De Novo Classification
FDA-Industry IVD Roundtable

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Acknowledgments

Presentation a joint effort -

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Why De Novo?

Avoid over-regulation of devices that should not be subject to PMA requirements

Avoid needless expenditure of FDA's resources that would occur if lower-risk devices were subjected to PMA requirements

Permit FDA to avoid time and resources consuming substantial equivalence determinations that rely on remote predicates

Source: Food and Drug Administration Modernization and Accountability Act of 1997 – Senate Report No. 105-43

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De Novo Draft Guidance: General Comments

- Pre *de novo* submission
  - Interactive
  - Clarity on device suitability for the de novo pathway
  - Opportunity to understand data needed for a successful petition
- Points to Consider
  - Role of literature in suitability determination
  - Combining the administrative screening and second predicate analysis when filing concurrent 510(k)/de novo petition following a PDS would reduce review time by 40 days
- Process Considerations
  - Transparent
  - Efficient
  - Predictable

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Transparency: PDS Content

Draft Guidance

Pre de novo and De novo petition

Regulatory history

Device info

Classification recommendation

Known & potential risks

Risk & mitigation (control types)

Test methods

Protocols

Targeted performance levels & anticipate risks

Data

Labeling

Viewed as Phases

Pre *de novo* Submission (PDS)

Suitable for *de novo*	Test methods & protocols	*De novo* petition & concurrent 510(k)
Regulatory history Device info Classification recommendation Known & potential risks Risk & mitigation (control types)	Test methods Protocols for bench and/or clinical testing Targeted performance levels Anticipated risks	PDS & 510(k) content + Data Labeling

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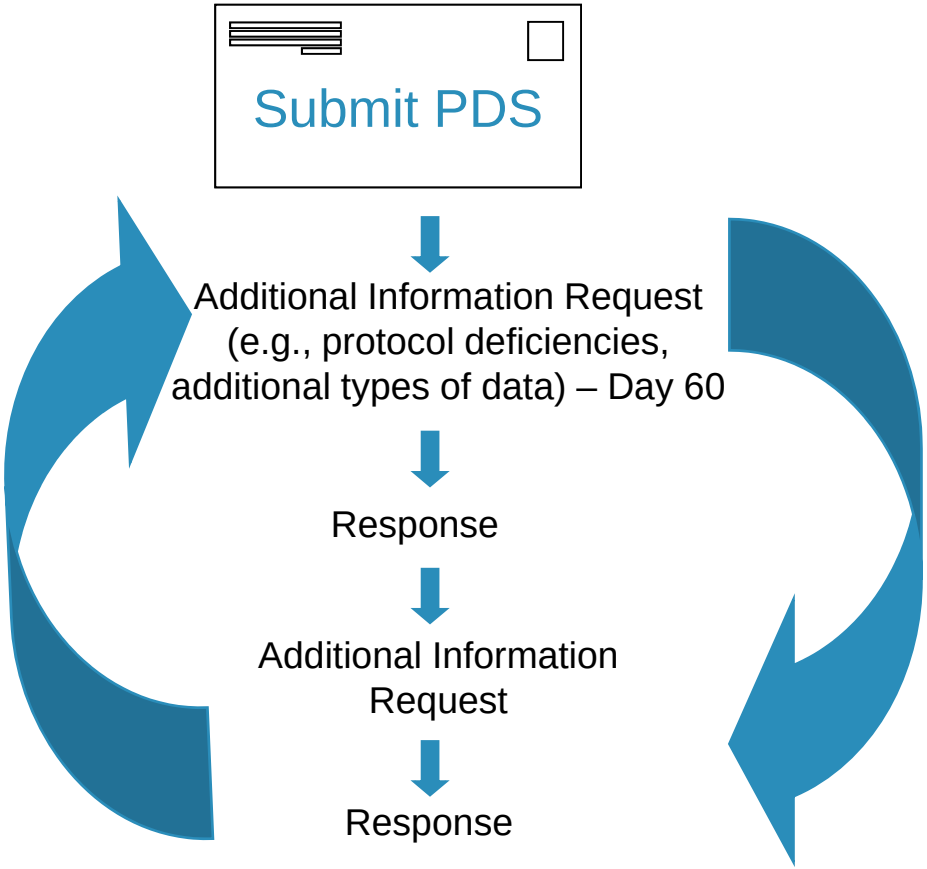
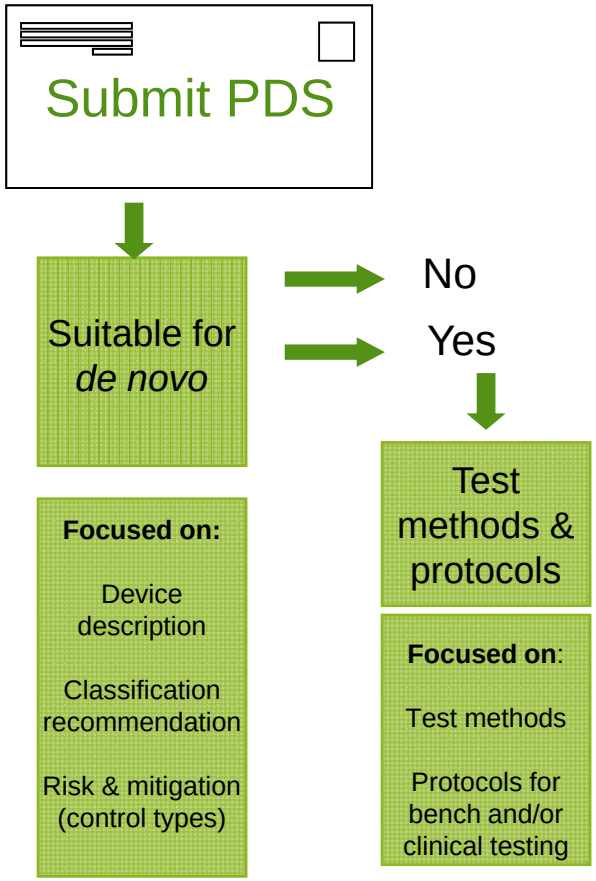
Efficiency: PDS Decision Points & Supporting Information

Potential for Multiple Cycles



Viewed as Phases



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Predictable: Are There Additional Mechanisms to Supplement the Proposed PDS Process?

Some thoughts for discussion:

De novo suitability – Information to make decision

(1) Principles for determining suitability coupled with statutory classification criteria at 513(a)

(2) Expanded table with more examples of risk and mitigation information

De novo petition – Methods & data

(1) Is there a role for essential principles (or similar types of evidentiary expectations)?

The Classification of an IVD medical device is based on the following criteria:

the intended use and indications for use as specified by the manufacturer…

the technical/scientific/medical expertise of the intended user…

the importance of the information to the diagnosis (sole determinant or one of several)…

the impact of the result (true or false) to the individual and/or to public health

(Abstracted from GHTF Principle of IVD Classification)

Example of "suitability principles"

Expand Table

Identified Risk	Recommended Mitigation Measures	Control Type (General or Special)
EXAMPLE: Adverse tissue reaction	Biocompatibility	Special
EXAMPLE: Device failure	Nonclinical Analysis and Testing	Special
	Labeling	Special
	Report to FDA	General
EXAMPLE: Failure to properly interpret test results	Labeling	Special

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Summary

- Step in the right direction
- Consider additional opportunities to enhance transparency, efficiency, and predictability
- Consider how best to use the de novo process to address
  - Avoid over-regulation of devices that should not be subject to PMA requirements
  - Avoid needless expenditure of FDA's resources that would occur if lower-risk devices were subjected to PMA requirements
  - Permit FDA to avoid time and resources consuming substantial equivalence determinations that rely on remote predicates
- Case studies for illustration and additional dialogue

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Case Study

A diagnostic company, Inova, has discovered a potential biomarker “xyz”. Existence of “xyz” in urine indicates vaginal infection in pediatric and adult female patients. An immunoassay was developed to detect this biomarker.

There is no predicate device and no reference method.

Published literature of “xyz” biomarker in Europe (significant number of publications).

Per the new guidance, there are two de novo pathways:

1) Pathway initiated by pre-de novo submission (PDS)

2) Pathway initiated by 510(k) submission

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Case Study 1: Pre De Novo Submission (PDS)

PDS to 510(k)/de novo petition process:

- Inova submitted the PDS with a request for a meeting 60 days from the submission date. At Day 45, Inova received FDA comments and questions.
- Inova prepares responses and discusses with FDA at the meeting (Day-60). Based on the meeting discussion, Inova submits to FDA additional information on Day-74.
- Day 134 (60 days from submitting the additional info), FDA sends recommendations regarding bench/clinical study protocols and issues a suitability letter indicating the device appears to be suitable for the de novo process.

Is the PDS process intended to be similar to the Pre-IDE, where the sponsor submits device information with proposed bench/clinical protocols to seek FDA's feedback?

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Case Study 1a: 510(k)/De Novo Petition Following PDS

- Inova submits the 510(k) concurrent with the de novo petition, which contains the information & data described in the PDS suitability letter.
- Day 45: Inova contacts FDA to request the review status and is informed FDA has initiated an in-depth scientific review.
- Day 60: FDA informs Inova a predicate device has been established by the de novo process in the interim since the PDS suitability review.
- FDA requests additional information to convert the submission into a Traditional 510(k).

1. In this scenario, since Inova followed the PDS suitability letter, what type of additional information will FDA request?
2. Would FDA request Inova conduct comparison testing to the new predicate device?
3. What is the review timeframe for the submission?

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Case Study 1b: 510(k)/De Novo Petition Following PDS

- Inova submits the 510(k) concurrent with the de novo petition, which contains the information & data described in the PDS suitability letter.
- Day 45: Inova contacts FDA to request the review status and is informed FDA has initiated an in-depth scientific review.
- Day 60: FDA issues an NSE letter indicating the de novo petition has been filed and will continue with the review.
- Day 120 (60 days from the issuance of the NSE letter): FDA sends AI letter to Inova. FDA review clock reset for another 60 days when Inova submits the formal responses to FDA. (134 PDS + 120 days 510(k)/de novo + ….)

1. In this scenario, how many 60-day cycles are permitted?
2. If FDA receives another Post PDS/510(k)/de novo petition for the same biomarker, would this second device have to wait for clearance of Inova's device in order to use it as a predicate?

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Case Study 2: 510(k) Followed by De Novo Petition

- Inova submits 510(k), which is followed by two AI requests and Inova taking the maximum number of days to respond to the AI requests.
- Day 270: Inova receives an NSE letter indicating the device is a candidate for de novo process under 513(f)(2) of the FD&C Act.
- Day 299: Inova submits a de novo petition. If FDA requests additional information, a 60-day cycle is expected.

1. What type of interaction/communication should a sponsor expect under this scenario?

2. Are AI requests focused on determination of new intended use or new types of technology?

3. Are AI communications focused on identifying the risks and special controls and adequate data to provide reasonable assurance of safety and effectiveness?

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