Reviewer's report

**Title:** New therapeutic approach to Tourette Syndrome in children based on a randomized placebo-controlled double-blind phase IV study of the effectiveness and safety of magnesium and vitamin B6

**Version:** 2  **Date:** 21 November 2008

**Reviewer:** Prathap Tharyan

**Reviewer's report:**

New therapeutic approach to Tourette Syndrome in children based on a study of the effectiveness and safety of magnesium and vitamin B6

1. Will the study design adequately test the hypothesis?

Yes

Clonidine (often with methylphenidate) is commonly used to treat Tourette’s syndrome- this could be mentioned in the background section.

2. Are sufficient details provided to allow replication of the work or comparison with related analyses: if not, what is missing?

· The hypothesis mentions a placebo control arm but there is no other mention of a placebo in the methods of the manuscript or the registration document under interventions (except in the flow diagram) or how this will be masked to prevent un-blinding of participants and investigators. More details of this are required to be mentioned explicitly.

· Will the allocation envelopes be serially numbered? This section needs re-wording to ensure that allocation concealment would indeed be maintained.

· Information on who will recruit subjects (keeping allocation and recruitment separate) and who will assess clinical outcomes is lacking as is who exactly will be blinded. Will adequacy of blinding be assessed?

· Will multiple raters be used to evaluate clinical outcomes using the specified rating scales? If so, what about inter-rater reliability?

· No details of how the PET data will be interpreted and what parameters will be assessed

2. Is the planned statistical analysis appropriate?

· Would not Repeat measures ANOVA with adjustments for baseline imbalances and scores be more appropriate than multiple t-test

· Since randomization was not stratified by concurrent treatments, it is possible this will need to be adjusted statistically.
3. Is the writing acceptable?

The word clinical “assay” seems to refer to clinical trial and could be substituted throughout. Tight editing for grammar and content could reduce the length of the manuscript and improve readability.