

## PubMed ‘Early Alerts’: A Pilot Study to Support Prospective Detection of Emerging Adverse Drug Events

Alfred Sorbello<sup>1</sup>, DO, MPH; Anna Ripple<sup>2</sup>, MLS; Olivier Bodenreider<sup>2</sup>, MD, PhD

<sup>1</sup>US Food and Drug Administration, Center for Drug Evaluation and Research, 10903 New Hampshire Avenue, Silver Spring, MD 20993, USA. <sup>2</sup>Lister Hill National Center for Biomedical Communications, U.S. National Library of Medicine, 8600 Rockville Pike, Bethesda, MD 20894, USA.

**Background:** The FDA traditionally monitors the safety of marketed drugs by analyzing reports submitted by manufacturers and consumers to the FDA Adverse Event Reporting System (FAERS). In order to enhance prospective detection of emerging adverse drug events (ADE), we investigated leveraging existing PubMed “MyNCBI” functionalities and searching resources to survey the biomedical literature for the latest published safety information in the use case of the new oral hepatitis C drugs.

**Methods:** Using PubMed “MyNCBI” cubby functionality, we established a search strategy designed to retrieve citations most recently added to PubMed and provide automated weekly emails (PubMed ‘Early Alerts’) with abstracts and links to available full text citations. The search strategy (Table 1) includes three criteria: (1) Drugs of interest; (2) Citation scope: citations from MEDLINE journals, as soon as they are entered in PubMed (prior to indexing); (3) Time Period: week of interest.

**Table 1: PubMed Search Strategy**

("drug A"[all fields] OR "drug B"[all fields] OR ...)	<i>Drugs of interest conjoined with the Boolean operator OR and searched in all fields including the Title, Abstract, and other terms (including Author Keywords) fields</i>
AND	
((publisher[sb] NOT pubstatusnihms[All Fields] NOT pubstatuspmcsd[All Fields] NOT pmcbook[All Fields]) OR inprocess[sb])	<i>Includes citations supplied by publishers that are not yet indexed and have not completed quality control, and includes citations in the review process; Excludes citations from non-MEDLINE journals (author manuscript or publisher-supplied citation submitted to PMC under the NIH Public Access Policy, book or book chapter citations available on NCBI bookshelf)</i>
AND	
"2015/Month/Day 15.00" [MHDA]:"2015/Month/7 Days Later 15.00" [MHDA])	<i>Restricts the search to a 7-day time period; MHDA is automatically added by PubMed for each weekly search—this is one of the parameters that can be set when stored searches are set up in the NCBI cubby.</i>

**Results:** A typical weekly PubMed ‘Early Alerts’ email delivery consists of 12-15 citations from domestic and international journals spanning 5-8 oral hepatitis C drugs of interest. The citations reflect human, animal, and *in vitro* research from the US and other countries with varied publication types, including reviews, letters, clinical trial reports, pharmacokinetic studies, case reports, and observational studies. Our search strategy is designed for recall. Its precision can be increased significantly by requiring the presence of specific words in the titles or abstracts (“safety”, “toxicity”, “adverse”, and “tolerability”).

**Conclusions:** By leveraging existing PubMed “MyNCBI” functionalities and searching resources, we can more efficiently canvass across a broad range of journals and publication types in PubMed for the latest drug safety data. This approach lessens reliance on time-consuming and often inefficient ad hoc searches, and it complements traditional approaches to finding relevant safety information on drugs of interest. Evaluation by FDA Medical Officers and Safety Evaluators indicates that the PubMed ‘Early Alerts’ complements their efforts to discover emerging ADEs as part of their regulatory review activities.

**Acknowledgements:** Funding support received from the FDA/CDER Critical Path Program and the Intramural Research Program, NIH, National Library of Medicine. **Disclaimer:** The views expressed are those of the authors and do not necessarily represent the views of the US FDA, the NIH, or the US Government.