De Novo Process

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Proposed Changes to *De Novo*

- Draft Guidance: "*De Novo* Classification Process (Evaluation of Automatic Class III Designation)"

  Issued October 3, 2011

Novel Device – 510k or PMA?

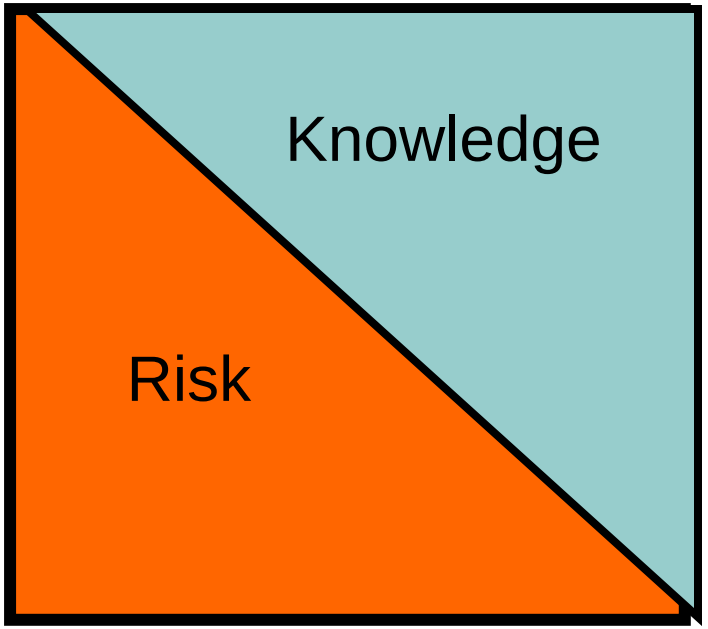
- Is a *de novo* submission appropriate for my device?

How are IVD Devices Classified?

Questions?

- Regulatory path determined using a risk-based approach
- Classification (I, II, or III) depends on risk

Class I – most 510(k) exempt



Low likelihood of harm

Class II - 510(k)

High or unknown likelihood of harm,

or how to prevent harm is unknown

Class III - PMA

Advantages of 510(k) Submission

- PMA application may be more complex than 510(k)
- PMA review and approval may take more time than 510(k) review
- No post market annual reports or PMA supplements for 510(k)
- Cost

Risk is Dependent Upon Intended Use

- Risk (and subsequently classification and submission type) is inherently tied to Intended Use of a device.

Risk is Dependent Upon Intended Use

- Level of FDA review and type of studies requested generally depend on the Intended Use claims; not always on type of technology or assay

- Prostate-specific antigen (PSA) testing with an indication for
- - "aid in detection of prostate cancer" (PMA)
- - "monitoring prostate cancer patients for disease progress" (510(k))

Use Established IVD Devices as a Reference

- Search our Classification Database to view classification and required submission type of devices similar to yours:

- http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpcd/classification.cfm

Use Established IVD Devices as a Reference

- Search our PMA and 510k Databases to compare your device claims to established intended use claims:

- http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm?IVDProducts=on

- http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm?IVDProducts=on

Is My Device First-of-a-Kind?

- Can the device be placed under existing regulations?
- Devices with novel technologies can often fit into the existing regulatory framework

Determining Classification with FDA

- 513g – Official request for classification of a currently unclassified device

- Pre-IDE submission – Informal interactive process allowing early assessment of device class, and least burdensome regulatory route to approved product

Understanding *De Novo*

Before FDA Modernization Act:

- **513 (f)(1) of F, D, & C Act automatically classifies devices that were not in commercial distribution prior to May 28, 1976 into Class III, requiring a pre-market approval (PMA)**

Understanding *De Novo*

FDA Modernization Act of 1997:

- **Provides a new mechanism for classifying new devices for which there is no predicate device**
- **Allows an automatic class III designation to be evaluated and overturned**
- **Appropriateness is determined on a case by case basis and is always risk based**

FDA Modernization Act of 1997 (FDAMA) - New Section 513(f)(2) of the F, D, & C Act. Amended November 21,1997

De Novo Candidates

- Lower risk IVD's for which there is no predicate
- Ancillary to other well-accepted methods for diagnosing a condition
- Discuss with FDA first before you begin the process

Not a Candidate

- Not for high risk IVD's
- Unable to determine ways to manage risk
- There is already a predicate device
- *De novo* process cannot be used to reclassify a device that is already in Class III

To Find Other *De Novo* Devices

- Search Federal Register (FR)
- Search 510(k) Database (through OIVD website)
  http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm?IVDProducts=on
  - Under “type” select: “Evaluation of Automatic Class III Designation”
  - Under “panel” select Chemistry, Immunology, etc.

New *De Novo* Guidance

- **One of 25 Action Items from *FDA's Plan of Action for Implementation of 510(k) and Science Recommendations***
  - Provide updated recommendations for interacting with FDA
  - Clarify the FDA review process
  - Describe the recommended content
- Original *de novo* guidance released in 1998

Goals

- Earlier, more productive, discussions between FDA and Industry
- More comprehensive *de novo* submissions
- More transparent and predictable *de novo* review practices

The *De Novo* Process

- A classification process
- Review process for safety and effectiveness

De Novo Process Comparison

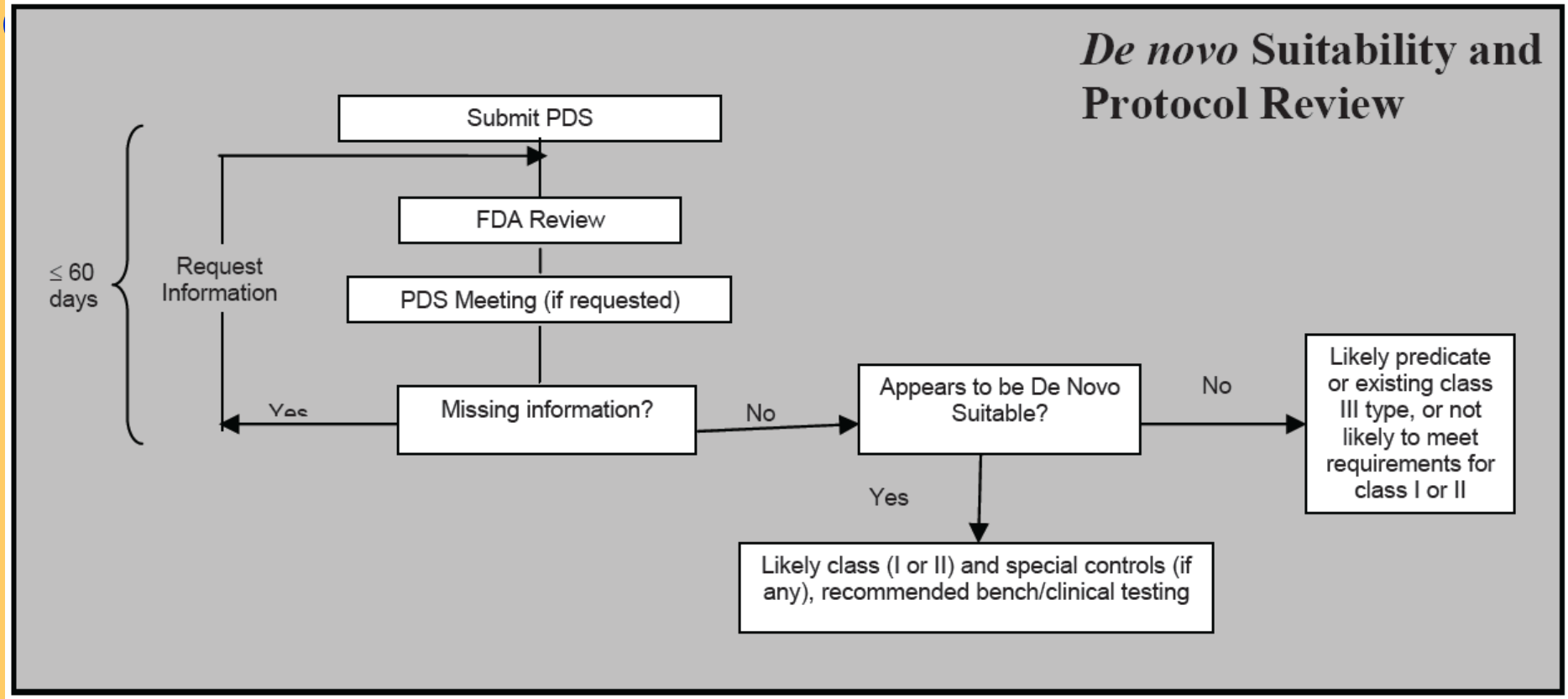
Current:

FDA and sponsor discuss possibility of *de novo* application informally through a teleconference or Pre-IDE.

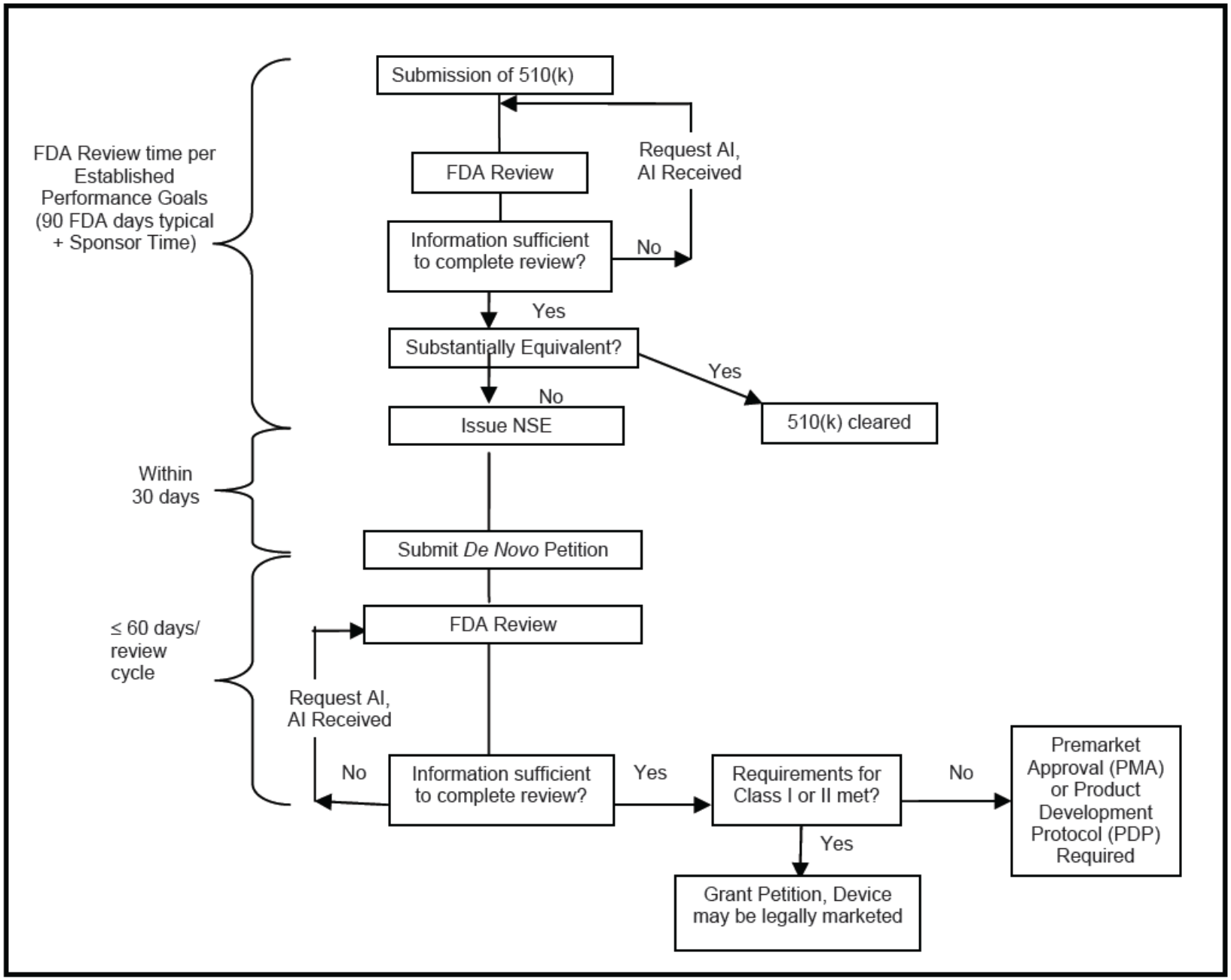
Proposed:

FDA and sponsor discuss possibility of *de novo* application more formally through a Pre *De novo* Submission (PDS)

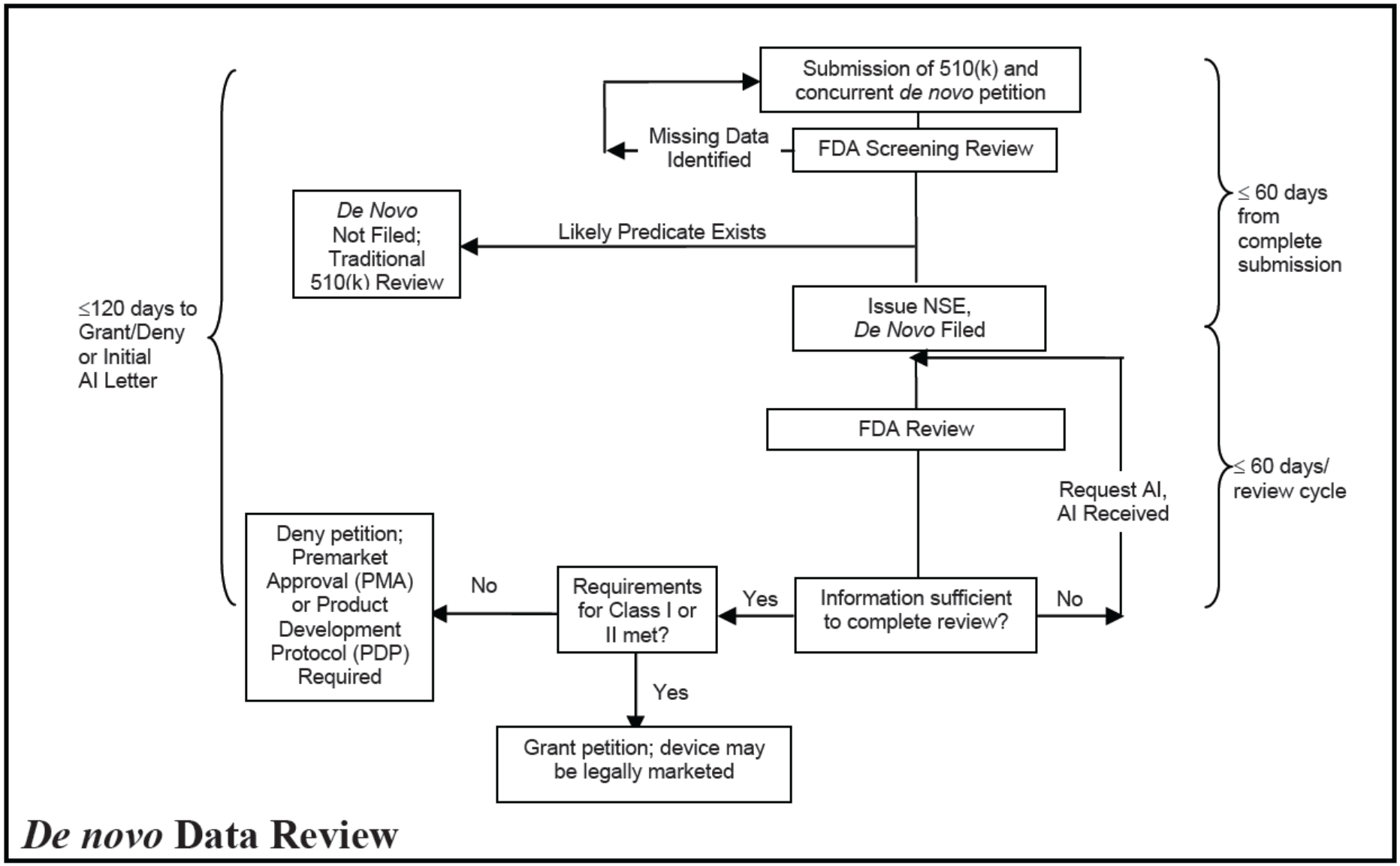
PDS Process


De novo Suitability and Protocol Review
Submit PDS
FDA Review
PDS Meeting (if requested)
Missing information?
Yes
Request Information
≤ 60 days
No
Appears to be De Novo Suitable?
No
Likely predicate or existing class III type, or not likely to meet requirements for class I or II
Yes
Likely class (I or II) and special controls (if any), recommended bench/clinical testing

De Novo Review – Traditional



De Novo Review – After PDS



After Completion of *De Novo* Studies

Current:

- *De novo* applications are submitted to the FDA as 510(k)s
- *De novo* 510(k) similar to traditional 510(k)
- Review of data completed within 90 FDA days at time of NSE

Proposed:

- Concurrent submission of 510(k) and *de novo* petition
- Review of data **not** likely complete at time of NSE (60 FDA days)

De Novo Language from NSE Letter:

The Food and Drug Administration Modernization Act of 1997 (FDAMA), in section 207, deals with the Evaluation of Automatic Class III Designation. Under this section a manufacturer, whose device is found to be not substantially equivalent to a predicate device, can request FDA to make a risk-based classification for their device. I believe that based on the review of your device, **it may be a candidate for Evaluation of Automatic Class III Designation**. Therefore, you may wish to make such a request of this agency.

Sponsor's *De Novo* Petition Should Include:

- Cover sheet identifying the submission as "Request for Evaluation of Automatic Class III Designation" or "*De Novo* Petition"
- Risk/benefit analysis
- Classification (your recommendation based on risk analysis)
- Discussion of proposed controls that would be needed to assure the safety and effectiveness of the device

Sponsor's *De Novo* Petition Should Include:

Current:

- 510(k) number on the NSE letter
- Statement of cross reference to the information in the 510(k)

Proposed:

- Statement of cross reference to the information in the PDS and concurrently submitted 510(k)
- Summary of all changes since the PDS submission

Purpose of Controls

- Tools to manage risk
- Give assurance that risk posed by the device is reasonably low

Examples of General Controls for Class I Devices

Regulations that:

- Requires registration and listing
- Prohibit adulterated or misbranded devices
- Restrict sale and distribution or use
- Govern good manufacturing practices
- Provide for notification of risks and of repair, replacement, or refund

Examples of Class II Special Controls

If general controls are inadequate, then one or more Class II Special Controls are also needed:

- Guidance Document
- Performance standards
- Device labeling
- Postmarket surveillance/data

Class II Special Controls Guidance Documents (SCGD)

- Can submit guidance suggestions with 510(k) submissions or at any time to FDA – recommended
- FDA follows good guidance practice (GGP)

FDA Review of the *De Novo* Petition

- Review the request
- Evaluate the risk
- Identify applicable controls
- Write Special Controls Guidance Document
- Classify the device
- Write the Approval Order
- Write FR notice of availability of SCGD

FDA Review of the *De Novo* Petition

Current:

- Content proposed as early as Pre-IDE submission
- Focused administrative effort once 510(k) review complete
- 60 calendar days

Proposed:

- Content proposed during PDS
- Administrative tasks performed concurrent with 510 (k) review
- 60 day review cycles

FDA Final Action

- Signed Approval Order classifying the device (Class I, II, or III)
- New device can be marketed
- 30 days after final, Approval Order published in FR

Summary of FDA's Review

- *De novo* confirmation
- Identifies deficiencies and ensures they are addressed
- New product code identified
- Special Controls Guidance Document (SCGD) prepared with input from sponsor.
- NSE letter
- Approval order

De Novo Responsibilities for Sponsor:

- Sponsor is responsible for providing information on risk and clinical utility to support a class II designation
- Draft of Special Controls Guidance (optional)
- Provide information that demonstrates safety and effectiveness [510(k)]
- Sponsor must send in the *de novo* petition requesting risk-based classification of the device

Advice

- Talk with FDA early in the process
- Utilize resources on OIVD web site
- Review available guidance documents
- Submit SCGD recommendations to FDA

Resources for *De Novo*

- Guidance document “New Section 513(f)(2) - Evaluation of Automatic Class III Designation” (Feb 19, 1998): http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080197.pdf

- Draft Guidance: “*De Novo* Classification Process (Evaluation of Automatic Class III Designation)” (Oct 3, 2011): http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM273903.pdf

Possible Legislative Changes

- Draft legislation could eliminate the requirement to submit a 510(k) prior to submitting a *de novo* petition:

  http://thomas.loc.gov/home/bills_res.html

  http://www.gpo.gov/fdsys/pkg/BILLS-112s1943is/pdf/BILLS-112s1943is.pdf

OIVD Website Resources

http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/default.htm

- Guidance documents
- Device advice
- 510(k) database
- OIVD phone and e-mail list