Reviewer’s report

Title: Inter-observer reproducibility of HER2 immunohistochemical assessment and concordance with fluorescent in situ hybridization (FISH): pathologist assessment compared to quantitative image analysis

Version: 3 Date: 20 March 2009

Reviewer: Richard Powell

Reviewer’s report:

No link was provided to the authors’ response letter, so comments are addressed to previous points and the extent to which the paper has been revised in accordance with previous comments. The revised manuscript does address many of the concerns about the explanations of the methods and the rationale for inclusion of data, but still leaves questions about some of the statistical results.

Major compulsory revisions:

(1) Kaplan-Maier survival still needs explanation, since P values still appear unfeasibly low. There is possible confusion in the nomenclature – the lower case “e” might suggest natural logs rather than base 10 logs, which would make the P values more reasonable, but if so this needs to be clarified (the text uses upper-case “E” rather than “X 10x”. The end-point is still not clear - overall survival or breast cancer related death/recurrences?

Minor essential revisions:

(1) Full bibliographic details needed for Ref. 40.

(2) Table 6, middle row “FISH 1.8=2.2” should be “FISH 1.8–2.2”

(3) Criteria for unscorable FISH is only in terms of core degradation – need to include any criteria for inclusion based on minimum number of cancer cells, heterogeneous amplification, or morphological characteristics of tissue.

Discretionary Revisions:

None

Language:

(1) p. 17, fifth line from bottom, remove “, etc.”

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I have no competing interests