Reviewer's report

Title: Exhaled and arterial levels of Endothelin-1 are increased and correlate to pulmonary systolic pressure in COPD with pulmonary hypertension. An imbalanced output in the breath between Endothelin-1 and Nitric Oxide.

Version: 2 Date: 28 April 2008

Reviewer: Emmanouil Paraskakis

Reviewer's report:

This is an interesting study about the assessment of FeNO and EBC ET1 in COPD patients with PAH. The study is well designed but there are a few major and minor revisions that I would like to point out:

Major Compulsory Revisions

1. As it is well known that both ET1 and FeNO production are oxygen depended, it would be essential to demonstrate if there is any difference of the ET1 and FeNO levels of the patients receiving long term domiciliary oxygen (5/12 in group 1, 6/36 in group 2 and 2/4 in group 3) compared with those not receiving long term oxygen. If there is actually an effect on ET1 and FeNO levels then the patients receiving long term oxygen should either excluded or form different groups and that might change the interpretation of the results.

2. All the patients with IPAH (group 3) were on bosentan which is an agent that normalizes the FeNO (Girgis et al Am J Respir Crit Care Med 2002) and affects the ET1 plasma levels (Hiramoto et al Circ J 2007). Although it should be stressed that IPAH is a rare disease it would be ideal if those patients were measured before treatment so their ET1 and FeNO levels would not been affected by the treatment. To my view this small group does not add much to the comparison since there is a significant difference between group 1 and 2 regarding ET1 and FeNO, so it should be either omitted or the limitations of the measurements of this group should be added in the discussion section.

Minor Essential Revisions

1. Although venous and arterial ET1 seems to give similar information, venous ET1 contrary to previous findings (Roland et al Thorax 2001) and to arterial ET1 did not correlated with any parameter of the patients. This finding should be discussed by the authors.

2. Figure legends (especially 1,2,3,8) are very extended and should be revised.

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

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

Declaration of competing interests:
I declare that I have no competing interests