Introduction and Regulatory Reference Sheet
Orthopaedic and Rehabilitation Devices Advisory Panel
Reclassification of Non-invasive Bone Growth Stimulator Devices
September 8-9, 2020

On September 8, 2020, the Orthopaedic and Rehabilitation Devices Advisory Panel (the Panel) will discuss and make recommendations regarding the reclassification of non-invasive bone growth stimulator devices.

FDA is proposing to reclassify non-invasive bone growth stimulator devices, which are currently regulated as class III devices, into class II.

At this meeting, the Panel will be asked to discuss the reclassification of non-invasive bone growth stimulator devices. The Panel will discuss the approved indications for use, the risks to health, the available safety and effectiveness information, and the potential special controls.

After this advisory panel meeting, the FDA will consider all available scientific evidence and the input from panel members in determining whether to reclassify these devices.

What data should be considered when making a classification recommendation?
Initial classification and reclassification decisions are based on existing information for legally marketed devices and their predicates. Although information on future technology or new indications applicable for these devices may be available, this information is not relevant to the deliberations of the Panel. The Panel must consider only the legally marketed cohort of each device type.

What are the definitions of Class I, Class II, and Class III?
Federal law (Federal Food, Drug, and Cosmetic Act, section 513) established the risk-based device classification system for medical devices. Each device is assigned to one of three regulatory classes: Class I, Class II, or Class III, based on the level of control necessary to provide reasonable assurance of its safety and effectiveness.

As device class increases from Class I to Class II to Class III, the regulatory controls also increase, with Class I devices subject to the least regulatory control, and Class III devices subject to the most stringent regulatory control.

The regulatory controls for each device class include:

- Class I (low to moderate risk): General Controls
- Class II (moderate to high risk): General Controls and Special Controls
- Class III (high risk): General Controls and Premarket Approval (PMA)

Class I, General Controls

A device is Class I if general controls are sufficient to provide reasonable assurance of the safety and effectiveness of the device. Examples of general controls are registration and listing, medical device reporting, labeling, and good manufacturing practices (GMPs). Devices may also be

considered Class I if the device "is not purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, and does not present a potential unreasonable risk of illness or injury."[1] Most Class I devices are exempt from submitting a 510(k) and can be marketed without a premarket submission. Examples of Class I devices include general manual orthopedic surgical instruments, manual arthroscopic instruments (e.g., cannula, drill guides, suture puncher), non-powered goniometers, and crutches.

Class II, Special Controls

A Class II device is "a device which cannot be classified as a Class I device because the general controls by themselves are insufficient to provide reasonable assurance of the safety and effectiveness of the device, and for which there is sufficient information to establish special controls to provide such assurance."[2] Examples of special controls are: performance standards, postmarket surveillance, patient registries, and special labeling requirements. Special controls may also include specific types of performance testing (e.g., biocompatibility, sterility, electromagnetic compatibility, pre-clinical testing) which FDA may outline in the regulation. Most Class II devices require clearance of a 510(k) prior to marketing. Sponsors are required to submit valid scientific evidence in their 510(k) demonstrating that the device is as safe and effective as a predicate device. Companies submitting a 510(k) for a device must demonstrate how any specified special controls have been met in order to receive marketing clearance. Examples of Class II devices include intramedullary fixation rods, intervertebral body fusion devices (i.e., cages), and resorbable calcium salt bone void fillers.

Class III, Premarket Approval

A Class III device is a device which:

1. "cannot be classified as a class I device because insufficient information exists to determine that the application of general controls are sufficient to provide reasonable assurance of the safety and effectiveness of the device," **and**
2. "cannot be classified as a class II device because insufficient information exists to determine that the special controls…would provide reasonable assurance of its safety and effectiveness," **and**
3. "is purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health," **or**
4. "presents a potential unreasonable risk of illness or injury."[3]

Class III devices require premarket approval prior to marketing the device and must provide valid scientific evidence to demonstrate that the device has demonstrated a reasonable assurance of safety and effectiveness through the submission of a PMA application. Examples of Class III devices include total artificial disc replacements, interspinous process spacers for non-fusion, and devices combined with bone morphogenetic protein (BMP).

What will the Panel be asked to consider in determining which device class to recommend?

[1] See Section 513(a)(1)(A) of the Federal Food, Drug, and Cosmetic (FD&C) Act.
[2] See Section 513(a)(1)(B) of the FD&C Act.
[3] See Section 513(a)(1)(C) of the FD&C Act.

Risks to Health

The FDA will present the risks to health that they have identified to be associated with use of the device type. The Panel will be asked to comment on whether they disagree with inclusion of any of the identified risks or whether they believe any other risks should be considered for this device type.

Safety and Effectiveness

The FDA will present available information regarding the safety and effectiveness of this device type as it relates to the indications for use and technology. The Panel will be asked to comment on the adequacy of the available scientific evidence with respect to safety and effectiveness for this device type and to determine whether the probable benefits to health from use of the device for the specific indications outweigh the probable risks. If safety and/or effectiveness are not established for this device type, or for specific indications or technology of the device type, PMAs should be required to establish safety and effectiveness.

Special Controls

The Panel will be asked to comment on whether any special controls can be identified to provide a reasonable assurance of safety and effectiveness in light of the available scientific evidence. If special controls can mitigate the identified risks to health, and safety and effectiveness have been established, it would be appropriate to recommend that this device type be classified into Class II, special controls.

What is a "reasonable assurance of safety"?

As defined in 21 CFR 860.7(d)(1), "There is reasonable assurance that a device is safe when it can be determined, based upon valid scientific evidence, that the probable benefits to health from use of the device for its intended uses and conditions of use, when accompanied by adequate directions and warnings against unsafe use, outweigh any probable risks. The valid scientific evidence used to determine the safety of a device shall adequately demonstrate the absence of unreasonable risk of illness or injury associated with the use of the device for its intended uses and conditions of use."

What is a "reasonable assurance of effectiveness"?

As defined in 21 CFR 860.7(e)(1), "There is reasonable assurance that a device is effective when it can be determined, based upon valid scientific evidence, that in a significant portion of the target population, the use of the device for its intended uses and conditions of use, when accompanied by adequate directions for use and warnings against unsafe use, will provide clinically significant results."

What are the practical implications of maintaining non-invasive bone growth stimulator devices in Class III?

If FDA chooses to maintain non-invasive bone growth stimulator devices in Class III, new devices or changes to existing devices would require approval of a premarket approval (PMA) application or PMA supplement in order to market the device. To support approval, the information in the PMA (including clinical data) would have to demonstrate a reasonable assurance of safety and effectiveness.

What happens if FDA decides to reclassify non-invasive bone growth stimulator devices into Class II?

If these devices are classified into Class II, these devices would become subject to the premarket notification [510(k)] requirements and any special controls specified in the final classification. Companies with existing legally marketed devices would be subject to the newly-defined special controls, and must ensure that their existing products meet all specified requirements. New devices and changes to existing devices that require a new submission to FDA would require a 510(k), demonstration that the special controls have been met, and a substantial equivalence (SE) determination.

What are the practical differences between PMA and 510(k) requirements?

A PMA application must provide all evidence to independently demonstrate a reasonable assurance of safety and effectiveness of the device. PMAs typically involve data from clinical trials of the specific device that support both safety and effectiveness, as well as detailed manufacturing information for the device. Conversely, a 510(k) submission can leverage existing information on predicate devices, including applicable clinical data, to support marketing clearance. For devices subject to 510(k), the premarket submission need only provide evidence that the device has indications and technological characteristics consistent with existing legally marketed predicate devices and meets any required special controls.

Once a PMA is approved, the PMA holder must report all design, manufacturing, and labeling changes made to the approved device to FDA via PMA supplements[4] and PMA annual reports[5]. PMA holders are also typically subject to ongoing postmarket requirements. 510(k) holders are not subject to as stringent postmarket oversight. For example, for 510(k) devices, companies do not need to submit many types of minor changes to a device or its labeling to FDA for review nor do they need to submit manufacturing changes or annual reports.

Regardless of the classification of these device types, FDA does not regulate the practice of medicine, specifically, which devices clinicians can use and how they use them.

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[4] Refer to FDA's Guidance for Industry and FDA Staff: 30-Day Notices, 135-Day Premarket Approval (PMA) Supplements and 75-Day Humanitarian Device Exemption (HDE) Supplements for Manufacturing Method or Process Changes (https://www.fda.gov/regulatory-information/search-fda-guidance-documents/30-day-notices-135-day-premarket-approval-pma-supplements-and-75-day-humanitarian-device-exemption).

[5] Refer to FDA's Guidance for Annual Reports for Approved Premarket Approval Applications (PMA) (https://www.fda.gov/regulatory-information/search-fda-guidance-documents/annual-reports-approved-premarket-approval-applications-pma).