

Pharmacovigilance and Drug Safety Compliance Update

**GAP Analysis: How We Get to
Where We Want to Be**

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Core PV Concepts

- Risk identification, collection of information
- Risk assessment, characterization of information
- Risk mitigation, communication or other action based on assessment
- Address known risks, potential risks, and missing information

Sources of PV Gaps

- Resources
 - Government PV resources have expanded via increased appropriations and an increase in the amount and dedication of user fees for safety, but resources are still limited
 - Private sector resources for IT and other PV investments are limited by reimbursement policies and market competition
 - The “science of safety” and its limitations

Sources of PV Gaps (continued)

- Authority and standards
 - FDAAA expanded FDA's authority to obtain PV information
 - FDA has explicit authority to order post approval studies or clinical trials to assess a known serious risk, assess signals of a serious risk, or to identify an unexpected serious risk when available data indicates the potential for a serious risk. Determination must be based on new information. Note that “new information can come from a variety of sources, including sources other than the sponsor. FDA has authority to order labeling changes.
 - REMS authority to require “elements to assure safe use”
 - Clinical trials data bank expanded, other information must be submitted, much of which is assessed and made public
 - Robust active surveillance

Sources of PV Gaps (continued)

- Guidance and standards for improving PV will evolve as science of what information is most useful and the IT to collect it improve over time
- Priorities and policies
 - Product “life cycle”
 - limitations of premarket trials
 - limitations of post market data
 - PV is a greater priority than ever before, but improvements will take time
 - PV will always be a work in progress, the “science of safety” is still evolving
 - PV “tensions” include liability, privacy, transparency/publicity, patient/provider culture
 - PV harmonization incomplete

Collection of Information

- Pharmacogenetics, IT, harmonization, and other factors are changing what is known or knowable about drugs
- There can be tension between the goal of greater “transparency” and access to PV information. Issues of confidentiality, liability, resources, and other factors can affect the quality and uniformity of information collected
- There is no apparent consensus on how much of what kind of information is needed to optimize PV

Characterization of Information

- Characterization of information is a work in progress, FDAAA's reports and studies reflect challenges in risk assessment and communication
- “Decisions about how to address a safety concern are often a matter of judgment, about which reasonable persons with relevant expertise may disagree.” (FDA Guidance, Drug Safety Information—FDA's Communication to the Public
- FDA focus on improving PV science, communication, and operations and management

The Future of Drug Safety (IOM) and FDAAA

- The Institute of Medicine's Report, "The Future of Drug Safety," identified a number of drug safety issues and provided recommendations
- Many of the IOM's recommendations are reflected in FDAAA
- FDAAA implementation will be a key to identifying and filling PV gaps

PV Gaps and FDAAA

- Office of Drug Safety is explicitly part of new drug review process
- Emphasis on product life cycle and recognition of limitations of pre-market clinical trials reflected in post-market authorities, resources, and responsibilities
- Greater allocations of resources, both appropriations and user fees, to drug safety
- Safety goals included in PDUFA goals
- Increase the amount and sophistication of active surveillance
- Public/private partnerships to make drug safety more effective and efficient

PV Gaps and FDAAA (continued)

- Expand FDA's drug safety expertise
- Increase FDA research on drug safety issues and establish Office of Chief Scientist
- Increase advisory committee input and reduce committee member conflicts of interest
- Expand posting of clinical trial and other data used for FDA product review
- Assess and make public post market study results
- Increase FDA authority to require studies or trials in response to safety signals, time limited dispute resolution
- Research and reports on risk communication

PV Gaps and FDAAA, Looking Ahead

- “[T]he Commissioner of Food and Drugs shall submit to the Congress a report on how best to communicate to the public the risks and benefits of new drugs and the role of the risk evaluation and mitigation strategy in assessing such risks and benefits” (FDAAA, section 904).
- “[T]he Secretary shall report to the Congress on the ways in which the Secretary has used the active postmarket risk identification and analysis system...to identify specific drug safety signals and to better understand the outcomes associated with drugs marketed in the United States” (FDAAA, section 905(c)).
- “[T]he Secretary shall improve transparency of information about drugs...by maintaining an Internet Web site that (A) provides links to drug safety information...and (B) improves communication of drug safety information to patients and providers” (FDAAA, section 915).

PV Gaps and FDAAA, Looking Ahead (continued)

- The Advisory Committee on Risk Communication shall advise the Commissioner on “methods to effectively communicate risks associated with the products regulated by the FDA (FDAAA, section 917). The Advisory Committee on Risk Communication shall perform regular reviews and evaluations to facilitate the dispensing of risk communication information to patients and providers (FDAAA, section 915).
- The Secretary shall report to Congress on procedures and processes for addressing ongoing post market safety issues (FDAAA, section 921).
- The Secretary shall conduct a pilot program to ensure that clinical trial information is non-promotional and is not false or misleading.

PV Gaps and FDAAA, Looking Ahead (continued)

- The Office of Chief Scientist shall “develop postmarket safety performance measures that are as measurable and rigorous as the ones already developed for premarket review” (FDAAA, section 602).
- The Reagan Udall Foundation shall “identify unmet needs in the development, manufacture, and evaluation of the safety and effectiveness, including post approval, of drugs and other products regulated by FDA (FDAAA, section 601).