May 2, 2019

Food and Drug Administration
Dockets Management Branch (HFA-305)
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. FDA-2018-N-4751: Modernizing FDA’s 510(k) Program; Request for Comments

Dear Sir/Madam:

On behalf of AdvaMed, the Advanced Medical Technology Association, I am pleased to submit these comments in response to the Food and Drug Administration’s (FDA’s or “Agency”) request for comments on Modernizing the Food and Drug Administration’s 510(k) Program.

The Advanced Medical Technology Association (AdvaMed) is the world’s largest trade association representing medical device and diagnostics manufacturers. AdvaMed’s member companies produce the innovations that are transforming health care through earlier disease detection, less invasive procedures and more effective treatments. AdvaMed has more than 400 member companies, ranging from the largest to the smallest medical technology innovators and manufacturers. AdvaMed advocates for a legal, regulatory and economic environment that advances global health care by assuring worldwide patient access to the benefits of medical technology. The Association promotes policies that foster the highest ethical standards, rapid product approvals, appropriate reimbursement, and access to international markets.

AdvaMed supports the current 510(k) program, which includes the ability to use older legally marketed devices as predicates, to the extent substantial equivalence can be demonstrated. The 510(k) program has demonstrated its effectiveness and durability over the years, and remains a critical component of the Agency’s “gold standard” for safety and effectiveness. When FDA announced its 510(k) Modernization Plan in November of 2018, we expressed our commitment to working with FDA and other stakeholders in reviewing and enhancing the current review paradigm. AdvaMed has also expressed support for potential alternative 510(k) pathways that emphasize adherence to recognized standards. Bringing safe and effective devices and diagnostics
to patients and physicians should be the focus of any comprehensive consideration of the future of the program. The relative age of a predicate represents one discrete aspect of a multi-faceted review paradigm that has significantly evolved over the decades.

Importantly, the age of a device, or whether iterative advances in technology are available, would be an arbitrary criterion for exclusion of a device as a predicate. This is because the predicate serves the role of appropriately classifying a device based on the existing body of scientific evidence. As part of the 510(k) submission review, each device is evaluated on its own merits based on scientific data, including any new technology introduced in the new device; the identified predicate is only one aspect of the submission and one aspect of FDA’s review.

Medical devices comprise diverse product groups. They range from bandages, wheelchairs (motorized and non-motorized), diagnostic tests, magnetic resonance imaging and computerized tomography equipment, to hip and knee implants. FDA has previously recognized an important attribute of medical devices: "Although drugs are molecules with short half-lives and long market lives, devices are often complex durable equipment with short market lives."\(^1\) As with all engineered products and technologies (e.g., computers, cell phones), medical device development is frequently evolutionary. Device development often results from clinician and patient feedback as well as innovations from other medical devices or even other industries (e.g., telecommunications and aerospace). The availability of additional features and accessories allows clinicians to make choices on what will provide the best outcome for their patients. For some devices, device changes introduce new technology, such as digital control or new materials. For other devices, changes are less frequent or not needed (e.g., orthopedic screws).

The 510(k) regulatory pathway ensures that diverse medical devices are appropriately regulated by creating a risk-based, science-driven classification system that includes a comprehensive and vigorous review of device performance and test data. 510(k) submissions for even simple devices may contain hundreds and in some cases thousands of pages of testing and data demonstrating safety and effectiveness and substantial equivalence, including, where appropriate, clinical testing. The 510(k) program has evolved since its enactment in 1976. By the 2000s, the program was different than its original conception, featuring multiple 510(k) pathways, authorizing FDA to establish standards that must be satisfied to support 510(k) clearance, and benefiting from the additional resources provided beginning with the advent of the medical device user fee program in 2002. According to FDA, 510(k) submissions now average 1,185 pages in length.\(^2\)

The 510(k) regulatory process has been, and remains, a successful program that ensures the safety and effectiveness of medical technology while encouraging device development and facilitating the availability of high-quality medical devices to improve patient care and meet the needs of clinicians and the American public. This critical regulatory program has tremendous significance in the everyday lives of our citizens but is too often misunderstood and mischaracterized.

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2. FDA Has Taken Steps to Strengthen The 510(k) Program (FDA Report released November 2018), p. 6.
It is estimated that 90% of medical devices reviewed by FDA have historically been authorized to be marketed in the U.S. through the 510(k) process. In 2017, the Center for Devices and Radiological Health (CDRH) cleared 3,173 devices through the 510(k) process, representing 82% of all devices approved and cleared. The 510(k) process ensures that medical devices are neither under-regulated nor over-regulated. It has served as an efficient and flexible means to appropriately regulate much of today's diverse medical technology, and it is only one part of a larger regulatory framework designed to ensure the continuing safety and effectiveness of medical devices.

AdvaMed believes that it is appropriate and necessary to evaluate programs on a routine basis to make adjustments and improvements. As noted above, FDA has made many important process improvements since the inception of the 510(k) program in 1976. For these reasons, we support the Agency's current review of the program and their objective of implementing continuous improvement. We believe that concepts such as the use of objective performance criteria have the potential to enhance the 510(k) process. We also, however, believe that FDA should have objective evidence that a fundamental change to the 510(k) process, such as limiting the use of older devices as predicates, would improve the program before seeking new legislative authority. We do not believe that such new authority is warranted, as FDA has current authorities to address safety concerns with respect to specific types of devices. Current authority allows FDA to up-classify medical devices, effectively removing them as predicates. FDA also has authority to impose special controls (e.g., device-specific data standards) for all moderate risk devices (Class II) where deemed appropriate, as well as to issue guidance documents with new or updated recommendations. FDA also has authority to ban a device, which removes it from the market and makes it ineligible to be used as a predicate.

Thus, AdvaMed believes that the current 510(k) process, including the ability to use older devices as predicates, is appropriate and does not create hurdles to the evolution of technology. Importantly, the age of a device, or whether iterative advances in technology are available, should not be a criterion for exclusion of a device as a predicate. Established devices for which the foundational technology has not changed in many years, such as sutures, spinal screws and rods, in vitro diagnostic (IVD) products and many other simple devices should not be disqualified as predicates because they are merely old, nor should devices relying on these predicates be called out in such a way that would suggest they are inferior. Further, using age as an exclusion criterion for a predicate device could imply that the benefit risk of an older technology has changed to the point that it is no longer acceptable. However, there are other mechanisms, such as risk management which are utilized by manufacturers to continually ensure that the benefit risk profile of a product remains acceptable. Companies are required through the application of the QSR (Quality System Regulation) to have a risk management system, and FDA has recognized the ISO 14971 standard for Risk Management for Medical Devices as an acceptable method to meet this require

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3 Shuren statement to Congress “Pathway to FDA Medical Device Approval: Is there a Better Way?” April 14, 2011

4 Statement from FDA Commissioner Scott Gottlieb, M.D. and Jeff Shuren, M.D., Director of the Center for Devices and Radiological Health, on transformative new steps to modernize FDA’s 510(k) program to advance the review of the safety and effectiveness of medical devices.
requirement. Utilizing risk management systems and standards, companies continually identify and mitigate risks associated with their devices.

There are many older devices that remain relevant as predicate devices because they meet current standards of care, represent a more affordable option than the latest technology and are well understood by the user. Even if newer versions of a device are available, there may be attributes of older predicates that are relevant to 510(k) submissions for devices introducing newer technologies. For example, older predicates could be especially important for Special 510(k)s where manufacturers use their own, previous-generation devices as predicates. An older predicate may serve as a valuable predicate because it may be made of materials that have a well-established track record of safety and demonstrated effective use. Reference to the 510(k) for that older product is useful and productive in demonstrating the safety of the material in the new device and allows for a more efficient review process because it can address issues such as materials, biocompatibility, and operating mechanisms. As a result, the FDA reviewer can concentrate on the new features of the device which could reference a different predicate device. In addition, for some IVD products, FDA identifies older technologies as required predicates in guidance documents because they are the “gold standards” to which the performance of new technologies must be compared (e.g., antimicrobial susceptibility tests).

Even prior to the 1990 amendments through which Congress codified FDA’s implementation of the Act's 510(k) requirement, manufacturers and the Agency typically compared new devices to the most recent version of their own predicate device. In the Safe Medical Devices Act of 1990, Congress strengthened the 510(k) process and effectively legalized advancing incremental differences between successive substantially equivalent devices so that devices cleared years after the first cleared device may differ substantially even though it remains under the same classification regulation. Through the 1990 amendments, Congress ensured that predicates embodied current technology and each 510(k) substantial equivalence determination could drive innovation one step further to enhance device safety and effectiveness.

“In the 510(k) Pathway, manufacturers generally rely on comparative testing against predicate devices to demonstrate that a new device is as safe and effective as the predicate device. Older predicates might not closely reflect the modern technology embedded in new devices, or our more current understanding of device benefits and risks.” According to the 510(k) decision-making criteria, when a device incorporates technology that is different than that of the cited predicate(s), the company is required to demonstrate that the new technology does not raise different questions of safety and effectiveness and that there are valid scientific means to evaluate the effects of changes in technology. This requirement is met when the company provides data to demonstrate the safety and effectiveness of the new device. FDA does not determine substantial equivalence solely on the comparison of the new device to the technology of the older predicate. In fulfilling its mandate to protect the public health, FDA requires data on the new technology introduced in the device.
In the request for comments on the use of older predicates, FDA stated:

Congress’ actions recognized that, from a commercial perspective, there is no incentive for a 510(k) submitter to pursue clearance of a device that was substantially equivalent to technology that was outdated and no longer in demand or use. Ultimately, it is the competitiveness of different technologies along with the features and benefits of those differences and the cost of including them that will determine the viability of a device in the marketplace.

With respect to the specific questions for which FDA has requested comments, AdvaMed provides the following:

1. **Should the FDA make public a list of devices, or manufacturers who make technologies that rely on predicates that have been on the market for more than a certain number of years (e.g., 10 years)?**

   No, AdvaMed does not believe that FDA should list devices or manufacturers that rely on predicates that have been on the market for more than a certain number of years. If an older predicate is useful for review of the new 510(k), then it should be allowed. Mere passage of time is not an appropriate determiner of scientific and/or clinical relevance. For example, a sponsor making a modification to its cleared device may cite an older version of its own device as the predicate, notwithstanding the existence of other devices of the same type cleared within the intervening years. There is no basis for correlating the use of an older predicate with an inferior safety or effectiveness profile.

   We can think of no useful purpose of publishing such a list. Placing such devices on a list may lead to the false impression that such devices are less safe or effective than other devices. Yet, older devices, or devices relying upon older predicates, are not less safe, for the reasons stated earlier in this letter and conversely, new technologies are not inherently safer. AdvaMed believes that publishing such a list will not drive anyone to develop devices with newer technology and may actually lead to well-established older devices being unnecessarily removed from the market.

   Further, FDA should consider the potential unintended consequences of creating such a list of commercially available devices which could create a false perception for patients, healthcare providers and foreign government agencies.

2. **Should the FDA consider using other criteria to inform our point of reference?**

   The 510(k) program is a program that has withstood the test of time. We believe publishing a list of devices based on the age of the predicate or other criteria could perpetuate misunderstandings of the 510(k) program. Instead, FDA should focus its efforts on educating stakeholders to explain how the program works, including the use of a predicate to classify a device, the testing and generation of device-specific data that is reviewed by FDA, and the role of technical national and international standards to guide device testing (e.g., biocompatibility, sterilization, electrical safety, magnetic resonance interference (MRI)).
3. **Are there other and/or alternative actions we should take to promote the development and marketing of safer, more effective 510(k) devices?**

FDA guidance documents and input to 510(k) submitters during pre-submission meetings are mechanisms the Agency may use to promote the development and marketing of safer and more effective 510(k) devices, including communicating to stakeholders the factors relevant to selection of a predicate for their device. Additionally, as noted above, FDA has the authority to issue special controls for a particular device type, where appropriate.

4. **Should the FDA consider certain actions that might require new authority, such as making at least some older devices ineligible as predicates?**

Current authority allows FDA to up-classify medical devices, effectively removing them as predicates. FDA also has authority to impose special controls (e.g., device-specific data standards) for all moderate risk devices (Class II) where deemed appropriate, as well as issuing guidance documents. FDA also has authority to ban a device, which removes it from the market and makes it ineligible to be used as a predicate. As we have noted above, AdvaMed does not believe that making older predicates ineligible is necessary or appropriate. FDA has sufficient existing authorities to regulate 510(k) devices, including setting forth special controls to address specific device types warranting additional action.

AdvaMed strongly supports the ongoing efforts of FDA to continuously improve and modify the 510(k) program. Through the years since the implementation of the device Act, Congress and FDA have modified the 510(k) program to ensure it accommodates changes in technology and healthcare.

Sincerely,

/s/

Ruey C. Dempsey RAC
Vice President
Technology and Regulatory