Letter to the Editor

Letter to the Editor: Editorial: When “Safe and Effective” Becomes Dangerous

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In his editorial about the important distinction between studies that assess effectiveness and those that evaluate safety, Dr. Leopold [2] emphasized that the burden often falls upon practicing physicians to understand the limitations of study design. It is critical for clinicians to understand the different types of evaluations and the limitations of each approach.

For medical and surgical devices, there are several distinct paths for

approval. A 510(k) [5, 6] is a premarketing submission made to the US Food and Drug Administration (FDA) to demonstrate that the device to be marketed is as safe and effective as—that is, substantially equivalent to—a legally marketed device that is not subject to premarket approval. For most devices cleared by the 510(k) process, clinical data are not required [5]. Premarket Approval (PMA), the most stringent type of device marketing application required by the FDA, is to be based on a determination by the FDA that the PMA contains sufficient valid scientific evidence that provides reasonable assurance that the device is safe and effective for its intended use(s) [6, 8]. According to the FDA website [8], the clinical investigations section of a PMA includes “study protocols, safety and effectiveness data, adverse reactions and complications, device failures and replacements, patient information, patient complaints, tabulations of data from all individual subjects, results of

statistical analyses, and any other information from the clinical investigations.”

Devices intended to benefit patients by treating or diagnosing a condition that affects fewer than 4000 individuals in the US per year [7] may be granted a Humanitarian Device Exemption (HDE) by the FDA. According to the FDA website [7], HDE applications are “not required to contain the results of scientifically valid clinical investigations demonstrating that the device is effective for its intended purpose, but must contain sufficient information for the FDA to determine that the device does not pose an unreasonable or significant risk of illness or injury, and that the probable benefit outweighs the risk.”

Certain biological products used in surgery, such as topical thrombin and fibrin sealants, are approved under a Biologics License Application [3]. For this type of application, the FDA reviews data from a clinical trial or another type of study in humans [3]. For human tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient (eg, bone and tendons), no premarket approval is required provided that certain criteria are met [4, 9].

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Even the largest and most carefully designed clinical studies cannot identify every potential safety issue [10]. Indeed, a committee convened by the Institute of Medicine [1] to review the 510(k) clearance process stated, “In practice, the assessment of substantial equivalence generally does not require evidence of safety or effectiveness of a device” [1]. However, the committee emphasized that it was “not suggesting that all, many, or even any medical devices cleared through the 510(k) clearance process and currently on the market are unsafe or ineffective” [1]. Although the FDA and manufacturers continually monitor the safety of devices and pharmaceutical products, practicing physicians can provide front-line observations that might not have emerged within the strict confines of a clinical trial.

In his editorial, Dr. Leopold wrote, “While efficacy can be demonstrated quickly, we often do not learn about the harms our interventions cause until much later” [2]. The admonition from the Editor-in-Chief of *CORR*[®] highlights the crucial role of clinicians in protecting patient safety.

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