Reviewer's report

Title: Responder Analyses and the Assessment of a Clinically Relevant Treatment Effect

Version: 2 Date: 20 June 2007

Reviewer: Stephen Senn

Reviewer's report:

General

I approve entirely of your thesis. It is nothing less than a scandal that the FDA and EMEA and drug regulatory agencies continue to place emphasis on so-called responder analysis. The definition of response is naive and the consequent rise in sample size simply adds to the cost of drug development and delays the introduction of treatment for patients. Judging by the frequency with which methodologically unsound papers on this topic are published in the medical press, it seems that the regulators’ confusion is shared widely by researchers, editors and referees. I hope that your paper will promote clearer thinking on this issue but, fear, alas, that this nonsense will continue.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

There are two points where I disagree (slightly) with what you claim.

1. You imply at one point that individual response could be determined by a cross-over trial. In fact even a cross-over trial is inadequate for this purpose. You need a cross-over with repeated periods. See Senn, S. J. (2004), Individual response to treatment: is it a valid assumption? British Medical Journal, 329, 966-968.

2. I think it is also not simple to judge response graphically as you imply. Certainly it is a necessary condition for response on the original scale to be additive for the distribution under active treatment and placebo to be identical but for location. However, it is not sufficient

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Discretionary Revisions (which the author can choose to ignore)

You might consider citing the following papers.


What next?: Accept after minor essential revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.