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FDA's 2021 Focus Areas Of Regulatory Science: 5 Trends To Watch

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One can easily argue that we have seen more innovation in the pharmaceutical industry in the last decade than in the past 50 years. The tools we use today to characterize and construct drug therapies, from next-generation gene sequencing technologies to CRISPR/Cas9, give us unprecedented capabilities to identify and treat new disease states. However, these technologies would not have been so influential in the absence of a regulatory framework within which to apply them. The FDA regulates the largest pharmaceutical market in the world and, as such, sets the bar suitably high for drug sponsors to demonstrate safety and efficacy.

In 2020, the FDA recognized that a new approach was required to keep pace with the rapid evolution of science and technology driving drug development, and it released the report Advancing Regulatory Science at FDA: Focus Areas of Regulatory Science (FARS) early in 2021 to identify and communicate areas requiring continued targeted investment. The acronym is apt, as the report is remarkably far reaching. Across the myriad of focus areas of the report's major FDA Strategic Initiatives (Public Health Preparedness and Response, Increasing Choice and Competition through Innovation, Unleashing the Power of Data, and Empowering Patients and Consumers), five key elements deserve our attention.

1. Patient-Centricity And Real-World Evidence

The COVID pandemic provided the push needed for telemedicine to get a foothold in modern healthcare standard of care. This crisis has not only proven the viability of telemedicine but has also reinforced the notion of patients managing their own health through the use of digital health solutions and patient portals where they can keep tabs on their own care and treatment. Improving the lives of patients requires a deep understanding of their medical conditions, their experiences, needs, and priorities. Patient-centricity can be described as "putting the patient first in an open and sustained engagement of the patient to respectfully and compassionately achieve the best experience and outcome for that person and their family." With a renewed emphasis on education co-creation, information access, and transparency, the FDA has embraced the era of patient-centricity to regularly engage consumers in patient listening sessions and patient-focused drug development public meetings.

Real-world data (RWD) are data relating to a patient's health status and/or the delivery of healthcare routinely collected from a variety of sources. Examples of RWD include data derived from electronic health records (EHRs), administrative claims, registries, patient-generated data, and data gathered from mobile devices and other digital health technologies. Real-world evidence (RWE) refers to clinical evidence about the usage, potential benefits, or risks of an FDA-regulated product derived from analysis of RWD. The FDA is committed to exploring the use of RWE in regulatory decision-making, including providing fit-for-purpose and clinically meaningful information about the safety and effectiveness of medical products. Support for many RWE initiatives includes funding a demonstration project known as RCT-DUPLICATE (Randomized, Controlled Trials Duplicated Using Prospective Longitudinal Insurance Claims: Applying Techniques of Epidemiology). The RCT-DUPLICATE initiative attempts to duplicate the results of recently completed clinical trials relevant to regulatory decision-making using RWE, based on health insurance claims data.

A key concept of patient-centricity was included in the 21st Century Cures Act, which introduced clinical outcome assessments (COAs). COAs capture how patients feel and function by measuring a patient's symptoms, mental state, effects of the disease or condition. Patient interviews and surveys are used to determine how messaging, labeling statements, and therapeutic claims affect patients' and consumers' understanding of their disease state and treatment as well as the patient's decision making.

2. Biomarker Research

One challenge drug developers have encountered is to define the mode and mechanism of action, especially in the rapidly expanding area of cell and gene therapy. In many cases, the ability to identify biomarkers that support the putative mechanism of action is the *only* path to establishing a defensible potency matrix and quality assurance argument.

Biomarkers can also play a critical role in bridging non-clinical results to clinical research. That is why the FDA and the National Institutes of Health (NIH) are working together to advance biomarker research by promoting consistent biomarker terms and concepts. A three-step qualification process for new biomarkers requires a letter of intent for the qualification of a development tool, a qualification plan, and a qualification package comprising the approach for defining the biomarker.

3. AI And Computer Modeling

The FDA has applied machine learning in a practical initiative to leverage artificial intelligence that looks for data anomalies in the agency's monitoring programs and to predict submission timing as a way to improve the efficiency of reviewing regulatory submissions.

The agency is encouraging the application of computer modeling as part of the product development life cycle. Model-informed product development (MIPD) aims to integrate information from diverse data sources to help relieve uncertainty and lower failure rates and to develop information that cannot, or would not, be generated experimentally. MIPD encompasses model-informed drug development (MIDD), an approach that involves developing and applying exposure-based biological and statistical models derived from preclinical and clinical data sources to inform drug development or regulatory decision-making.

Computer modeling can inform researchers on the efficiency of clinical trial designs, providing evidence for efficacy, product performance, and safety predictions. The willingness of the agency to stray from a classical clinical trial design is a big acknowledgement that alternative approaches may be equally effective in demonstrating safety and efficacy.

4. Advanced Manufacturing

One by-product of the COVID-19 pandemic was that it exposed many nations' dependence on external suppliers for chemical precursors, active pharmaceutical ingredients (APIs), and critical drug therapies. In response, the FDA has renewed its support for advanced manufacturing technologies. *Advanced manufacturing* is a collective term for innovatively applied or new medical product manufacturing technologies and processes that can improve quality, enhance efficiency, address shortages of medical products, or speed time-to-market. Advanced manufacturing techniques being applied to FDA-regulated medical products include additive manufacturing (also known as 3D printing), continuous manufacturing, modularization, and "smart" manufacturing. There are examples across all medical product areas that include continuous manufacturing and modularization. "Smart" manufacturing concepts use automation, digitization, and artificial intelligence to streamline production methods, collect process control data, and ultimately use algorithms to adaptively control or make decisions about production or release. The FDA's emphasis on advanced manufacturing — in particular, continuous manufacturing — is a major driver behind the resurgence of onshoring initiatives within the U.S.

5. The Power Of Data

Perhaps the most strategic initiative is the FDA's focus on harnessing the power behind data, and a significant expanding area is digital health. Digital health technologies (DHTs) use computing platforms, digital connectivity, software, and sensors for healthcare and related uses. We see digital platforms moving healthcare from the clinic to patients by improving understanding of patient behavior and physiology outside traditional clinical settings and enabling early therapeutic interventions. In clinical trials, telehealth tools provide important opportunities to gather information directly from patients at home in decentralized clinical trials, or as part of pharmacovigilance, and gather frequent or continuous medical data from patients as they go about their lives. But DHTs can use advanced algorithms susceptible to potential errors, which may lead to malfunction or misinterpretation of health data. Consequently, regulatory science tools and methods—such as simulations to test algorithm performance— need to be developed to protect data integrity and improve overall reliability of DHTs.

Conclusion

FDA's Focus Areas of Regulatory Science capture an agency that is looking to provide meaningful regulatory insight on new and emerging approaches to drug development and governance. While we have touched on a few of the major initiatives underway within the FDA, the FARS report provides insight as to the agency's current thinking across a large number of strategic initiatives to meet scientific and technological issues for the foreseeable future.

About The Author:

Bikash Chatterjee is CEO of Pharmatech Associates. He has over 30 years' experience in the design and development of pharmaceutical, biotech, medical device, and IVD products. His work has guided the successful approval and commercialization of over a dozen new products in the U.S. and Europe. Chatterjee is a member of the USP National Advisory Board and is the past chairman of the Golden Gate Chapter of the American Society of Quality. He is the author of Applying Lean Six Sigma in the Pharmaceutical Industry and is a keynote speaker at international conferences. Chatterjee holds a B.A. in biochemistry and a B.S. in chemical engineering from the University of California at San Diego.

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