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Regulatory Perspectives – Where We Came from, Where Are We Today, Where Are We Headed?

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1. Introduction

While frequent employment of the phrase "regulatory science" by regulators and academics arose within the last three decades, "science" applied to "regulation" of medicinals dates back many centuries. Descriptive science characterized the earliest classifications of medicinal substances, employed for self-regulation by apothecaries and physicians. Later, development of chemical and biological techniques permitted more precise descriptions of biological and drug products, which were adaptable to development of quantitative product specifications for governmental regulation of manufacturers. Motivated by need to protect and support public health, advanced regulatory science has been applied to research regulatory standards and requirements. Advanced regulatory science is currently being researched and intensively applied in both medical product regulation and development. Ever more novel regulatory science is likely to contribute in a crucial way to undreamed of advances in pharmaceutical development and improved public health.

2. Materials and methods

Sources for the author's perspective of the origins, evolution and future of regulatory science include published histories of pharmacopeias, pharmaceutical science and regulation, and the author's observations during a half-century of experience in medical practice, drug and regulatory research and tenure at the U.S FDA.

3. Results

Pharmacopoeias, containing description of drug substances and methods of production, evolved from Egyptian times forward. Application of analytical chemistry for more precise pharmacopeial specifications in the USA dates to the 1820 establishment of the U.S. Pharmacopeia, a nongovernmental organization.

The transition from 'self-regulation" of drug compounding and quality by apothecaries and medical practitioners to governmental regulation, requiring science-based specifications, commenced in the latter half of the 19th Century. Motivated by disastrous consequences of impure vaccines and poisonous patent medicines led to passage of the Biologics Control Act (1902) and Food and Drugs Act in 1906, requiring derivation and enforcement of science-based product quality standards for manufacturing and truthful labeling.

Regulatory science comprised biological and chemical research to inform analytical methods and regulatory standards for product quality during the first decades of the 20th Century. The 1938 elixir of sulfanilamide and 1960 thalidomide tragedies, motivated stringent safety and efficacy requirements for drug approval, necessitating advanced regulatory science to derive standards for safety, and biostatistical analytics applied to randomized controlled clinical trials.

Motivated by realization of the importance of bioavailability and drug metabolism, advances in pharmaceutical sciences, quantitative clinical pharmacology and biostatistics led to methods for development of bioequivalence standards and clinical pharmacology requirements. These disciplines, have proved key for establishment of regulatory guidance and medical product development procedures for optimizing dosages utilizing population pharmacometric approaches are optimal for safe and effective therapies.

Needs for regulatory guidance and standards for gene, cell-based immunotherapies, and complex therapies to meet unmet medical needs and for rare diseases have prompted novel regulatory science for speeding regulatory approval. Regulatory encouragements for application of model-informed approaches including PKPD, PBPK, and systems modeling and simulation; adaptive clinical trials; real-world evidence; and Bayesian statistics are among the latest targets for research and application in regulatory science.

Currently, advanced regulatory science research by Agency and academic scientists is leading to greater speed, economy and informativeness of medical product development and regulation. There is all reason to expect continued expansion and intensification of research and application of novel regulatory science to meet public health needs of the future.

4. Conclusions

Currently, advanced regulatory science research by Agency and academic scientists is leading to greater speed, economy and informativeness of medical product development and regulation. There is all reason to expect continued expansion and intensification of research and application of novel regulatory science to meet public health needs of the future.

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