To: [redacted]
Cc: [redacted]
Subject: RIS-232

August 31, 2003

Dear [redacted]

I have hesitated to write you this letter, hoping in part that you would have spoken to me.

I want to remind you that I was extensively involved in the design of the RIS-232 and RIS-82 trials. As you remember [redacted] had organized the consulting for these trials several years ago. Early on [redacted] and I worked with him both in meetings and in Titusville. In addition there were several meetings in Philadelphia. As the protocol developed I contributed substantial portions to it, and then to training, co-leading the 2 investigator meetings, and early trial consultation. Over this time I worked extensively with [redacted] initially and others.

As [redacted] and others can attest, I would not have done this simply to provide consultation but with the expectation of collegial collaboration and authorship.

Therefore you understand my concern when it turns out that the trial had been analyzed some time ago, presented to others, and then extensively discussed in unofficial ways at meetings.

Although I expressed these concerns to [redacted], and he did arrange a rather brief briefing on June 9 with [redacted] I thought I'd wait for you to actually contact me.

Respecting fully any confidentiality agreement that I have with Janssen, it is obvious to me and to others who may not be so bound and who have learned about the data that this trial is on its face nearly completely negative. Not because "psychosis of AD" was not a viable target but because a substantial proportion of subjects who were enrolled should not have been enrolled, and would not have been prescribed antipsychotics if they had been ordinary clinic patients. These were subjects who probably nominally fulfilled "psychosis" for entry into the trial, by having been rated on one or two delusion or hallucination items of the Behave-AD but who clearly had no severity of psychotic symptoms or associated behavioral disruption. Thus to a large extent this is a failed study because of inappropriate subject selection.

That you might find an effect when you sub-select more agitated patients will not get you a claim for "psychotic agitation" as some might be advocating.

As it was 4 years ago, FDA will clearly be concerned with the low psychosis scores on a rating scale not meant for this kind of clinical trial, not to mention the ongoing safety issues of CVAEs and deaths.

Entirely separately, Janssen has been sitting on the trial results for a long time. Yet it has a moral and ethical responsibility to publish results quickly and in a way that they can be understood and makes clinical sense. It has an obligation to publish not just the clinical efficacy data which could very well be informative and supportive of the use of risperidone if considered properly, but also the safety data, including events that have been labeled in the past as "cerbrovascular adverse events" and deaths.

This is my main reason for writing. Janssen had the opportunity to present this data, for example, at the IPA meeting in Chicago last week. It also has the opportunity to present it at the upcoming ACNP and ICGP meetings in San Juan, Puerto Rico and should do so.

The second matter of your excluding me from collegial collaboration in a trial that I was is one I would be happy to discuss with you or anyone else at Janssen.

Please note that all of what I wrote above was learned or inferred outside of any confidentiality agreement I have with Janssen. However, based on what was presented to me under the confidentiality agreement, it is clear that Janssen has not been able to consider the outcomes of Ris-232 properly, in a way to understand what the trial results do say, or to understand the clinical significance of the outcomes, and would benefit from crisp clinical and expert advice. Clearly psychotic agitation is not a helpful construct.

Regards

[redacted]