Signal Detection in Small Safety Databases

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On September 29, 2010, the FDA published a new final rule amending the IND safety reporting requirements under 21 CFR Part 312 to improve safety monitoring in clinical trials. Under this new regulation, effective March 28, 2011, all trials involving an investigational new drug (IND) application are held to more stringent analysis and reporting guidelines for adverse events. One specific requirement of the regulation is that sponsors should have a systematic approach in place for safety surveillance of their entire safety database. This signal detection process extends throughout the investigational lifetime of a drug and is designed to determine if the incidence any adverse events associated with a study drug is higher than their incidence associated with other drugs or placebos. It is intended to aid in detection of safety signals present at low frequencies that may escape detection by looking solely at individual trials. Several methods for analyzing large safety datasets aggregated across multiple studies have been published, but publications regarding signal detection in smaller safety databases are scarce.

The NIAID, NIDDK, and JDRH -fund the Immune Tolerance Network (ITN) which includes a portfolio of several smaller clinical trials, many of which are under INDs held by DAIT, NIAID or by the investigators. To comply with the new regulations, attempts were made to extend the methods for analyzing large databases for use on much smaller scale analyses of single studies or groups of studies. This poster will focus on the feasibility of extrapolating a variety of methods used on large databases to smaller studies. We will also display graphical tools developed to enhance the evaluation of possible adverse event signals and discuss additional ways to group safety data for further analysis.

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