Reviewer’s report

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

Version: 1 Date: 31 Dec 2015

Reviewer: Nigel Rawson

Reviewer's report:

Most of my concerns have been dealt with by the authors. However, I have the following comments:

1. The authors focus on my example of acetarsol, which was withdrawn in Mauritius for hematologic reasons. This was simply an example to ask the authors to comment on whether a drug being withdrawn in only one or two countries implied that the product was solely approved in those countries or in multiple countries because the issue remains that they do not know which drugs were approved in which countries. The withdrawal data are only one side of the analysis. While they mention this in their Discussion and point to other authors having the same problem, they downplay the impact that this lack of information has on their results.

2. The authors have taken my comment that after 1985 where 81% of the withdrawn products were discontinued within 5 years of the first ADR report and used it in their Discussion, but do not make the point that I was indicating which is that there has been an improvement since thalidomide in the time taken to withdraw drugs after an ADR report. Instead, they amalgamate my comment that their data do not allow any understanding of how many patients were impacted by the ADRs. Both points should be acknowledged separately, not mixed. The authors could easily revise their statement and should do so.

3. Reviewer 2 uses Lexchin's 5% figure for the rate of drugs withdrawn in Canada. Due to an incorrect analysis, Lexchin over-estimates the true figure of 3% (Rawson NSB. New drug approval times and safety warnings in the United States and Canada, 1992-2011. J Popul Ther Clin Pharmacol 2013; 20: e67-81). The authors should correct the rate.

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

Yes

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

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

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.
Not relevant to this manuscript

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