The FDA: Doctors, Investigators, and Translational Research

The policies of the US Food and Drug Administration (FDA) will affect the developmental course of any therapeutic, diagnostic, or preventative agent aimed at being marketed in the United States. As such, the FDA impacts almost all translational research. Put more bluntly, no research will be translated as a product to the US medical market until it is approved by the FDA.

I wrote a book entitled *The FDA for Doctors* (Eaglstein, 2014), which was recently published by Springer, said to be the largest academic press in the world. I had been working on the book episodically for some years and had a hard time finding a publisher. Several publishers of medical books declined, believing the book would not be of interest to doctors. The publishers explained that they succeed by publishing cardiology books for cardiologists, endocrinology books for endocrinologists, dermatology books for dermatologists, and so forth. They felt a book on the FDA, because it was not focused on a given specialty, would not be purchased by doctors. For specialists engaged in translational research, I strongly disagree.

My more-than-casual interest in the FDA first came through performing clinical studies aimed at FDA approval. I later helped with the FDA's long-delayed review of the efficacy of drugs approved for marketing before efficacy was required, the so-called Drug Efficacy Study Implementation review. I have served as a member and ultimately the chair of FDA's dermatologic drug advisory committee, and when I was a Robert Wood Johnson Heath Policy Fellow, for a short time I was given the lead role in FDA oversight for the US Senate by way of the Labor Committee. During this time, I, too, decided that most doctors seem little interested in the FDA. I felt this disinterest was largely the result of doctors receiving limited formal training about the FDA while in medical school and then becoming overwhelmingly busy in the practice world.

Why wouldn't doctors be curious about an agency that determines which drugs, biologicals, and medical devices can be sold in the United States, an agency that mandates what can and must be on the labels of all therapeutics and what can be said to doctors and in advertisements? Few individuals realize that because of the FDA's policies, the United States is one of only two countries that allow direct-to-consumer drug advertising. The FDA must approve even a drug's name before it can be sold, and its authority actually covers 25% of the US economy, including foods, drugs, biologics, devices, cosmetics, and tobacco products. How many doctors know that the definitional difference between a drug and a device is that devices do not act chemically? And that more than 95% of new medical devices receive FDA approval without any required human testing? Although most doctors know that human clinical trials, phases I, II, and III, are required for drug approval, few realize that the clinical trials, especially phase III, are the most costly part of drug development. For completely new drugs, this cost is now estimated to be in the $2 billion range (Tufts Center, 2014).

There are probably many reasons that doctors are not more interested in an agency whose policies and regulations control so much of what we need to prevent, diagnose, and treat disease. For one thing, the practice of medicine is controlled by the states, which issue licenses to practice medicine. The FDA is a federal agency whose powers derive from the federal control over interstate sales. That is, the FDA

Journal of Investigative Dermatology (2015) **135**, 2555–56.
doi:10.1038/jid.2015.258

© 2015 The Society for Investigative Dermatology

has no authority over the practice of medicine. As such, although science and medicine are often at the heart of FDA matters, the FDA's powers, responsibilities, and actions derive mainly from laws and legal constructs that inherently reside in the legal rather than the medical purview.

I recognize that many of the *JID*'s readers are not medical doctors. However, like medical doctors, academic and other researchers have received little formal education about the FDA. Most investigators, even basic scientists, aspire to have their work result in clinical application, even if that occurs sometime in the distant future. The *JID*'s editor, Barbara Gilchrest, selected "Progress in Translational Research" as the journal's 2015 theme "to celebrate the impressive progress" in translational research (Gilchrest, 2015). A subsequent editorial (Parrish *et al*., 2015) highlighted the need for academic investigators, physicians and nonphysicians alike, to be informed about the process of having their work translated to the clinic. The editorial gave as an example the need to forgo quick publication or presentation of findings to obtain patents, which are critical to incentivizing companies or venture capitalists to invest in the translational process.

In a similar manner, and realizing that almost all translation to the bedside in the United States is dependent on FDA marketing approval, knowledge about the agency—especially its regulatory categories and its preclinical as well as clinical requirements—will be useful in guiding researchers in directions that are most advantageous to the ultimate translation of their findings and technologies. For example, by knowing the difficulties of large-scale production and characterization of large protein molecules made by microorganisms (biologics), investigators might at the earliest possible stage seek small molecules able to mimic the effect achieved with large molecules to have a potential small-molecule drug. Recognizing the need for a stable molecule might dispose researchers to select this criterion at the earliest stage. Knowledge of the definition and approval pathways for devices might dictate the use of certain experimental approaches and an alertness to devices already on the market that might serve as predicates, thus greatly reducing the requirement for preapproval clinical testing. Similarly, knowledge of regulatory categories such as combination drug–device and device–drug can be useful early in the game. Of course, much of the work involved in ultimately obtaining FDA approval, especially the chemistry, manufacturing, and control requirements and long-term toxicology, cannot usually be done by academic investigators. However, the insights afforded by knowing more about the process might well help to shorten the "valley of death," the period between the discovery of a potential drug and when the support for translational work is secured.

In summary, I believe that all medical scientists and physicians would not only help themselves but also ultimately help society by becoming more conversant with the FDA's roles and its processes for carrying them out. It was with those beliefs in mind that my book was written. The book can serve as a primer for medical students, postdoctoral fellows pursuing medical research, and all those intrigued by translational research at any time in their careers. Information about the FDA and its goals, policies, and requirements can be found in many other places as well, including the agency's websites.

CONFLICT OF INTEREST
The author states no conflict of interest.

William H. Eaglstein
Chairman Emeritus, Department of Dermatology and Cutaneous Surgery, University of Miami, Miami, Florida, USA

Correspondence: William H. Eaglstein, 100 1st Street #304, Los Altos, California 94022, USA. E-mail: weaglstein@gmail.com

REFERENCES

Eaglstein WH (2014) *The FDA for Doctors*. Springer: Cham, Switzerland. 93 pp

Gilchrest BA (2015) Progress in translational research. *J Invest Dermatol* 135:1–3

Parrish J, Schachter S, Dempsey M *et al*. (2015) Facilitating translational research. *J Invest Dermatol* 135:1463–5

Tufts Center for the Study of Drug Development (2014) How the Tufts Center for the Study of Drug Development pegged the cost of a new drug at $2.6 billion. http://csdd.tufts.edu/files/uploads/cost_study_backgrounder.pdf