



DIA 2014 50th Annual Meeting

Celebrate the Past – Invent the Future

June 15 – 19, San Diego (CA) Convention Center

Session 319 – Signal Detection: Challenges & Strategic Aspects

Signal Detection: Challenges & Strategic Aspects explored three different aspects of signal detection that significantly influence the overall quality of pharmacovigilance for a product.

Dr. Michael J. Klepper (President and Founder, Drug Safety Navigator, LLC) discussed the critical role of proper identification and assessment of premarketing signals in maintaining a favorable benefit-risk profile throughout a product's life cycle. He specifically emphasized that because there are many instances of false signals, a new signal does not mean that there is a new risk. However, one unrecognized clinically significant safety signal is all it takes to raise doubts over a drug's future.

Dr. Klepper presented additional opportunities for identifying premarketing signals and stressed paying attention to nonclinical data, clinical study reports and ongoing safety review. He categorized approaches to signal detection into pre-specified (data that reach a predetermined threshold) and random (for example, a cluster of cases) and signal identification/verification processes based on the type of adverse reaction. He emphasized that signal detection is very challenging because many signals are not pre-specified, are often subjective and are not

always clinically relevant. Problems such as limited exposure, incomplete case information, poorly written narratives or limited access to safety data can make this process even more complex, although many of these problems can be avoided. Determining causality and clinical significance require a standardized approach; Dr. Klepper provided many valuable examples of such an approach from his professional experience. One of the key points he shared is the need for committed, ongoing safety review as *“in the fields of observation, chance favours only those minds that have been prepared”* (Louis Pasteur).

Stella Stergiopoulos (Senior Project Manager, Tufts Center for the Study of Drug Development) shared her research as well as her perspective on the optimization of practices and systems for reporting and tracking drug-related adverse events in ambulatory and institutional settings. She first introduced the Tufts Center for the Study of Drug Development (TCSDD) as an independent, academic group focusing on drug development, scientific, regulatory, economic and management policy. She then surveyed the regulatory background for adverse drug event reporting and explained current trends for signal detection.

Data on the strengths and limitations of the MedWatch Program, derived from a Tufts CSDD study that analyzed over 10 million adverse event reports for their completeness and accuracy, indicated that although FDA upgrades to the MedWatch reporting system are delivering improvements to information accuracy, additional improvements in adverse event reporting from the institutional setting may be required. She concluded by overviewing a current CSDD study on mapping the process of adverse event reporting.

Dr. Alan Hochberg (Sr. Process Development Leader, F. Hoffman-La Roche Ltd.) shared his perspective on the current trend of stakeholders publishing pharmacovigilance data and safety signals; this array of stakeholders includes academic institutions, insurers, nonprofits, and web businesses, in addition to sponsors and regulators. The process of signal detection has undergone tremendous change in recent years. It was traditionally a mandated industry responsibility, while programs established at regulatory agencies not only varied in methodology and priority but also in disclosing their methodologies and priorities. Today, signal detection among regulatory agencies has experienced an evident move towards a more proactive and transparent process. Dr Hochberg provided an example of FDA-EMA assessment of pancreatic safety of incretin-based drugs, compared strengths and weaknesses of signal detection at academic institutions, discussed particularities of signals raised by payers and lawyers, and elaborated on the emerging involvement of social media in the signal detection process. He proposed that new ways of approaching signal detection offer opportunities for early and independent identification and communication of safety risks, while acknowledging the risk of discouraging patient use of effective treatments based on premature or faulty communication. He also recognized an unmet need for reconciliation of pronouncements, accounting for biases and for variations in the quality of evidence, and concluded by posing the critical question: Who can meet this need?

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