Reviewer's report

Title: International Active Surveillance Study of Women Taking Oral Contraceptives (INAS-OC Study)

Version: 3 Date: 15 June 2009

Reviewer: Kavita Nanda

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Major Compulsory Revisions

1. Why did you choose to look at this particular regimen? Why not look at other pills, such as other so called 3rd generation progestins compared with 2nd generation? Or look at continuous or other extended regimens. The fact that you have chosen this particular pill does make it seem like this is a marketing study, despite the claims of independence.

2. Page 4. You present a detailed account of adjudication for DVT. But what about for the other primary outcomes?

3. Page 6. Will the participants provide written informed consent?

4. Page 7. Will the participating physicians be given incentives to recruit a certain number of DRSP/EE 24d users?

5. Page 8. How will contraceptive information be collected and how often? Will it be validated by prescription databases or clinic records?

6. Page 8. Again what about other outcomes-how will they be confirmed?

7. Page 9. Will there be any monitoring of the sites? To verify informed consent enrollment procedures, look at source docs, etc.?

8. Page 10. You need to define what will be included as an ATE.

9. Page 10. What is the difference in incidence of VTE and other outcomes that you are trying to rule out? I.e., the degree of inferiority of the new treatment compared with the standard treatment that your study attempts to exclude?

10. Page 11. What is the primary analysis population?

11. Page 12. What about GCP? This is not a randomized trial but many principles still apply. Will you follow GCP?

12. Page 12. What is the four-eye principle?


14. Page 13. How can you state that “All known confounders will be accounted for”? How? For example you would not have information on factor V Leiden a known confounder.

15. Page 13. How does the chosen design minimize the impact of referral and misclassification bias?
16. Page 13. How does the chosen design minimize the impact of the healthy user effect?

Minor Essential Revisions

1. Page 2. Do you mean 24 in the following statement “it can be assumed that a 21-day regimen of DRSP/EE 24d would not be associated with a higher risk of venous thromboembolism (VTE) than DRSP/EE 21d.”?

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests