Reviewer's report

Title: Direct Acting Antivirals in Hepatitis C: A Systematic Review of Neuropsychiatric Risks and Psychiatric Drug Interactions

Version: 3 Date: 27 March 2013

Reviewer: David Back

Reviewer's report:

This is an important topic and the authors have given us a thorough review which will be useful to HCPs seeking to optimise the use of DAAs in the treatment of Hep C.

I have some comments (mostly minor)

1. Page 2. Line 8. pharmaceutical companies?

2. Page 4 Line 13. Both agents inhibit P-gp and telaprevir may inhibit renal transporters. These statements should be referenced.

3. Page 5. Line 4 & 6 of Methods. Some concern that the searches only went to Sept 2012. This is such a fast moving field that I would strongly urge the authors to include articles to March 2013 - else you are losing 6 months of possible important material.

4. Page 6 Line 14. I would like to see some additional input here on the level of evidence and make it clear that this was only done in the context of treatment of depression.

5. Page 7 Line 13. Slightly confused. In Table 2 the notes state that Level 4 is anecdotal or expert opinion whereas here it implies it is literature based. Clarify.

6. Page 8, Line 4. Somewhere (either here or Table 2) would like to see a comment about the Dec 11 QT warning with escitalopram and citalopram.

7. Page 8 Line 8. Sentence beginning 'Therefore, selection .....' is not clear.

8. Page 8 Last line. Does not make sense. glucuronidation is conjugation!


10. Page 14. Last lines. Do the authors consider that it is realistic that future drug interaction studies will correlate changes in DAA and psychotropic drug levels with HCV treatment outcomes and relapse. Most DDI studies have PK endpoints.

11. Table 2. Why if citalopram and escitalopram have the same metabolic pathway will citalopram levels likely increase while escitalopram have been shown to decrease with TVR?

12. Table 2. Need some comment for nefazodone.

13. Table 4. Clozapine. Is it realistic to advocate TDM?

14. Table 4. Paliperidone. I understood that this drug is substantially renally
excreted with little evidence for CYP2D6 or CYP3A4 in vivo.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

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