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actapsych@rm.dk [actapsych@rm.dk]  
Sent: Tuesday, 7 July 2015 7:27 PM  
To: jon.jureidini@adelaide.edu.au  
Subject: Acta Psychiatrica Scandinavica - Decision on Manuscript ID  
ACP-2015-5105

Dear Professor Jon Jureidini

I have now received the assessments of your manuscript - ID ACP-2015-5105 entitled "The Citalopram CIT-MD-18 Pediatric Depression Trial: Deconstruction of Medical Ghostwriting, Data Misrepresentation and Academic Malfeasance". The comments from the reviewers can be found at the bottom of this e-mail. Based on these I invite you to revise your manuscript according to the reviewers' comments.

One of the reviewers noted this in the comments to me: " However, it is not very well written or presented, and at present is not in a state to be published in an academic journal. There is almost no attempt to contextualise the data within the relevant literature, and the Results section could be written and presented more clearly and with more detail. The paper gives the impression of something that was written for other purposes, maybe a report." I in particular ask you to pay attention to these comments.

Moreover, the legal aspects of your paper should be clarified. I therefore ask you to get a comment from your university's lawyer about the lawfulness of the material, in particular the question about public access to the material used.

Please notice that if we decide to publish your paper in the Acta Psychiatrica Scandinavica, we will publish it in our December issue this year.

To revise your manuscript, log into <https://mc.manuscriptcentral.com/actapsych> and enter your Author Center where you will find your manuscript title listed under the feature "manuscripts awaiting revision".

You will be unable to make your revisions on the originally submitted version of the manuscript. Instead, revise your manuscript using a word processing program and save it on your computer. Please also highlight the changes to your manuscript within the document by using the track changes mode in MS Word or by using bold or colored text. Once the revised manuscript is prepared, you can upload it and submit it through your Author Center.

When submitting your revised manuscript, you will be able to respond to the comments made by the reviewers in the space provided. You can use this space to document any changes you make to the original manuscript. In order to expedite the processing of the revised manuscript, please be as specific as possible in your response to the reviewers.

**IMPORTANT:** Your original files are available to you when you upload your revised manuscript. Please delete any redundant files before completing the submission.

Please forward your revised version within 30 days from the above date, otherwise we will consider the case closed.

Please notice that at this stage of the process we cannot guarantee a publication of your manuscript. A decision to publish your manuscript is also dependent on the result of the reviewers' assessments.

Once again, thank you for submitting your manuscript to the Acta Psychiatrica Scandinavica. I look forward to receiving the revised version of the manuscript.

Best regards  
Acta Psychiatrica Scandinavica

Povl Munk-Jørgensen  
Editor

Reviewer(s)' Comments to Author:  
Reviewer: 1

#### Comments to the Author

Definitely, this is a very unique and important article deserving rapid publication.

Given the fact that this report comes from the US and that the authors seek for publication in a European/Scandinavian journal, there should be a clear

statement about the cultural background of the trial and the report.

This should start with the title (The Citalopram CIT-MD-18 Pediatric Depression Trial in the United States. ....), should continue with the abstract (rephrase objective), and should be made clear also in the first paragraph of the introduction.

Furthermore, it should be indicated by the ®symbol both in the abstract and

in the first paragraph that Celexa and Lexapro are US brand names for Citalopram and Escitalopram, respectively, and that Forest stands for Forest

Research Institute (describe function of the institute).

From reading the results, it does not become sufficiently clear how the primary outcome measures were substituted by post hoc outcome measures (page 8).

It is a common procedure to regard a difference at  $p=0.052$  as a trend for significance (page 9). This could be admitted in the manuscript to avoid further discussion.

Does the typo in the cited sentence " Any patient...." on top of page 10 stem from the protocol or from the authors of this manuscript?

Both in the introduction and the discussion a comment on the broader frame

of reference of drug trials in children might add to the value of the paper.

For instance, there could be a reference to the higher vulnerability of the developing brain and the lower efficacy of most psychotropic medications including the higher risk of adverse events in this young population.

In addition, the concern about a worldwide trend of prescribing more drugs

to children could be mentioned (as evidenced also in this journal recently).

Similarly, it could be addressed that the US absorbs the vast majority of worldwide drug prescriptions for children.

Reviewer: 2

#### Comments to the Author

I have read this paper carefully and write to you alone and do not include any reviewer comments.

In essence, we have been informed on multiple occasions over the last

decade

in particular about inappropriate conduct in undertaking pharmaceutical trials and in their reporting, with particular concerns about psychiatrists being accorded prominent authorship status without being in charge of the

data or even aware of the probity of the evidence. I am not aware of any paper that has been published in any journal that details a number of the inappropriate practices so well or in such detail and therefore, if it were to be published, it would be a prominent piece that would attract considerable attention. While the first two authors acknowledge that they have had legal support in giving evidence to the legal challenge mounted by

a group of plaintiffs, if the article were to be published it would need to be over-viewed carefully by a lawyer to ensure that the journal was not compromised legally. This may be relatively straightforward if the lawyer were to judge that everything reported here had been considered in court and

therefore was 'public' information. However, that may not be so.

Reviewer: 3

Comments to the Author

This manuscript provides extensive primary source documentation of corporate intent to mislead the anticipated professional readership of Am J Psychiat regarding the effectiveness of citalopram in treatment of major depressive episodes in youth. Because of the importance of documentation

that no selective reporting by the authors of this submitted manuscript occurred, it is reasonable that they be asked to make such a statement.

Similarly, the corporations and other agents engaged in the planning, funding, and preparation of the citalopram study manuscript, as well as those individuals engaged in the writing or review of such writing of the citalopram manuscript, should be provided opportunity to comment on the

actions described in the manuscript submitted to Acta that involve putative

distortion of facts and recommendations. However, a professional journal generally has little or no staff or budget to utilize in investigative inquiry. If any court system or regulatory system evidence has been brought

regarding the citalopram study and preparation of the original manuscript, some of such may be germane to what might be published in Acta. For several reasons, the judicial/regulatory system is best suited to address many of the actions asserted in this manuscript. That said, there is still a useful societal and professional value of publication of such a manuscript

in a respected, widely read journal such as Acta.

Reviewer: 4

### Comments to the Author

The paper uses archival documents released during court proceedings to document the process of ghost-writing, and the manipulation of study data by

a drug company. The content is interesting but could be improved.

Introduction:

Reference to some more general data on rates of use of antidepressants in children would be useful, along with a description of existing literature on ghost-writing (e.g. David Healy's work) and previous findings of publication

bias in antidepressant research, including the meta-analysis by

Whittington

et al which included unpublished data and found few effects.

Methods:

Note it is 'materials and methods'

Some more description of the process of analysis would be useful, such as comparison between published report and study data revealed in the confidential documents, including the study protocol, scrutiny of e mails and other correspondence relating to authorship and manuscript production.

In the description of the power calculation, is it specified what effect size they were aiming to detect?

Results:

Overall this section could be more clearly presented and more data would be

useful.

I would suggest the section is divided into a sub-section on 'authorship' and one on 'results' or 'data', and to incorporate the first paragraph in the second section.

I would not describe the e mail about authorship that is quoted on P 7 as 'banter'. I agree this is a very important quote, but to my mind it simply states the bold fact that the writer and author are not the same under this system of authorship, and might not have been meant light-heartedly.

The statement that there is no evidence the manuscript was circulated to the

other authors is potentially libellous, so the authors need to be very sure that they have grounds to make this suggestion, and provide more evidence to

back it up. Are they sure they have seen all the correspondence about the trial? Are there e mails suggesting these authors agree to be authors

without evidence that they have seen the manuscript?

The data on the results of the study is difficult to follow. The authors seem to be making two substantive points: first that the original, per-protocol primary outcome was not statistically significant (although it was very nearly so, which should be acknowledged), and was inflated by adding the unblinded participants; second – an interaction effect was not reported.

It is difficult to judge the situation with the effect size, so I wouldn't make this a big point, but just it is worth mentioning.

I wanted to know if any other outcomes were misreported. Was the response

criterion used in the published paper the same as the one in the protocol? Were the other secondary outcomes like the CGI reported accurately in the published paper? Were the reasons for the dropout of the five citalopram subjects reported? Was there any other discrepancy in how adverse events were reported?

On the subject of the Lundbeck trial, why should the company have been expected to know the results if it had not been published? I agree it seems likely, but not certain that they should have known.

Discussion:

This section should relate the findings back to the literature covered in the introduction, and should mention the similar analysis of study 329. It needs to stress why this sort of analysis is important.