

McClellan Envisions Lifecycle Approach to Drug Surveillance

By Catherine Varmazis

June 23, 2008 | BOSTON | Rising drug development costs and public frustration about major drug recalls highlight the need for an active, post-market drug surveillance system, Mark McClellan told attendees at the recent Post-Approval Summit.*

McClellan, former head of the FDA and currently chairman of the Reagan-Udall Foundation, said declining success rates in Phase III clinical trials are not always related to a drug's effectiveness. Rather, he said, they can be attributed to the costs of following up on questions about the safety of drugs in particular settings, such as tracking down rare side effects, determining the effects of long-term use, and concerns about off-label use.

Citing legislative changes, public expectations, and technological gains, McClellan said, "it's going to be a new world" with reauthorization of the FDA Amendments Act (AA) last fall—one in which lots more data will be available, and clinical trials will be more transparent. Active post-market surveillance is critical for the development of personalized medicine, he said, and if done right, will be "an opportunity to move away from current bifurcated, costly and time-consuming pre-market/post-market process" to a more continuous "improvement lifecycle approach."

The Reagan-Udall Foundation that McClellan heads—a private/public organization chartered by Congress in the AA—is one example of the kind of private/public partnerships that will play a major role in this "new era" of active surveillance.

The current practice of characterizing safety issues in Phase III will be replaced by a population-based approach in which drugs are monitored while in active, long-term use, McClellan predicted. To accomplish that, the AA envisions the FDA and its private sector partners having the capacity to do active surveillance on a population of 25 million Americans by 2010 and on 100 million by 2012. "Such an approach is very different from the current system based on 'spontaneous adverse events report' to manufacturers and one-off studies," he said.

Key elements in such a system of post-market active surveillance include:

The ability to aggregate data: Existing separate databases have to be connected in a HIPAA-compliant way using distributed networks. That way, individual, identifiable patient data stays behind the firewall of each organization that owns that data and only key data about the drug itself is aggregated. This approach requires consistent methods of gathering data and reporting on findings.

Better biostatistical methods to enable adaptive trials, randomized trials, and better signal-extraction techniques. "With a dataset of 100 million people, the challenge is not to detect a signal, but to determine whether it is clinically meaningful," said McClellan. This

requires better methods for identifying unusual trends and for following up on apparent cases of adverse events to confirm that they're real.

Better communication strategy: "We have to find better ways to talk to the public about what we know and why we don't know more, and what steps are under way to fix problem," said McClellan. The FDA should clearly inform the public about what it is doing to resolve ambiguous issues.

Better governance: There needs to be broad-based and transparent approach, not only a government-run approach because most data will come from the private sector.

Sustainability: Development of consistent data strategy across all the nodes of the system to pull data together and do the analysis. "We should be able to learn a lot more without necessarily spending a lot more. It's a different way of spending money – a redirection – and we have not yet worked out a way to do that," concluded McClellan.

*May 14-15, 2008, at the Harvard Medical School.