Safety Works at GlaxoSmithKline

BY ALISSA POH

Several years ago, recognizing the need for more efficient access to new sources of safety information, GlaxoSmithKline (GSK) joined forces with ProSanos Corporation in developing SÆfetyWorks, a web-based software system for drug surveillance that leverages observational databases, namely health care insurance claims and electronic health records, as rich sources of safety information. It simultaneously interrogates multiple databases, allowing pharmacovigilance professionals to more accurately compare the information therein with data from traditional sources like adverse event reports or epidemiological studies.

"These databases have three things in common: patients, prescriptions [representing drug exposures], and diagnoses [representing conditions]," says Stephanie Reisinger, senior VP for product development at ProSanos. "So the big-picture idea here is organizing data related to these three factors, and looking for a relationship between when a patient takes a drug and a condition that occurs afterwards, temporally to that prescription."

It's a timely development, since interest in utilizing observational data is growing within the drug safety community. But systematic approaches toward accomplishing this goal have, to date, been few and far between. Prior to SÆfetyWorks, GSK scientists wishing to analyze observational databases "did it kind of piecemeal," says Gregory Powell, manager of global clinical safety and pharmacovigilance at GSK and team leader for this project, noting it was "very expensive and time-consuming, it could take six to 12 months. Now we can combine as many analyses as we want, so the incremental cost is minimal, which wasn't the case before."

Multi-Question Approach

"Not only were previous analyses costly, people would just ask one question per database," says Edward Pattishall, GSK's VP for clinical safety. "SÆfetyWorks normalizes data from multiple sources such that you can ask the same safety question of different databases in real time. If you get the same answer with multiple databases, you have more confidence that there's an issue."

GSK scientists first contemplated technologies for manipulating observational data back in 2005. Two years later, the company engaged ProSanos to collaboratively formulate their plan into software. As Reisinger puts it: "GSK developed a proof-of-concept for their idea. We took that and turned it into something their safety scientists could touch, sign on to, and make work."

The project team faced two key hurdles early on: drug and condition vocabularies had to be normalized, and inconsistent data storage formats standardized to enable systematic identification of potential drug safety issues.

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For the first, the group selected two reference ontologies—MedDRA for describing conditions and SNOMED CT for describing drugs—to which all observational databases with their disparate vocabularies and coding schemes were converted. They also developed a "person-time analysis data model"—built on standard concepts found within all observational databases—for the purpose of addressing the second challenge.

Advances in technological know-how, not to mention increased storage capabilities at lower cost, made SÆfetyWorks feasible where, even a few years earlier, it wouldn't have been cost effective. "You could say the stars aligned in our favor, given that we're now able to manipulate terabytes of data," Powell says.

SÆfetyWorks users have three tools for rapidly analyzing observational data. They can use the Natural History module to better understand drugs and diseases by exploring—across multiple databases—gender breakdown, age range, and average length of drug exposure, among other statistics. The Screening module is essentially data mining; a broad-reaching look at all conditions occurring in a patient, without

Stephanie Reisinger, ProSanos Corp.; Ed Pattishall and Gregory Powell, GlaxoSmithKline

focusing on any particulars. Both modules produce information in under an hour for small cohorts (thousands of patients), and less than a day for large cohorts (millions of patients). On the other hand, the Risk Estimation module zooms in on suspicious indications, letting users explore these and estimate the potential risk.

"We've done a lot of validation work, looking at examples of past safety issues in published literature and verifying that our results were similar to these studies," Powell says. For example, the group used SÆfetyWorks to retrospectively evaluate pergolide (Permax), FDA-approved for Parkinson's disease in 1988, but withdrawn nine years later over concerns about leaky cardiac valves. In a case study conducted in less than two days, they found that a safety signal for pergolide first surfaced in 2001, and further evidence connecting the drug with valve disease appeared by 2002. They've also explored fracture risk in patients taking antidepressants (as a drug class). "We found a small but probably real risk, and we'll need to alert [antidepressant] prescribers and put it on the labels," Pattishall says.

It took about a year for SÆfetyWorks to be fleshed out. Soon after its implementation at GSK in 2008, the collaborators decided that their new system was ready to be spotlighted in this year's Best Practices. ProSanos also acquired marketing rights to the software, and several regulatory agencies have since expressed interest in possibly making use of SÆfetyWorks, among them the FDA.

The SÆfetyWorks team is hardly resting on its laurels. Besides insurance claims and health records, they're in the process of incorporating laboratory data for patients, and information on procedures performed, into the system. Pattishall says this will allow a better definition of both patient populations and disease outcomes that occur during medications. They're also considering a European database, to more accurately reflect medical practices in other regions.

"We put a significant amount of hard work into developing SÆfetyWorks, so it's gratifying that *Bio•IT World* recognized this," Powell says. And beyond such validation, SÆfetyWorks' profile should gain in visibility. "Hopefully there'll be more users," Pattishall adds, "as this will more rapidly improve drug safety in patients, which is our main interest." •