Reviewer’s report

Title: Estrogen receptor alpha (ERα) mRNA copy numbers in immunohistochemically positive-, and negative breast cancer tissues

Version: 3 Date: 15 February 2007

Reviewer: Michael C MacLeod

Reviewer’s report:

This study is a useful albeit small step forward. The reviewer with the most negative opinion, Dr. Spyratos, makes several valid points, some of which the authors have answered adequately in the last revision. The basic underlying problem appears to be that the study was designed to use material at hand, rather than to collect the samples needed to directly assess the question of interest. Thus, we are left with an unspecified mixture of biopsy samples and mastectomy samples, some previously assessed by IHC, others by ligand-binding assays, trying to answer a question that is probably only relevant in the case of biopsies. Also, the use of GAPDH as the control gene is problematic, as pointed out by the reviewer. However, it is not clear that a better single "control" gene for this purpose is known (certainly none are proposed by the reviewer), and the use of a panel of control genes which might provide a more robust assay would be prohibitively expensive in clinical use. Even with these caveats, the data are suggestive that this could be a useful approach and are fairly interpreted and clearly presented. On balance, I would agree with the other two reviewers and publish this paper as is. Undoubtedly it will require larger, prospective trials with cleaner design, probably at multiple centers, to bring this technology to the clinic. This is a first step in that direction.