EXHIBIT 4

Unknown

From: Murray Michael MF
Sent: Thursday, March 23, 2000 11:55 AM
To: Jones Martin AM - PHMS
Cc: Mullen Jamie JA; Goldstein Jeffrey JM; Tumas John JA
Subject: HELP FW: Meta Analyses

Importance: High

Attachments: RE: Meta Analyses; RE: Meta Analyses; TD0004.doc; TD0005 version 2.doc

RE: Meta Analyses

Martin,
I think we need your help on this one. Can you please read the attached messages. Can me, you, Jeff, and Jamie discuss this in Paris. I don't understand why we got such vast differences in these anayses.
Thanks,
Mike

Mike Murray

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From: Tumas John JA
Sent: Thursday, March 23, 2000 10:05 AM
To: Goldstein Jeffrey JM; Murray Michael MF
Subject: FW: Meta Analyses
Importance: High

Jeff and Mike,

Here's the analyses that I got from Emma. I've also attached a message that I sent to her yesterday asking for clarification.

The data don't look good. In fact, I don't know how we can get a paper out of this.

My guess is that we all (including Schulz) saw the good stuff, ie the meta analyses of responder rates that showed we were superior to placebo **and** haloperidol, and then thought that further analyses would be supportive and that a paper was in order. What seems to be the case is that we were highlighting the only good stuff and that our own analysis support the "view out there" that we are less effective than haloperidol and our competitors.

Once you have a chance to digest this, let's get together (or telelconference) and discuss where to go from here. We need to do this quickly, because Schulz needs to get a draft ready for APA and he needs any additional analyses we can give him well before then.

Thanks,

John

RE: Meta Analyses

From: Westhead Emma EK
Sent: Wednesday, March 22, 2000 12:44 PM
To: Tumas John JA
Cc: Shadwell Pamela PG
Subject: RE: Meta Analyses

Hi John,

Some of the work you need has already been completed within the Commercial Support Team. I attach the relevant technical documents for your information.

TD0004.doc (94 KB) TD0005 version 2.doc (127 KB)

I've tried to summarise below our current position with this data:

CGI

- Meta-Analysis has been done by CST vs haloperidol (TD005). No superiority of Seroquel over haloperidol was seen - although we can claim we are 'as least as effective' as haloperidol'.
- Seroquel vs placebo. A meta-analysis has not been performed, this could be progessed with the CST.

BPRS

- Meta-analysis has been performed on BPRS total, anxiety item, factor I, factor V, hostility item, hostility cluster and mood cluster for those patients who were symptomatic at baseline (TD004). No superiority of Seroquel over haloperidol was seen - although we can claim we are 'as least as effective' as haloperidol'.
- A similar meta-analysis was performed vs placebo on the same items. Superiority of Seroquel over placebo was seen in this case.

SANS

- A meta-analysis of SANS scores has been done for placebo and is contained within the new promotional guide (available for the Handover). Superiority of Seroquel over placebo.
- I don't believe many haloperidol studies actually recorded SANS but will check this.

Hence, for the BPRS analysis we haven't covered all of the items suggested by Dr Schulz. However, given that we are seeing a consistent picture of similar efficacy to haloperidol, I don't think we would seen anything different when analysing the other individual items. It depends on your focus - would you be happy to state "as least as effective" as haloperidol.

I propose that we could progress the following:

- a meta-analysis of CGI, seroquel vs placebo
- consider wether SANS data was recorded in haloperidol studies
- Discuss with Dr Schulz the focus of the meta-analysis of BPRS/CGI vs haloperidol before any extra work is done to look at items not yet analysed.

Could you consider these proposals and also let me know what your exact deadline is? I'll need to feed this in against the current work being progressed within the CST.

Kind Regards - sorry for the lengthy reply!
Emma

From: Tumas John JA
Sent: 22 March 2000 15:42
To: Westhead Emma EK
Subject: FW: Meta Analyses

Hi Emma,

It seems that Martin will not be easy to reach during the next week or so. Do you have a feel for how doable the below is? Dr. Schulz is supposed to have a draft manuscript for us by APA in May and I expect he will need the below in order to do so.

Thanks,

John

From: Tumas John JA
Sent: Monday, March 20, 2000 1:39 PM
To: Jones Martin AM - PHMS
Cc: Westhead Emma EK; Goldstein Jeffrey JM; Gavin Jim JP
Subject: Meta Analyses

Dear Martin,

You may be aware that Jeff and I met with Drs. Shulz and Tandon in Chicago a couple of weeks ago to discuss a few review manuscripts. The one with Dr. Schulz was conceived as a result of the responder meta analyses that were used for his APA (and CPNP) abstracts. After formulating an outline for the manuscript, Dr. Shulz put together a list of other meta analyses that would be needed in order for him to progress the manuscript. Below is a list of additional analyses Dr. Schulz has requested. Could you let me know the feasibility of these requests?

I've attached a first draft of the poster for CPNP that I sent to Dr. Schulz.

Best regards,

John

Meta analyses comparing quetiapine to haloperidol and placebo:

1) Total BPRS
2) CGI
3) BPRS Factor scores, ie thought disorder, anxiety, depression, negative symptoms.
4) Individual BPRS items: hallucinatory behavior, suspiciousness, flattened affect.
5) SANS
6) Control for factors:
    a) age
    b) gender
    c) length of illness.

<<File: Schulz.doc>>