MAED Tool: FDA-Developed Tool for Adverse Event Data Signal Detection in Clinical Safety Analysis

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Background and Overview
MAED, one of the earliest tools developed by the Computational Science Center, is a web-based SAS application running behind a Java GUI for analysis of adverse events (AEs). MAED stands for MedDRA-based Adverse Event Diagnostics. Medical and statistical reviewers use MAED as an aide in safety signal detection, using adverse event (AE) data coded to the Medical Dictionary of Regulatory Activities (MedDRA). It is assumed that AEs are coded using MedDRA version 6.0 or later. Either preferred terms (PTs) or prefer term codes can be used for analysis.

Safety signal detection assessments include assessment of 1) individual reported AE terms by level of the MedDRA hierarchy or SMQ (See Table 1). Analyses by level of the MedDRA hierarchy or SMQ class (narrow-, broad-scope, or algorithmic) are summarized in a of report of frequency and risk estimators between comparison groups (e.g. test drug vs. placebo). MAED Tool is based on the basic statistics with Multiple Risk Estimators including: Odds ratio (OR), Risk difference (RD), Relative risk (RR), P-value for all MedDRA terms (complete hierarchy) and all levels of SMQ.

This report provides reviewers with automated analyses by level of the MedDRA hierarchy or SMQ (See Table 1). Analyses by level of the MedDRA hierarchy or SMQ class (narrow-, broad-scope, or algorithmic) are summarized in a of report of frequency and risk estimators between comparison groups (e.g. test drug vs. placebo). MAED Tool is based on the basic statistics with Multiple Risk Estimators including: Odds ratio (OR), Risk difference (RD), Relative risk (RR), P-value for all MedDRA terms (complete hierarchy) and all levels of SMQ.

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The above report can be easily obtained following MAED launch through a web browser. The input data for these analyses are end-user supplied and can be clinical trial datasets or post-marketing datasets. Items in the red box indicate SMQs options

Methodology and Maintenance
The successful deployment, maintenance and upgrading of MAED Tool is due to a number of factors; it is the single tool that is served by a server environment maintained by the OCS, the architecture design is clear and scalable, project management is run using Agile methodology and uses JIRA as tracking system; regular releases include bug fixes and security updates

Given updates of the MedDRA dictionary, source code management is maintained and reviewed in SonarCube as a standard process. MAED Tool updates MedDRA dictionary twice a year and also updates analysis algorithm for the algorithmic SMQ accordingly. The use of Puppet Automated Deployment Tool reduces risk and speeds deployment. EPLC and Application configuration are well maintained and documented. Since 2015 when metrics were first collected, the number of users (Figure 1) and frequency of analyses (Figure 2) per user have increased.

What's next?
MAED is a powerful signal detection tool widely adopted by reviewers in the Office of New Drugs, Office of Surveillance and Epidemiology, and the Office of biostatistics at CDER. To enable increased functionality, OCS is looking into further improvements to the end-user experience. There include incorporation of FDA internal review-based Customized MedDRA Query, broadening use in postmarketing use by pilot testing using FAERS data and analytic approaches used for postmarket reports. To enable this scale up of use, OCS needs to add support to existing OIMT governance, more Agile-friendly and explore opportunities to further improve the tool. The successful deployment and maintenance of MAED over 10 years serves as a model for enterprise tool development and maintenance.

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