Reviewer's report

Title: Invasive meningococcal disease epidemiology and control measures: a framework for evaluation

Version: 1 Date: 17 September 2006

Reviewer: Adam Finn

Reviewer's report:

General

The authors describe a fairly sophisticated population-based mathematical model for prediction of the impact of different immunisation strategies upon the occurrence and consequences of meningococcal disease.

I have advised developers of other such modelling systems previously on the clinical assumptions that need to be made to drive such models and therefore have some familiarity with them I am also familiar with the epidemiology and impact of meningococcal disease and with the available vaccines. However I am not a mathematical modeller and cannot comment on technical aspects of the design of this model which are, in any case, not described in detail in this paper.

The model uses individuals, but also has some standardised parameters based on means (such as age of high school drop out, size of community). It can take into account not only general immunisation but also immunisation done in response to outbreaks.

Any such model is limited by the degree to which the mathematical algorithms used reflect the true complexity of real population effects and the accuracy of the assumptions used to drive the model. Regarding the former, as far as I can judge, the model is at least as good as and probably better than average. Regarding the latter, there are important gaps in knowledge – notably about the efficacy and duration of protection both against invasive disease and against carriage of conjugate vaccines given to adolescents. However, as new data emerge on this, they can be fed into the model to produced revised outcomes.

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

I may have missed something, but was left feeling unsufficiently clear precisely what the assumptions were that were fed into the model to produce the illustrative predictions shown in the figure on page 31 (?figure 2) The legends says nothing. In particular what rate of uptake by 12 year olds is used and is this one that can realistically be expected to be achieved across the board in the USA based on success with current programmes in adolescents?

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

End page 2 start page 3

“aided by facilitated through…”

Need to pick one verb for this sentence

Page 13

Analysis settings

What rate of uptake was assumed for routine immunisation of 12 years olds (as opposed to immunisation in response to outbreaks) in this illustration? Does the model assume this uptake rate is uniform or does it allow for variable uptake rates within and across communities?

Discretionary Revisions (which the author can choose to ignore)

Page 3
“That vaccine, however, has relatively poor efficacy in younger children, does not prevent carriage of the disease, and does not provide long-lasting protection”

Although it is commonly stated, I believe it is not really know whether polysaccharide vaccines can impact on colonisation. Certainly A and C polysaccharides can induce mucosal immune responses (. Infection and Immunity 2000; 68: 2692-2697 and Infection and Immunity 2001; 69: 4337-4341)

**What next?:** Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No

**Declaration of competing interests:**

I have received reimbursement of costs and honoraria to attend and to speak at conferences from Sanofi-Pasteur in the past 5 years and am in negotiation with them concerning involvement in conduct of a clinical trial. Income received has been paid into an educational fund held on my behalf by my employer.