PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Uterotonic Drug Quality: An Assessment of the Potency of Injectable Uterotonic Drugs Purchased by Simulated Clients in Three Districts in Ghana
AUTHORS	Cynthia K. Stanton, Alissa Koski, Patience Cofie, Ellie Mirzabagi, Breanne Grady and Steve Brooke

VERSION 1 - REVIEW

REVIEWER	Mariana Widmer Technial Officer Reproductive Health and Research World Health Organization I declare no conflict of interests.
REVIEW RETURNED	06/02/2012

THE STUDY	Reference 4 page 7 line 10: it might be better to change it for WHO Action Programme on Essential Drugs 1993 (Document WHO/DAP/93.6)

REVIEWER	Jennifer Blum Senior Program Associate Gynuity Health Projects USA
REVIEW RETURNED	16/03/2012

GENERAL COMMENTS	In the Summary: I don't think the first bullet under article focus is needed for this paper and not sure its indisputable. I suggest deleting or editing this statement regarding uterotonic effect on maternal morbidity and mortality. Abstract: First sentence in objectives can be delted. For conclusions, one thing that struck me when reading the paper is that only 10% of samples bought a health facility pharmacies, so i wonder if the conclusion is about "quality of injectible drugs purchased from drug sellers and pharmacies at the peripheral level in Ghana" I think the statement can be stronger than there "may be a serious problem" there really seems to be one. Introduction: in the first line for clarity between injectible ergo and ergo tablets suggest you write "injectible ergometrine". Can you double check WHO recs, I am not sure they say "refrigeration is feasible". .. you are probably right, but pls check. Methods: I think this could be shortened - especially paras 2 and 3. Are all the author disclosures now required as part of main manuscript? Seems to detract from getting to the results... Results: I am interested in the fact that 10% of samples were from

	public health facility pharmacies. Really, the data are about what the quality of uterotonics are bought mostly outside of these facilities. I think this point should be made stronger if possible and I am also curious to see the results of active ingredient on uterotonics bought from public health facility pharmacies (albeit only 10%) and other sources. it would be interesting to know the quality of drug purchased by a mobile peddler vs a market vs a public health facility pharmacy, for instance. On page 13, can you explain what these other drugs are - reader might be interested "Buscopan, Ladymax, Menstrogen..." Discussion: I think the first sentence, to me, is really the conclusion of uterotonics bought outside of public health facility pharmacies... First paragraph on page 17, suggest rewording so that you avoid saying "clearly warrant" twice in the same paragraph. Page 17, the questions that aren't specific to Ghana are interesting but I don't think the question of what approaches to data colletion should be promoted and for which objective is the most interesting. Do we need more data about uterotonic quality still? I think we have a pretty good idea of what is out in the field. I think the questions that aren't specific to Ghana are more related to what is described in teh paragraph above - how can more countries be proactive about buying quality drug, tracking drug sellers, issuing guidelines, not collecting data on uterotonic drug quality.

VERSION 1 – AUTHOR RESPONSE

Reviewer: Mariana Widmer

• Questions whether our Reference #4 is appropriately placed. In this revised version of the manuscript we have corrected the error and have changed the order of References #3 and 4.

Reviewer: Jennifer Blum

• Suggests that we delete or edit the first sentence of the abstract. We have edited the sentence such that it stresses prevention and treatment of maternal mortality and morbidity.

• Requests that the first sentence in the Abstract (under the sub-heading “objectives”) be deleted. We have deleted this sentence.

• Notes that we also visited public health facility pharmacies in addition to private sales points, and thus questions the first sentence under sub-heading “Conclusions” that there may be a problem with uterotonic drug quality at the peripheral setting in Ghana. We have edited the sentence by removing the clause “at the peripheral level” and state that uterotonic drug quality is a problem in the three districts of our study.

• Suggests that it would be helpful to see the % of active ingredient of uterotonic drugs by type of point of sale. We did not include this in the original manuscript because the n of ampoules in our various categories are small. We would like to point out that we do state in the text that

o “Figures 1 and 2 illustrate the number of ampoules of oxytocin (..and ergometrine) by incountry registration status of the product and by type of point of sale”.

o “None of the oxytocin ampoules purchased were from a registered manufacturer of oxytocin”.

o “All of the oxytocin ampoules from unregistered manufacturers were outside specification for active ingredient.

o “One third of the oxytocin ampoules from manufacturers with pending registration status were outside specification for active ingredient”

o Page14, 2nd paragraph.

Thus, we have not made any changes to address this comment.

• Suggests that it would be interesting to know the quality of drug purchased by a mobile peddler vs a market vs a public health facility pharmacy, for instance. We state in the text that “No uterotonics were successfully purchased from mobile peddlers, herbal/home clinics or markets” (page 13, 2nd paragraph, 2nd sentence). Thus, we have not made any changes to address this comment.

• Requests that we explain the purpose of the other drugs purchased by mystery clients (for example: Buscopan, Ladymax, Menstrogen). We have added a sentence to briefly describe the purpose of Buscopan and have deleted reference to Ladymax and Menstrogen as their purpose and provenance is unclear. See page 13, 2nd paragraph, 2nd sentence.
• States that the first sentence of the Discussion pertains to the data only from uterotonic drugs purchased from the private sector. We respectfully disagree; the percentages cited reflect the entire sample (which includes public sector sources), the sale of unregistered drugs is shown via graphics in the manuscript to occur in the public and private sectors and the 4th point in this sentence refers to both public and private sectors. Thus we have not made any changes here.
• Suggests the phrase “clearly warrant” not be used twice in the same paragraph on page 17 (1st paragraph). We have edited the paragraph such that the 2nd use of “clearly warrant” is replaced with “strongly support”.
• Suggests that we do not need additional information on uterotonic drug quality, and thus the comments about the best approaches to data collection are of lesser interest to the paper. The authors respectfully disagree with the reviewer. The most recent data on uterotonic drug quality in the literature dates from the 1990’s. As noted in the paper, tracer drugs which are carefully monitored via post-marketing surveillance are generally restricted to ARVs, anti-malarials and antibiotics and tend to be supported by large-scale international funding (The Global Fund, Roll-back Malaria, etc.). We hope that our paper will encourage additional data collection on the quality of uterotonic drugs. Thus, we have not made any changes to address this comment.