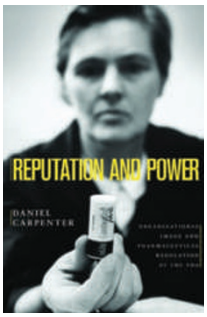
Power struggle



Reputation and Power: Organizational Image and Pharmaceutical Regulation at the FDA

by Daniel Carpenter

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Early in Daniel Carpenter's book on the Food and Drug Administration, he makes the following observation: "There were variable readings of the FDA in different quarters of American industrial society, images of the regulator that ranged from cooperative enforcer to vigilant purity cop to industry bully to vanguard assessor to bought-off corporate servant." One might believe that Carpenter is referring to the current state of affairs but in fact he is alluding to how the FDA was thought of in the 1940s. Has anything changed over the past seventy years, particularly in how this agency is viewed? Carpenter deals with this and many other current issues facing the FDA in his excellent and thorough treatise on this most controversial government agency. This book provides not just a history of the FDA but analyses its evolution, its sources of power and the sway it holds over health issues not just in the United States but literally around the world.

Carpenter's goal is to leave readers "with an appreciation of the historical and political complications of US pharmaceutical regulation". First, by going through the history of the FDA, he shows how the agency evolved and how it shaped the modern system of pharmaceutical regulation. He then turns to the operation of this system and describes how the FDA not just influences but controls the conduct of research and development in the US.

Not surprisingly, major changes in the regulation of medicines have resulted from major crises. Early on, the authority of the FDA was quite limited. However, an anti-infective drug, 'Dr. Massengill's Elixir Sulfanamide', introduced in 1937 caused over a hundred deaths, creating fears over the safety of medicines and potions that were being sold. The outrage from the public led Congress to pass the Federal Food, Drug and Cosmetic Act of 1938, which Carpenter characterizes as "one of the most important regulatory statutes in American and perhaps global history." This Act endowed the FDA with the sole authority to reject the marketability of any new pharmaceutical product. It is on this role as gatekeeper that the FDA's power is based.

The FDA's initial mission was focused on the safety of medicines; over the next two decades they began to broaden their efforts into evaluating the efficacy of new drugs as well. During the 1940s and 1950s, the FDA began asking drug sponsors for more and more data on their compounds. Drug sponsors bemoaned the increased requirements and physicians believed that their role in evaluating the efficacy of new drugs to be compromised. However, these debates ended with another crisis — thalidomide.

The role of Frances Kelsey and the FDA in preventing the marketing of thalidomide, which stopped the tragic birth defects from occurring in the US, has been well documented, but Carpenter provides more context. This also ended the debate in Congress about limiting the FDA's power and led to the Kefauver–Harris Amendments (1963) and IND (Investigation New Drug) Regulations (1963). These acts fused FDA's role as cop, gatekeeper and protector, and created the now standard three phases of clinical testing and the desired goals of each phase.

The pendulum of favoured status began to swing back in the late 1970s and 1980s. Political changes were driven by the Reagan administration desirous of less government regulation, the 'drug lag' — where medicines' approval outside of the US was much faster — and the rise of patient advocacy groups who wanted early access to experimental drugs. Carpenter contrasts the FDA's behaviour on Laetrile (which proved to be 'snake oil') with the anticancer agent, cisplatin, to show how the FDA was able to silence their critics and be flexible when true life-saving medicines could be made available on a limited basis.

In the book's second part, Carpenter teaches how the FDA used the development of certain drugs to help set policy, particularly around the risk-benefit profile of new drugs. Carpenter focuses most of this part on how the FDA uses its influence to control the entire spectrum of R&D activities. The FDA can force hospitals and academic centres to make changes to their internal procedures by threatening to disqualify them as suitable sites for doing clinical research. They can shut down pharmaceutical manufacturing sites if specific protocols are not followed. Although the FDA cannot legislate, its 'Guidelines' effectively drive policy. On ignoring a guideline such as the 'General Considerations for the Clinical Evaluation of Drugs', a pharmaceutical company runs the likely outcome of its drug being rejected outright by the agency. Such examples hammer home Carpenter's main point that the power wielded by the FDA far outstrips the authority and resources given by Congress.

The author, however, misses an opportunity to teach valuable lessons around the Vioxx story. Vioxx was the second of the COX-2 inhibitors approved by the FDA, Celebrex being the first. These compounds were the first of a new class of arthritis treatments designed to provide pain relief without the attendant gastrointestinal side effects. Cardiovascular issues with Vioxx only surfaced after long-term studies in colon-cancer prevention. What is missing in Carpenter's account is the fact that, thanks to FDA guidance, such studies are now closely monitored by independent drug-safety review boards and that when unforeseen problems occur, the trial is halted, the drug programme is reviewed and the drug can even be pulled from the market. A major outcome from the COX-2 Advisory Committee meetings held in 2005 was that all anti-inflammatory agents seemed to share the potential for adverse cardiovascular effects. An FDA supporter could argue that the Vioxx story shows that the FDA's regulatory systems are indeed effective.

On the whole, however, this is a small point. This is the definitive book on the FDA. Carpenter has crafted an extremely meticulous account of the organization. His detailed history of the agency is fascinating and the stories that he provides capture a vivid picture of its evolution. His lessons about the growth of the power and influence of the FDA are important for anyone who is involved in the discovery, development and registration of any new medicine. This book should be read by a wide audience, from people involved in regulatory affairs to the CEOs of newly formed biotech companies. All will come away with a better understanding of what is needed in developing a successful new drug. ❐

REVIEWED BY JOHN LAMATTINA

John LaMattina is the former president of Pfizer Global Research and Development and author of Drug Truths — Dispelling the Myths of Pharmaceutical R&D