Reviewer's report

Title: Do pneumococcal conjugate vaccines provide any cross-protection against serotype 19A?

Version: 2 Date: 4 August 2009

Reviewer: Hanna Maria Nohynek

Reviewer's report:

This is an important contribution to the discussion on cross protection by different pneumococcal conjugate vaccines (PCV) on those serotypes which in large scale use of the vaccine have behaved differently than expected. All of the authors work for GSK, and have declared their conflicts of interests. A suspicious reader could interpret the paper as part of the company’s marketing campaign of their newly licensed 10-valent PCV, but to my best understanding, the authors have thoroughly reviewed the existing literature, made their choices based on the selection of the most specific endpoints of interest (i.e. invasive disease, and acute otitis media rather than pneumonia, which would have given them one more vaccine and some more papers to refer to), and written their understanding of the observations from both academic and public health points of view. My detailed comments follow.

• Major Compulsory Revisions

1. The magnitude of the 19 A pneumococcal disease burden (invasive as well as mucosal infection) at least for some of the countries referred to would be good to mention in the Background for the less learned audience. Now it is presumed that everyone knows what kind of incidences and magnitudes of rises the authors are talking about.

2. Table 1. a) The vaccine efficacy values would make more sense, if the table included absolute numbers of subjects and numbers of 19F and 19A findings. The reader could thus have better idea on the robustness of the observations the authors refer to. b) in the context of this manuscript as a review, it does not make sense to refer to a meta-analysis (ref #14). I would rather like to see the authors break the meta-analysis results into numbers and VE estimates from the original papers as the 4 studies arise from such different populations (as actually mentioned by the authors in the Discussion).

3. Table 2. As above, the reader could understand the robustness of the statements better if absolute numbers of trial participants and 19F and 19A isolates where given. In addition, I would prefer seeing confidence intervals for all Odds Ratios rather than p-values.

4. Not only the number of doses of pneumococcal conjugate vaccine (PCV) but the initial time point of the first dose given is important when making observations...
on impact of PCV on carriage. It has been demonstrated that PCV cannot eradicate already established carriage. This needs to be shortly discussed as it is not explicitly stated when referring to reference #13 (which as a conference abstract may not be easily accessed).

• Minor Essential Revisions

In Summary Box, add “by” in the sentence in the 3rd bullet point (“The limited protective…”)

• Discretionary Revisions

None.

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

In the past 5 years, I have received reimbursements for technical advise (pneumococcal conjugate and HPV vaccines development) and teaching (travel health) from GlaxoSmithKline, Wyeth, and SBL vaccines.