Reviewer's report

Title: Drug shortages in European countries: a trade-off between market attractiveness and cost containment?

Version: Date: 28 May 2014

Reviewer: Lynda Doward

Reviewer's report:

This is a potentially interesting article. However, there are aspects to the manuscript that require revision before this could be considered for publication. I feel that if the authors address the points below, this could be a valuable addition to the scientific literature.

Major Compulsory Revisions

General Comments

The focus of the article is not totally clear. The aim of the study, as stated in the Abstract, is to ‘develop a standardized template that covers all aspects involved in drug shortages’. The study goal, as stated in the Background section (page 4, line 15) is to ‘reveal and identify a typology of drug shortages in European countries’.

The aims and objectives of the study should be clearly stated (and consistent between Abstract and manuscript body).

It is currently unclear whether the reporting template was intended solely for use in the current study, as a means of standardizing data collection, or whether the authors propose this template as a tool for data collection by competent authorities in the future. Please clarify this point.

Furthermore, if the study goal is to present an overview of the situation in Europe, it is unclear why so much of the manuscript is devoted to reporting the situation in the USA. Although European data are presented in the results section, much of the text in the Discussion is dedicated either to the USA, or to a comparison of the US and Europe. For example, on page 9, lines 5-17 include a detailed description of the US situation relating to economic issues and MMA. Similarly, on page 9 (last two lines) and page 10 (lines 1-7) there is a detailed discussion again about the FDA. The corresponding information relating to EMA / Europe is scant. While it may be useful to draw parallels between the two regions, the discussion contains too much US-based detail at the expense of the EU. If the authors intend to conduct a comparison of the US and the EU, then this should be presented as an objective, and US data should be presented alongside the EU data. If the focus is on the EU, then the discussion should be rewritten to redress the current imbalance.
The level of English needs improvement throughout. There are too many examples of poor or inaccurate English to mention in detail, but some examples are given below:

Attention needs to be given to ensuring that the correct tense is used throughout. For example, the Abstract contains the phrases ‘results are based’ and ‘typology and drug shortages is mapped’. First of all, the latter should read ‘are’ mapped. Second, the present tense contradicts used in both of these statements contradicts the past tense used in the Methods section in the manuscript body.

Examples of English language requiring improvement:

Page 1, lines 2-3: ‘a medicinal product which hinders to meet the demand of the product’. This statement makes no sense in English. Hinders what? The ability of the manufacturers or suppliers? Please clarify or

Page 1, line 16: ‘drug shortages ever more’. Again, this makes no sense. Do you mean ‘drug shortages increasingly’?

Page 9, line 2: ‘In case the cause is known’ – do you mean ‘for cases where the cause is reported’? The use of ‘in case the cause’ is very clumsy English.

Majority is used throughout without a preceding ‘a’ (as in ‘a majority’). Please correct this.

To address these, and the other many examples of incorrect or clumsy English, I would recommend that the authors have the manuscript edited by an English language specialist before re-submission.

Methods Section

It is not absolutely clear from the methods section, what the authors actually did. Currently, data sources are presented, along with the fact that a reporting template was produced (although no information is given on how this was developed). Was the literature review conducted to yield information on shortages? Or was this simply used to inform on the sites / bodies from which data on shortages could be collected? Which sources were used to gather the data presented in the results section? Just those presented in Table 1? Or the results of the literature search too.

Please could the authors rewrite this section to allow the reader to ascertain precisely what research was conducted.

Results Section

Page 6, lines 13-16: It is not clear where these data have come from (see comment 3 above).

There is some confusion around past, present and predicted shortages in paragraph 3. This may be compounded issues surrounding mixed tenses. However, I do feel that the authors need to expand this section and separate out
the information relating to these as far as possible.

Please clarify and provide more information around the statement ‘were information about the end-date is present, the shortage is announced to be permanent’. If there is an end-date, can it be permanent? Who has announced this? Please also replace ‘were’ with ‘where’.

I would also suggest that the authors include a table outlining the reported causes. It would greatly assist the reader to have a table highlighting the five broad groups and their corresponding components.

Discussion Section

Page 8, lines 20-23: Please expand the discussion around the scope of the reporting systems in each country. It is unclear what the authors mean by Italy having the broadest scope.

Page 10, lines 1-7. There is too much information relating to the US. Please condense this or consider moving to the ‘Background’ section.

Page 10, lines 21-22. Please clarify the statement ‘supply quotas are currently more reproached’

Minor Essential Revisions

Background Section

Page 1, line 5: ‘alternative therapy which can’. Do you mean ‘can’ or ‘may’? ‘Can’ implies that these always cause adverse events, ‘may’ implies that there is potential for adverse events to occur. Please clarify.

Page 1, lines 8-9 ‘the origin of a drug shortage problem can possibly be located at both the supply and demand side’ do the authors mean ‘both’ or ‘either’. Please clarify.

Page 1, line 17: ‘from about 60 cases in 2005 to more than 200 cases in 2010’. I assume that ‘cases’ here means number of drugs for which a shortage has been reported? Or is it number of reported incidents? Please clarify.

Results Section

Page 6, line 13: ‘Figure 2 shows the relative number’. Figure 2 actually shows percentages not numbers. I would suggest that both n-values and %s are included in all figures.

Page 8, line 2: ‘reporting systems distinct’ should read, ‘reporting systems distinguish’

Page 11, line 15: EMA has been given in full on page 5. Please just use acronym.
Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Not suitable for publication unless extensively edited

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