FDA De Novo Program

Orthopaedic and Rehabilitation Devices Panel Meeting

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Peter J. Yang, PhD, RAC
De Novo Program Lead
Division of Submission Support
Office of Regulatory Programs
Office of Product Evaluation and Quality
Center for Devices and Radiological Health
U.S. Food and Drug Administration

Medical Device Classification (summary)

- **Class I devices: general controls**
  - Registration and listing of manufacturing facilities
  - Quality System requirements (including good manufacturing practices)
  - Medical Device Reporting (adverse events)
  - Prohibitions against misbranding/adulteration

Generally **exempt** from FDA premarket review

- **Class II devices: general controls and special controls**, which can include:
  - Specific bench testing requirements
  - Specific labeling requirements
  - Specific clinical or postmarket requirements

Devices are **cleared** through the **510(k)** process and demonstration of "substantial equivalence"

- **Class III devices: general controls and premarket approval** (PMA)
  - Demonstrate "reasonable assurance of safety and effectiveness" for the proposed intended use
  - Review of manufacturing changes to the device
  - Ongoing annual reporting requirements
  - Conditions of approval, including postmarket requirements

Devices are **approved** through **PMA** process

What Is a De Novo Request?

- A type of premarket submission that, like a 510(k) or PMA, allows for marketing the device if granted
- Intended for **new types of devices** that are low-to-moderate risk that are otherwise automatically classified into class III
- Request to classify the device into class I or class II based on **reasonable assurance of safety and effectiveness** (**not substantial equivalence**)
- If granted:
  - FDA **creates a new classification regulation**
  - the new device type is regulated through 510(k), if class II
  - the De Novo device serves as the first predicate device of its kind

Is the Product Eligible for De Novo?

- **Must be a medical device (Section 201(h) of FD&C Act)**
- **Must not fit into any existing classification regulation**
  - Doesn't fit into existing Class I/II regulation, i.e., no predicate device (not substantially equivalent (NSE))
    - Includes unclassified preamendments devices
  - Doesn't fit into existing Class III regulation
- **No approved PMA(s) for same device type**

Classification Process – Goals

1. Determine if probable benefits outweigh probable risks
2. Identify probable risks to health for the device/product
3. Determine level of control needed:
   - general controls only = class I
   - general controls + special controls = class II

Together, these provide reasonable assurance of safety and effectiveness.

Benefit-Risk Assessment

- Based on totality of evidence in the De Novo request
- Assessment of probable benefits
- Assessment of probable risks
- Assessment of additional factors, for example:
  - Uncertainty
  - Patient perspectives
  - Addressing unmet medical need

New Classification Regulation

- Number (e.g., 21 CFR 888.XXXX)
- Name (name of device type)
- Identification
  - Intended use(s)
  - Key technological characteristics
  - Describes what FDA believes to be a single device type with a shared intended use and technology

Risk/Mitigation Table

Identified Risks to Health	Mitigation Measures
Infection	Reprocessing validation Labeling
Adverse tissue reaction	Biocompatibility evaluation
???	???
???	???

- **Risk to Health:** Written from the patient's perspective
- **Mitigation Measures:** Categories of testing or other requirements which, together, mitigate a particular risk to health
- Risks and mitigations will be dependent on a device's intended use and technology (example in subsequent slides)

Special Controls (Class II)

- Special controls are legal requirements for all devices in the regulation and are written into the new classification regulation
- Special controls include, and are not limited to:
  - Non-clinical (bench) testing requirements
  - Clinical validation requirements
  - Labeling requirements
  - Some postmarket requirements
    - Postmarket studies are not intended to address premarket questions
- **The De Novo device must meet its own special controls**

When a De Novo Is Granted

- New device may be legally marketed
  - Subject to applicable requirements
- New classification regulation is established
- New device may be used as a predicate device for similar devices to be cleared via 510(k)
- FDA publishes Decision Summary
- FDA publishes new regulation in the Code of Federal Regulations (CFR)

Panel Questions in Context

- FDA is asking questions today about the **benefits and risks** of the NUsurface Meniscus Implant.
- FDA is soliciting input from outside experts who will provide non-binding recommendations to the FDA regarding this De Novo request


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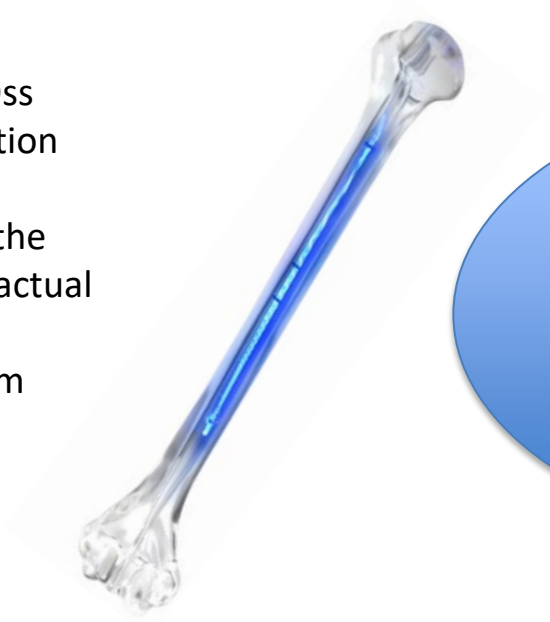
Example De Novo - IlluminOss

Indications for Use: IlluminOss Photodynamic Bone Stabilization System (PBSS) is indicated for skeletally mature patients in the treatment of impending and actual pathological fractures of the humerus, radius and ulna from metastatic bone disease.



Eligible – Different technological characteristics that raise different questions of safety/effectiveness

Example De Novo – IlluminOss New Classification Regulation

- Number: *21 CFR 888.3023*
- Name: *In vivo cured intramedullary fixation rod*
- Identification: *An in vivo cured intramedullary fixation rod is a prescription implanted device consisting of a balloon that is inserted into the medullary canal of long bones for the fixation of fractures. The balloon is infused with, and completely encapsulates, a liquid monomer that is exposed to a curing agent which polymerizes the monomer within the balloon creating a hardened rigid structure.*

Example De Novo – IlluminOss Risk/Mitigation Table (excerpt)

Identified Risks to Health	Mitigation Measures
Adverse tissue reaction resulting from: • Balloon leakage • Device materials	Biocompatibility evaluation Labeling
Infection, including wound complications	Sterilization validation Reprocessing validation Shelf life testing Pyrogenicity testing Labeling
Bone fracture resulting from: • Device bending, cracking, or fracture • Device migration or instability, including initial inadequate fixation • Inability to properly deploy or remove device	Non-clinical performance testing Labeling
Soft tissue damage including transection or laceration of neural, vascular, or muscular structures.	Non-clinical performance testing Labeling
Pain and/or loss of function resulting from: • Balloon leakage • Device bending, cracking, or fracture • Device migration or instability, including initial inadequate fixation • Inability to properly deploy or remove device	Non-clinical performance testing Labeling

Example De Novo – IlluminOss Special Controls

1. Non-clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use. The following performance characteristics must be tested:
   a. Mechanical testing must be conducted on the final device to assess burst, abrasion, bending, and torsion in static and dynamic conditions.
   b. Mechanical testing must demonstrate the integrity of the balloon including testing for leaks, ruptures, and release of cured/uncured material.
   c. Performance testing must demonstrate that the device can be inserted and removed.
   d. Performance testing must demonstrate the ability, in the event of a leak, to remove the uncured material from its in vivo location.
   e. Performance testing must demonstrate the reliability and accuracy of the curing method used.
   f. Thermal safety testing must be conducted to evaluate the temperature rise during curing.
2. Electrical safety, electromagnetic compatibility (EMC) testing, and electromagnetic interference (EMI) testing must be conducted for all electrical components.
3. All patient-contacting components must be demonstrated to be biocompatible.
4. Performance data must demonstrate the sterility and pyrogenicity of patient contacting components of the device that are provided sterile.
5. Performance data must validate the reprocessing instructions for any reusable components or instruments.
6. Performance data must support the shelf life of the system by demonstrating continued sterility, package integrity, and system functionality over the established shelf life.
7. Technological characterization of the device must include materials, curing agents, and a description of the operating principles of the device, including the delivery system and devices which initiate the curing process.
8. Labeling must include the following:
   a. A detailed summary of the device technical parameters.
   b. Information describing all materials of the device.
   c. Information describing how to perform the procedure and use the device, including the delivery system and devices which initiate the curing process, as well as how to remove the device and any uncured materials.
   d. A shelf life.
   e. Validated methods and instructions for reprocessing any reusable components or instruments.