Reviewer's report

**Title:** Ageing and long-term smoking affects KL-6 levels in plasma, sputum and lung with significant correlations to COPD severity

**Version:** 2 **Date:** 22 February 2011

**Reviewer:** Jadwiga Wedzicha

**Reviewer's report:**

Thank you for asking me to review this paper.

The paper studies KL6 levels in patients with COPD, and non-smokers. The rationale is a good one as KL6 is closely involved with mucin production and mucous production is linked to disease progression in COPD.

However I do have a few reservations:

1. I am not sure about the patients population and how representative it is – only Stage 4 GOLD COPD patients were on inhaled steroids and that is unusual as according to clinical practice guidelines one would expect at least Stage 3 and 4 to be treated with inhaled corticosteroids

2. The patient numbers rae relatively small for a COPD biomarker study – with the maximum of 40 patients in the COPD group and much less in the induced sputum and immuno-cytochemistry analyses.

3. There is an emphasis on ageing in this paper but the mean age of he COPD patients is only 61 with a small SEM – although the age range is up to 79, I think there must be few patients over 70. the middle aged smokers with no COPD have a mean age of only 52. I do no think that one can comment much about the effects of ageing in such a small and relatively young population.

4. In the immunochemistry group, we also have AAT deficient patients that complicates the analysis and could be left out.

5. There is no follow up longitudinal study that will be useful.

I think this is not quite up to the mark – if they had a larger sample size, then that would be better but I think the sample size is too small for such a heterogeneous condition such as COPD.