Reviewer's report

Title: The Methodology for Developing a Prospective Meta-Analysis in the Family Planning Community

Version: 1 Date: 20 February 2011

Reviewer: Jesse Berlin

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MINOR ESSENTIAL REVISIONS

1. Page 5: It may be helpful to draw a slightly clearer distinction between the usual multicenter study and PMA. In particular, you argue here that (in addition to the flexibility) it’s an advantage of PMA that individual sites can recruit a “feasible” number of subjects. That’s true relative to a typical meta-analysis, in which individual studies would presumably (although I admit, not necessarily) be powered adequately to address their respective questions, but it’s not an advantage relative to a multicenter study. Are you saying that it’s OK NOT to power the studies at the individual sites, and instead, power the overall PMA? I’m not arguing with the principle, just for a shade more clarity.

2. Page 6: Some may want to interpret the word “pooled” as “combining into one big database and treating as one study.” This (as you know) ignores the retention of stratification by “study” in the analysis. Please add a reminder of the need to retain such stratification throughout the study, including (especially) in the analysis.

3. Page 8: Just an opinion, but I don’t know if I’d go as far as saying, left to themselves, the sites “would LIKELY report incompatible data.” Doesn’t this depend on the field? I would suggest you soften this to say something like, “could potentially generate incompatible data.”

4. Page 8: What do you mean by the analysis being more “accurate?” Less biased (in the statistical sense)? This is a vague term, as it’s not clear in which sense you mean it.

5. Page 8-9: You don’t mention the need for a protocol for the combined analysis? I would definitely mention this point (and assume you already have, or are working on, such a protocol)?

6. Page 9: I would suggest you add some caution around the concept of unique patient populations at each site. The worst case is complete overlap between site and subpopulation. If stratification by site = stratification by subpopulation, then you can’t separate out whether effect modification results from site or from population factors. This is just a caveat.

7. Page 9: I very much (as a former academic) appreciate the point about
authorship on individual site studies, but this raises the question above, about adequate statistical power at individual sites. If each site is underpowered, how do individual sites report results that have inadequate power or precision (and fail to reach statistical significance)? I know it’s easily possible to do proper reporting, but my point is that the site-specific results may best be interpreted in the context of the overall PMA.

8. Page 10: IUD’s may be ideal for SOME women, but certainly not all women. I don’t know that I’d make a sweeping generalization, as you do here, by referring to IUDs as “ideal.”

9. Page 10: I would suggest that you need more (especially since you’re not in a family planning journal) on the motivation for evaluating misoprostol. What’s the basis for thinking it should work? Is there truly equipoise?

10. Page 11: What was the predetermined sample size at each site? What was the justification for that sample size? What is (was?) the planned sample size overall? What power to detect what effect size does the overall PMA have? This may well be the topic of another paper, but it’s an important piece of this paper, as well.

11. Page 12: Who will do the final combined analysis? Is there a coordinating center? How was the decision made about who does the final analysis? Is this the role of the Cochrane review group (the Fertility Regulation Group)? Please clarify. This is a helpful point to make for those considering conducting a similar type of PMA.

12. Page 14: It’s not clear what you mean by “homogeneous data”. Presumably, you mean something like “using the same definitions of endpoints, the same data collection methods, etc..” The word “homogeneous” could be interpreted as a result (as in similar findings across sites).

13. Discussion (or Methods): Are there plans for any subgroup analyses? Another advantage of PMA is that it allows subgroups to be defined in advance, and may even provide power for treatment comparisons within subgroups.

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.

Declaration of competing interests:

I am a full time employee of Johnson & Johnson Pharmaceutical Research and Development. I don’t see any potential conflict for this methodologic paper generated by that employment.