April 2, 2015

Dear BMJ Editors:

Thank you for your provisional acceptance of the manuscript. Per your letter dated April 1, 2015, we respond to each request below:

Section 1: General

1. Online and print publication: we accept publication of both online and the PICO summary in print. The PICO was provided to you previously.

Section 2: Editors’ comments

**BMJ Comment 1**: “…in the discussion there is a point: ‘no sponsor chose to release a CRL included in this study, although nothing prevents one from doing so.’ Please add here as well about the onus on the FDA to increase transparency.”

**Authors’ response:** The discussion section (page 15, first full paragraph) already includes FDA disclosure of the CRLs as one of three policy options, alongside sponsor release of the CRL:

> Three potential approaches to reducing the gap between the information provided in CRLs and that provided in PRs are: 1. Sponsors could release the CRLs themselves, although they did not choose to do so for any of the CRLs in this study; 2) Sponsors could release more complete PRs; and 3) **FDA could itself make the CRLs public, although this would likely require a change in FDA’s regulations.** A thorough discussion of these options is beyond the scope of this paper. (Emphasis added)

Accordingly, we believe no such addition is needed.

**BMJ Comment 2:** The paper continues to have several abbreviations which make for a tedious read. We would prefer if you expand these abbreviations.

**Authors’ response:** We expanded the following abbreviations – New Molecular Entity (NME); Center for Drug Evaluation and Research (CDER); Electronic Data Gathering, Analysis, and Retrieval (EDGAR); International Conference on Harmonisation (ICH); and Document Archiving, Reporting, and Regulatory Tracking System (DARRTS), but retained other abbreviations that were more common or more widely recognized.

**BMJ Comment 3:** We wonder if it might be possible for you to share an example of a CRL identifying the statements and classifying into domains and sub-domains
Authors’ response: Unfortunately, we are unable to share a complete response letter given current U.S. legal prohibitions against such disclosure.

BMJ Comment 4: In the conclusions, it is written: “FDA will consider these issues as it charts its future policies.” We don't see the need for this declaration and it may not fit with the objective of the research paper.

Authors’ response: The sentence has been deleted.

Section 3: Layout/additional information

1. Title: We have modified the title to include the study design (cross-sectional study).
2. All other layout issues have been addressed in the previous revisions and additional information (authorship/copyright/funding statements, etc.) has been provided.

Sincerely,

Peter Lurie, MD, MPH
Associate Commissioner for Public Health Strategy and Analysis
U.S. Food and Drug Administration