FDA's Safety And Performance-based Pathway: An Alternative To Substantial Equivalence For 510(k) Submissions

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Since the inception of the 510(k) program, the 510(k) clearance of medical devices has been based on their proven substantial equivalence with claimed predicate device(s). In concert with the goal of adopting the least burdensome approaches, the FDA provides an alternate pathway based on proven safety and performance characteristics, instead of devices' equivalence to other predicates. This pathway is an expansion of the abbreviated 510(k) pathway, applicable to some well understood low to moderate-risk class II device categories. The FDA has released and continues to release device-specific guidelines to encourage manufacturers to opt for this approach for their device approvals. The FDA also conducts webinars and workshops to assist industry stakeholders understand the pathway.

The pathway is voluntary and is not mandated by the FDA. Though the manufacturer is not required to prove substantial equivalence of its device with a predicate device, the manufacturer is still required to identify a predicate device in the scope of the submission. Manufacturers can opt for the safety and performance-based pathway if the device has the same indications for use as the identified predicate, its technological characteristics do not raise any different safety and effectiveness concerns than the identified predicate, and it meets all the FDA-identified performance criteria for the given device. If any of the above factors are not met, the manufacturer can opt to submit a traditional, special, or abbreviated 510(k).

The FDA has so far identified performance and safety criteria and testing methodologies for spinal plating systems, orthopedic non-spinal metallic bone screws and washers, magnetic resonance receive-only coils, cutaneous electrodes for recording purposes, and conventional foley catheters, and the final guidance is in effect for each. The draft guidance for soft (hydrophilic) daily wear contact lenses has been released, with the final guidance not yet available. For each type of device, the guidance includes the description of the device, the types of devices included and excluded under the purview of the safety and performance-based pathway, applicable performance criteria that are to be met by the device, and the recommended testing methodologies. A brief outline of these device categories is detailed in the table below.

Table 1: Safety and Performance-based Pathway Device Categories

Device	Device Class	Regulation	Product Codes	Device Types	Intended Use / Device Description	Out of Scope
Orthopedic Non-spinal Metallic Bone Screws and Washers	II	21 CFR 888.3040	HWC	Screw, fixation, bone	• Bone screws: orthopedic non-spinal fracture fixation, osteotomy, or small joint fusion or arthrodesis	• Bone screws and washers intended for mandibular, maxillofacial, cranial, and orbital fracture fixation or for use in spine • Devices intended for use with suture or chord components as part of implant system
	II	21 CFR 888.3040	HTN	Washer, bolt, nut	• Washers: intended for use with bone screws only to aid in load distribution at the screw head/bone interface	
Cutaneous Electrodes for Recording Purposes	II	21 CFR 882.1320	GXY	Electrode, cutaneous	• Non-invasive, single use electrodes intended to be used on normal, healthy, clean, intact skin for recording	• Dry electrodes • Reusable cutaneous electrodes • Cutaneous electrodes intended for stimulation or for use in MR environment • Electrodes regulated under other regulations • Electro-conductive media devices and needle electrodes
Spinal Plating Systems	II	21 CFR 888.3060	KWQ	Appliance, fixation, spinal intervertebral body	• Anterior cervical or anterior/ lateral thoracolumbar spinal plating systems intended for fixation of vertebral bodies for purpose of stabilizing the spine for fusion	• Plating systems attaching to the posterior spine or the occiput
Conventional Foley Catheters	II	21 CFR 876.5130	EZL	Catheter, retention type, balloon	• Drainage is accomplished by inserting the catheter through the urethra into the bladder • The catheter is retained by use of a balloon inflated in the bladder, which is attached to the distal end of the catheter	• Three lumen catheters, catheters treated to enhance their lubricity, suprapubic catheters, and antimicrobial catheters
Magnetic Resonance Receive-only Coils	II	21 CFR 892.1000	MOS	Coil, magnetic resonance, specialty	• MR receive-only coils are intended for hydrogen/proton imaging, have no patient contact, or have limited contact with intact skin to produce images of human anatomy for general diagnostic use by trained clinicians • Only air-cooled MR coils • Receive-only radio-frequency (RF) coils	• MR coils intended for specific clinical conditions • Water-cooled and cryogen-cooled electronics
Soft Hydrophilic Daily Wear Contact Lenses	II	21 CFR 886.5925	LPL	Spherical or toric lenses	• Intended to be worn directly against the cornea and adjacent limbal and scleral areas of the eye for the optical correction of ametropia (myopia or hyperopia with or without astigmatism) • The lenses are designed to be frequent replacement or daily disposable lenses	• Lenses to correct presbyopia, to enhance or alter the apparent color of the eye, to act as a bandage or therapeutic lens • Lenses for the management of keratoconus or irregular corneal conditions • Lenses with special optical performance beyond that of correcting ametropic (e.g., blue light filtering), with special physical performance (retains moisture, lubricates, reduces deposits) and with special health performance characteristics (e.g., relieves dry eye)

The performance criteria defined in these guidelines ensure that the new device is at the least equivalent to legally marketed devices, in terms of safety and performance. The safety and performance can be demonstrated based on the FDA's recognized consensus standards, the FDA guidance, special controls, scientific literature, or submission of historical data. While opting for this pathway, the manufacturer should

not use performance criteria suggested in standards that are not recognized by the FDA. Some tests would require complete test protocols and all test reports and the summary of test results and declaration of conformity would be sufficient for submission, as a part of 510(k) application.

When the performance criteria are included in the FDA recognized consensus standard and the manufacturer uses the same testing methodology included in the FDA recognized consensus standard, submitting a declaration of conformity would suffice under this pathway. When the performance criteria are established by the FDA in the safety and performance guidance for a given device category and the test methodology from the FDA recognized standard is adopted by the manufacturer, a summary of results should accompany the declaration of conformity. In cases where the performance criteria are established by the FDA in the safety and performance guidance for a given device category and the test methodology is recommended or specified by the FDA, a testing protocol is required. If the test methodology is neither included in the recognized standard nor recommended by the FDA, or if the manufacturer uses its in-house test method as an alternative, the manufacturer shall submit the complete test report. However, manufacturers should note that the FDA does not consider performance criteria that are not included in the device-specific safety and performance-based guidelines.

The table below shows the data that should be included in the submission under various possible scenarios.

Table 2: *Data required under various possible scenarios.*

Type of Performance Criteria and Methodology the FDA identified for Safety and Performance-based Pathway		
Performance Criteria	***Testing Methodology***	***Safety and Performance-based Pathway 510(k) Submission Should Include***
FDA-recognized standard	FDA-recognized standard	Declaration of Conformity
FDA-established	FDA-recognized standard	Results Summary and Declaration of Conformity
FDA-established	FDA-recommended or specified	Results Summary and Testing Protocol
FDA-established	None specified/recommended or alternative to the FDA-specified methodology used	Complete Test Report

The submission process, cover letter, Refuse To Accept (RTA) checklist requirements, the review process, e-copy requirements, and MDUFA fees remain the same as for other types of Pre-Market Notification pathways like traditional 510(k), abbreviated 510(k), and special 510(k). The timeline for the FDA to review and make a decision on a 510(k) submitted under the safety and performance-based pathway is 90 FDA days.

To comply with the RTA policy guidance, the manufacturer shall include the sections listed below in the same order. Where a particular section is not applicable for a given device category, the manufacturer can retain the section heading and include the statement, “This section does not apply” or “N/A” for ease of review by the FDA staff. The statement should provide the rationale for why a particular section is not applicable for the device.

1. Medical Device User Fee Cover Sheet (Form FDA 3601) 2. CDRH Premarket Review Submission Cover Sheet (Form FDA 3514) 3. 510(k) Cover Letter 4. Indications for Use Statement (Form FDA 3881) 5. 510(k) Summary or 510(k) Statement 6. Truthful and Accuracy Statement 7. Class III Summary and Certification 8. Financial Certification and/or Disclosure Statement (Forms FDA 3454 and FDA 3455) 9. Declarations of Conformity and Summary Reports	10. Device Description 11. Executive Summary/Predicate Comparison 12. Substantial Equivalence Discussion 13. Proposed Labeling 14. Sterilization and Shelf Life 15. Biocompatibility 16. Software 17. Electromagnetic Compatibility and Electrical Safety 18. Performance Testing – Bench 19. Performance Testing – Animal 20. Performance Testing – Clinical 21. Other

Table 3: *Required sections for safety and performance-based pathway.*

The manufacturer shall demonstrate the device's compliance to a standard through the declaration of conformity to the standard, results summary, or a summary report, if recommended in any relevant device-specific guidance, testing protocols, and/or a complete test report demonstrating that the new device meets the FDA-identified performance criteria. The manufacturer shall identify a predicate and provide a trade name, model number, name of the 510(k) submitter/holder, and 510(k) number, if available. Though the safety and performance-based pathway does not require the manufacturer to compare performance specification testing with a predicate device, the manufacturer shall provide a comparison with predicate device in terms of indications for use and technology. For other sections of the 510(k) technical file, i.e., Proposed labeling, sterilization and shelf life, biocompatibility, software, electromagnetic compatibility and electrical safety, and performance testing, the data shall be submitted in terms similar to a typical 510(k) technical file, though it is not a direct comparison with the predicate device.

Below is an example of the test methodologies, performance criteria, and data submission requirements defined for MR coils.

Table 4: *MR coil requirements as per the safety and performance-based pathway.*

Test	***Test Methodology***	***Submission Requirement***	***Performance Criteria***
Image Signal to Noise	• IEC 62464-1 Magnetic resonance equipment for medical imaging - Part 1: Determination of essential image quality parameters	Summary of results and Declaration of Conformity	• >130 (for 1.5T coils) • >215 (for 3T coils) (using the lowest

	• National Electrical Manufacturers Association (NEMA) MS 1 Determination of Signal-to-Noise Ratio (SNR) in Diagnostic Magnetic Resonance Imaging • NEMA MS 6 Determination of Signal-to-Noise Ratio and Image Uniformity for Single-Channel, Non-Volume Coils in Diagnostic Magnetic Resonance Imaging (MRI) • NEMA MS 9 Characterization of Phased Array Coils for Diagnostic Magnetic Resonance Images (MRI)			SNR measure over all imaging coils, planes, and anatomical regions)
Image Conformity	• IEC 62464-1 Magnetic resonance equipment for medical imaging - Part 1: Determination of essential image quality parameters • NEMA MS 3 Determination of Image Uniformity in Diagnostic Magnetic Resonance Images • NEMA MS 6 Determination of Signal-to-Noise Ratio and Image Uniformity for Single-Channel, Non-Volume Coils in Diagnostic Magnetic Resonance Imaging (MRI) • NEMA MS 9 Characterization of Phased Array Coils for Diagnostic Magnetic Resonance Images (MRI)		Summary of results and Declaration of Conformity	• Worst-case non-uniformity < 50% (e.g., without any optional software correction algorithms applied)
Surface Heating	• NEMA MS 14 Characterization of Radiofrequency (RF) Coil Heating in Magnetic Resonance Imaging Systems		Summary of results and Declaration of Conformity	• Temperature criteria as defined by ANSI/AAMI ES 60601-1: <41°C for both normal use and single fault (coil not plugged in) condition
	•			•
Acquired Image Quality	• Sample clinical images from all target anatomical locations are reviewed to determine that the images produced by the device are of sufficient quality for diagnostic use		Statement from a U.S. Board Certified or international equivalent qualified physician	• Statement from a U.S. Board Certified or international equivalent qualified physician (e.g., radiologist, radiation oncologist) that images are of diagnostic quality and sample clinical images to support the ability of your coil to generate diagnostic quality images

Decoupling Circuit	• Inspection of circuit diagrams	Circuit diagrams and description of decoupling mechanism	• Presence of decoupling mechanisms
Immunity, electrostatic discharge	• IEC 60601-1-2 Medical electrical equipment – Part 1-2: General requirements for basic safety and essential performance – Collateral Standard: Electromagnetic disturbances – Requirements and tests	Summary of results and Declaration of Conformity	• Pass at ±8 kV contact, ±2 kV, ±4 kV, ±8 kV, ±15 kV air
General electrical / mechanical safety	• AAMI/ANSI ES60601-1 Medical electrical equipment - Part 1: General Requirements for Basic Safety and Essential Performance • IEC 60601-2-33 Medical electrical equipment - Part 2-33: Particular requirements for the basic safety and essential performance of magnetic resonance equipment for medical diagnosis	Summary of results and Declaration of Conformity	• Demonstration that the device performs safely and as anticipated in its intended use environment

The safety and performance-based pathway offers a cost-efficient way for device manufacturers to gain market access in the U.S., as the number of samples that are required to be tested are reduced by half. The FDA is expected to issue a draft and final guidance(s) for additional device types that qualify for the safety and performance-based pathway.

About The Author:

Jeffrey S. Eberhard is with Freyr and has more than 15 years of experience in the medical device industry serving many key roles in regulatory affairs, quality management systems (QMS), and risk assessment and mitigation. He has led various U.S. device approval projects, including pre-market notifications (510(k)). Jeffrey has developed ISO 13485 and safety testing programs and designed programs for safety, efficacy, and clinical research. Jeffrey has vast expertise in sterile medical devices as well as dermal and oral care medical devices.