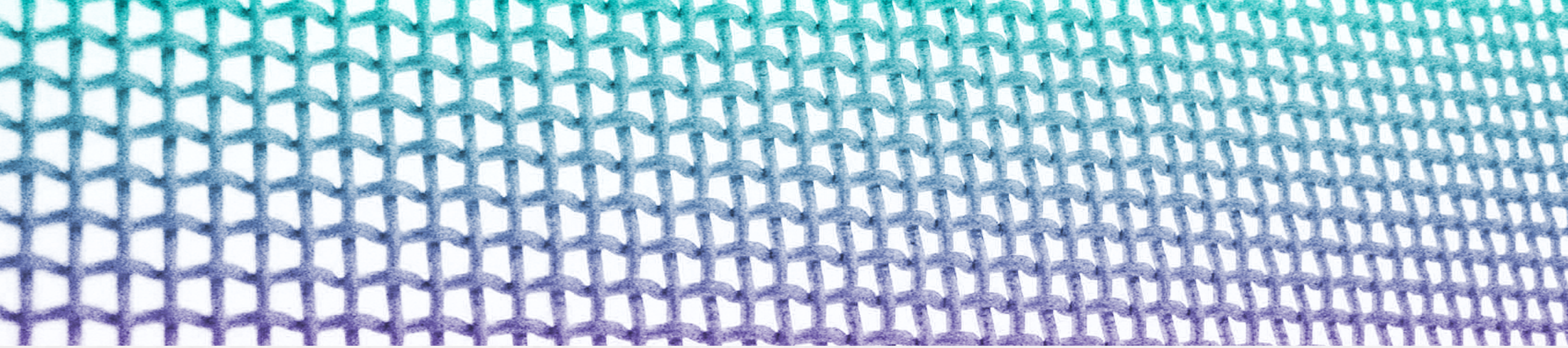
CLASSIFICATION:

WHEN "EQUIVALENCE" MEANS "SAFETY"

The FDA must clear most medical devices before they can be sold to the public. This article refutes a claim that the FDA's process for clearing devices does not provide the "reasonable assurance of safety and effectiveness" Congress intended. The claim, which was first suggested in Medtronic v. Lohr, 518 U.S. 470 (1996), arose because Congress initially grandfathered devices sold before 1976 and then allowed new devices to be cleared if they were "equivalent" to pre-1976 devices. But after 1976, the FDA used medical panels to "classify" devices. Today, most devices are cleared because they are equivalent to post-1976 devices whose safety and effectiveness were independently assessed when they were classified. That assessment provides the reasonable assurance Congress requires and makes the Lohr dictum no longer applicable.

The many well-reasoned explanations as to why the Lohr dictum should no longer be followed have overlooked a fundamental question, which, if asked, greatly strengthens the argument for distinguishing *Lohr*.

That 1996 Supreme Court dictum declared that the "focus" of most of the FDA's medical device regulation process was "not safety." The Court said this because Congress had allowed the FDA to clear for sale new devices "equivalent" to others that had "never been formally reviewed … for safety or efficacy" because



That 1996 Supreme Court dictum declared that the "focus" of most of the FDA's medical device regulation process was "not safety."

they were sold before the medical device law went into effect in 1976[2]. In other words, Congress had grandfathered them.

The idea that the FDA was not focusing on safety is, to say the least, peculiar. Congress has charged it with a duty to provide "reasonable assurance" that medical devices are safe and effective.[3] In recent years, commentators have offered a number of reasons why the FDA today is in fact providing that assurance for the devices it clears. They have pointed to 1990 statutory amendments that strengthened the requirements for clearance and to the FDA's pronouncements about that process.[4] But the idea that the clearance process "is focused on *equivalence*, not safety" has been hard to shake.

These commentators have simply assumed that all clearance through what is called the 510(k) process is based on pre-1976 devices, or, as the General Accounting Office has put it, "iterations" of those devices.[5] In other words, clearance of a new device might be based on equivalence to a post-1976 device, but that device would, in turn, have been cleared as being equivalent to a pre-1976 device, all without any stand-alone look at safety and effectiveness. In answer to the question "equivalent to what?" they have assumed the answer was ultimately a pre-1976 device.

But both the governing statute and the regulatory history provide a different answer for many, if not most, medical devices. In the Act, Congress instructed the FDA to convene medical panels to classify devices. And where after 1976 the FDA classified a device or group of devices as presenting a low or moderate risk, the statute authorized clearance based on equivalence to the classified device.[6] So for these devices, the answer to the question "equivalent to what?" is quite different. It is "equivalent to a device classified by the FDA as being safe and effective."

In order to look at how the classification process has worked, it is helpful to examine the governing law as it has been applied to one particular product group, surgical mesh.

The scheme Congress enacted in 1976 and revised in 1990 requires the FDA to place devices in classes according to the amount of regulation needed to provide "reasonable assurance of safety and effectiveness." Those that need the least are in Class I. Those that may additionally need only what are called "special controls" are placed in Class II. And those whose risks are sufficiently great or unknown are placed in Class III and subjected to special scrutiny and regulation. *See* 21 U.S.C. § 360c(a)(1). But the purpose in all cases is to provide that reasonable assurance.

Congress in 1976 instructed the FDA to create medical panels to classify devices. The panel members, paid for their work, were to be persons who "possess skill in the use of, or experience in the development, manufacture, or utilization" of the devices. 21 U.S.C. § 360c(b)(2). They were to be organized "according to the various fields of clinical medicine and fundamental science in which devices intended for human use are used." 21 U.S.C. § 360c(c)(1). Panels had to explain why Class III treatment was not necessary to provide reasonable assurance of safety and efficacy if they were evaluating devices to be implanted in the human body. 21 U.S.C. § 360c(c)(2). Before the FDA adopted a recommendation, it was to publish the panel recommendations in the Federal Register and invite public comment. Again, if the FDA decided not to place an implantable device in Class III, it was to provide "a full statement of the reasons." 21 U.S.C. § 360c(d)(2)(B).

So it was with surgical mesh.

In 1978, the FDA assigned three classification panels the job of evaluating surgical mesh: General and Plastic Surgery, Orthopedic Device, and Gastroenterology and Urology. They were to classify devices based on "[p]anel members' personal knowledge of, and clinical experience with, the devices under review." 47 Fed. Reg. 2810, 2812 (Jan. 19, 1982). In their deliberations, they considered risks such as infection, foreign body reaction and discomfort. *Id.*

In 1982, the panels recommended that surgical mesh (21 CFR § 878.3300) be placed in Class II. Their report said that surgical meshes have "an established history of safe and effective use." 47 Fed. Reg. 2810, 2817 (Jan. 19, 1982). It said they "meet a generally accepted satisfactory level of tissue compatibility." *Id.* The panels cited medical literature to support their conclusions. *See id.* at 2817-2818.

The FDA tentatively agreed with the classification "because of the extensive clinical usage of surgical mesh over a long period of time and because there is sufficient

The scheme Congress enacted in 1976 and revised in 1990 requires the FDA to place devices in classes according to the amount of regulation needed to provide "reasonable assurance of safety and effectiveness."

information available to establish a performance standard that would provide reasonable assurance of the safety and effectiveness of the device." Id. at 2817. The FDA noted that surgical meshes had then been in use for 20 years. *See id.* It cited three studies on the use of polypropylene mesh, and noted that one of them:

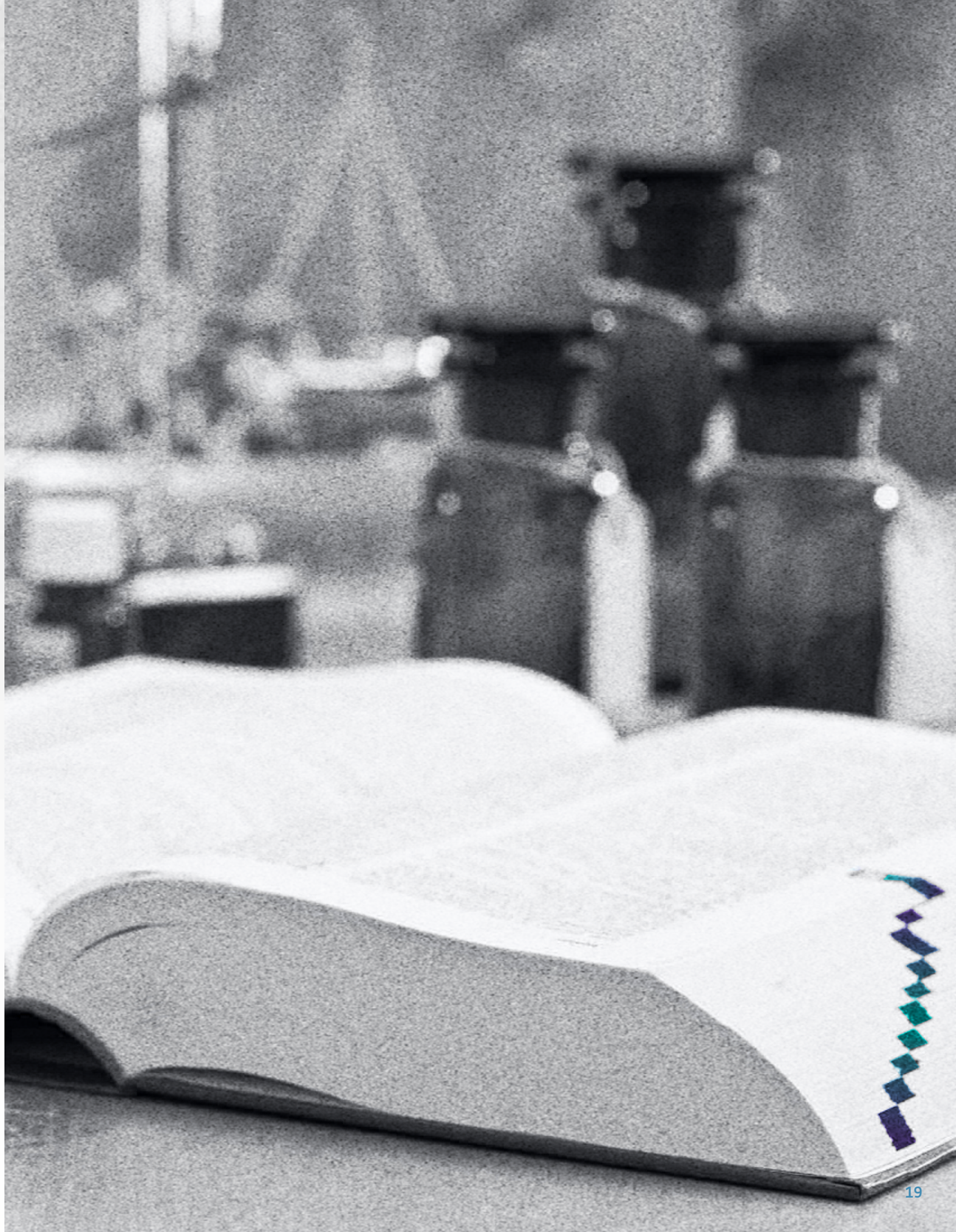
> *reported on 53 patients for the repair of incisional hernias with polypropylene mesh. During 8 years (1970-1978), there was no operative mortality and the mesh had been uniformly well tolerated. The recurrence rate was found to be 11 percent, a distinct improvement over the era before the mesh was used.*

Id. at 2817, citing Gerald M. Larson and Harold W. Harrower, *Plastic Mesh Repair of Incisional Hernias*, 135 American Journal of Surgery 559 (April 1978). That study declared that complications from use of mesh were "rarely serious," that mesh did not increase the frequency of wound infection," and that polypropylene mesh "does not appear to degrade or lose strength in patients." *Larson et al.*, 135 American Journal of Surgery at 562. The FDA also cited an earlier one-year dog study that found a "minimal foreign body reaction" to the mesh.[7] The FDA published the classification along with others and invited public comment.

In 1988, after reviewing the comments and holding public hearings, the FDA published the final classification of surgical mesh as Class II. 53 Fed. Reg. 23856 (June 24, 1988). It rejected a claim that Class II devices were not safe and effective until a performance standard was adopted. *Id.* at 23860. It reiterated that the "biocompatibility of [surgical mesh and certain other devices] "has been established through their successful use for a number of years" and "the probable benefit to health from proper use of these devices outweighs an[y] likelihood of illness or injury resulting from their use." *Id.* at 23861. With respect to surgical mesh, it said Class II performance standards might be needed, however, because "long-term biocompatibility" was still an issue. *Id.* at 23862.

In 1996, Ethicon, Inc. submitted a 510(k) notification for the sale of "Modified PROLENE* polypropylene nonabsorbable synthetic surgical mesh." See http://www. accessdata.fda.gov/scripts/cdrh (K963530)[8]. The predicate device was PROLENE* polypropylene mesh, which was identified as a "Class II Medical Device, 21 CFR §878.3300." The notification describes the product as being composed of knitted filaments "identical in composition" to that used in a suture product whose safety had been approved. It provides the labeling that will be used, including the statement that the material "is not absorbed nor is it subject to degradation or weakening by the action of tissue enzymes." It offers no clinical data, other than one 28-day animal test, but recites that the predicate mesh has "a long established history of safe clinical use as an implantable material." The FDA cleared the device.

So for this product, there was, contrary to *Lohr*, a formal expert panel and FDA review of safety and effectiveness, which led to classification of the predicate device. The determination by the FDA that the new product was equivalent in safety and effectiveness was thus an affirmative finding that the new device was, in fact, both safe and effective.



Given the prominent role that classification plays in the statute and in the history, it is worth asking why its role has been overlooked in the debate over *Lohr*. The closest any of the commentators on *Lohr* have come is to say that the FDA system "uses data" in the 510(k) notice to determine classification.[9]

For one thing, some Class III products may still be cleared based on equivalence to pre-1976 devices. Like the device at issue in *Lohr*, they have not been found safe enough to be placed in Class II, yet the FDA has still not required that they go through the approval process.[10]

Another potential problem is that the FDA, when it adopted a regulation identifying devices that qualified for predicate status, did not follow the simple statutory language, which says any post-1976 device "which has been classified in class I or II" can be a predicate.[11] Instead it said devices which "have been reclassified from class III to class II or I," which is narrower and confusing. This is not a problem for surgical mesh, an implantable device, because Congress classified all implantable devices as Class III until a medical panel decided otherwise.[13] But it suggests a narrower group than the statutory language would permit.

Another problem is that the FDA itself has not emphasized the importance of classification when it has defended the 510(k) process. It was only recently that it declared

> *[b]ecause devices are classified according to the level of regulatory control necessary to provide a reasonable assurance of safety and effectiveness, classification of a new device through the 510(k) process requires FDA to determine the issues of safety and effectiveness presented by the new device.* [14]

Whatever the reason, when any court confronts the *Lohr* dictum, it needs to ask the question "equivalent to what?" If the answer is a device in a group that the FDA and its medical panels have classified as being safe and effective, then the dictum should be reversed, for in that circumstance "equivalence *is* safety."

And there is a broader point. Where Congress has told the FDA how to provide "reasonable assurance" of safety and effectiveness, and the FDA has done what Congress has instructed, it is not within the proper province of a court to disregard what the FDA has done simply because it disagrees with the methods Congress chose. *Lohr* was a peculiar case in which the FDA had not yet done what Congress had told it to do with a Class III product. But where the FDA has acted, its action should be respected. That should be true even when it has classified a device as being so safe as to be entirely exempt from the 510(k) or any other premarket review process. ■

Whatever the reason, when any court confronts the *Lohr* dictum, it needs to ask the question "equivalent to what?" If the answer is a device in a group that the FDA and its medical panels have classified as being safe and effective, then the dictum should be reversed, for in that circumstance "equivalence *is* safety."

1. Butler Snow LLP, Ridgeland, Miss. The firm represents Ethicon, Inc. in mesh litigation.
2. Medtronic Inc. v. Lohr, 518 U.S. 470, 493 (1996).
3. 21 Mutual Pharm. Co. v. Bartlett, 133 S. Ct. 2466 (2013).
4. See Ralph F. Hall and Michelle Mercer, *Rethinking Lohr: does "SE" Mean Safe and Effective, Substantially Equivalent, or Both?*, 13 Minn. J.L. Sci. & Tech. 737 (2012) (article "questions whether litigants and courts have ignored major statutory and regulatory changes"); James M. Flaherty Jr., *Defending Substantial Equivalence: An Argument for the Continuing Validity of the 510(k) Premarket Notification Process*, 63 Food & Drug L.J. 901, 907-916 (2008) (survey of statutory and regulatory changes). See also FDA, The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]/ Guidance for Industry and Food and Drug Administration Staff (2014) at p. 6 ("principles of safety and effectiveness underlie the substantial equivalence determination in every 510(k) review").
5. GAO, Medical Devices/ FDA Should Take Steps to Ensure That High-Risk Device Types Are Approved through the Most Stringent Premarket Review Process 13 (2009).
6. 21 U.S.C.§ 360c(f)(1)(A)(predicate device can be post-1976 device which "has been classified in class I or II").
7. Francis C. Usher, *Hernia Repair with Knitted Polypropylene Mesh*, 117 Surgery Gynecology and Obstetrics 239, (1963). See also B.T. Casebolt, *Use of Fabric Mesh in Abdominal Wall Defects*, 72 Missouri Medicine 71 (1975) (evaluating 35 cases over periods of up to nine years).
8. The entire 510(k) can be found at *Lewis v. Johnson & Johnson*, United States District Court for the Southern District of West Virginia, No. 2:2:12-cv-4301, Dkt. 128-17.
9. *See* Hall and Mercer, supra n.4 at 782 & n. 246 (referring to the "accompanying scientific data" in the 510(k) notice).
10. *See* n.4, supra.
11. 21 U.s.C. 360c(f)(1(A)(i).
12. 21 CFR § 807.92(a)(3).
13. 21 U.S.C. § § 513(c)(2)(C), (d)(2)(B).
14. FDA, The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications {510(k)]/Guidance for Industry and Food and Drug Administration Staff (July 28, 2014).

By Luther Munford

By Erin Lane[1]