Reviewer's report

Title: Delays in the post-marketing withdrawal of drugs to which deaths have been attributed: a systematic investigation and analysis

Version: 2 Date: 6 November 2014

Reviewer: david menkes

Reviewer's report:

The authors have chosen an important topic, thus far virtually unexplored, and conducted a careful, descriptive analysis of drug withdrawal due (at least in part) to deaths

Major compulsory revisions:

1. Presumably the market share and profitability of particular drugs would influence industry’s attitude to withdrawal; has this been considered? Likewise, it is unclear how industry’s role should fit with that of regulators, and of course this will vary country by country, as will the quality of evidence required to prompt withdrawal.

2. Another aspect worthy of mention concerns drugs, notably psychotropics, not withdrawn but known to cause death (this could be added to Discussion or considered as a limitation)

Minor essential revisions

3. Rounding down to the first year of a decade could significantly skew results and it seems strange that a launch year for a drug could not be reasonably obtained. Can this be justified?

4. Disagreements resolved by discussion seems vague; how often did this occur?

5. Results (e.g., p values) are presented without indication of statistical analyses used.

6. On page 9: a number of drugs were withdrawn due to overdose deaths – why these and not countless others known to be lethal in overdose?

discretionary revisions

7. On page 10: The statistics do not add up in paragraph 3 unless more than one study per drug was applied, in which case this should be mentioned

8. On page 17: Incentivising the reporting of adverse events is a promising idea but requires study and may plausibly lead to over-reporting.

9. A subtle anti-industry flavour pervades some of the text; while drug companies
doubtless do contribute to the phenomenon under study, an expanded, more objective treatment of this would strengthen the paper. For example, commercial conflicts of interest are presumably fundamental to this problem and are referred to rather too briefly with one paragraph and three citations (30-32).

**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 in relation to this paper