

"FDA in the Twenty-First Century: The Challenges of Regulating Drugs and New Technologies"

Holly Fernandez Lynch and I. Glenn Cohen, editors, 2015, 551 pages, Columbia University Press, \$64.99

Review by Norman M. Goldfarb

"FDA in the Twenty-First Century: The Challenges of Regulating Drugs and New Technologies" is the book Robert Califf should be reading to prepare for his new position as the FDA's Commissioner of Food and Drugs. If he hasn't already, expect him to say that the agency's challenge is to change the wheels on a very large moving car. This book is essential reading for anyone who wants to understand the powerful forces driving the FDA's evolution...or loss of primacy in keeping the nation healthy.

This book has been selected for
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Essential reading for clinical research professionals

The following excerpts present some of the challenges faced by the FDA:

The deeper threat to FDA's role in the regulatory firmament of the twenty-first century is not that it is inadequately performing its core functions in assessing the safety of food and therapeutic products but rather that this focus on product "safety" — at least in the relatively acontextual manner FDA has tended to assess that variable — is increasingly unimportant in a new world of focus on product cost, consumer behavior, and consumption patterns...

[T]he greatest challenges going forward involve allocation, price and cost-effectiveness, as opposed to abstracted notions of "safety" and "efficacy." Yet FDA is jurisdictionally limited and bureaucratically disinclined from addressing such issues. The end result going forward is an apparent mismatch between FDA's core regulatory competencies and the most urgent policy issues in its broader domain...

In the future, *ex ante* FDA approval will cease (if it has not already) to be the most important regulatory event in a new therapeutic product's life cycle; far more important will be the decision by public and private payers to include that product on their reimbursable formulary.

In this new world, FDA's reluctance to embrace comparative effectiveness analysis places it at the margins of current policy thinking about comparative efficacy, which has become a central subject of inquiry in the health research and health care delivery systems in the United States and elsewhere. Exemplifying this disinclination to innovate, FDA in 2008...rejected a recommendation to require new drugs to be tested against existing therapies, explaining that "[w]e believe that [a requirement of drug-drug trials instead of placebo control] is inconsistent with U.S. law and policy because it would impose a standard for the design of clinical trials that is different from the standard of 'adequate and well-controlled investigations' that the act requires us to apply."...

The regulatory fixation on premarket activities, which we refer to as "premarket syndrome," contributes to a range of problems that can negatively impact both patient health and the health care system. Premarket clinical trials are typically

conducted under controlled conditions that generally do not reflect how a drug will be used in the real world and rarely assess whether a drug is actually more effective than existing therapies. These trials are often of short duration, so rare or longer-term side effects may remain hidden for many years, by which point the drug is already widely prescribed. Moreover, drugs are frequently prescribed “off label” to patients and disease groups never assessed in clinical trials...

Two recent trends — one in drug development and one in drug regulation — are reinforcing the importance of moving drug evaluation beyond the premarket stage. First, in recent years the pharmaceutical industry has been showing a growing interest in developing drugs for niche markets where the symptoms of premarket syndrome can be particularly acute. The narrow population base for these therapies often inherently limits the amount of safety and efficacy data available to support their approval — a fact that heightens the importance of assessing the benefits and risks of these drugs through the ongoing collection and analysis of postmarket data...

[T]here are the much broader and more amorphous kinds of messages about a drug’s risks that may be contained in reports put forward by entirely independent actors based upon their own reviews or analyses conducted without any direct input from either regulators or drug sponsors. This category includes everything from summaries in third-party drug databases to entries in drug compendia to comprehensive meta-analyses published in academic medical journals. Again, any of these, but particularly the latter, may be picked up, amplified, and/or modified by other communication channels so they reach a much wider audience than their initial dissemination...

Although FDA has spent almost four decades regulating computerized devices, its oversight remains piecemeal and sporadic, relying heavily on nonbinding guidance. FDA has never written comprehensive rules tailored to software. In the 1990s, FDA hinted that it was contemplating such a rule but never proposed one. In 2011, the agency explained that it never created an “overarching software policy” because “the use of computer and software products...grew exponentially and the types of products diversified and grew more complex.”

The book includes 27 chapters by 44 contributors:

- Historical Themes and Developments at FDA Over the Past Fifty Years
- A Global and Innovative Regulatory Environment for the U.S. FDA
- FDA and the Rise of the Empowered Patient
- After the FDA: A Twentieth-Century Agency in a Postmodern World
- The Future of Prospective Medicine Under the Food and Drug Administration Amendments Act of 2007
- Global Trends Toward Transparency in Participant-Level Clinical Trials Data
- Conflicts of Interest in FDA Advisory Committees: The Paradox of Multiple Financial Ties
- The Crime of Being in Charge: Executive Culpability and Collateral Consequences
- Recalibrating Enforcement in the Biomedical Industry: Deterrence and the Primacy of Protecting the Public Health
- Prospects for Regulation of Off-Label Drug Promotion in an Era of Expanding Commercial Speech Protection
- The FDCA as the Test for Truth of Promotional Claims
- Why FDA’s Ban on Off-Label Promotion Violates the First Amendment: A Study in the Values of Commercial Speech Protection

- Speed Versus Safety in Drug Development
- Overcoming “Pre-market Syndrome”: Promoting Better Postmarket Surveillance in an Evolving Drug-Development Context
- FDA’s Public Health Imperative: An Increased Role for Active Postmarket Analysis
- The Drug Efficacy Study and Its Manifold Legacies
- Drug Safety Communication: The Evolving Environment
- Innovation Policy Failures in the Manufacturing of Drugs
- From “Recycled Molecule” to Orphan Drug: Lessons from Makena
- FDA, Negotiated Rulemaking, and Generics: A Proposal
- The “Follow-On” Challenge: Statutory Exclusivities and Patent Dances
- New Wine in Old Bottles: FDA’s Role in Regulating New Technologies
- Analog Agency in a Digital World
- Twenty-First-Century Technology with Twentieth-Century Baggage: FDA Regulation of Regenerative Medicine
- Device-ive Maneuvers: FDA’s Risk Assessment of Bifurcated Direct-to-Consumer Genetic Testing
- A New Regulatory Function for E-Prescriptions: Linking FDA to Physicians and Patient Records
- Race and the FDA

The book is available in bookstores.

Reviewer

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