antonio, Texas on June 8, 2004 reported: "talked prolactin and findling (sic) he did not know infor (sic) and was curious about it, showd (sic) safety info and how risp (sic) is safe." (J-TX3024570) The same sales representative visiting another physician in San Antonio a few days later reported that the physician was concerned about the safety of prolactin and fertility. The rep told the physician "about prolactin article from findling (sic) and studies up to 3 yrs. (sic) have not shown any problems int(sic) this area." (J-TX3026249)

11. RIS-INT-41

Croonenberghs J, Fegert JM, Findling RL, De Smedt G, Van Dongen S, "Risperidone in children with Disruptive Behavior Disorders and Subaverage Intelligence: A 1-year, Open-label Study of 504 Patients," Journal of the American Academy of Child and Adolescent Psychiatry 2005; 44: 64-72.

Message:

"Risperidone was well tolerated and effective in the long-term treatment of disruptive behavior disorders in children with subaverage intelligence." (Abstract, 64)

"Our data demonstrate that long-term treatment with risperidone is generally well tolerated and that children and adolescents receiving long-term treatment with risperidone appear to have a stable response under study conditions in which there were frequent reevaluations." (Conclusion, 71)

Wells Healthcare was another medical communication company that developed manuscripts for J&J, its "client." The production schedule that Wells Healthcare prepared for J&J made clear that it assumed primary

responsibility for drafting, writing, and revising articles. The external author was to approve the product and make minor (if any) comments. Thus, on May 27, 2002 Wells HealthCare sent J&J a Production Schedule for RIS-INT-41.

"Wells Healthcare Communications will manage the production and journal submission of this paper. Production of the paper includes: a paper outline; 3 draft reviews (where the 3rd draft is approved for submission to agreed journal); liaison with authors; production of up to 3 professionally drawn black and white figures. The paper should be no longer than 4500 words (including references). Following submission to journal, Wells Healthcare will make minor revisions based on referee's comments. Major re-writes or re-submissions will be subject to additional charge." (J-TXCID 1480794)

After outlining its tasks and schedule, the document listed five authors: J. Croonenberghs, J. Fegert, R. Findling, B. Lyons, G. De Smedt, three external, two internal. (J-TXCID1480795) When the study appeared, one internal author was removed and another substituted. The production schedule assigns them no tasks and does not even provide for their review.

The document also included a draft of the conclusions, giving a message that J&J would want to transmit:

"Risperdal is well tolerated during a year long study. Risperdal is associated with significant improvements in behavior. Risperdal is the only antipsychotic with long-term safety and efficacy data in this population. Risperdal dose can be tailored to the individual needs of the patient." (J-TXCID1480798) When the paper appeared in the Journal of the American Academy of Child and Adolescent Psychiatry in 2005, the conclusions mirrored the earlier message.

J&J and Wells Healthcare considered RIS-INT-41 a secondary publication whose goal was to educate the target audience about its product and reinforce the messages in primary publications. By the Wells Healthcare definition, secondary publications constituted "the recycling of data already presented in primary publications." (J-TXCIDrev1492301) "These will reinforce the clinical messages in the primary publications and add the marketing messages not covered in the primaries." (J-TXCIDrev149302) In all: "The secondary publications need to fulfill the following objectives: Educate the target audience about the disease area; Prepare the target

audience for the primary publications; Reinforce the messages in the primary publications; Fill the 'message gaps' left by the primary publications; *Ensure continued positive noise about the product and the disease area.* " (Italics added, J-TXCJDrev1492319)

Thus, secondary publications were marketing activities presented in the guise of scientific publications rather than outright advertisements. It was necessary to have "authors," titles and affiliations. In this sense, ghostwriting was an essential element in the marketing campaign. J&J arranged for "ghosts" so as to give promotional materials credibility, in the process subverting scientific integrity and misleading payors.

11. RIS-AUS 5

Brodaty, H, Ames D, Snowden, J, Woodward M Kirwan J, Charnette R, Lee, E, Lyons B, Grossman F, " Randomized Placebo-Controlled Trial of Risperidone for the Treatment of Aggression, Agitation, and Psychosis of Dementia," Journal of Clinical Psychiatry 2003; 64: 1708-1714.

Conclusions: "Treatment with low dose (mean=0.95)mg/day) risperidone resulted in significant improvement in aggression agitation and psychosis associated with dementia." (134)

"The reduction in aggression was not secondary to sedation or to the antipsychotic properties of risperidone, indicating a direct effect of risperidone on this behavior." (140)

This article reveals how ghostwriting by a J&J team was incorporated into a manuscript to minimize unfavorable data on serious adverse events experienced by participants taking risperidone. J&J repeatedly intervened to edit the text so as to best serve its marketing goals.

RIS-AUS-5 was an investigator-initiated placebo controlled trial of risperidone funded by J&J. The authors had submitted the manuscript to the Journal of Clinical Psychiatry and apparently received a "revise and resubmit" response from the journal. J&J wanted changes made to the manuscript. It was concerned about the presentation of some findings in the Results Section, particularly those reporting Serious Adverse Events. J&J wanted two sentences deleted. (Vergis Exhibit, 1990) The first: "No serious cerebrovascular events occurred in the placebo group." The second: "Two of

the 5 patients in the risperidone group who had a stroke died." (J-TX4221449)

The email chains of Vincent Nye of J&J-Belgium, key marketing/scientific personnel in J&J U.S., and Dominic Barnes, medical director of J&J-Cilag Australia, (who was to discuss the changes with Henry Brodaty, the principal investigator), demonstrates how J&J intervened in a scientific publication. On April 19, 2002 Nye informed his colleagues that the changes made in the manuscript which included deleting the two sentences in the Serious Adverse Effects section, had been approved by four key J&J staff members and that he was ready, to send them to Henry Brodaty, the principal author. (Vergis Exhibit, 1990) "Should you have any additional comments please let me know by Monday April 22. We will submit to Henry Brodaty on Tuesday April 23. The idea is that Henry addresses the changes to the Journal and they come back with questions/comments and this is expected to happen in the near future." (J-TX4221447) On April 26, 2002, Nye again wrote to colleagues that since he had not heard from them, "I presume the proposed attached changes to the RIS-AUS-5 manuscript are accepted by the group. The next step is to discuss with Henry Brodaty via Dominic Barnes.... Probably Henry will seek input from the other investigators and we can expect comments from them." (Vergis Exhibit, 1990 J-TX4221447)

On June 11 2002, Dominic Barnes sent J&J both Brodaty's response and his comments embedded in "BLOCKS". (Vergis Exhibit, 1993) "FIRST, I think we should resist watering down the reporting of AEs. Stroke is a much more appropriate term than cva. SECOND I'm comfortable with the rewordings, but not with the dropping of information/interpretation. THIRD I am not in favour of the use of the term CVA instead of stroke. Stroke is an accepted clinical term whereas the term CVA dates from the 1950s when nobody knew what the pathology was. CVA is not really acceptable terminology." (J-TX3183837) Brodaty also indicated that he would resist some changes: "This is an efficacy paper, so not too much focus on SE. CAN DE-EMPHASISE BUT NOT TOO MUCH -EFFICACY PAPERS GENERALLY DO PROVIDE DATA ON SEs. (J-TX4183838)

J&J turned to Excerpta Medica International, assigning it the task of communicating with the authors to see if they could insert language that would be more favorable to its product. On October 9, 2002 Hester Kulpers, the Plan Manager, Strategic Publication Planning of Excerpta Medica

International, wrote J&J that the authors were insistent: "Please find attached for your review the response prepared by the authors to accompany the revised RIS-AUS-5 manuscript (together with the original comments from the reviewers). In short, based on the authors' request, in the results section we changed CVA to stroke in the following sentence: 'Regarding cerebrovascular disorder, in the risperidone group, 5 patients suffered a stroke and 1 had a transient ischemic attack (TIA).'" Knowing the desire to minimize the Serious Adverse Events associated with Risperdal in comparison to the placebo, Hester met with one of the J&J authors, Fred Grossman, and made additional changes that would be favorable to Risperdal. "In liason (sic) with Fred and Grant, the following was included in the discussion. Cerebrovascular disorders were reported in 18 (sic) patients, (5 patients in the risperidone and 3 in the placebo group) Patients suffering a CVA had significant predisposing medical risk factor (sic) across treatment and placebo groups." (Vergis Exhibit-1992; J-TX4210554)

J&J still remained concerned and involved. On October 14, 2002, Janet Vergis communicated her concerns. "I have concerns about the additional comments added to the discussion. They appear to simply be restating more results as opposed to discussing the implications and really only add to the amount/percentage of text spent on CVA." (Vergis Exhibit, 1992; J-TX4210553) Instead, Vergis proposed: "Changing the first sentence in the discussion section to delete the number of patients and simply state 'Cerebrovascular disorders were reported in more patients treated with risperidone than with placebo.'" (Vergis Exhibit, 1992; J-TX4210552) On October 16, Hester responded with new language: "Cerebrovascular disorders were reported in more patients treated with risperidone than with placebo. Patients suffering a cerebrovascular event had significant predisposing medical risk factors. This study, however, was not designed to stratify by risk factors? across treatment and placebo groups." (Vergis Exhibit 1992; J-TX4210551)

To further obscure negative findings about Risperdal, J&J decided to ghostwrite a commentary to accompany RIS-AUS-5. (Vergis Exhibit, 1992) On October 18, 2002, Mahmoud informed his colleagues about his communications with John Shelton, the publisher of the JCP: "I have spoken with John Shelton several times, and he has been in touch with the editor (Alan). They accept the idea of an accompanying commentary to be published with the AUS-5 manuscript. We would need to have it authored by someone recognized in the field.... We will now need to contact the

outside author with a sense of real urgency to make this happen Are we 100% clear on what we want discussed in such a commentary? I feel it should not be focused on stroke (!), but we need to balance how much we use the vehicle to communicate on the stroke issue (how much of the text should be on stroke?)” Mahmoud also noted that the journal planned to publish the article in the December of January issue. (J-TX4210550)

That same day Ronald Kalmeijer, the Director of Marketing CNS, responded to Mahmoud: “Ramy, Outstanding news!!! Could you take the lead in gost (sic) writing the letter to the editor. Within such a tight time frame I don’t think it will be feasible to get high quality, accurateness and business needs.” (Vergis Exhibit 1992; J-TX4210549) Marketing was also in favor of a commentary. On October 21, 2002, Bridget Ross, the Director of the Business Unit of CNS, Dementia-Neurology & Eldercare wrote: “This is great news – congrats! I will be speaking with the team here about this and could probably suggest an individual or two for the commentary—if this would be of value.” (Vergis Exhibit 1992; J-TX 4210549)

Although J&J produced a draft of the commentary, they decided not to pursue it. On December 31, 2002, Mahmoud informed his colleagues “This editorial is canceled.” (J-TX479531)

The article as published reflected some, albeit not all, of J&J’s ghostwriting. It did not contain the sentence: “No serious cerebrovascular events occurred in the placebo group.” The fact that 2 of the 5 patients in the risperidone group who had a stroke died became a phrase in a sentence that discussed the most frequent causes of death. “The most frequent causes of death were pneumonia (3 in the risperidone and 1 in the placebo group) and stroke (2 in the risperidone group).” (140) Finally, Vergis’ effort to eliminate the numbers of patients suffering adverse events did not succeed. In the published article the sentence regarding cerebrovascular events read: “Regarding cerebrovascular adverse events, in the risperidone group, 5 patients suffered a stroke and 1 had a transient ischemic attack (TIA). (140) In any event, J&J’s deep involvement in the process of writing and publication worked to the detriment of scientific integrity.

J&J sales reps’ call notes indicate that physicians in Texas were concerned about giving patients a product that might cause cerebrovascular adverse events (CAE). J&J explained to its sales reps in its CAE Package Insert Revision Backgrounder April 1, 2003: “CAEs include not only

stroke, but also temporary events like a transient ischemic attack (TIA)." (J-TX2166952) For example, a sales rep referred to a physician in Pearland Texas as "CAE shy," and indicated that the rep would provide the Brodaty article information on the next call. (J-TX2820810) In another instance, a sales rep visiting a physician in Houston Texas reported that he addressed the physician's "concerns w/CAE using brodaty." (sic) (J-TX2907501)

13. RIS-OUT—66

RIS-OUT-66 provides an example of how J&J subverted the integrity of scientific research by not publishing data that was unfavorable to Risperdal. In November 1998, J&J entered into a Research Agreement with Covance Health Economics and Outline Services Inc. to "Examine the association between use of antipsychotic agents and clinical events related to drug-induced hyperprolactinemia such as amenorrhea." (Grogg Exhibit 1583) (J-TX2767095) J&J agreed to pay Covance \$194,520.00 in five installments based upon completion of study milestones and a final report. (J-TX2767102) Covance, in turn, agreed that all information developed from the study was J&J's property as was the decision to publish the data. "Covance will prepare a final report to JanssenIf the decision is made to publish then the principal investigator from Covance will lead the development of the manuscript. Other employees from Covance or Janssen...could be coauthors." (J-TX2767101)

J&J's internal documents reveal that its goals were more commercial than scientific, seeking to demonstrate Risperdal's superiority to competitor's drugs. In its Quarterly U. S. Outcomes Research Status Report 1Q 1999, J&J looked to RIS-OUT-66 "to demonstrate that the incidence of prolactin-related side effects is low with Risperdal, is not elevated relative to conventionals, and possible that it is lower." (Grogg Exhibit 1584) In April 2000, an internal report on RIS-OUT-66 observed, "Initial results do not support Risperdal advantage. Further Analysis planned." (Grogg 1585) In a report on October 4, 2000, the decision was made to forego publication. "Results do not support Risperdal advantage. Internal report distributed for review—no follow-up planned." (Grogg Exhibit 1586)

9) Did defendants disguise promotion of Risperdal through the use of advocacy and third party organizations?

Yes. Advocacy organizations are powerful stakeholders in the formation of policies on access to health care resources. As J&J noted in 2003: "Advocacy groups greatly influence patient acceptance and awareness of new medications as well as reimbursement support for the treatment." (JTXCID0043568) In light of this power and the public trust they enjoy, advocacy organizations should be open and transparent in their relationships with their contributors, including the pharmaceutical companies. They should disclose the sources of their funding, the purposes of the funding, and the exact sums.

In light of their special standing, J&J should have placed a firewall between their marketing departments and advocacy organizations. In disregard of these obligations, J&J exercised undue influence, in particular with the Texas chapter of the National Alliance on Mental Illness (NAMI). J&J financially supported organizations that represented advocates and patient voices. J&J's goal was to have these organizations promote public policies that were in J&J's best marketing interests, including open formularies and a preeminence in purchasing for Risperdal. Both on the part of J&J and on the part of NAMI, there was a notable absence of transparency. Neither Texas decision makers, Medicaid payors nor policy makers could know that NAMI was receiving funding from J&J; were they aware of the facts, the groups would have been equipped to make more informed decisions. One telling incident reveals J&J's strong preference for acting outside of the public eye. In 2004, one of the leaders of Texas NAMI, Joe Lovelace, responded via email to queries from a New York Times reporter and openly copied J&J employees on it. J&J was distressed by his action, apparently not wanting it known that Lovelace kept the company informed. "We need to contact Mr. Lovelace to request that he remove all J&J names from any future communications to NYT reporter." It should be taken care of "ASAP." (J-TXCID1102836)

NAMI figured very prominently in J&J's marketing strategies. Already in 1995, J&J was using Texas NAMI, through its then president, Joe Lovelace, to advocate for expanding the use of Risperdal. (Vaughan Exhibit, 712) In its 1996 "Risperdal Business Plan," J&J set forth its plans to use NAMI to help "Build Anti-Psychotic Market." The plan declared: "In order to increase the size of the anti-psychotic market, our efforts need to be focused on public education." It went on to explain: "This ties in very well to the 1996 NAMI Anti-Discrimination Campaign that Janssen is committed to and will play a very important role.... This is a great opportunity to

leverage both NAMI and Janssen interests through the 'Treatment Works' program, the Public Service Announcement (PS) developed by Janssen, early intervention, and schools/military programs." (J-TXCID0022943)

In 1999, as J&J explained in its Reimbursement Management Business Review (J-TXCID 0070906): "Partnering efforts with Advocacy continue to grow. Advocacy is a strong force in opening closed markets and maintaining access in existing open markets." This was particularly important because of the need to: "Leverage their [advocates] influence to minimize any negative impact on atypical dollars due to budget shortfall." (J-TXCID 0070903, 06).

J&J's June 6, 2000 Business Plan outlined many of the components of this approach: "Continue pivotal partnerships with national, state and local advocacy organizations (e.g. NAMI, NMHA)." The "Deliverables" include visits to national offices of NAMI, giving "appropriate and guided funding at national and local levels," supplying "key Risperdal information for publication in journals, newsletters, etc." And: "Positioning key speakers at regional meetings." J&J also trained patient advocacy group lecturers on the "intricacies of public speaking" (with press, legislators etc.) The goal is "to target key advocacy leaders and ready them for tough battles regarding access to services and medications." J&J wanted to be known as a prime "consumer advocate" so as to "Ensure Risperdal atypical drug access is clearly highlighted as an important mental health issue." There was a quid pro quo in these arrangements: "NMHA commitment to return their support (advocacy) in kind to issues important to Janssen and Risperdal access." (CID09-0017994-5; Roman Exhibit, 129; J-TXCID 1395178)

The very same formulation appeared in the Public Health Systems & Reimbursement 2001 Texas Business Plan. As its "Mission Statement" declared: "Support CNS Sales by working proactively with Public Mental Health Care Systems to identify, maximize and protect Risperdal sales opportunities." With particular regard to "Advocacy NAMI Texas," the J&J "Goal" was to "Continue to develop relationship /partnership to enhance Risperdal access." Its "Tactics" included: "Monthly calls on Administrators.... Advisory Board participation...Conference support and participation...." (J-TXCID 1395178)

To these same ends, in 2002, when Joseph Lin of CNS Marketing was setting forth his Media Management Plan, he proposed both to support

family/patient advocacy groups and to "Identify and further develop relationships with key advocacy groups." NAMI was prominent among them. Lin also proposed a Children's Mental Health Summit, with NAMI to be included, whose "output" included publishing position papers for media, government, and academia. (Lin Exhibit, 1071; J-TXCID1261302)

To insure that NAMI would promote its marketing interests, J&J wanted to increase its presence at NAMI annual meetings and to "influence speaker selection." (J-TXCID 0069351) It was also prepared to fund a variety of NAMI activities. Already in July 1995, Paulo Costa, President of J&J Research Foundation, informed Laurie Flynn, Executive Director NAMI, that J&J would serve as a founding sponsor for NAMI's National Campaign to End Discrimination against People with Severe Mental Illness." (J-TXCID 0064040) In 1995, J&J would provide \$300,000; in 1996, \$500,000; and in 1997, \$500,000. In addition to financial contributions, Costa told Flynn, J&J "will also provide programs that have received import and support of NAMI, which are designed to support the national campaign." J&J explained its commitment: "Recognizing NAMI's effectiveness as a public advocate we feel strongly that funding should be 'front-loaded' in earlier years and directly targeted to the general public and key influentials." Costa listed nine other NAMI programs that J&J was considering funding and should J&J do so, NAMI would receive on average \$1 million per year for the next three years. To supplement this funding, "Janssen employees are willing to devote their time and effort in supporting your anti-discrimination efforts. We can also offer you the in-house marketing expertise to assist you in your drives for membership." J&J accepted NAMI's offer to participate on the national campaign's steering committee. Bruce Given, Group Vice President, would participate and "be in attendance at this year's NAMI Annual Meeting."

NAMI was so central to J&J's marketing strategy that the company spared no effort to buttress NAMI's capacity. Two slides that were part of the Public Sector & Institutional Business: Public Health Systems and Reimbursement presentation of J&J employee Roman, reveal the company tactics. (J-TXCID 1391272)

Slide 1: 2000 Goals and Key Accomplishments: ADVOCACY

Consumer Media Training: With the tremendous response to the 1999 program, conduct at least one more during 2000. The CMT

teaches the intricacies of public speaking (e.g. public hearings, meetings with state officials) TV and written press. The overall goal is to target key advocacy leaders and ready them for tough battles regarding access to services and medications.

State/Local Programs: Continue pivotal partnerships with national, state and local advocacy organizations (e.g., NAMI, NMHA) mental health coalitions and state health trade associations. *Ensure these same groups clearly understand our concerns with access, understand the cost/dose comparative profile among the atypicals and ready to advocate on behalf of RISPERDAL and the atypicals as warranted.* (Italics added)

SLIDE 2: 2002 Goals & Objectives: ADVOCACY:

Advocacy Advisory Board

NAMI/NMHA annual meetings: Influence speaker selections and increase PHS& R representation at national meetings (Public Health Systems & Reimbursement)

Develop/Feature Joe Lovelace (NAMITX)

Empower advocacy to publicly support and work toward increasing state funding, as well as supporting cost-weighting factors among atypicals

To these same ends, in 2002, in response to negative media publicity about psychopharmacology, J&J established an Advocacy Advisory Panel. The first meeting took place in Miami, March 19-20. The panel was composed of 19 members, 9 of whom were from NAMI. (Ten were from a kindred advocacy organization, Mental Health America.) All attendees were presidents or executive directors of state programs. A second meeting was to be held in 2003. (Josephson 23541-47) (Lin Exhibit 1071, J-TXCID1261313)

The objectives spelled out J&J's interests:

Impact of treatment guidelines on quality of care
Access to atypical antipsychotics and legislative actions

Clinical understanding of antipsychotics
 Impact of non-adherence to all medications
 Coalition building with alternative associations

J&J was also prepared to give NAMI \$12,500, in the form of an unrestricted educational grant "in support of NAMI's distribution of the J&J video: 'The Science of Schizophrenia: Milestones to the Millennium,' the A&E Investigative Report: 'The Worst Disease,' and the PBS program, 'The Visionaries.' We are excited about the opportunity to assist NAMI as you disseminate resources to your affiliates and other key mental health community representatives. We look forward to continuing to partner with NAMI." To have a so-called patient advocacy group with standing in the community distribute company products was a victory for J&J's marketing. (October 19, 2000, Nadia Dac Project Director CNS, to Charles Harman, NAMI-JAN 0220; see also Payson Exhibits, 1522, 1529)

J&J's interests in having NAMI as well as other advocacy groups fulfill its marketing aims continued to be powerful. In 2005, for example, J&J representatives worked with advocacy groups to increase the Texas use of Risperdal in its community mental health centers. As one rep described the process: "I went into the NAMI. I said listen, I'm working as an advocate to try to get open access." (Daniels Deposition 185) What was not said was J&J's financial stake in access. The appearance was of doing well by mentally ill patients, not doing well by J&J's sales charts. (Daniels Deposition, 175-180)

NAMI, for its part, sought J&J support, although it did not disclose the extent of the funding. It regularly reported to J&J to demonstrate the ways by which the organization's efforts furthered the company's interests.

A report to J&J (Sid Frank) from NAMI (1997) described the progress made by its Campaign to End Discrimination in the Care and Treatment of the Mentally Ill: (J-TXCID 0064020)

1. Federal Parity for mental health care:
 Flooded White House with Calls and Letters:
2. Media Outreach:

NAMI placed ad in Washington Post under the headline: "Stand Tall, Mr. President."

NAMI partnered with the Rand Institute to promote a study in JAMA on the cost of parity for the care and treatment of mental illness.

3. Membership Marketing

NAMI also mailed 2000 letters asking state legislators to join NAMI, assisted by NAMI board member Garnet Coleman, the Texas representative who sponsored and helped pass the state's parity act. NAMI included in the mailing copies of THE DECADE OF THE BRAIN which featured information on the latest anti-psychotic medications. (J-TXCID 0064020)

Relations between NAMI and J&J officials were very close. In October 1998, for example, NAMI's Laurie Flynn thanked Sid Frank for providing \$500,000 for the Campaign to End Discrimination. She noted that NAMI had 185,000 members and over 1,140 affiliate organizations. She addresses him as Sid, signs it Laurie, and writes in the margin: "I deeply appreciate your support and look forward to working with you." (J-TXCID 0064109)

It is not surprising, therefore, to read an internal NAMI email of December 11, 2000, from Charles Harman to colleagues, with the "Subject: Jan\$\$en" Harman wrote that J&J would continue to fund NAMI in 2001 "equal to the previous years. First check which is a portion of next year's grant" was \$350,000. (NAMI-Jan-0217)

To make certain that J&J support continued, Harman kept J&J officers fully informed about the NAMI activities that would please the company. "Attached are two letters to key Senators from Dr. Richard Birkel [NAMI's executive director] regarding proposed legislation that we believe would restrict access to medications used to treat people with mental illness. NAMI continues to fight to protect access to treatment through strong advocacy on the state and federal levels. Please let me know if you have any questions about this issue." (Charles Harman to Alex Gorsky July 25, 2002)

So too, he told Laurie Snyder that NAMI programs aimed:

- To drive the local, state and national debate on mental illness system reform
- To improve treatment outcomes by advancing evidence-based and emerging science-based practice
- To reach out to under-served and priority populations
- To rebuild the NAMI grassroots by strengthening the network of state and affiliate organizations (J-TXCID011410)

"In addition to the Campaign, we continue to have an interest in collaborating on a national, region and state basis with Janssen." (December 6, 2002, ...410)

The exercise of improper influence by J&J and NAMI's readiness to further J&J's interests is particularly evident in the activities undertaken by Joe Lovelace, the preeminent figure in Texas NAMI.

Lovelace received funding from J&J not only for the organization but personally, noting in his deposition that he deposited the monies in his wife's law firm account because "she needed the money...there was a loss there." (Lovelace Deposition, 86) He also "expressed a desire," as J&J's Coard informed colleagues, "to partner with Janssen as a consultant," which several of them considered "a tremendous asset to Janssen in current and future initiatives." (J-TXCID 1559353) Lovelace advocated for J&J's interests, and trained other community and NAMI members to do so as well. He was a frequent speaker for J&J between 2000 and 2003. (Deposition Exhibits, 1753, 1755, 1766, 1767; J-TXCID 0079268) He worked hand in hand with J&J to get Risperdal Consta favorably positioned in Texas Medicaid. When asked whether he "worked with people at Janssen to try to get Texas Medicaid to cover Risperdal Consta," he replied yes. (Lovelace Deposition, pp. 174-175, 191; J-TXCID 0142701) He arranged to have NAMI host meetings with "key members of the legislature and the executive branch" of the Texas government, thereby giving J&J access to them. (Lovelace Deposition, 178-179) Lovelace kept J&J well informed of his activities with Texas medical benefit personnel on behalf of Risperdal Consta, and the J&J employees carefully evaluated and reviewed his efforts. As one internal J&J email noted: "Joe Lovelace's email outlining what he plans to do with his meeting with the Tx Medical benefit Medical Director was discussed. Everyone on the call was satisfied with the objectives, agenda, and level of responsibility." (J-TX4460370) (See also Lovelace

Exhibit, 1770, 1786, J-TXCID 1130103 for documents demonstrating how J&J used Lovelace to ensure coverage for Risperdal Consta.)

Many of the activities that Lovelace carried out in conjunction with J&J violated principles of transparency. When asked if he let state officials know that he was copying the emails with them to J&J, he replied no. (Lovelace Deposition, pp. 193-194) When asked "did you ever let on to the Texas Medicaid folks that you were reporting at each stage and at each step to Janssen your interactions with people at Texas Medicaid?" he responded: "The answer to each step is no" (Lovelace Deposition, 216-217) Thus, when he wrote to Texas representative John Davis to promote Risperdal Consta, his email openly copied other Texas officials but did not openly copy J&J employees—although he sent it to them as well. (J-TXCID rev0086242) He also received travel payments and honoraria from J&J, including to Europe and Hawaii. (Lovelace Deposition 143, 149-150; see also Lovelace Exhibits, 1741, 1743, 1745, 1747, 1751, 1753, 1755-57, 1759, 1761, 1764-69) Lovelace was so indifferent to obvious conflict of interest considerations that he tried to get J&J to bring him onto its staff as a consultant. (Lovelace Deposition, 156, 160; J-TX4057588) J&J itself took no steps to remedy the situation.

The value of Lovelace to J&J went beyond his own work for them to include his training of community and NAMI members to advocacy. When asked if he would have NAMI members "come up to testify and relate their personal stories," he responded by noting that when he had a chairman of a legislative insurance committee from Amarillo, he "made sure that a person in his church sat down in front of him." (Lovelace Deposition, 72) "You can't imagine how good advocates this folks are just in the raw state. And when you bring them in and talk to them and give them talking points and they sit and observe the process, they do pretty effectively." And if Lovelace himself did not inform legislators of his J&J links, these advocates surely did not do so either. (Lovelace Deposition, 74) When asked whether there was a session between 1995 and 2005 when NAMI was not using grass roots advocacy, Lovelace replied "we were there." When asked: "Every Time?" he answered, "Yes." (Lovelace Deposition, 70)

In sum, the J&J-NAMI collaboration allowed the company to use a health advocacy organization to disguise its marketing interests. That NAMI was a willing partner does not make J&J any less culpable. It was the company funds that fueled the operation. To use an

organization that presents itself as the public voice of the mentally ill in order to enhance marketing strategies is an egregious example of the exercise of undue influence.

A handwritten signature in cursive script, appearing to read "David Rothman".

David J. Rothman

October 15, 2010