Reviewer's report

Title: Do serum biomarkers really measure breast cancer?

Version: 2 Date: 13 January 2009

Reviewer: Emanuel Petricoin

Reviewer's report:

This is a much improved and very interesting manuscript. However, I still have a few questions based on the revisions and comments by the authors in their cover letter

Minor Essential Revisions:

1. Why not mention and discuss the fact that sensitivity and specificity held up in an independent test set? This is an important aspect of the paper, and provides confidence in the signature identified. I really feel that the paper is strengthened by this addition and associated discussion!

2. The authors provide product information about Luminex analytical sensitivity, but this was not the basis of my question. I'd like to know what the CV of each analyte was - what is the inter and intra assay reproducibility? For example, the first patient delineated in the supplemental information lists a VEGF measure of 427. Firstly, is this the average of the two replicates? what was the individual values obtained from each of the two runs? What if this patient sample were run the next day- what would the result be. This question goes to the heart of the matter in signature-based markers- how reproducible are the analyte readings, and then the compounded CV when you combine them together. This detail requires more discussion and information that I cannot find in the revised version

Given that each sample was run in duplicate, I cannot find where this is mentioned in the manuscript as well...

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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

Declaration of competing interests:

I declare that I have no competing interests