Reviewer's report

Title: Correlation of breast cancer risk factors with HER-2/neu protein overexpression according to menopausal and estrogen receptor status.

Version: 1 Date: 13 November 2004

Reviewer: Robert Millikan

Reviewer's report:

General:
The authors present an interesting study of risk factors for HER2+ and HER2- breast cancer. The study is small, many of the ORs are imprecise, and there are some problems with the data analysis and interpretation. But the study provides important, worthwhile information.

Major Revisions:

1. The OR results in Table 3 (adjusted for age) differ considerably from the ORs in Table 4 (multivariate adjusted). This suggests the presence of confounding, and that the age adjusted estimates are not the best (most valid) estimates. Only ORs adjusted for confounding should be presented.

2. p. 11 It is not correct to interpret case-only ORs as estimates of risk. Rather, they estimate ratios of odds ratios. For example, the case only OR of 3.12 in Table 4 for abortion in premenopausal women should not be interpreted as a measure of "increased risk" but as a measure of the relative strength of the association for HER2+ versus HER2- breast cancer.

3. Methods p. 5 What was the time period for ascertainment of cases and controls? 1990 through 2002 for cases is listed in Abstract but not in the Methods section of the paper. Were cases consecutively diagnosed and not selected for family history or other characteristics. Were cases invasive only, or was DCIS included?

Minor Revisions:

4. Background p. 4. "etiological heterogeneity...rather than prognosis." These are not mutually exclusive, and need not be "either or."

5. p. 6 How were the cut points for BMI chosen? Were HRT and OC use classified as any use, or was there a threshold for positive?

6. p. 7 What was the retrieval rate for tumor blocks?

7. p. 15 The discussion of recall bias and selection bias needs to be clarified. What does "inevitable" mean in this context? Exposure can still be misclassified due to memory or reporting differences between cases and controls.

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

Level of interest: An article of importance in its field

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.