Reviewer's report

Title: Improved Detection of Human Papillomavirus DNA in Cervical and Breast Tissues by Touchdown General Primer PCR and Optimized Sample DNA Concentration

Version: 1 Date: 24 August 2005

Reviewer: Philip Castle

Reviewer's report:

General

I think that this is a reasoned and carefully performed study. I have a few general concerns that need to be addressed:

1. I don't like the title, given that the role of HPV in breast cancer is uncertain at best. The authors make this point clear in the discussion but this is a long paper, etc. I think that the title could be much more conservative and still convey the main objective of the paper.
2. The authors need to better emphasize that increased detection is not necessarily useful in clinical applications. Since current tests already detect the bulk of precancer and cancer, the increased analytic sensitivity cannot help clinical sensitivity but can reduce clinical specificity.
3. One limitation that should be discussed is that they did not address assay reliability.
4. I guess that this is the advantage of an on-line article but there seemed to be a great number of figures, etc.

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

1. I do not agree with the approach of testing only HPV- abnormal cytology specimens to determine if an assay is better than another---a number of papers have urged against this approach because of potential bias. It is likely that if we were to test "touchdown" negative specimens by the standard GP5+/6+, some would have tested positive. Or, GP5+/6+ positives might have tested negative by "touchdown". A proper approach would be to retest all specimens or a stratified sample of specimens in a masked fashion. Then present to the readers a two by two table with Kappa stats and McNemar's test. Secondarily, details about which types were missed, etc.

2. An additional concern is that the FFPE tissues could have been contaminated when they were cut leading to elevated HPV positivity by the more sensitive touchdown assay. What PCR precautions were taken? Did the authors run any tissues that are known to be HPV-? For example, I do not think that anyone would attribute brain cancer to HPV infection.

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

Discretionary Revisions (which the author can choose to ignore)
What next?: Accept after minor essential revisions

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: No

Declaration of competing interests:
I declare that I have no competing interests