Comments on the Assessment Report: Adefovir dipivoxil and peginterferon alfa-2a for the treatment of chronic hepatitis B - the HIV and blood-borne virus group of the British Association for Sexual Health and HIV (BASHH)

1) We are increasingly uncomfortable with the final conclusion that (section 10, page 161)
'….sequential strategy of pegylated interferon alfa, followed by lamivudine, with adefovir added as salvage therapy is increasingly likely to be the optimal intervention'

Although the cost-effectiveness analysis took into account acquisition of resistance from mono-therapy with nucleoside/nucleotide analogues (lamivudine and adefovir) and the continued e-seroconversions after prolonged adefovir therapy, we are not sure whether the following were accounted for:

a) The cost-implication of 'flares' associated with the acquisition of resistance mutations
b) The psychological consequences to an individual with compensated cirrhosis who progresses to hepatic decompensation as a result of a hepatic 'flare' associated with HBV mutation.
c) The cost-implication and wider impact of transmission of HBV mutants (this is mentioned briefly in section 7). There is some suggestion already that many of these mutant viruses may be transmissible to HBV-vaccinated individuals (see Cooley et al. AIDS 17(11):1649-1657, 2003).
d) The uncertainty of future treatment options for patients failing sequential therapy with lamivudine and adefovir (although a number of nucleoside/nucleotide analogues are in the pipeline their effectiveness against multiply mutant viruses is yet to be established).

The future long term suppressive therapy for HBV should take into account the combination treatment paradigms applied to HIV treatment and the 'biological plausibility' that non-IFN combination therapies will lead to less resistance acquisition.

Although, long-term data for this strategy is, as yet lacking, most experts agree (D Mutimer. J Hepatol. 2005 Jun 20; [Epub ahead of print]), that combination therapy may indeed be the standard of care in the future.

For these reasons we strongly suggest that the assessment document suggests that treatment strategies may change in the future, and policy makers and healthcare funding organisations need to adopt to guidance issued by national/international experts as new evidence comes to light.

2) Although mentioned in research needs (section 9.3.3) and in section 10, we would like the document to be explicit that the treatments and strategies outlined (in terms of cost-effectiveness) do not apply to patients with HIV/HBV co-infection where incidence, disease progression rates, response to therapy and acquisition of resistance to mono-therapy with lamivudine, and treatment strategies (treating both HIV and HBV with combination therapy that includes tenofovir and lamivudine) are very different to HBV mono-infected patients.

Guidance for treating HBV in the context of HIV co-infection is issued by the British HIV Association (BHIVA) and is regularly up-dated as new evidence accumulates (see http://www.bhiva.org/guidelines/2004/HBV/index.html).

3) Given the concerns of treatment of HBV in the context of HIV co-infection we would also suggest that there is a recommendation that all patients with HBV infection should be tested for HIV before commencing therapy