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: 27 October 2014
Reviewer: Joel Lexchin

Reviewer's report:

Major compulsory revisions

As someone who has previously published on drug withdrawals for safety reasons I found this manuscript very interesting but I am concerned that the authors are combining different groups of drugs into a single theme. Some of the drugs were withdrawn because the deaths occurred even with proper use of the drugs, some because the deaths seemed to be due to improper use of the drugs (overdose with pentobarbital and co-proxamol) and some where only single strengths were withdrawn (e.g., the 150 mg dose of bicalutamide was withdrawn from the Canadian market because of accelerated deaths but the 50 mg dose is still available). This leads me to my second major concern, which is the accuracy of some of the secondary sources that the authors used in constructing their database. In my previous research I found that the WHO Database of Consolidated List of Products was not always accurate. Did the authors rely on a single source for information about withdrawals or did they try and confirm the information from a second source?

I also have a number of more specific concerns:

Page 6, last paragraph:

How did the authors deal with the situation where death was cited as a reason for withdrawal in one (or more) country but not as a reason for withdrawal in others?

Drugs are sometimes prescription only in some countries and OTC in others. How did the authors resolve this issue?

Page 10, Evidence for withdrawal:

The authors should define how they are using the term precautionary principle.

Page 15, first paragraph:

The authors need to describe what they mean by “addressing” the problem.

Page 15, second paragraph:

Describe the established standard procedure in one of the countries.

Minor essential revisions:
Finally, there are a couple of places where the word choice is not quite correct:

Page 6, 5th line from the bottom:
It should be either “medicines” or “medications” not “medicaments”.

Page 13, 8th line from the top:
It should be “per capita” not “per caput”.

**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