Reviewer's report

Title: Characterisation of an aerosol exposure system to evaluate the genotoxicity of whole mainstream cigarette smoke using the in vitro gammaH2AX assay by High Content Screening

Version: 1 Date: 29 December 2013

Reviewer: daniel smart

Reviewer's report:

1. Materials & Methods; Smoke exposure/WMCS treatment; paragraphs 1/2 (Minor Essential Revision)
   It is not clear how many cigarettes were smoked for the exposure. Was the smoke from only 1 cigarette used for the 3 h exposure or was a number of cigarettes smoked continuously throughout the exposure period?

2. Materials & Methods; WMCS treatment; paragraph 2 (Major Compulsory Revision)
   Was RCC measured directly after the 3 h exposure? If so, it is reasonable to assume that there would have been negligible effects on cell viability after this short exposure period. A "recovery" period would be required for the manifestation of any cytotoxicity. Can this be clarified and expanded upon?

3. Results; WMSC genotoxicity assessment; paragraph 2 (Major Compulsory Revision)
   Contrary to these data, published literature has indicated that aerosols from flue-cured tobacco are generally more genotoxic than 3R4F counterparts in mammalian assays. Interestingly, it appears that 1 mM etoposide-induced gH2AX responses between cigarette exposures differed by approximately 35% (lower when used alongside M4A). Could an overall reduced assay response when evaluating M4A genotoxicity account for this apparent discrepancy with published data or is 3R4F more genotoxic than M4A specifically when using the WMCS/gH2AX assay?

4. Figure 4 A and B (Minor Essential Revision)
   It is not clear what the dotted lines represent. Can this be clarified in the legend?

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

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.