Customizing a Commercial Rule Base for Detecting Drug-Drug Interactions

Ervina Resetar[a], MS, Richard M. Reichley[b], RPh, Laura A. Noirot[a], BS, Wm Claiborne Dunagan[a,b], MD, and Thomas C. Bailey[a, b], MD

[a]Washington University School of Medicine, Department of Internal Medicine, St. Louis, MO
[b]BJC Healthcare, Center for HealthCare Quality and Effectiveness, St. Louis, MO

Abstract
We developed and implemented an adverse drug event system (PharmADE) that detects potentially dangerous drug combinations using a commercial rule base. While commercial rule bases can be useful for rapid deployment of a safety net to screen for drug-drug interactions, they sometimes do not provide the desired rule sensitivity. We implemented methods for enhancing commercial drug-drug interaction rules while preserving the original rule base architecture for easy and low cost maintenance.

Introduction
Adverse Drug Events (ADEs) occur in up to 6.5 % of hospitalized patients.[1] Dosage errors in prescribing are one of the most common causes of ADEs.[2] Commercial rule bases can be used to rapidly deploy systems to screen large numbers of medication orders for potentially dangerous drug combinations. The effectiveness of a commercial rule base can be enhanced to provide desired rule sensitivity. We customized commercial rules for drug-drug interactions by implementing concepts of 'time between interacting medications' and 'medication sequence' to achieve desired rule sensitivity.

Methods
We implemented a commercial rule base (Cerner Multum, Kansas City, MO) with drug-drug interaction rules at Barnes Jewish Hospital (BJH), a university teaching hospital, and two community hospitals in the BJC HealthCare System. The vendor's rule base consisted of nearly 77,000 drug-drug interaction rules classified by severity that ranks from 1 being minor, to 3 being major drug interaction. Although the vendor's rule base provides a 'drug-interaction elimination half-life' value for each drug, there is a wide inter-patient variation for these values especially for patients with renal and hepatic impairment. Therefore, we implemented the concepts of 'time between medication orders' and 'medication order sequence' to provide an adequate cautious interval following discontinuation of certain medications during which medication may still be part of patient's active drug regimen.

Results
Implementation of the 'time between medication' concept provided an interval following discontinuation of a medication during which starting another medication might result in an adverse event (e.g. MAOI and SSRIs). The 'medication sequence' allowed further customization of rules that use the time between medications concept where the sequence of medications is relevant. By implementing the two concepts, we were able to customize 146 rules from the vendor's rule base. Due to the overwhelming alert volume produced by activating all vendor provided drug-drug interaction rules, we first activated only those rules that were in place prior to the commercial rule base implementation. The majority of these active rules belong to the major drug interaction severity group. Our domain experts are currently analyzing performance of the remaining 7,000 + major drug-drug interaction rules to determine which ones should be activated.

Table 1. Drug-drug Interaction Rules by Severity

Interaction Severity*	Rules	Active Rules by Hospital		
		A	B	C
1	8246	16	16	16
2	60833	73	74	74
3	7902	490	552	550

* Severity scale provided by vendor
1 – minor drug interaction, 2 – moderate drug interaction,
3 – major drug interaction

Conclusions
Implementing drug-drug interactions rules directly from a commercial rule base usually does not provide the desired rule sensitivity. With relatively simple customization techniques, additional rule functionalities can be gained while preserving the original rule base architecture for easy updates and maintenance.

References
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[2] Leape LL, Bates DW, Cullen DJ, et al. Systems analysis of adverse drug events. JAMA. 1995;274:35-43.