Reviewer’s report

Title: Post-marketing withdrawal of 462 medicinal products because of adverse drug reactions: a systematic review of the world literature

Version: 0 Date: 16 Dec 2015

Reviewer: Joel Lexchin

Reviewer's report:

The revised version of this manuscript has addressed some of my concerns but some still remain.

1. The authors have still not used the published literature that documents drug withdrawals due to safety problems. In some cases the published articles could only document withdrawals by cross-referencing multiple different sources including the grey literature.

2. Figure 1 is somewhat misleading. It lists 9 databases that the authors searched. The implication is that all 9 were searched to look for withdrawn drugs, but the last three - PubMed, Medline and Google Scholar - were only searched to look for the first reported ADR.

3. The authors continue to use 1950 as the start of modern drug regulation whereas my contention is that a better date would be post-thalidomide.

4. The authors determined which countries had withdrawn a drug from the WHO database and the newly developed database that they refer to. Has there been any assessment about the accuracy of these databases. If not this should be noted.

5. What is the basis for the assumption that if a drug is withdrawn in one country in a continent it is likely to have been withdrawn in other countries in the same continent?

6. The authors need to make it clear that they are referring to Australasia and Oceania as a "continent".

7. The figure of 2% of drugs approved by the FDA having been subsequently withdrawn is well below the Canadian figure of 5% for the 5-year periods between 1985 and 2009 - see Lexchin Open Medicine 2014;8:e14-e19.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

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If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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