Reviewer's report

Title: A Pipeline To Extract Drug-Adverse Event Pairs From Multiple Data Sources

Version: 2 Date: 11 September 2013

Reviewer: Gianluca Trifiro

Reviewer's report:

I read with interest this paper, which is aimed at describing a pipeline for drug safety signal detection. The research topic is highly relevant. As follows, some major and minor criticisms:

Major revisions

1. Authors should pay carefully attention to the terminology being used. In particular, this study cannot in no way identify adverse drug reaction (implying causality assessment) but rather adverse event (based only on statistical association). I suggest reconsidering the tile and the objective of the pipeline. Moreover, correct definition of safety signal should be taken into account. Signal concerns a new or incompletely documented drug-adverse event association. Thus, by definition, a known-adverse event association should not be considered as signal if found through the pipeline.


3. Objective of the study should be more clearly described

4. Methods: what is the rationale for choosing the study drugs a part from being cited in other papers? Are then results generalizable to other drugs belonging to different drug classes? Authors should comment on it. In addition, the types of medication should be revised: carbamazepine is antiepileptic drug and not antipsychotic either antidepressant; In would distinguish between antidepressants (trazodone, and paroxetine) and antipsychotics (olanzapine and ziprasidone; why not including any old typical antipsychotics which are in the market since longer period?)

5. Results: why results has been reported only for bupropion? Authors should describe results for all the study drugs trying to use visualization which may summarize results. The disagreement between different sources (as well as
additional value of each source) should be better analysed and discussed. In general results should be described using more quantitative and measurable parameters.

6. Table 1. Some important safety concern are not listed: a) stroke and all-cause mortality for olanzapine; b) sexual disorders for paroxetine. The list of safety concerns for each drug should be revised by experts in pharmacovigilance. Why no know AE has been reported for orphine?

Minor revisions

1. Introduction: replace “correlation between drugs…” with “causal association between drugs…”

2. Introduction: ADAMS does not fully relate to the topic


5. Methods: indicate from which section of label of buproprion the information on safety have been extracted

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests