De Novo Classification Requests

FDA Small Business Regulatory Education for Industry (REdI)

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Office of Regulatory Programs

Office of Product Evaluation and Quality

Center for Devices and Radiological Health

IlluminOss

No predicate device

What would you do?

Learning Objectives

- Identify the eligibility criteria for De Novo classification
- Summarize the classification goals and elements needed to grant a De Novo request
- Identify resources for composing a De Novo request
- Describe the De Novo review process

What Is a De Novo Classification Request?

De Novo Classification

- **New device type**
  - Intended for devices that are automatically classified into Class III
- **Risk-based classification**
  - Request to FDA to classify new device into Class I or Class II

De Novo Classification

- **Granted De Novo request**
  - Creates new classification regulation
  - Regulates new device type through 510(k) pathway
  - Authorizes marketing in U.S.A.

Is Your Product a New Device Type?

- **Must be a medical device (Section 201(h) of FD&C Act)**
- **Must not fit into any existing classification regulation**
  - No predicate device
  - Doesn't fit into existing Class III regulation
- **No approved PMA(s) for same device type**

IlluminOss (DEN160062)

Intended Use

- Fracture fixation in various long bones

Technological Characteristics

- Intramedullary (IM) fixation rod
- Polymer-based
- Constructed at time of surgery

IlluminOss (DEN160062)

Possible Similar Regulation

21 CFR 888.3020

Intended Use

✓ Same

Technological Characteristics

× **Different**

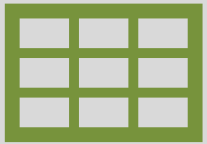
Eligible – Different technological characteristics raise different questions of safety/effectiveness

De Novo Classification Goals

1. Determine if the probable benefits outweigh the probable risks to health
2. Identify probable risks to health
3. Determine level of control needed to mitigate risks:
   - general controls only = *Class I*
   - general controls + special controls = *Class II*

De Novo Classification Elements

Benefit-Risk Assessment



Risk/Mitigation Table

Special Controls (Class II)

New Classification Regulation

Knowledge Check

Which is not true of a new device type?

1. Meets the definition of a medical device
2. Fits into an existing classification regulation
3. No approved PMAs for this same device type

Preparing a De Novo Request

Suggested Resources

- CDRH Device Advice – De Novo Classification Request
- De Novo Classification Process (Evaluation of Automatic Class III Designation)
- Acceptance Review for De Novo Classification Requests

Q-Submission

- Introduce your device to FDA review team
- Discuss regulatory pathway/eligibility
- Obtain feedback on evidence to support classification:
  - Non-clinical performance testing and methods
  - Clinical study design
  - Benefit/risk considerations

See "Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program"

Benefit-Risk Assessment

- Based on totality of evidence (primarily clinical)
- Assessment of probable benefits and probable risks
- Assessment of additional factors, for example:
  - Uncertainty
  - Patient perspectives
  - Addressing unmet medical need

See "Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approval and De Novo Classifications"

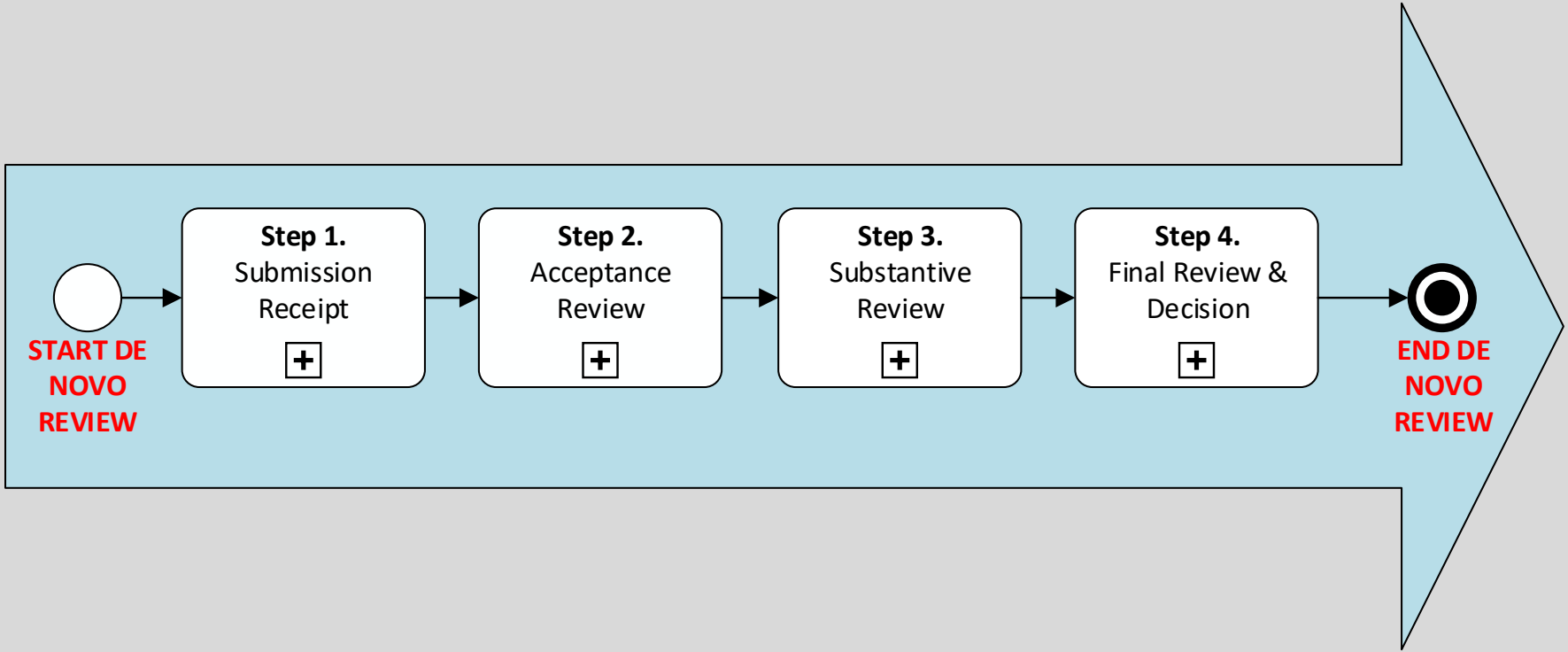
De Novo Review Process

Overall Process and Timeline

Goal → Final decision by FDA Day 150

- Typically two separate review cycles (75 days each)
  - 1st cycle: issue request for Additional Information
  - 2nd cycle: render final decision (**grant** or **decline**)

De Novo Review Process



1 – Submission Receipt

- De Novo sent to Document Control Center (DCC)
- DCC verifies following criteria are met:
  - Applicable user fee is paid
  - Valid electronic copy (eCopy) is provided
- If above criteria are met, De Novo is assigned to lead reviewer

2 – Acceptance Review

- Determine if De Novo is administratively complete
- Intend to complete review within 15 calendar days of receiving original De Novo
- Once accepted, proceed to substantive review

See "Acceptance Review for De Novo Classification Requests"

3 – Substantive Review

- Classification summary – verify device is eligible
- If eligible:
  - review all information in the De Novo
  - identify any questions (deficiencies)
- Send request for Additional Information (AI), which stops review clock
- 180 days to provide complete responses

4 – Final Review and Decision

- Submit responses to AI letter, which restarts the review clock
- Determine if complete responses provided
- Review responses, including any new data
- Render final decision: **grant** or **decline**

Decline Decision

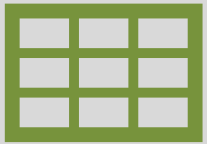
- Reasons for a **decline** decision:
  - Benefits do not outweigh risks
  - Can't develop/determine if special controls mitigate risks
  - Ineligible (1st review cycle)
- Decline order will be issued to requester
- Decline order will identify all outstanding deficiencies

Granting Decision

- ✓ **Determine probable benefits outweigh probable risks**
- ✓ **Identify probable risks to health**
- ✓ **Determine level of control needed to mitigate risks to health**
  - General controls only = *Class I*
  - General controls + special controls = *Class II*

De Novo Classification Elements

Benefit-Risk Assessment



Risk/Mitigation Table

Special Controls (Class II)

New Classification Regulation

IlluminOss – Benefit/Risk Assessment

- Based primarily on IDE clinical study
  - Prospective, multi-center, historically controlled
  - 81 subjects treated with subject device
- Also incorporates non-clinical studies, for example:
  - Mechanical testing
  - Biocompatibility testing

See DEN160062 – Decision Summary

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

IlluminOss – Special Controls (excerpt)

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.
    [truncated]

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.

New Classification Regulation

- Number (e.g., 21 CFR 862.XXXX)
- Name (name of device type)
- Identification
  - Intended use(s)
  - Key technological characteristics

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.

Knowledge Check

To grant a De Novo, the probable benefits of the device must outweigh the probable risks to health.

1. True
2. False
3. It depends on the device type

After a De Novo Is Granted

- FDA sends granting order
- De Novo device may be legally marketed
  - Subject to applicable requirements, including special controls
- New classification regulation is established
- De Novo device may be used as a predicate device

After a De Novo Is Granted

- FDA updates De Novo Database
  - Granting order
  - Decision Summary
- FDA publishes notice in Federal Register
  - Mechanism for updating Code of Federal Regulations

Summary

- De Novo pathway is intended for new device types.
- A granted De Novo creates a new classification regulation.
- Classification is determined by benefit-risk assessment and risk mitigation measures.

Resources

Slide Number	Cited Resource	URL
5	CDRH Device Advice – Classify Your Device	www.fda.gov/medical-devices/overview-device-regulation/classify-your-medical-device
12	CDRH Device Advice – De Novo Classification Requests	www.fda.gov/medical-devices/premarket-submissions/de-novo-classification-request
12	De Novo Classification Process (Evaluation of Automatic Class III Designation)	www.fda.gov/regulatory-information/search-fda-guidance-documents/de-novo-classification-process-evaluation-automatic-class-iii-designation
12, 19	Acceptance Review for De Novo Classification Requests	www.fda.gov/regulatory-information/search-fda-guidance-documents/acceptance-review-de-novo-classification-requests

Resources

Slide Number	Cited Resource	URL
13	Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program	www.fda.gov/regulatory-information/search-fda-guidance-documents/requests-feedback-and-meetings-medical-device-submissions-q-submission-program
14	Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approval and De Novo Classifications	www.fda.gov/regulatory-information/search-fda-guidance-documents/factors-consider-when-making-benefit-risk-determinations-medical-device-premarket-approval-and-de
25	DEN160062 – Decision Summary	www.accessdata.fda.gov/cdrh_docs/reviews/DEN160062.pdf
31	De Novo Database	www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/denovo.cfm

Questions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