De Novo Classification Process (Evaluation of Automatic Class III Designation)

Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE

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For questions regarding this document, contact Melissa Burns, 301-796-5616, melissa.burns@fda.hhs.gov or CBER's Office of Communication, Outreach and Development at 1-800-835-4709 or 301-827-7800.

When final, this document will supersede "New Section 513(f)(2) - Evaluation of Automatic Class III Designation, Guidance for Industry and CDRH Staff" dated February 19, 1998.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Office of Device Evaluation
Office of In Vitro Diagnostics and Radiological Health

Center for Biologics Evaluation and Research

Preface

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Or contact:

Office of Communication, Outreach and Development, HFM-40
Center for Biologics Evaluation and Research
Food and Drug Administration
10903 New Hampshire Ave., Building 71, Room 3128, Silver Spring, MD 20993-0002
Internet:
http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/default.htm
Tel: 800-835-4709 or 240-402-7800
E-mail: ocod@fda.hhs.gov

De Novo Classification Process (Evaluation of Automatic Class III Designation)

Draft Guidance for Industry and Food and Drug Administration Staff

This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

1. Introduction

The purpose of this document is to provide guidance on the process for the submission and review of a request (hereafter a "*de novo*") under section 513(f)(2) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act), also known as the *de novo* classification process. This process provides a pathway to Class I or Class II classification for medical devices for which general controls or general and special controls provide a reasonable assurance of safety and effectiveness, but for which there is no legally marketed predicate device.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

Throughout this guidance document, the terms "we," "us" and "our" refer to FDA staff from the Center for Devices and Radiological Health (CDRH) or the Center for Biologics Evaluation and Research (CBER) involved in the review and decision-making aspects of the *de novo* classification process. "You" and "your" refers to the submitter of a *de novo* and/or related materials.

2. Background

A device may be classified in class III and be subject to premarket approval via several different regulatory vehicles. In accordance with the criteria at section 513(a)(1)(C) of the FD&C Act, FDA may promulgate a regulation classifying, or issue an order reclassifying,[1] a device *type* into class III based on the risks posed by the device and the inability of general and special controls to provide reasonable assurance of the safety and effectiveness of the device. All particular devices of such a type are considered to be in class III and such devices are not eligible for the *de novo* classification process.

Alternatively, devices of a new type that FDA has not previously classified based on the criteria at section 513(a)(1) of the FD&C Act are "automatically" or "statutorily" classified into class III by operation of section 513(f)(1) of the FD&C Act, regardless of the level of risk they pose or the ability of general and special controls to assure safety and effectiveness. This is because, by definition, a new type of device would not be within a type that was on the market before the 1976 Medical Device Amendments or that has since been classified into class I or class II. Thus, there would be no available predicate device.

This second scenario is what Congress targeted when it enacted section 513(f)(2) of the FD&C Act as part of the Food and Drug Administration Modernization Act of 1997 (FDAMA). The process created by this provision, which was referred to in FDAMA as the Evaluation of Automatic Class III Designation, will be referred to as the "*de novo* process"[2] throughout this guidance document. Congress included this section to limit unnecessary expenditure of FDA and industry resources that could occur if lower risk devices were subject to premarket approval (PMA) under section 515 of the FD&C Act. Section 513(f)(2) has allowed manufacturers to submit a *de novo* to FDA for devices "automatically" classified into Class III by operation of section 513(f)(1). As enacted by FDAMA, in order to submit a *de novo*, a device first had to be found not substantially equivalent (NSE) to legally-marketed predicate devices through a premarket notification (510(k)).

Section 513(f)(2) was modified by section 607 of FDASIA, which created an alternative *de novo* pathway that does not require that a device be reviewed first under a 510(k) and found NSE prior to submission of a *de novo*. Under the new *de novo* pathway, if a person believes their device is appropriate for classification into Class I or Class II and determines there is no legally marketed predicate device, they may submit a *de novo* without a preceding 510(k) and NSE (hereafter "direct *de novo*").

FDA is issuing this draft guidance to provide updated recommendations for interactions with FDA related to the *de novo* process, including what information to submit when seeking a path to market via the *de novo* process. When final, this guidance will replace "New Section

[1] Prior to the Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA), FDA reclassified devices under section 513(e) of the FD&C Act through rulemaking; FDASIA changed this to an order process.
[2] The process has been termed "de novo" because it requires the agency to evaluate novel devices anew, in accordance with the criteria at section 513(a)(1) of the FD&C Act.

513(f)(2) – Evaluation of Automatic Class III Designation, Guidance for Industry and CDRH Staff," dated February 19, 1998.

3. The *De Novo* Process

In accordance with section 513(f)(2), you may submit a *de novo* requesting FDA to make a classification determination for the device according to the criteria at section 513(a)(1) of the FD&C Act. The *de novo* must include a description of the device and detailed information and reasons for any recommended classification (see section 513(f)(2)(A)(v) of the FD&C Act). FDA must make a classification determination for the device that is the subject of the *de novo* by written order within 120 days of the request (see section 513(f)(2)(A)(iii) of the FD&C Act).

If the submitter demonstrates that the criteria at section 513(a)(1)(A) or (B) of the FD&C Act are met, we will grant the *de novo*, in which case the specific device and device type is classified in class I or class II. The device may then be marketed immediately and serve as a predicate device. We will publish a notice in the Federal Register announcing the classification and the controls necessary to provide reasonable assurance of safety and effectiveness. If the *de novo* is declined, the device remains in class III and may not be marketed.

3.1 When the *De Novo* Process May Be Used

FDA will consider *de novos* for devices that are not within a device type that has been classified under the criteria at section 513(a)(1) of the FD&C Act. This includes devices which do not fall within any classification regulation, where the *de novo* requester either determines that there is no predicate device or has received an NSE determination on a 510(k) submission. For devices that have already undergone 510(k) review, FDA will consider a *de novo* if the device has been determined to be NSE due to: (1) the lack of an identifiable predicate device, (2) new intended use, or (3) different technological characteristics that raise different questions of safety and effectiveness. Devices that have been found to be NSE solely due to lack of performance data would generally be ineligible for the *de novo* process.[3] On the other hand, if the device is within a type for which there is an existing Class III classification regulation or one or more approved PMAs, the appropriate mechanism for classification into class I or II would be reclassification under section 513(e) or (f)(3).

In addition, the following criteria should be met for a device for which a *de novo* is submitted:

[3] This is because, using the 510(k) decision process, FDA ordinarily only considers the adequacy of performance data after finding a device has the same intended use as the predicate and technological characteristics that do not raise different questions of safety and effectiveness from the predicate, indicating the device type has been classified and there is a device that could reasonably serve as a predicate for substantial equivalence review.

- The device should be low to moderate risk and should appear, based on what is known about the device, to meet the statutory standards for classification into class I or class II under section 513(a)(1) of the FD&C Act, i.e., general controls or general and special controls would provide reasonable assurance of the safety and effectiveness of the device; and

- You should sufficiently understand and be able to explain all of the known risks and benefits of the device as well as how all known risks can be effectively mitigated and device effectiveness can be assured through the application of general controls or general and special controls[4].

3.2 Submitting *De Novo* Information for FDA Review

This guidance describes two mechanisms for interacting with FDA regarding a device for which *de novo* may be appropriate:

- Pre-Submission (Pre-Sub). A Pre-Sub is not required in order to obtain FDA review of a *de novo*, but is a useful way for submitters to facilitate early feedback from FDA. A Pre-Sub would allow FDA to provide feedback on whether a device may be suitable for the *de novo* process and/or to advise you on the documentation needed in a subsequent *de novo*. The primary advantage of a Pre-Sub is that it provides an opportunity to obtain our preliminary perspective on the likely regulatory controls necessary to provide a reasonable assurance of safety and effectiveness as well as feedback on the evidence, including performance and/or clinical data, that will likely be necessary to support the *de novo*. By obtaining this feedback, you are more likely to optimize your resources in collecting safety and effectiveness evidence needed to support a *de novo*, without the need to perform additional tests. This should also facilitate the review of a subsequent *de novo*.

- *De Novo*. A *de novo* may be submitted with or without a preceding 510(k). The success of a *de novo* that is filed without a Pre-Sub will depend more heavily on how well you search for a potential predicate device, identify the risks and special controls (if applicable), and define and collect adequate data to provide reasonable assurance of safety and effectiveness.

The *de novo* process is outlined in Attachment 1.

In preparing de novo information to submit, we suggest you review publicly posted information, including decision summary documents, for recently granted CDRH *de novos*

[4] For more information on benefit-risk determinations, please see *Guidance for Industry and Food and Drug Administration Staff – Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approvals and De Novo Classification* (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm267829.htm).

available on our website at http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHTransparency/ucm232269.htm.

3.2.1 Pre-Submission (Pre-Sub)

A Pre-Sub may be submitted early in the development process for a device; however, we believe it is most useful after you have identified the proposed intended use and key aspects of the device design sufficient to permit a meaningful discussion. A Pre-Sub related to a future anticipated *de novo* should contain sufficient information to enable us to provide guidance on the test methods and protocols to be used for the collection of performance data. A Pre-Sub is strongly recommended prior to the submission of a *de novo*, especially for devices we have not previously reviewed under a 510(k). *De novo* Pre-Subs will be handled in accordance with our normal pre-submission process. For information on Pre-Subs, please see *Guidance for Industry and FDA Staff, Requests for Feedback on Medical Device Submissions: The Pre-Submission Program and Meetings with Food and Drug Administration Staff (Pre-Sub Guidance)* (http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM311176.pdf). Note that a Pre-Sub may also be filed during review of a *de novo*, as described in the "Submission Issue Meetings" section of the guidance.

In addition to the recommended content for all Pre-Subs (device description, proposed intended use/indications for use, previous submissions, etc.), we suggest that a Pre-Sub prior to a *de novo* also include:

- Proposed Class (I or II) and proposed applicability of 510(k) requirement (exempt or not exempt). Describe why you believe general or general and special controls are adequate to provide reasonable assurance of safety and effectiveness. If you propose Class II and believe future devices of the same type should be exempt from 510(k), justify why premarket notification should not be required.
- The searches of FDA public databases and other resources, including terms, used to establish that no legally marketed device of the same type exists. Provide a list of regulations, PMAs, and/or product codes that may relate to or are potentially similar to the subject device. You may also provide a rationale for why the subject device does not fit within and/or is different from any identified regulations, PMAs, and/or product codes.
- Specific questions regarding review issues relevant to a planned *de novo*. Where necessary for us to consider these specific questions, the Pre-Sub should also include the following:
    - Identification of each risk associated with the device and the reason for each risk (tracing back to risk analysis, clinical testing, etc.). Briefly describe any ongoing and/or planned protocols/studies that need to be completed to collect the necessary data to establish the device's risk profile.
    - Information regarding the safety and effectiveness of the device. Cite the available data/studies relating to the device's safety and effectiveness. Briefly

describe any ongoing and/or planned protocols/studies that need to be completed to collect the necessary safety and effectiveness data.

- Protocols for performance and clinical testing, including how they will address the risks you anticipate and targeted performance levels that will demonstrate that general controls or general and special controls are sufficient to provide reasonable assurance of safety and effectiveness. If preliminary data are available that can help facilitate protocol design and establish final performance characteristics, you are encouraged to submit this information as well.
- The proposed mitigation(s)/control(s) for each risk based on the best available information at the time of the submission. Highlight which mitigations are general controls and which are special controls. Provide details on each recommended mitigation (e.g., specific testing required, labeling, etc.) in the submission.

Examples of questions to pose to FDA in a *de novo* Pre-Sub include:

- Based on the device description, its intended use/indications for use, and/or technological characteristics, and information on the search performed for legally marketed devices, does FDA believe the device may be ineligible for *de novo* because it is likely that a predicate device or appropriate Class III regulation exists or that reclassification would be more appropriate because approved PMA(s) exist?
- Are there other risks, in addition to those identified in the Pre-Sub, given the intended use/indications for use for the device?
- If applicable, are there other controls, in addition to those identified in the pre-sub, that should be considered to provide a reasonable assurance of safety and effectiveness for the device?
- Are the performance study protocols sufficient to allow for the collection of data from which conclusions about device safety and/or effectiveness can be drawn?
  - Is the identified level of concern the appropriate level of concern for the device software?[5]
  - What, if any, additional biocompatibility and/or sterility testing would be appropriate?
- If clinical data are needed, are the proposed trial design and selected control group appropriate?

After you submit your Pre-Sub, we may ask you for clarification or to provide more information. You may also request meetings with us. For more information on Pre-Subs and meetings with FDA staff, please see the Pre-Sub Guidance.

[5] For more information on software, please see *Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices* (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089543.htm)

3.2.2 *De Novo* Application

The *de novo* should include all information and evidence regarding the safety and effectiveness of the device that you are aware of, including the general controls or general and special controls that you believe would provide reasonable assurance of safety and effectiveness. The *de novo* should establish the risk profile of the device, the benefits of device use, and provide data demonstrating that general controls or general and special controls support a classification of Class I or Class II. Attachment 2 contains the suggested content of a *de novo*.

For *de novos*, sponsors must submit at least one valid electronic copy (eCopy). See section 745A(b) of the FD&C Act and FDA's eCopy guidance, *eCopy Program for Medical Device Submissions*, available at http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM313794.pdf. *De novos* (and subsequent submissions, as applicable) submitted without valid eCopies will be placed on hold and the review clock will not start until a valid eCopy is received.

3.3 Address for *De Novos*

For devices regulated by CDRH, *de novos* should be submitted to:

U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center – WO66-G609
10903 New Hampshire Ave
Silver Spring, Maryland 20993-0002

For devices regulated by CBER, *de novos* should be submitted to:

U.S. Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center -WO71-G112
10903 New Hampshire Ave.Silver Spring, Maryland 20993-0002

4. FDA Review Process for *De Novo*

4.1 510(k)s Followed by *De Novo*

If, at the end of our review of a 510(k), we determine that a device is NSE due to lack of a predicate, a new intended use or different types of technology issues, we will consider whether the device may be suitable for review under the *de novo* process. The 510(k) review will occur per standard review practices for 510(k)s and in accordance with current performance goals. If the device appears to present a low to moderate risk and we believe general controls or general and special controls may provide reasonable assurance of safety

and effectiveness, we may indicate in the NSE letter that the product may be appropriate for the *de novo* process under section 513(f)(2) of the FD&C Act. Inclusion of this language within an NSE letter does not indicate that sufficient information currently exists within the 510(k) submission to support a successful *de novo*, but simply indicates that given the risk profile of the device, it seems reasonable that *de novo* may be an appropriate classification pathway.

4.2 *De Novos*

Once a *de novo* is received, whether or not it is preceded by a 510(k), we will verify that another submission for the same device is not under review (e.g., Pre-Sub, 510(k) or PMA). We will not review two submissions for the same device simultaneously. If we identify another submission for the same device, we will not begin review of the *de novo* and will notify you that to start the review, you would need to withdraw the other submission. If the other submission has not been withdrawn within 90 calendar days, we will consider the *de novo* withdrawn.

We will also check that the content of the *de novo* includes the information required by 513(f)(2). As provided by section 513(f)(2)(A)(ii) of the FD&C Act, in order to submit a direct *de novo*, the submitter must determine that there is no legally marketed device upon which to base a determination of substantial equivalence. Under section 513(f)(2)(A)(i), a de novo preceded by a 510(k) must be for a device type that has not been previously classified; thus, if you submit a *de novo* after receipt of an NSE, you should confirm that no device of the same type has legally entered the market since the time of the NSE. See Attachment 2 for discussion of what information you should submit in the classification summary. *De novos* that lack information to determine whether a potential predicate device exists may be placed on hold. As provided by section 513(f)(2)(v) of the FD&C Act, if you are recommending that your device be regulated as a Class II device, you must also submit an initial draft proposal for applicable special controls.[6] If you are recommending Class II and have not provided a draft proposal for applicable special controls, we will place the *de novo* on hold. If your *de novo* is placed on hold, the review clock stops and we will notify you that it is on hold pending receipt of information regarding potential predicates or a draft proposal for special controls. In the event you do not provide the requested information within 180 calendar days, we will consider your *de novo* to be withdrawn.

Next, we will conduct a classification review of legally marketed device types. We will analyze whether an existing legally marketed device of the same type exists, including

[6] Per 21 CFR 860.3(c)(2), special controls include "the promulgation of performance standards, postmarket surveillance, patient registries, development and dissemination of guidance documents (including guidance on the submission of clinical data in premarket notification submissions in accordance with section 510(k) of the act), recommendations, and other appropriate actions as the Commissioner deems necessary to provide such assurance." Typical special controls include specific performance testing requirements, which may include performance and/or clinical testing, and labeling requirements.

whether a predicate has been recently established through the *de novo* process.[7] If a likely predicate device exists or your device falls under a class III classification regulation, or if it is a direct de novo and the device is not low-moderate risk, we intend to decline your *de novo* and notify you of the basis for our decision. If the device falls within a class III classification regulation or there is one or more approved PMAs for the same type of device and we believe general and/or special controls may be adequate to provide a reasonable assurance of safety and effectiveness, we intend to discuss with you the process for reclassification under section 513(e) or 513(f)(3) of the FD&C Act, which are the appropriate pathways for such types of devices to be reclassified in class I or class II. If no existing legally marketed device of the same type is identified, we will continue our review.

Upon successful completion of the submission and classification review, FDA will begin the substantive review of the *de novo*. If the *de novo* is missing information and/or data necessary to determine whether general controls or general and special controls can provide reasonable assurance of safety and effectiveness, we may issue an additional information (AI) letter or request information via interactive review. Issuance of an AI letter stops the review clock, and once you provide a complete response, the clock will resume and review will continue.[8] If you fail to provide a complete response within 180 calendar days of the date of the AI request, we will consider the *de novo* to be withdrawn. If a *de novo* is withdrawn due to failure to submit adequate information, a new *de novo* is required to reinitiate review of the device under the *de novo* process.

If general controls or general and special controls are insufficient to provide reasonable assurance of safety and effectiveness or the information and/or the data provided in the *de novo* are insufficient to determine whether general controls or general and special controls can provide a reasonable assurance of safety and effectiveness, we will decline the *de novo* and you may not legally market the device. You may either submit an application for premarket approval (PMA) under section 515 of the FD&C Act or collect additional information in an attempt to address the issues and submit another *de novo*.

If your data and information demonstrate that general controls or general and special controls are adequate to provide reasonable assurance of safety and effectiveness, we will grant the *de novo*. If a *de novo* is granted, we will issue you a written order granting the *de novo* and specifying the classification of the device into either class I or class II and whether the device

[7] We do not anticipate that *de novos* for the same device type will frequently be under review concurrently. However, in cases where a *de novo* is granted while another device of the same type is under *de novo* review, after a *de novo* is granted, FDA intends to notify the submitter of the *de novo* still under review that a predicate has been established and the *de novo* is declined. You may leverage all information in the *de novo* but will still be required to demonstrate substantial equivalence in a subsequent 510(k).

[8] In rare instances, we may seek input on a *de novo* from a Classification Panel of the FDA Medical Devices Advisory Committee. In such instances, we will likely need to extend the overall review timelines to allow time for scheduling and conducting an Advisory Committee meeting.

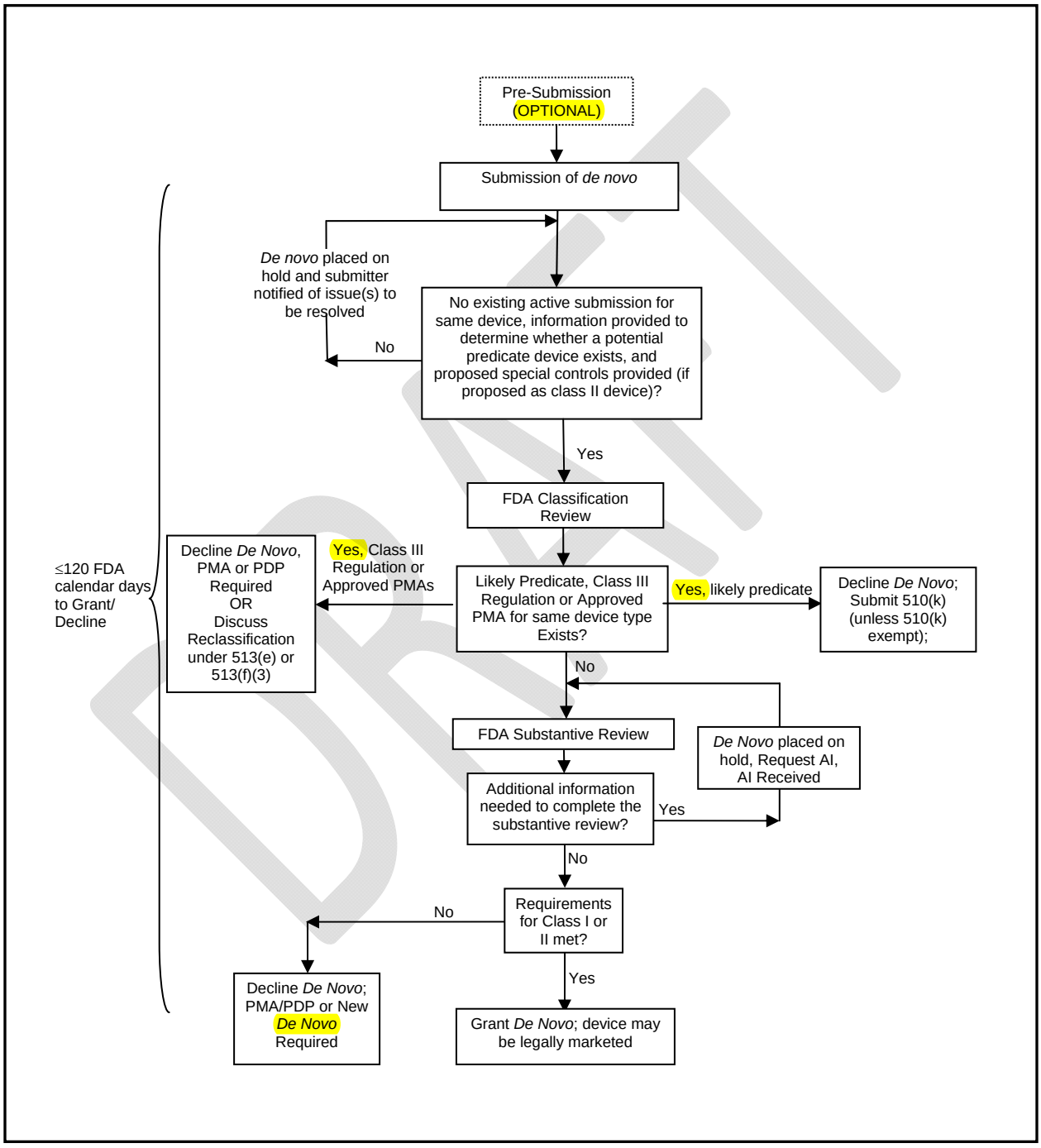
is exempt from premarket notification requirements.[9] For class II devices, we will also identify special controls. Once you receive a written order granting the *de novo*, you may immediately begin marketing the device subject to the general controls and any identified special controls. We will then publish an order in the Federal Register providing public notice of the decision, which will result in codification of the device's identification, classification, and applicable requirements in Title 21 of the Code of Federal Regulations (device classifications are at parts 862 – 892).

If a *de novo* is granted, we intend to make the written order to the submitter granting the *de novo* and a summary of our review of the *de novo* available on the CDRH website (see http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHTransparency/ucm232269.htm) or the CBER website (see http://www.fda.gov/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/default.htm). All information posted to the FDA website will be redacted to protect any confidential commercial, trade secret, or personal privacy information in accordance with 21 CFR Part 20.

[9] Exemption from premarket notification means that future devices of the same type (or modifications to the original *de novo* device that do not result in a new type of device) do not need to be reviewed in a 510(k), subject to the limitations of exemption. For additional information on exemption from premarket notification, see *Procedures for Class II Device Exemptions from Premarket Notification, Guidance for Industry and CDRH Staff* (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080198.htm)

Attachment 1

De Novo Process



Attachment 2

Recommended Content of a *De Novo*

The cover letter for a de novo should clearly identify "De Novo Request"

If significant data for any of the sections below are contained in a previous submission, you may provide cross-reference to the information. Any cross-references should include applicable volume/section/page numbers as appropriate.

Administrative Information:
Applicant name, contact name, address, phone, fax, e-mail.

Regulatory History:
Describe any prior submissions to FDA for the device, including any 510(k)s and related NSE decisions, IDEs, Pre-Subs, and/or previously withdrawn or declined *de novo*s.

For any previous submissions where we provided feedback, please identify how you have responded to the identified issues.

Device Information and Summary:
Provide the device name, device description, indications for use statement (including prescription and/or over the counter), and a description of all main functions, technological characteristics, components, and accessories. Include a summary of the directions for use/usage instructions. Identify the target population including demographics information, diseases, and/or symptoms to be treated, etc.

Change Summary (if appropriate):
Describe in detail any changes made to your device or proposed indications since any prior Pre-Sub or 510(k), as appropriate. This summary should include changes to the device as well as changes to test protocols and/or labeling.

Classification Summary:
For direct *de novos*, describe your search for legally marketed devices of the same type. Provide a list of regulations, approved PMAs, and/or product codes that may relate to or are potentially similar to the subject device. You should also provide a rationale for why the subject device is different from and/or does not fit within any identified regulations, PMAs, and/or product codes.

If the same device (same technology and same indication(s) for use) has been previously found NSE due to lack of a predicate, new intended use, or different questions of safety and effectiveness, only the relevant 510(k) number should be submitted for this section along with a summary of this search performed since the NSE was issued.

Classification Recommendation:
Recommended Class [I or II] and recommended applicability of 510(k) requirement [exempt or not exempt]. Describe why you believe general controls or general and special controls are adequate to provide reasonable assurance of safety and effectiveness. If you are proposing Class II and believe the device type should be exempt from 510(k), justify why premarket notification should not be required.

Proposed Special Controls (for Class II devices ONLY):
Provide proposed special controls along with cross-references to other information within the submission demonstrating that the device meets these special controls.

Supporting Protocols and/or Data:
Provide a summary of all performance and clinical testing that provide a reasonable assurance of safety and effectiveness for your specific device and that demonstrate that general controls or general and special controls are sufficient to provide a reasonable assurance of safety and effectiveness. The summary should include the objective of the testing, a description of study design, and a description of the results. For human subject testing, the summary should also describe the study population, selection and exclusion criteria, duration, data collection methodology, observed adverse reactions, and statistical analysis. The summary should include links to appendices, etc., which contain the detailed final protocols and supporting data.

Summary of Benefits:
Provide information supporting the effectiveness of the device. Cite the available data/studies supporting effectiveness. This section may include references to available published literature, where applicable.

Summary of Known and Potential Risks to Health:
List each risk and identify the reason for each risk (tracing back to risk analysis, clinical testing, etc.). Summarize the studies completed and how they support safety.

Risk and Mitigation Information:
Provide a table showing the proposed mitigation(s) for each risk. Identify which mitigations are general controls and which are special controls. Provide specific section and page numbers where the details on each recommended mitigation (e.g., specific testing required, etc.) can be found in the submission.

Identified Risk	Recommended Mitigation Measures	Supporting Data Contained in *De Novo*
EXAMPLE: Adverse tissue reaction	Specified Biocompatibility Testing Requirements (special control)	Testing in compliance with recognized standard (Section XX, page XXX)
EXAMPLE: Device failure due to XXX (mechanical failure, software anomaly, use error, etc.)	Specified Performance Testing (special control), Device Specific Labeling Requirements (special control),	Test protocols and results (Section XX, pages XXX) Draft device labeling

	Medical Device Reporting (MDR) (general control)	(Section XX, pages XXX)
EXAMPLE: Failure to properly interpret test results	Device Specific Labeling Requirements (special control)	Draft device labeling (Section XX, pages XXX)

Benefit-Risk Considerations:

Provide a discussion demonstrating that, when subject to general controls or general and special controls, the probable benefits to health from use of the device outweigh any probable injury or illness from such use.[10]

Device Labeling:

Proposed device labeling that clearly indicates the proposed intended use and indications for use, limitations, contraindications, etc.[11]

[10] For information on benefit-risk determinations and factors considered, please see *Guidance for Industry and Food and Drug Administration Staff - Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approvals and De Novo Classifications* (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm267829.htm).

[11] Labeling is defined in section 201(m) of the FD&C Act, 21 U.S.C. 321(m), as "all labels and other written , printed or graphic matter (1) upon any article or any of its containers or wrappers, or (2) accompanying such article." Labeling may include package inserts, instructions for use (for patient and/or physician, as applicable), service manuals, etc.