Reviewer’s report

Title: Genotype distribution of human papillomavirus (HPV) in cervical cytologic specimens in a region of southeast Spain.

Version: 1 Date: 17 March 2009

Reviewer: Jennifer Smith

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This paper presents data on the prevalence of HPV in different grades of cervical neoplasia among 432 cytologic specimens collected in clinical practice in SouthEast Spain.

General points:

Abstract:

Ie the point that low percentage of HPV 18 and the remarkable prevalence of HPV 58 might reduce the effectiveness of the vaccination campaign in this region:

I am concerned about this statement. It is important to differentiate HPV prevalence results found in the population, versus those found in LSIL lesions, versus those found in HSIL and those found in ICC. HPV prophylactic vaccines target the oncogenic HPV types that are most common in ICC. Thus, it is misleading to conclude that if HPV 16 and 18 are not the most common types in HSIL, LSIL or within the population that the vaccine efficacy will be compromised. Based on global review, HPV types 16 and 18 are found to be the most common types in ICC in all geographical regions surveyed. In actuality, the number of HPV types identified in each stage of cervical disease decreases with increasing grade of cervical disease, thus being lower in ICC than in HSIL or than in LSIL.

Introduction:

Please add a reference concerning the statement that there are more than 200 HPV types..is this referring to humans or other species?

Please add a caveat ie the 20-30% prevalence of multiple infections—results are clearly dependent upon the HPV typing assay used.

Also, please include a caveat that the data on HPV vaccine cross-protection has not necessarily proven to be clinically relevant. I would thus put caveats on this when cross-protection is referred to in the text.

Ie the statement, “the effectiveness of HPV vaccines will depend upon the particular HPV genotype/distribution of the region”. Please see comments above under the abstract section. This statement seems to presume that certain types will replace others (niche hypothesis), although this has not been proven and
may be purely theoretical. This should be make clear in the introduction and/or methods section.

Methods:

Please clarify how the data on the follow-up of the 42 women was used in these analyses.

The decision to include two different assays for HPV detection and combining results needs to be further justified, particularly given that different HPV tests will likely result in different sensitivities for the detection of different individual types.

Results:

The figures on the overall prevalence of HPV found among all women included in this study are not particularly useful, given that these data are dependent upon the proportion of women with HSIL, LSIL and normal diagnoses. I would suggest, thus, present the HPV results by each stage of cervical disease (normal, LSIL, HSIL), rather than combined figures.

I would suggest eliminating the data on the 14 women with undetermined cytological status. Given that this is not a representative population based sample, these data do not add much.

Please include an analysis of A5 and A9 limited to women with normal cytology.

Please provide the data on the prevalence on the most common HPV types as single type infections. This is particularly important for low risk type HPV 6, which in most cases will be accompanied with another high-risk type.

Discussion:

Please carefully indicate which results you are referring to (normal, LSIL or HSIL) for each study included in the discussion.

Please add a reference concerning the lower sensitivity of HPV 53 in currently available diagnostic tests.

Line 262, it is difficult to compare the prevalence of multiple infections in Munoz et al (all invasive cervical cancer cases) with that of the present study, which has different grades of cervical disease less severe than ICC.

Line 307-310, the statements about HPV vaccine cross protection here seem a stretch. If my understanding is correct, cross protection is likely due to closer phylogenetic grouping, rather than competition between different HPV subtypes.

Tables:

Table 1, unclear what the others category. Please add data on negative HPV results and missing results, if applicable.

Table 2. Please clearly define “other” and “co-infections” below the table.
References:

Please kindly update the references, as many are out of date.

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

**Quality of written English:** Needs some language corrections before being published

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

**Declaration of competing interests:**

I have received grants or honoraria from GSK or Merck during the past five years.