Reviewer's report

Title: Revisiting the technical validation of tumour biomarker assays (or how to open a Pandora's box)

Version: 1 Date: 9 March 2011

Reviewer: anne Vincent-Salomon

Reviewer's report:

This review is interesting and should be accepted with discretionary revisions.

Here are my suggestions:

1. In the introduction, the authors should briefly mentioned the new or other available biomarkers such as in blood (CTC, circulating DNA) and emphasize that not only tumor-derived biomarkers are to be submitted to careful validation and accurate protocols.

2. At the end of the last paragraph of "Validation: when and why?", regarding internal quality control, I think it is important to give examples "breast cancer based" such as ER and PR and HER2 for which the normal glands should be respectively positive for ER/PR and negative for HER2 before the marker is interpreted and signed out.

3. I personally don't like the term "hazards" in the second paragraph of "Validation assay for novel biomarkers". I would favor "multiple steps in tissue preparations difficult to be perfectly standardized» ?

4. To be added in the list of pre-analytical variables "dehydration steps in the V.I.P. device " added before paraffin embedding.

5. At the end of the paragraph listing the key issues with immunohistochemistry, it should be added that when a biomarker is used in routine, internal statistics have to be performed to be sure that the lab's results are in agreement with others;

6. Finally in figure 2, I would add for FFPE tissues: use of multi-tissue blocks for positive and negative controls.

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.