Medical Device Development: Regulation and Law, 4th Edition
Review by Norman M. Goldfarb

Medical Device Development: Regulation and Law, 4th edition is the essential handbook for medical device professionals. Indeed, one can question the bona fides of a medical device regulatory expert who has not read the book or does not, at least, keep a copy handy for reference.

The book is written in a practical and straightforward manner, as illustrated by this excerpt from the chapter on clinical studies:

Number of Clinical Investigations Required for Approval

Clinical trials involving medical devices pose some unique challenges as compared to clinical trials involving drug products. Unlike drug trials, which have well-defined phases as specified in drug regulations, FDA does not typically mandate that companies perform device trials in a predefined series of phases. It is somewhat difficult to make broad generalizations regarding the stages, or “phases,” of device trials because they vary so markedly depending on the technology and medical procedures involved. Section 513(a)(3)(A) of the FDC Act (21 U.S.C. § 360c(a)(3)(A)) as amended by Section 217 of FDAMA indicates that “one or more” clinical investigations would be required for premarket approval of medical devices. However, each device poses its own unique challenges and concerns. And in clinical development programs for devices, preliminary phases may or may not be required, especially if safety has been established based on preclinical testing or the theoretical lack of risk. Postapproval studies raise different issues than preapproval studies, as discussed later.

Nevertheless, it is safe to say that for clinical studies used to support PMAs, CDRH historically has placed a greater emphasis on the conduct of pilot or feasibility trials (the terms are often used interchangeably) before allowing pivotal trials to begin, so that potential problems can be addressed before a pivotal trial is initiated. As discussed earlier, early feasibility studies are limited clinical investigations of a device early in development, typically before the device design or specific indications have been finalized. This type of study may, or may not, be the first in human study wherein a device for a specific indication is evaluated for the first time in human subjects. Traditional feasibility studies are clinical investigations that are commonly used to capture preliminary safety and effectiveness information on a near-final or final device design to preliminarily evaluate the safety of the investigational device and to adequately plan an appropriate pivotal study. Pivotal studies are clinical investigations designed to collect definitive evidence of the safety and effectiveness of a device for a specified intended use, typically in a statistically justified number of subjects. It is important to note that devices are not required to pass through each of these stages. Historically, CDRH also typically requested traditional feasibility studies in cases where the safety profile of the device is largely unknown, such as...
when there are outstanding safety questions. CDRH has proposed to allow a staged pivotal trial in cases where certain outstanding questions can be answered concurrently with enrollment of a limited number of subjects in *Guidance for Industry: Clinical Investigators, Institutional Review Boards, and Food and Drug Administration Staff: FDA Decisions for Investigational Device Exemption (IDE) Clinical Investigations* (August 2014). For example, FDA has sometimes required pivotal studies for devices with questionable safety profiles to include a run-in phase with a small number of patients in order to evaluate preliminary safety before a larger cohort of patients is enrolled. Once an IDE supplement containing the necessary additional information for the run-in patients is submitted to FDA and found to be acceptable, the agency will permit the sponsor to expand enrollment partially or to the full sample size.

The book includes 16 chapters:

- The Framework for Regulation of Medical Devices
- The 510(k) Premarket Notification Process
- Device Modifications Requiring a 510(k) Notice
- FDA Regulation of Device Software and Digital Health Technology
- The Investigational Device Exemption Application: Overview of the IDE Process and Humanitarian Devices
- Medical Device Clinical Studies
- The Premarket Approval Application
- Review of Premarket Approval Application
- PMA Supplements
- Medical Device Reclassification
- The Regulation of *In Vitro* Diagnostics
- The Quality System Regulation
- Compliance
- Medical Device Exports and Imports
- Product Jurisdiction and Regulation of Combination Products
- Working Well with FDA

**Reviewer**

Norman M. Goldfarb is Chairman of MAGI and Chief Collaboration Officer of WCG. Contact him at 1.650.465.0119 or ngoldfarb@magiworld.org.