Author's response to reviews

Title: Improving Global Health Governance to Combat Counterfeit Medicines: A Proposal for a UNODC-WHO-Interpol Trilateral Mechanism

Authors:

Tim K Mackey (tmackey@ucsd.edu)
Bryan A Liang (brliang@ucsd.edu)

Version: 2 Date: 30 September 2013

Author's response to reviews: see over
Dear Dr. Denyer:

Thank you for your 26 September 2013 email and reviewer comments for the manuscript titled *Improving Global Health Governance to Combat Counterfeit Medicines: A Proposal for a UNODC-WHO-Interpol Trilateral Mechanism* (Manuscript ID: MS 6550769041045634). As directed by your correspondence, we are submitting a revised manuscript with changes highlighted using the tracked changes function in MS word that addresses all editor and reviewer comments and suggestions.

Below, please find the editor and reviewer’s comments and how each is addressed in the revised manuscript. Reviewer comments are in **bold**; our responses are in *italics*, with quoted text from the revised manuscript in 10 point font. The convention of pX, ¶A (i.e., page X, paragraph A) is adopted to indicate from where in the revised manuscript the text we reproduce arises.

I thank you for the opportunity to submit this revised manuscript and look forward to your comments.

**EDITORIAL COMMENTS:**

As you will see, the reviewers are generally very positive about your article, but suggest a number of minor changes to help improve the readability of your manuscript. As you know, in addition to the reviewers reports, we also sought advice from an editorial board member - thank you for your patience whilst we did this. The editorial board member raised a further interesting point we would like you to address regarding differentiating between counterfeit and substandard medicines:

??I do differentiate counterfeits, intentionally made, from unintentional substandard products. Dealing with unintentional substandard products requires a range of remedial activities that may include criminal prosecution for negligence but also must include educational and other activities to help well-meaning manufacturers rather than always jailing them.

The authors are correct when they want to separate intellectual property issues from public health issues. In my view, substandard products can be classified as intentional or unintentional as the WHO definition goes. One can also classify them as hazardous to the patients when little or no active ingredient is present or not hazardous when the product is properly made but labelled as being made by someone other than the manufacturer cited.
I am oversimplifying but I trust you get my point.

We thank the editorial board member for this important comment and request for clarification. Indeed, defining the issue is difficult, but we also agree that the nuances between counterfeit medicines made intentionally and unintentionally substandard or hazardous requires additional discussion. We have clarified what we constitute as a “dangerous counterfeit medicine” focusing on products intentionally made substandard and where criminal intent is involved in deceiving the consumer regarding the quality or authenticity of the medicine. Our revised language is provided below:

Global Scope of Counterfeit Medicines
Harm arises from a wide spectrum of detected dangerous counterfeit medicines across therapeutic classes, with quality, manufacturing, and/or provenance issues that make the product ineffective and/or harmful. In this discussion, we focus on the subset of “dangerous counterfeit medicines” that are intentionally made substandard, ineffective or are adulterated as well as instances where there is a criminal intent to deceive regarding the authenticity or origin of the medicine. In the case of dangerous counterfeit medicines, there is a clear public health risk given that these products can be harmful to health, there is fraud or criminal intent involved, and/or the authenticity/quality of the medicine cannot be assured. This differs from instances where unintentionally medicines are made substandard and do not meet the legally required quality specifications (e.g., such as an error in authorized manufacturing).[1] In these unintentional cases, legal principles of negligence and, if reckless or egregious, possible criminal sanctions may still apply. Yet for illicit activities and intentional fraud, a range of other remedial activities must also be explored to determine an appropriate regulatory and legal response. [p.5, ¶1]

REVIEWER 1 COMMENTS:

Major Compulsory Revisions:

1. I have no major compulsory revisions. However, on Page 8 it should be made clearer that WHO doesn't have any enforcement jurisdiction in countries. As mentioned, WHO is limited to providing information, suggestions and expertise if the resources are available.

We thank the reviewer for this important comment and clarification regarding the limitations of WHO in enforcement and reiterating its primary functions. We have amended the language as suggested below:

Several key international entities have attempted to address the global counterfeit medicines issue. These include WHO, UNODC, Interpol, and the World Customs Organization (“WCO”). Most notably, beginning in 1988, WHO has repeatedly issued resolutions and guidance, while also attempting to be actively engaged in developing policies, programs and governance activities (including its Good Governance for Medicines programme) in an attempt to ensure access to safe medicines and combating counterfeit drugs.[3, 31] However, it should be noted that WHO does not have enforcement capabilities, cannot specifically address criminal or law enforcement issues, and generally engages in technical capacity building if resources are available. These limitations hamper any attempted response to dangerous counterfeit medicines where the criminal element is involved. [p.8, ¶2]

Minor Revisions:

2. Bottom of page 5 estimates of the global market for counterfeit drugs mentions the
over used $75 billion. Suggest that the authors use other estimates for example the World Customs Organization estimates the falsified drug market is $200 billion. This will show the range and our lack of information on the topic.

We thank the reviewer for this comment and for suggesting the use of other estimates to show the wide range and lack of information we have on the global trade of counterfeit medicines. We have incorporated this suggestion below:

Available estimates have placed the global market for counterfeit medicines between $75-200 billion, indicating that this is a multibillion dollar illicit enterprise, but also highlighting the wide range and general lack of reliable information on the topic.[12,15] [p6, ¶1]

3. Recommend that that comments about operation Pangea by Interpol document the number of web sites closed. (The authors mentions millions of counterfeit drugs seized by operation Pangea but the paragraph topic is the internet. The number of internet site shut down should be mentioned.

We thank the reviewer for this comment and agree that the estimated number of Internet sites shut down would also provide the reader additional information/context to this enforcement effort. We have totaled all reported Operation Pangea website closures and included in the amended language below:

Addressing online counterfeit distribution using multi-sector efforts such as the International Criminal Police Organization’s (“Interpol”) enforcement action Operation Pangea I-VI has resulted in millions of counterfeit pill seizures and some 40,000 total websites shut down, but appears to have not stemmed the continued proliferation of illicit online pharmacies.[20, 27] [p7, ¶carryover paragraph]

Discretionary Revisions:

4. Last paragraph page six, first sentence needs clarifying--PSI collects information counterfeit, diverted and stolen pharmaceuticals, not just counterfeit. It is later explained but I believe it would be better if it were upfront in the paragraph.

We thank the reviewer for this important clarification and suggestion to introduce this information earlier in the paragraph. We have modified the language as suggested below:

Publicly available data collected by the Pharmaceutical Security Institute (“PSI”), a not-for-profit organization of pharmaceutical industry security directors collecting and analyzing information on global pharmaceutical crime (which includes in addition to counterfeit incidents, illegal pharmaceutical diversion, and theft), also shows increasing criminal activity: an alarming 77% overall global increase in incidents of pharmaceutical crime were verified from 2005-2011 (1,123 to 1,986 incidents) involving 532 different pharmaceutical products.[28, 29] PSI information is based on an incident-based reporting system, verified in a similar fashion to information collected by law enforcement agencies and is sourced from PSI pharmaceutical member and non-member companies, law enforcement agencies, healthcare/regulatory agencies, and open-source media reports. To be included, a counterfeit product, using WHO definitions, must be supported by factual information validated by a team of multilingual criminal analysts from PSI.[30] [p7, ¶1]
5. The article is not easy to understand mainly due to the use of acronyms and the many international organizations described. If one is not familiar with the area I believe it will be a difficult read. The table does help, but perhaps a diagram or flow chart of the groups recommended and their role in the proposed organization would help. Just a suggestion.

We thank the reviewer for this comment and agree that the article can be confusing for readers due to the large use of acronyms and many international organizations described. In addition to the table, we also have included in the manuscript a figure detailing the groups recommended and their role in the proposed governance structure. We more explicitly reference this figure and have also made some additions to improve its understandability below:

In order to move forward, the respective technical expertise, international legitimacy, financial and non-financial resources, and leveraging of existing partnership networks between these organizations must be coordinated to create a cohesive and transparent governance framework. Given UNODC’s emerging strengths as an open governance forum for broader stakeholder mobilization and its UN mandate through CCPCJ, a trilateral governance mechanism under the auspices of UNODC with active participation of WHO and Interpol should be established.[34] We propose the basic structure and primary roles of the organizations participating in this mechanism in Figure 1. [p12-carryover, ¶2-carryover]

Figure 1: Trilateral Working Group on Counterfeit Medicines
REVIEWER 2 COMMENTS:

1. The manuscript is well-written and the authors present convincing arguments for consolidating 3 reputable organizations into a trilateral mechanism. In order for this mechanism to be effective, emphasis on surveillance and the proper identification of a counterfeit should be made. Proper data collection is fundamental for justifying the appropriate action. But the focus of this paper is a review of what needs to be done and suggest that the technical/specific elements be the subject of another manuscript. In general, the manuscript is very comprehensive, and touches on all the elements required for the suggested mechanism to be effective.

   We thank the reviewer for their constructive and helpful comments and completely agree that an emphasis on surveillance and the proper identification of counterfeit medicines is crucial in any solution. We further agree that proper data collection must be a fundamental and priority component to inform policymaking and enforcement. In the below revised language, we further emphasize the need for investment in transparent and evidence-based surveillance and confirmation of counterfeit status for this issue. We also believe that this is a critical reason for continued engagement and participation of WHO give its expertise in this area. Thank you very much for this comment.

Most importantly, dangerous counterfeit medicines place all patients at risk, from developed to developing countries, formal and informal economy sectors, from rural clinics to tertiary care centers, and from resource-poor to high-income settings.[2, 11] Yet, global trafficking of counterfeit medicines is difficult to quantify, largely due to the criminal element of the trade and lack of adequate surveillance.[2, 3][p.5-carryover, ¶2-carryover]

... Importantly, WHO can assess and recommend measures to promote public health issues arising from dangerous counterfeit medicines and contribute specialized scientific and public health knowledge to this effort. WHO could then concentrate on core issues of improving safe medicines access, strengthening health systems for better surveillance, developing monitoring and evaluation protocols for sourcing/distributing safe drugs, strengthening domestic drug regulatory and pharmaceutical governance capacity, and collecting data and studying the epidemiology of counterfeit drugs to enhance UNODC and Interpol efforts. Paramount to this effort is the need for more accurate and reliable data on the prevalence of dangerous counterfeit medicines and surveillance and laboratory capacity for proper identification of dangerous counterfeit pharmaceuticals. Indeed, proper and robust data collection is fundamental for justifying appropriate regulatory, legal, and law enforcement action. Efforts could include enhancement of data collection under the WHO’s SSFFC Global Surveillance and Monitoring Project by harmonizing reporting fields and collecting information from a variety of sources (including drug regulatory, customs, and law enforcement authorities) to form a centralized database. This infrastructure would provide a better evidenced-base in determining the true scope of the global counterfeit medicines trade.[50][p16, ¶1]

Thank you for your consideration and constructive comments. We look forward to your comments regarding this revised manuscript.

Best wishes and regards,

Authors