a proposed rule or modification by issuing an order within 60 days of the date the proposed rule or modification was published in the **Federal Register** for public comment.

(b) *Standard of review.* The Commission will approve a proposed rule or modification if the Commission finds that the proposed rule or modification is consistent with the Act and the applicable rules approved by the Commission. If the Commission disapproves a rule or modification, it will make recommendations to the Authority to modify the proposed rule or modification within 30 days of such disapproval.

(c) *Effect.* A proposed rule or modification will not take effect unless it has been approved by the Commission.

By direction of the Commission.

April J. Tabor,

Secretary.

[FR Doc. 2021–21306 Filed 10–4–21; 8:45 am]

BILLING CODE 6750–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 860

[Docket No. FDA–2018–N–0236]

RIN 0910–AH53

Medical Device De Novo Classification Process

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is issuing a final rule to establish requirements for the medical device De Novo classification process under the Federal Food, Drug, and Cosmetic Act (FD&C Act). This final rule establishes procedures and criteria related to requests for De Novo classification (''De Novo request'') and provides a pathway to obtain marketing authorization as a class I or class II device and for certain combination products. These requirements are intended to ensure the most appropriate classification of devices consistent with the protection of the public health and the statutory scheme for device regulation. They are also intended to limit the unnecessary expenditure of FDA and industry resources that may occur if devices for which general controls or general and special controls provide a reasonable assurance of safety and effectiveness are subject to premarket approval. The final rule implements the De Novo classification process under the FD&C Act, as enacted by the Food and Drug Administration Modernization Act of 1997 (FDAMA) and modified by the Food and Drug Administration Safety and Innovation Act (FDASIA) and the 21st Century Cures Act (Cures Act).

DATES: This rule is effective January 3, 2022.

ADDRESSES: For access to the docket to read background documents or comments received, go to *https://www.regulations.gov* and insert the docket number found in brackets in the heading of this final rule into the ''Search'' box and follow the prompts, and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240–402–7500.

FOR FURTHER INFORMATION CONTACT: Sergio de del Castillo, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. 2431, Silver Spring, MD 20993, 301–796–6419.

SUPPLEMENTARY INFORMATION:

Table of Contents

I. Executive Summary
A. Purpose of the Final Rule
B. Summary of the Major Provisions of the Final Rule
C. Legal Authority
D. Costs and Benefits
II. Table of Abbreviations/Commonly Used Acronyms in This Document
III. Background
A. Need for the Regulation/History of This Rulemaking
B. Summary of Comments to the Proposed Rule
C. General Overview of Final Rule
IV. Legal Authority
V. Comments on the Proposed Rule and FDA Response
A. Introduction
B. Description of General Comments and FDA Response
C. Comments and FDA Response on Use of Advisory Committees and Bundling Devices
D. Comments and FDA Response on De Novo Request Information Disclosure
E. Comments and FDA Response on Facility Inspections
F. Comments and FDA Response on Definitions
G. Comments and FDA Response on De Novo Request Format
H. Comments and FDA Response on De Novo Request Content
I. Comments and FDA Response on Criteria for Accepting a De Novo Request
J. Comments and FDA Response on Criteria for Granting or Declining a De Novo Request
K. Comments and FDA Response on Availability of the De Novo Classification Process for Combination Products
VI. Effective Date
VII. Economic Analysis of Impacts
VIII. Analysis of Environmental Impact
IX. Paperwork Reduction Act of 1995
X. Federalism
XI. Consultation and Coordination With Indian Tribal Governments
XII. References

I. Executive Summary

A. Purpose of the Final Rule

This rule establishes new regulations implementing the medical device De Novo classification process under the FD&C Act, which provides a pathway for certain new types of devices to obtain marketing authorization as class I or class II devices, rather than remaining automatically designated as a class III device, which would require premarket approval under the postamendments device classification section of the FD&C Act.

The De Novo classification process is intended to provide an efficient pathway to ensure the most appropriate classification of a device consistent with the protection of the public health and the statutory scheme for device regulation. When FDA classifies a device type as class I or II via the De Novo classification process, other manufacturers do not necessarily have to submit a De Novo request or premarket approval application (PMA) to legally market a device of the same type. Instead, manufacturers can use the less burdensome pathway of premarket notification (510(k)), when applicable, to legally market their device, because the device that was the subject of the original De Novo request can serve as a predicate device for a substantial equivalence determination.

B. Summary of the Major Provisions of the Final Rule

This rule establishes procedures and criteria for the submission and withdrawal of a De Novo request. It also establishes procedures and criteria for FDA to accept, review, grant, and/or decline a De Novo request. While several comments object to sections or subsections of the proposed rule, almost all comments voice support for the objective of the proposed rule: To establish regulations implementing the De Novo classification process. The rule provides that:

- A person may submit a De Novo request after submitting a 510(k) and receiving a not substantially equivalent (NSE) determination.
- A person may also submit a De Novo request without first submitting a 510(k), if the person determines that

there is no legally marketed device upon which to base a determination of substantial equivalence (SE).

- FDA will classify devices according to the classification criteria in the FD&C Act. FDA classifies devices into class I (general controls) if there is information showing that the general controls of the FD&C Act are sufficient to reasonably assure safety and effectiveness; into class II (special controls) if general controls, by themselves, are insufficient to provide reasonable assurance of safety and effectiveness, but there is sufficient information to establish special controls to provide such assurance; and into class III (premarket approval) if there is insufficient information to support classifying a device into class I or class II and the device is a life-sustaining or life-supporting device or is for a use which is of substantial importance in preventing impairment of human health or presents a potential unreasonable risk of illness or injury.
- Devices will be classified by FDA by written order.
- A De Novo request includes administrative information, regulatory history, device description, classification summary information, benefits and risks of device use, and performance data to demonstrate reasonable assurance of safety and effectiveness.
- FDA may refuse to accept a De Novo request that is ineligible or that is not sufficiently complete to permit a substantive review.
- After a De Novo request is accepted, FDA will begin a substantive review of the De Novo request that may result in either FDA requesting additional information, issuing an order granting the request, or declining the De Novo request.
- FDA may decline a De Novo request if, among other things, the device is ineligible or insufficient information is provided to support De Novo classification.

The rule also describes our practices for the conditions under which the confidentiality of a De Novo file is maintained.

C. Legal Authority

This rule is being issued under the device definition provision of the FD&C Act, the combination products provision of the FD&C Act, the device classification section of the FD&C Act, the De Novo classification section of the FD&C Act, the general rulemaking section of the FD&C Act, and the inspection section of the FD&C Act.

D. Costs and Benefits

The final rule clarifies the De Novo classification process for certain medical devices to obtain marketing authorization as class I or class II devices, rather than remaining automatically designated as class III devices under the FD&C Act. A more transparent De Novo classification process could improve the efficiency of obtaining marketing authorization for certain novel medical devices. The medical device industry will incur one-time costs to read and understand this rule. Over 10 years, the annualized cost estimates a 7 percent discount rate range from $0.01 million to $0.17 million, with a primary estimate of $0.09 million. The annualized costs over 10 years at a 3 percent discount rate range from $0.1 million to $0.15 million, with a primary estimate of $0.08 million.

II. Table of Abbreviations/Commonly Used Acronyms in This Document

Abbreviation or acronym	What it means
510(k)	Premarket Notification
CDRH	Center for Devices and Radiological Health
CFR	Code of Federal Regulations
EUA	Emergency Use Authorization
FDA	Food and Drug Administration
FD&C Act	Federal Food, Drug, and Cosmetic Act
FDAMA	Food and Drug Administration Modernization Act of 1997
FOIA	Freedom of Information Act
FR	Federal Register
GLP	Good Laboratory Practice
HDE	Humanitarian Device Exemption
IDE	Investigational Device Exemption
IC	Information Collection
ICR	Information Collection Request
NSE	Not Substantially Equivalent
OMB	Office of Management and Budget
PHI	Protected Health Information
PMA	Premarket Approval Application
PRA	Paperwork Reduction Act of 1995
Pub. L.	Public Law
QSR	Quality System Regulation
Ref.	Reference
RFD	Requests for Designation under 21 CFR 3.7 (§ 3.7)
SE	Substantially Equivalent
SSED	Summary of Safety and Effectiveness Data
U.S.C.	United States Code

III. Background

A. Need for the Regulation/History of This Rulemaking

In the **Federal Register** on December 7, 2018 (83 FR 63127), FDA issued a proposed rule entitled ''Medical Device De Novo Classification Process'' and requested comments on the proposed rule by March 7, 2019. This rule establishes procedures and criteria for the submission and withdrawal of a De Novo request. It also establishes procedures and criteria for FDA to accept, review, grant, and/or decline a De Novo request.

B. Summary of Comments to the Proposed Rule

FDA received comments on the proposed rule from several entities, including medical device associations; industry, medical and healthcare professional associations; public health

advocacy groups; law firms; and individuals. While several comments object to sections or subsections of the proposed rule, almost all comments voice support for the objective of the proposed rule: To establish regulations implementing the De Novo classification process. Comments raise concerns or request clarification regarding several issues, including:

- De Novo request information disclosure,
- facility inspections,
- devices that collect protected health information,
- training of FDA reviewers,
- the definitions,
- the De Novo request format,
- the De Novo request content,
- the criteria for accepting a De Novo request,
- the criteria for declining a De Novo request,
- the availability of the De Novo classification process for combination products, and
- the information needed to support FDA's determination to grant a De Novo classification request.

C. General Overview of Final Rule

FDA considered all comments received on the proposed rule and made changes, primarily for clarity and accuracy and to reduce burden in meeting regulatory requirements. On its own initiative, FDA is renumbering the sections to make them easier for De Novo requesters and the public to research and use. On its own initiative, FDA is also making minor technical changes to make the regulatory history, withdrawal, nonclinical studies, and classification summary provisions clearer. FDA also changed the word ''guidance'' to ''guidelines'' in the definition of Class II at § 860.3 (21 CFR 860.3) on its own initiative for consistency with the language used in section 513(a)(1)(B) of the FD&C Act (21 U.S.C. 360c (a)(1)(B)) and with § 860.123 (21 CFR 860.123) in the final rule. Finally, on its own initiative, FDA is adding requests for information regarding the class in which a device has been classified or the requirements applicable to a device under the FD&C Act that are submitted in accordance with section 513(g) of the FD&C Act, to the regulatory history information required to be included in a De Novo request under proposed § 860.234(a)(3) (21 CFR 860.234(a)(3)) (see § 860.220(a)(3) in the final rule). In the preamble of the proposed rule, FDA described section 513(g) requests for information as one of the submissions it was proposing to require requesters to identify as part of the regulatory history section of a De Novo request (see 83 FR 63127 at 63132). However, a reference to section 513(g) of the FD&C Act was inadvertently omitted from the proposed regulatory text included in the proposed rule. The changes from the proposed rule include the following revisions, additions, and removals.

- Renumber the proposed De Novo section numbers as follows:

TABLE 1—RENUMBERED SECTIONS

Proposed section No.	Renumbered section No.	Section name
860.201	860.200	Purpose and applicability.
860.223	860.210	De Novo request format.
860.234	860.220	De Novo request content.
860.245	860.230	Accepting a De Novo request.
860.256	860.240	Procedures for review of a De Novo request.
860.267	860.250	Withdrawal of a De Novo request.
860.289	860.260	Granting or declining a De Novo request.

- Revise the De Novo request confidentiality provision (§ 860.5(g)) to clarify that after an order granting a De Novo request is issued, data and information in the De Novo file that are not exempt from release under the Freedom of Information Act (FOIA) (5 U.S.C. 552) are immediately available for public disclosure; and to replace certain references to ''De Novo request'' with ''De Novo file.''
- Revise the De Novo format requirements as follows:
  - ○ Remove the requirement to cite the volume number in the table of contents if the De Novo request consists of only one volume,
  - ○ remove the requirement to provide a fax number when submitting a De Novo request, and
  - ○ clarify that the De Novo request must be submitted as a single version in electronic format.
- Revise the De Novo content requirements as follows:
  - ○ Add section 513(g) requests for information to the regulatory history requirement in proposed § 860.234(a)(3) (see § 860.220(a)(3)) and change the term ''use'' to ''device'' in the regulatory history requirement so the text more accurately refers to an application for ''humanitarian device exemption''.
  - ○ Revise the order of the proposed requirements for the content of a De Novo request in proposed § 860.234(a)(9) through (11) (see § 860.220(a)(9) through (11) in the final rule).
  - ○ Revise § 860.220(a)(7) and (a)(9) (this final rule renumbers proposed § 860.234(a)(7) as § 860.220(a)(7)) to clarify that the information required is that known to or that reasonably should be known to the requester.
  - ○ Remove ''laboratory'' to clarify § 860.220(a)(13)(i) and (a)(15)(i) (this final rule renumbers proposed § 860.234(a)(13)(i) and (a)(15)(i) to § 860.220(a)(13)(i) and (a)(15)(i)) requires a summary of each nonclinical study.
  - ○ Move the phrase, ''as appropriate,'' in § 860.220(a)(15)(i) to clarify that not all of the identified nonclinical studies may be applicable to the subject device.
  - ○ Revise § 860.220(a)(15)(i) to clarify that a De Novo requester must include a protocol and complete test report for each nonclinical study.
  - ○ Revise § 860.220(a)(15)(i) to clarify that a De Novo request must only include a statement regarding compliance with good laboratory practice (GLP) requirements in part 58 (21 CFR part 58) for nonclinical studies that are subject to part 58.
- Revise the provisions for withdrawal of a De Novo request to make minor technical changes.
- Revise the provisions for granting a De Novo request to specify that FDA will publish a notice of the classification order in the **Federal Register** within 30 days after granting the request.
- Revise the provisions for declining of a De Novo request to clarify that FDA will decline a De Novo request by written order and moves the grounds for which FDA may decline a De Novo request from § 860.260(b) into § 860.260(c).

IV. Legal Authority

The FD&C Act establishes a comprehensive system for the regulation of medical devices intended for human use. Among the provisions that provide authority for this final rule are sections 201(h), 503(g), 513(a) and (f), 701(a), and 704 of the FD&C Act (21 U.S.C. 321(h), 353(g), 360c(a) and (f), 371(a), and 374). This final rule establishes regulations to implement the De Novo classification process created by section 207 of FDAMA (Pub. L. 105–115) and amended by section 607 of FDASIA (Pub. L. 112–144) and section 3101 of the Cures Act (Pub. L. 114–255).

V. Comments on Proposed Rule and FDA Response

A. Introduction

We received several sets of comments on the proposed rule by the close of the comment period, each containing one or more comments on one or more issues. We received comments from medical device associations, industry, medical and healthcare professional associations, public health advocacy groups, law firms, and individuals. We describe and respond to comments in sections V.B through V.K. We have numbered each comment to help distinguish between different comments. We have grouped similar comments together under the same number, and, in some cases, we have separated different issues discussed in the same comment and designated them as distinct comments for purposes of our responses. The number assigned to each comment or comment topic is purely for organizational purposes and does not signify the comment's value or importance or the order in which comments were received.

B. Description of General Comments and FDA Response

Several comments made general remarks supporting the proposed rule without focusing on a particular proposed provision. Almost all comments supported the objective of the proposed rule: To establish regulations implementing the De Novo classification process. Several comments also requested that FDA make changes without focusing on a particular provision of the proposed rule. In the following paragraphs, we discuss and respond to such general comments.

(Comment 1) A commenter states that FDA should retain patient safety as its number one priority and integrate cybersecurity into the De Novo request process, and that science should support any decisions.

(Response 1) FDA agrees with this comment. As part of the cybersecurity review for premarket submissions for devices that contain software (including firmware) or programmable logic as well as software that is a medical device, FDA recommends that medical device manufacturers assess the impact of threats and vulnerabilities on device functionality and end users/patients as part of the cybersecurity review (Ref. 1).

(Comment 2) A commenter requests FDA to adopt an abbreviated procedure and a reduced user fee for De Novo requests when the requester believes that its device meets the criteria for classification in class I under section 513(a)(1)(A)(ii) of the FD&C Act, because the commenter believes that it would help provide more timely access to low-risk devices and conserve valuable FDA premarket review resources without compromising public health protection.

(Response 2) We do not agree that the procedure proposed by the commenter would be more efficient than the procedures described in FDA's proposed rule. The De Novo classification process provides a pathway for certain devices to obtain marketing authorization as class I or class II devices, rather than remaining automatically designated as class III under section 513(f)(1) of the FD&C Act. FDA makes the determination that a device is class I or class II under section 513(f)(2) of the FD&C Act using the criteria in section 513(a) of the FD&C Act. The process proposed by the commenter would require an abbreviated submission with only some of the information FDA proposed to require in a De Novo request when the requester believes that its device meets the criteria for classification as a class I device. The proposed process would also add a step to the Agency's review process for such devices by requiring FDA to determine within 15 days of receiving the request either that the device meets the criteria for classification into class I or that additional information is required to make the classification determination.

The FD&C Act provides 120 days for review of a De Novo request, regardless of the ultimate classification determination. In FDA's experience, 15 days is not a workable timeframe for the Agency to complete a substantive review of a submission for a new device type to determine that the device meets the criteria for classification into class I. Further, the commenter's suggested abbreviated initial submission omits information that is important for FDA's classification determinations, such as information on probable risks to health associated with use of the device. Therefore, under the commenter's proposed process, FDA would usually, if not always, need to require additional information within 15 days. In § 860.220(a) of this final rule, FDA has identified the required contents of a De Novo request taking into account the Agency's experience with the types of information needed to make a determination on a De Novo request. If a requester believes that some of the required information is not applicable to its device, the requester may submit a justification for omitting that information pursuant to § 860.220(c).

We also note that the proposed process does not appear to provide for any FDA action other than requesting additional information or classifying the device. Section 513(f)(2) of the FD&C Act provides for FDA to decline a De Novo request.

With respect to the user fees applicable to a De Novo request, the Medical Device User Fee Amendments of 2017 amended the FD&C Act to authorize FDA to collect user fees for certain premarket submissions received on or after October 1, 2017, including De Novo requests (see section 738 of the FD&C Act (21 U.S.C. 379j)). The fees are set by statute (section 738(a)(2)(A)(xi) of the FD&C Act) and therefore any changes to such fees are outside the scope of this rulemaking.

(Comment 3) A commenter concerned about the design of a remote monitoring system containing software states that as part of the De Novo request, a manufacturer should provide information on whether the device collects protected health information (PHI). The same commenter requests that the Health and Human Services' Office for Civil Rights should complete a review prior to the De Novo request being granted by FDA. A commenter states that a PHI pre-approval plan should be reviewed with the impact and patient experience included in the overall De Novo request grant.

(Response 3) Standards for the use and disclosure of protected health information by certain entities are set forth in regulations implementing the Health Insurance Portability and Accountability Act of 1996 (HIPAA) (Pub. L. 101–191), which are outside the scope of this rulemaking. To demonstrate a reasonable assurance of safety and effectiveness for software devices, documentation related to the requirements of the quality system regulation (QSR) (21 CFR part 820) is often a necessary part of the premarket submission. See also ''Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices'' (Ref. 2). As part of QSR design controls, a manufacturer must ''establish and maintain procedures for validating the device design,'' which ''shall include software validation and risk analysis, where appropriate.'' (§ 820.30(g)). As part of the software validation and risk analysis required by § 820.30(g), software device manufacturers may need to establish a cybersecurity vulnerability and management approach, where appropriate. Such cybersecurity design controls help to ensure device security, including protection of health information.

(Comment 4) A comment recommends FDA provide additional training for FDA reviewers on De Novo classification to assist FDA reviewers in more thoroughly understanding the devices and how to review De Novo requests with the broader view of assessing the nature of the devices and their value to the patient.

(Response 4) FDA currently provides training to FDA staff on the De Novo classification process. With the publication of this final rule, FDA intends to update its current training to be reflective of the requirements of the final rule. FDA also understands that patient input can be an important consideration during FDA's review of a De Novo request, as reflected in our guidance for industry and FDA Staff, ''Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approval and De Novo Classifications'' (Ref. 3) and ''Patient Preference Information—Voluntary Submission, Review in Premarket Approval Applications, Humanitarian Device Exemption Applications, and De Novo Requests, and Inclusion in Decision Summaries and Device Labeling'' (Ref. 4).

(Comment 5) A commenter proposes that unless required by the FD&C Act or the device is of high public health importance, FDA defer the identification of special controls for devices being granted De Novo classification until after the De Novo request is granted and FDA can make a general assessment of all class II devices. The same commenter also requests that FDA prioritize the identification of special controls for all class II devices.

(Response 5) Because special controls are necessary to assure the safety and effectiveness of class II devices, FDA does not agree with the commenter's proposal. FDA believes it is important to identify the appropriate special controls for class II devices at the time FDA grants the De Novo request. The granting of the De Novo request does several things: It allows the device to be marketed immediately, creates a classification regulation for devices of the type, and permits the device to serve as a predicate device (section 513(f)(2)(B) of the FD&C Act) (Ref. 5). Because these consequences flow from the grant of a De Novo request, and because special controls are necessary to reasonably assure the safety and effectiveness of a class II device, FDA will continue to identify special controls at the time that it grants a De Novo classification request.

The request that FDA prioritize the identification of special controls for all class II devices is outside the scope of this rulemaking.

(Comment 6) A comment recommends that medical device applicants be encouraged to perform and/or review studies that address the effect of the device on patient function, because the commenter states that, for all populations, the ability to function at work, at home, and with family is an important outcome.

(Response 6) Where relevant to the intended use of a device, FDA currently would take patient function into account in evaluating the safety and effectiveness of the device. As part of its initiative for patients to engage with FDA, FDA has incorporated patient perspectives into the total product life cycle, including in the premarket evaluation of devices (Refs. 4 and 6).

(Comment 7) A comment objects to the placement of all the De Novo request regulatory requirements in part 860 and suggests that the Center for Devices and Radiological Health (CDRH) separate requirements for the information needed to classify a device type from requirements for the information needed to authorize a specific low to moderate risk device for marketing by placing the latter in a separate regulation for ''Premarket Approval of Novel Class I and II Medical Devices.''

(Response 7) FDA disagrees with this comment. The De Novo classification provisions will be housed in part 860 of the CFR with the other device classification subparts. We recognize that, because the De Novo classification process includes a pathway to obtain marketing authorization for a specific device, placement of the De Novo classification regulations may not be as straightforward as the other classification regulations. FDA believes that part 860 is the most appropriate fit.

(Comment 8) A comment asserts that some devices, especially implantable devices, are inappropriately classified as class II instead of class III because these devices are ''potentially life-saving or life-threatening.'' The comment further indicates that the De Novo pathway should not replace the PMA pathway for implanted devices that are not eligible for 510(k) clearance and recommends that FDA document whether the increase in De Novo grants over the past few years indicates a movement from 510(k) clearance of devices to De Novo or from PMA review to the less stringent De Novo pathway before finalizing the proposed rule.

(Response 8) Altering the statutory standards for device classification and marketing authorization is outside the scope of this rulemaking. FDA classifies devices according to the statutory criteria set forth in section 513(a)(1) of the FD&C Act. Therefore, if FDA determines that general and special controls are sufficient to provide a reasonable assurance of safety and effectiveness for a potentially life-supporting device, FDA must classify that device into class II (see section 513(a)(1)(B) of the FD&C Act). Congress added section 513(f)(2) of the FD&C Act as part of FDAMA to limit unnecessary expenditure of FDA and industry resources that could occur if devices for which general controls or general and special controls provide a reasonable assurance of safety and effectiveness were subject to premarket approval under section 515 of the FD&C Act (21 U.S.C. 360e). As enacted by FDAMA, to submit a De Novo request, a device first had to be found NSE to legally marketed predicate devices through a 510(k). Section 513(f)(2) of the FD&C Act was modified by section 607 of FDASIA, which created an alternative mechanism for submitting a De Novo request that does not require that a device be reviewed first under a 510(k) and found NSE prior to submission of a De Novo request. If a person believes their device is appropriate for classification into class I or class II and determines, based on currently available information, there is no legally marketed predicate device, they may submit a De Novo request without a preceding 510(k) and NSE.

(Comment 9) A comment objects to making De Novo devices immediately available as a predicate device because the commenter suggests that it puts patient safety at risk and does not reward innovation. The commenter proposes a ''safe harbor'' of several years where the De Novo device cannot be used as a predicate.

(Response 9) FDA disagrees with this comment. Section 513(f)(2) of the FD&C Act provides that any device classified through the De Novo pathway ''shall be a predicate device for determining substantial equivalence'' and does not impose a waiting period for such devices to be used as predicates.

C. Comments and FDA Response on Use of Advisory Committees and Bundling Devices

(Comment 10) A comment requests FDA to revise § 860.1 to limit the use of advisory committees to cases of high-risk, life-supporting, or life-sustaining devices, or to classification panels because the commenter states that referring a De Novo request to an advisory committee should be unusual, as the devices that are the subject of such requests generally present low to moderate risk.

(Response 10) We disagree with this proposed revision. This comment is directed specifically to the De Novo classification process, and § 860.1 applies to both premarket and postmarket classifications and reclassifications. In addition, we do not agree that the only time we should seek advice from an advisory committee is in cases of high-risk, life-supporting, or life-sustaining devices, or in a classification panel; FDA may refer a matter to an advisory committee because it chooses to do so at its own discretion (see our guidance ''Procedures for Meetings of the Medical Devices Advisory Committee'' (Ref. 7).) For example, the Agency may present a matter before an advisory committee if the matter is of significant public interest or there is additional or special expertise provided by the panel that could assist FDA in its decision making.

(Comment 11) A comment asks FDA to revise the De Novo ''Purpose and applicability'' provision (the final rule renumbers the proposed § 860.201(b) as § 860.200(b)) to clarify that a De Novo request may also be submitted for a group of related devices because a commenter states that, in some cases, more than one related device should be submitted for De Novo classification.

(Response 11) FDA disagrees with this comment. Generally, it is not appropriate to bundle multiple devices in a single De Novo request. For example, FDA would not grant a De Novo request that would require FDA to create more than one classification regulation. If an applicant feels that they have a situation where it makes logical sense to bundle multiple devices into one De Novo request, it would be advisable to discuss proactively with FDA in advance of submission of the De Novo request.

D. Comments and FDA Response on De Novo Request Information Disclosure

(Comment 12) A comment requests that FDA revise the De Novo file confidentiality provision in § 860.5(g) so that it follows the approach for PMAs concerning confidentiality because the commenter asserts requesters are entitled to maintain confidentiality for information submitted to FDA through the De Novo process even if some information relating to the De Novo request has been disclosed publicly. Another comment requests that FDA revise the provision regarding disclosure of the existence of a De Novo request before an order granting the request is issued to clarify that such disclosure is governed by the trade secrets and confidential commercial information provisions in § 20.61 (21 CFR 20.61). A different comment questions why CDRH could not disclose the existence of a De Novo request and the date of its acceptance for review or the date it was refused.

(Response 12) FDA is making minor revisions to refer to the ''De Novo file'' instead of the ''De Novo request'' in four places in § 860.5(g) for consistency with the language used in § 860.5(g)(1) and to align with similar language used in 21 CFR 814.9 regarding confidentiality of information in a PMA file. FDA otherwise disagrees with the comments requesting revision of the proposed De Novo request confidentiality requirements. The provisions in § 860.5(g)(2) and (3) provide that, before an order granting the De Novo request is issued, FDA may not publicly disclose the existence of or data and information contained in a De Novo file, unless such information has already been publicly disclosed or acknowledged by the De Novo requester. Therefore, if a requester publicly acknowledges only the date and existence of a De Novo request submission, that acknowledgment would not, by itself, make underlying data and information in the De Novo file publicly available for disclosure under § 860.5(g). Further, the requester cannot have confidentiality concerns about information it has already publicly disclosed. This approach is concordant with FDA's general public information regulations at § 20.61 and § 20.81 (21 CFR 20.81). Under § 20.61, information submitted to FDA that qualifies as trade secret or confidential commercial information is generally exempt from public disclosure, but § 20.81 provides that records otherwise exempt from disclosure are available for public disclosure to the extent that they ''contain data or information that have previously been disclosed in a lawful manner to any member of the public, other than an employee or consultant or pursuant to other commercial arrangements with appropriate safeguards for secrecy.''

Regarding why FDA will not disclose the existence of a De Novo request that has not been publicly disclosed or acknowledged, disclosing the existence of the De Novo request would disclose the requester's intent to market the device. Consistent with FDA's approach in other premarket programs, we generally consider an applicant's intent to market a device to be confidential commercial information where the applicant has kept that intent confidential. This approach is supported by the Supreme Court's recent decision in *Food Mktg. Inst.* v. *Argus Leader Media,* 139 S. Ct. 2356, 2363 (2019).

(Comment 13) Some comments requested more clarity on how and when data and information may be disclosed by FDA, and some comments suggested that the data and information disclosed after FDA issues an order granting a De Novo request should only be available following a FOIA request. A commenter also recommended changes to clarify that the requester would have an opportunity to review and redact trade secret information before the release of any data and information in the De Novo request. Another commenter recommended that CDRH draft and post on its website a summary of the information submitted to support FDA's classification determination and require De Novo requesters to prepare summaries of data and information submitted to support the safety and effectiveness of the specific device that could be posted in FDA's De Novo database to align with public disclosure of 510(k) and PMA summaries.

(Response 13) As discussed in response to the previous comment, prior to sending an order granting the De Novo request to the De Novo requester, FDA will not disclose the data or information contained in the De Novo file, unless the De Novo requester has publicly disclosed or acknowledged such information (§ 860.5(g)(3)). To provide more clarity and to help ensure that information exempt from release is appropriately protected, we are revising § 860.5(g)(4) to make clear that after FDA sends an order granting the De Novo request to the De Novo requester, FDA may immediately disclose any safety and effectiveness information and any other information in the De Novo file that is not exempt from release under FOIA.

FDA disagrees with the comments requesting FDA to limit the release of data and information contained in a granted De Novo request to situations in which the Agency has received a FOIA request for that information. FDA proactively discloses information of interest to the public on a regular basis. For example, granting a De Novo request allows marketing of the particular device that is the subject of the request, creates a classification regulation for devices of this type, and permits the device to serve as a predicate device (section 513(f)(2) of the FD&C Act; Ref. 5). FDA believes that information regarding granted De Novo requests and summaries of safety and effectiveness information that formed the basis of FDA's granting decisions should be publicly posted without waiting to receive a FOIA request for that

information. With respect to affording requesters an opportunity to review and redact records that may contain trade secret information before they are disclosed, FDA will follow its existing pre-disclosure notification requirements in § 20.61.

Since 2010, FDA has posted on its website classification orders and redacted decision summary documents for devices classified through the De Novo classification process. This approach is analogous to our current approach for other marketing authorization pathways: summaries of safety and effectiveness information that formed the basis of FDA's decisions are posted on FDA's website for PMA approvals, available at *https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm*; and for 510(k) clearances, 510(k) summaries are available at *https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm.* We believe the comment suggesting that FDA require a De Novo requester to prepare a summary of safety and effectiveness information for public posting to align with PMA and 510(k) procedures confuses the requirement for a PMA to include a summary that allows the reader to gain a general understanding of the data and information in the application (§ 814.20 (21 CFR 814.20(b)(3))) with the publicly posted detailed summary of safety and effectiveness data (SSED) on which an approval or denial decision is based for a PMA. Although some PMA applicants may submit draft SSEDs, the final SSEDs posted online are FDA documents. The De Novo decision summary is intended to present an objective and balanced summary of the scientific evidence that served as the basis for the decision to grant a De Novo request. Because the Agency already prepares such documents and determines what information supports its decision to grant the De Novo request, FDA is not revising the final rule to require requesters to prepare a similar summary, as this commenter requests. We believe the information that the commenter indicates would be of interest to healthcare providers and patients is already made publicly available through FDA's current approach.

E. Comments and FDA Response on Facility Inspections

(Comment 14) A comment supported facility inspection prior to granting or declining a De Novo request because the commenter states that it is essential for safety in the case of novel medical devices. Several comments wanted to delete either all of subsection § 860.240(c) (this final rule renumbers proposed § 860.256(c) as § 860.240(c)) or paragraph § 860.240(c)(2) (this final rule renumbers proposed § 860.256(c)(2) as § 860.240(c)(2)) or revise subsection § 860.240(c) because the commenters state these provisions are unduly burdensome or that FDA lacks statutory authority to require facility inspections to assess implementation of the QSR (part 820).

(Response 14) Several comments objected to proposed § 860.256(c) (this final rule renumbers proposed § 860.256(c) as § 860.240(c)), which relates to the inspection of relevant facilities prior to granting or declining a De Novo request and argued that the FD&C Act does not give FDA this inspection authority. FDA disagrees with the comments, and, as described below, is finalizing the provision with clarifying changes. The inspection would be done only in the two circumstances specified in the regulation. Based on past experience, inspections in these circumstances should arise with a small percentage of De Novo requests.

1. Clinical and Nonclinical Data

As explained in the proposed rule preamble, an inspection prior to its De Novo decision is used to help FDA determine whether clinical or nonclinical data were collected in a manner that ensures the data accurately represents the risks and benefits of the device, in accordance with section 513(a)(1)(C) of the FD&C Act. FDA has been conducting such inspections when data integrity and quality concerns arise during its review of a De Novo request, and information from these inspections has been critically important to the Agency's De Novo determination. For example, based on review of the clinical data provided in the De Novo request, FDA may determine that the results of a clinical investigation are clinically or physiologically improbable. An inspection may be conducted to verify the integrity of the data.

In another example, FDA may receive a whistleblower complaint alleging misconduct at one or more clinical investigational sites, and the results from the clinical investigation are used to support a De Novo request. Our assessment of the subject device is dependent on the veracity of the complaint. FDA inspections of one or more investigational sites to assess the veracity of the complaint would help determine whether evidence submitted in support of the De Novo request (*e.g.,* data from a particular site) needs to be excluded from FDA's consideration.

2. Quality System Regulation and Current Good Manufacturing Practices

For certain devices with critical and/or novel manufacturing processes that may impact the safety and effectiveness of the device, FDA also believes that an inspection may be necessary for FDA to determine whether general controls, including the QSR (part 820) for devices and current good manufacturing practices (21 CFR part 4, subpart A) for combination products, are adequate to provide a reasonable assurance of safety and effectiveness of the device, or whether special controls to mitigate risks must be developed. Such inspections are not for the purpose of reviewing for compliance with the QSR. Rather, the purpose of such an inspection is to gather information on critical and/or novel manufacturing processes, the methods and procedures used, and such additional information as may be necessary to assess the safety and effectiveness of a drug or biologic constituent part of a combination product. Such information will help classify the device type by providing an understanding of critical and/or novel manufacturing processes to determine if the device type is of low to moderate risk, to determine if general controls and special controls can effectively mitigate the probable risks to health, and to determine if the product specifications can reasonably be met. In some circumstances, this information can only be obtained by an inspection—and not any other means, such as through review of standard operating procedures—because it requires a detailed understanding of how manufacturers, in practice, carry out complex and/or safety critical processes, methods, or procedures. In these situations, the information obtained from an inspection would be necessary for FDA to make a De Novo determination.

For example, FDA may receive a De Novo request for a permanent implant with a coating that contains the same active ingredient that is in a new drug application (NDA) approved drug product. The combination product is intended to reduce the risk of surgical site infections. The safety and effectiveness of the combination product is linked to the ability of the manufacturer to ensure consistent levels of drug coating and drug release batch-to-batch. Probable risks associated with inconsistent coating or inconsistent drug release may include local/systemic toxicity, reproductive/genotoxicity, antibiotic resistance, and infection. An inspection would help assess the sampling methodology and laboratory

controls used by the manufacturer to ensure consistent levels of drug coating and drug release batch-to-batch. Such information would be critical to FDA in its De Novo determination because assessment of the sampling methodology and laboratory controls at the manufacturing facility would aid in FDA's determination that the product has consistent levels of drug coating and drug release batch-to-batch. This information would enable FDA to determine whether the proposed special controls are sufficient to reasonably assure safety and effectiveness or if additional controls are needed.

In another example, FDA may receive a De Novo request for a device that is provided sterile using a novel sterilization method for which there is little or no published information and limited or no history of FDA evaluation of sterilization development and/or validation data. Probable risks associated with inadequate sterilization may include risk of infection or contamination. An inspection of the facility where the device is sterilized would be critical to determining if special controls regarding sterilization validation are sufficient to mitigate the device's probable risks, verify that the novel sterilization method can feasibly be carried out, and determine if additional controls are needed to mitigate the risks associated with inadequate sterilization to reasonably assure the device's safety.

One commenter objected to inspections used to assess whether QSRs are adequate to ensure that critical and/or novel manufacturing processes that may impact the safety and effectiveness of the device are controlled on the grounds that such inspections require either a warrant or specific statutory authorization under the Constitution. Section 704(a)(1) of the FD&C Act grants FDA authority to enter and inspect ''any factory, warehouse, or establishment in which food, drugs, or devices are manufactured, processed, packed, or held for the introduction into interstate commerce or after such introduction.'' 21 U.S.C. 374. In addition, FDA intends to undertake inspections only in limited circumstances when the inspection is to help determine whether to grant a De Novo request from a firm and determine whether the proposed special controls are sufficient to reasonably assure safety and effectiveness or if additional controls are needed under section 513(f)(2) of the FD&C Act.

F. Comments and FDA Response on Definitions

(Comment 15) A comment proposed several changes to the ''Supplemental data sheet'' definition because not all implanted devices are class III, and another comment recommended changes to Form FDA 3429 (General Device Classification Questionnaire).

(Response 15) These comments are moot because, in a separate rulemaking (see 83 FR 64443 at 64454 through 64456, December 17, 2018, effective March 18, 2019), the definitions for the terms ''Supplemental data sheet'' and ''Classification questionnaire'' were removed from § 860.3 and the prior requirements to provide Form FDA 3427 (Supplemental Data Sheet) and Form FDA 3429 (General Device Classification Questionnaire) were removed from §§ 860.84 and 860.123.

(Comment 16) A comment requests that FDA keep the individual paragraph designations in the definitions section (§ 860.3) because the commenter states it is helpful to industry to be able to cite a specific term by paragraph designation.

(Response 16) FDA disagrees with this comment. FDA believes it would be easier for industry to locate definitions listed alphabetically. FDA has taken a similar approach in its labeling and unique device identification regulations (see 21 CFR 801.3 and 830.3). FDA further believes that it is not difficult to cite to alphabetical definitions within § 860.3.

G. Comments and FDA Response on De Novo Request Format

(Comment 17) A comment asks FDA to revise the proposed De Novo request format requirements to clarify that the application can be a single version in electronic format, conforming it to FDA's proposed rule, ''Medical Device Submissions: Amending Premarket Regulations That Require Multiple Copies and Specify Paper Copies To Be Allowed in Electronic Format'' (83 FR 46444, September 13, 2018).

(Response 17) FDA agrees that a De Novo request may be submitted as a single version in electronic format, which is currently eCopy and, in the future, may be a different electronic format. De Novo requests currently must be submitted as a single eCopy, in accordance with section 745A(b)(1) of the FD&C Act (21 U.S.C. 379k–1(b)(1)) and FDA's guidance, ''eCopy Program for Medical Device Submissions,'' issued April 27, 2020 (Ref. 8). Section 745A(b)(3) of the FD&C Act requires the presubmission and submission types enumerated in section 745A(b)(1) (including De Novo requests), any supplements to such presubmissions or submissions for devices, and any appeals of action taken with respect to such presubmissions or submissions, including devices under the Public Health Service Act, to be submitted solely in electronic format as specified by FDA in guidance. Once FDA issues guidance under section 745A(b)(3) of the FD&C Act, the Agency can require De Novo request submissions in electronic formats other than eCopy. We are revising paragraph § 860.210(a) (this final rule renumbers proposed § 860.223(a) as § 860.210(a)) to require submission of a De Novo request as a single version in electronic format).

(Comment 18) A commenter states it is overly prescriptive to require a specific format for a De Novo request.

(Response 18) We do not agree that the format FDA is requiring is overly prescriptive. Section 860.210 (this final rule renumbers proposed § 860.223 as § 860.210), the format section, requires that the De Novo request be signed by the requester or an authorized representative, be designated as a ''De Novo request,'' and be written or translated into English. FDA believes it is easier for FDA reviewers to find required information if the De Novo request information is provided in a specific format, thereby facilitating more efficient review and processing of the request.

(Comment 19) Because a De Novo request may contain only one volume, a comment asks FDA to revise the De Novo request format paragraph to qualify that the table of contents of a De Novo request reference a volume number only if the De Novo request contains more than one volume.

(Response 19) FDA agrees that it is unnecessary to cite the volume if the De Novo request does not contain more than one volume. We are revising paragraph § 860.220(a)(1) (this final rule renumbers proposed § 860.234(a)(1) as § 860.220(a)(1)) accordingly.

H. Comments and FDA Response on De Novo Request Content

(Comment 20) Some comments request FDA to revise the ''Device description'' provision at § 860.220(a)(6)(ii) ((this final rule renumbers proposed § 860.234(a)(6)(ii) as § 860.220(a)(6)(ii)) because the commenters state some of the terminology is more typically used to describe drugs than devices. The commenters suggest that ''component'' is more applicable to devices than ''ingredient,'' and that some components may not be ''functional'' but may still be important to a De Novo

classification decision. A commenter states the term ''principal components'' is appropriate because it signals that the submitter should identify the device's primary components but need not identify every component. Another commenter similarly suggests the term ''major components'' would be appropriate.

(Response 20) FDA disagrees that ingredient is an atypical term for a device. For example, in vitro diagnostic device labels generally are required to include the quantity, proportion, or concentration of each reactive ingredient for a reagent (21 CFR 809.10(a)(3)).

In addition, FDA does not agree with requiring only a device's principal or major components to be described in a De Novo request. FDA is requesting identification of all functional components or ingredients that comprise the subject device or combination product so that FDA has sufficient understanding of the device to evaluate whether general controls or general and special controls are sufficient to provide reasonable assurance of safety and effectiveness. We would consider any component of the device relating to how the device operates be a functional component. It was not our intent to limit the identification of the components or ingredients of the device or combination product. To that end, we disagree with the commenters' proposed edits to require identification of only major or principal components.

(Comment 21) Comments on the summary of studies (this final rule renumbers proposed § 860.234(a)(13)(ii) as § 860.220(a)(13)(ii)), the technical sections (this final rule renumbers proposed § 860.234(a)(15)(i) and (iii) as § 860.220(a)(15)(i) and (iii)), and the bibliography (this final rule renumbers proposed § 860.234(a)(16)(i) as § 860.220(a)(16)(i)) that are part of the required content of a De Novo request ask that FDA limit the required information to that ''necessary to determine the classification of the device.'' The commenter states that it is necessary to clarify that data unrelated to classification of the device (*e.g.,* for other indications) do not need to be submitted and that the focus of the application is to determine the classification of the device.

(Response 21) FDA does not agree with these comments and does not believe the requested clarifications are necessary. Under the FD&C Act, FDA determines the classification of a device that is the subject of a De Novo request (section 513(f)(2) of the FD&C Act). The requirements for the content of a De Novo request reflect the information that, in FDA's experience, generally is necessary to determine if general or general and special controls are sufficient to provide a reasonable assurance of safety and effectiveness of the device that is the subject of the De Novo request. To the extent the requester believes that certain required content for a De Novo request is not applicable to its device, the requester has the option under § 860.220(c) (this final rule renumbers proposed § 860.234(c) to § 860.220(c)) to omit that information and submit a statement that specifies the omitted information and justifies the omission. FDA will notify the requester if it does not accept the justification.

Further, § 860.220(a)(15) (this final rule renumbers proposed § 860.234(a)(15) as § 860.220(a)(15)) already specifies that the required technical sections must include data and information ''in sufficient detail to permit FDA to determine whether to grant or decline the De Novo request.'' Therefore, we believe it is already clear the information required in the technical sections under § 860.220(a)(15)(i) and (iii) (the final rule renumbers proposed § 860.234(a)(15)(i) and (iii) as § 860.220(a)(15)(i) and (iii)) and the related summary of studies under § 860.220(a)(13) (the final rule renumbers proposed § 860.234(a)(13) as § 860.220(a)(13)) is information focused on FDA's classification determination. In addition, the bibliography of published reports required under § 860.220(a)(16)(i) (the final rule renumbers proposed § 860.234(a)(16)(i) as § 860.220(a)(16)(i)) is limited to reports ''that concern the safety or effectiveness of the device.'' Published reports concerning the safety or effectiveness of the device that is the subject of the De Novo request would be useful to FDA's evaluation of the request.

(Comment 22) Some comments object that FDA's proposed requirements for the data and information submitted in a De Novo request are overly broad or potentially confusing. One commenter supports requirements for a thorough review of existing data but requests that the requirement to submit '' 'all' available data . . . should be clarified to indicate that which is reasonably attainable by'' the De Novo requester. Other commenters request that FDA change the phrase ''known or reasonably known'' in certain provisions of § 860.220(a) (this final rule renumbers proposed § 860.234(a) to § 860.220(a)) to ''known or reasonably available to'' the requester. These commenters indicate that the ''known or reasonably known'' standard does not clarify to whom the required information is known or reasonably known. A commenter also indicates that the proposed language could lead FDA reviewers to decide a De Novo requester is ''hiding something'' if the submission lacks information known to the reviewer but not the requester. Another commenter states that use of the term ''reasonably available'' instead would ''impl[y] that the sponsor must engage in reasonable effort to obtain the relevant information.''

(Response 22) FDA did not include provisions in the proposed rule using the phrase ''all available data'' as one comment suggests, but we believe limiting all of the required information for a De Novo request to that ''reasonably attainable by'' the requester is inappropriate. In some cases, for example, a requester may know of studies or reports concerning the safety or effectiveness of the device but be unable to obtain them for some reason (*e.g.,* the requester must pay to gain access to a registry containing the relevant data). In these cases, it is still useful to provide to FDA the information about such studies or reports that is known or reasonably should be known to the requester, even if complete information about or copies of such studies or reports is unavailable to the requester. For example, FDA may have a greater ability to access a publication with more complete information.

In response to these comments, FDA is revising § 860.220(a)(7) and (9) (this final rule renumbers proposed § 860.234(a)(7) as § 860.220(a)(7) and renumbers § 860.234(a)(11) as § 860.220(a)(9)) to clarify that the information required is that known to or that reasonably should be known to the requester. The intent of requiring a De Novo request to include information that is known or reasonably known to the requester is to ensure that the requester engages in a reasonable effort to provide relevant information and does not omit information important to FDA's determination to grant or decline the De Novo request because of a failure to conduct reasonable searches for such information. As explained in the proposed rule, for example, the summary of known or reasonably known probable risks to health associated with the use of the device required in the De Novo request under § 860.220(a)(9) ''should be based on the best available information at the time of submission of the De Novo request.'' (83 FR 63127 at 63133) These requirements help ensure that FDA's evaluation of a

De Novo request is based on complete and quality information and minimize review staff's need to request additional information. We believe the term ''should reasonably be known'' appropriately captures the intent of these requirements.

(Comment 23) A comment requests that FDA provide more flexibility in the standard for valid scientific evidence for De Novo devices as a way to address lower risk devices, rather than requiring only less-detailed summary information for some components of a complete De Novo request.

(Response 23) FDA disagrees with the comment. As in other device classification processes, FDA relies upon valid scientific evidence in determining the safety and effectiveness of a device that is the subject of a De Novo request (§ 860.260(e) (this final rule renumbers proposed § 860.289(d) as § 860.260(e)). This is unchanged by the requirement to provide summaries of certain information as part of a De Novo request. In addition, the required content of a De Novo request must include, in addition to such summaries, technical sections containing nonclinical study results, software information and testing, and clinical investigation results with sufficient detail to allow FDA to make a determination on the De Novo request.

Regarding the commenter's request for ''flexibility'' in the standard for valid scientific evidence, FDA does not believe any change is necessary. FDA's regulatory definition of valid scientific evidence already makes clear that ''[t]he evidence required may vary according to the characteristics of the device, its conditions of use, the existence and adequacy of warnings and other restrictions, and the extent of experience with its use'' (§ 860.7(c)(2)). FDA has also issued guidance explaining its approach to making benefit-risk determinations in the context of De Novo requests, which is a flexible, patient-centric approach tailored to the type and intended use of the device. See our guidances ''Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approval and De Novo Classifications'' (Ref. 3) and ''Consideration of Uncertainty in Making Benefit-Risk Determinations in Medical Device Premarket Approvals, De Novo Classifications, and Humanitarian Device Exemptions'' (Ref. 9).

(Comment 24) A commenter states FDA should focus on device design to improve device safety. The same commenter asserts that all premarket applications (PMA, 510(k), and De Novo requests) should include a design and development plan, design input, output, design reviews, verification, validation, transfer, and all design changes.

(Response 24) FDA agrees that device design is important to device safety. Manufacturers are already required under part 820 (QSR) to focus on device design (§ 820.30, Design controls). Additionally, FDA may require additional verification or validation information for specific design features or inspect relevant facilities, where appropriate (§ 860.240, this final rule renumbers proposed § 860.256 as § 860.240).

(Comment 25) Because a commenter notes that ''manufacturer'' is used elsewhere in the proposed rule and because some commenters state that many companies no longer use Fax machines, the comments request that FDA revise the ''Administrative information'' provision of the De Novo request content section to add a reference to ''manufacturer,'' in addition to owners and operators, and to remove the reference to Fax machines from § 860.220(a)(2) (this final rule renumbers proposed § 860.234(a)(2) as § 860.220(a)(2)).

(Response 25) FDA agrees to remove the reference to Fax machines and is revising paragraph § 860.220(a)(2) (this final rule renumbers proposed § 860.234(a)(2) as § 860.220(a)(2)) accordingly. However, we do not agree that it is necessary to add a reference to ''manufacturer'' in this provision. In the final rule, § 860.220(a)(2) requires that the De Novo request include the establishment registration number of the owner or operator submitting the De Novo request, if applicable, because certain ''owners or operators,'' as defined in 21 CFR 807.3(f), are the entities required to register and submit listing information under 21 CFR part 807. Use of the terms ''owner'' and ''operator'' in § 860.220(a)(2) does not mean that a device manufacturer is unable to submit a De Novo request. The registration and listing requirements apply to owners or operators of establishments who are ''engaged in the manufacture, preparation, propagation, compounding, assembly, or processing of a device intended for human use,'' unless they are exempt under 510(g) of the FD&C Act or FDA regulations (see 21 CFR 807.20).

(Comment 26) A comment requests FDA revise the indications for use paragraph (§ 860.220(a)(5), this final rule renumbers the proposed § 860.234(a)(5) as § 860.220(a)(5)) in the De Novo request content section to include references to intended use and the meaning of that term for the purpose of determining substantial equivalence because intended use will be relevant to 510(k) submissions made after FDA grants a De Novo request. The commenter also suggests the revisions would align more closely with the PMA requirements in § 814.20(b)(3).

(Response 26) FDA does not agree with this comment and believes that the indications for use requirement is aligned with § 814.20(b)(3)(i) and the definitions in Appendix D of FDA's guidance, ''The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]'' (Ref. 10).

(Comment 27) A few commenters state it is unnecessary and places a potentially unrealistic burden on the De Novo requester to provide a ''complete'' device description; the comments request FDA require a ''device description.''

(Response 27) FDA disagrees with these comments and is retaining the word ''complete'' in § 860.220(a)(6) (this final rule renumbers the proposed § 860.234(a)(6) as § 860.220(a)(6)). The word ''complete'' is appropriate in this context and not overly burdensome. FDA does not expect an excessively detailed description of the device, but there must be sufficient detail to describe the aspects of the device that could affect safety or effectiveness. A complete device description is necessary for FDA to classify a device.

(Comment 28) Comments on the requirement to describe alternative practices (§ 860.220(a)(7), this final rule renumbers proposed § 860.234(a)(7) as § 860.220(a)(7)) either support the requirement as facilitating classification and improving transparency, or request revisions to reduce the burden of describing known or reasonably known alternative practices and procedures. The comments suggest revising the provision to instead ask for a summary related to the standard of care for a disease or condition for which the device is indicated as it bears on the device's proposed classification or assessment of probable benefits and risks.

(Response 28) FDA disagrees with the comments to limit the description of alternative practices. We do not believe this requirement requires extensive unnecessary efforts, as some of the commenters suggest. As explained in the proposed rule, this requirement is intended to capture alternative biologic, device, or drug practices or procedures. An understanding of available alternative practices or procedures that are used to diagnose, treat, prevent, cure, or mitigate the disease or condition for which the device is

intended or that similarly affect the structure or function of the body is one of the factors FDA considers in its benefit-risk assessments to determine the appropriate classification for a device. For example, for a device indicated to treat a rare condition for which there are no alternative treatments, FDA may accept greater uncertainty in the evidence regarding the device's probable benefits and probable risks. Furthermore, FDA does not agree with the assumption that a standard of care exists for all diseases or conditions for which a device is intended.

(Comment 29) Comments request that FDA rearrange the order of the provisions in proposed § 860.234(a)(9) through (11) (this final rule renumbers proposed § 860.234(a)(9) as § 860.220(a)(11) and this final rule renumbers proposed § 860.234(a)(11) as § 860.220(a)(9)). Commenters suggest that the risks and mitigations form the basis for the classification recommendation and accordingly request that the *Summary of risks and mitigations* provision (proposed § 860.234(a)(11) precede the *Classification recommendation* provision (proposed § 860.234(a)(9)). Commenters further suggest that the *Proposed special controls* provision (proposed § 860.234(a)(10)) should immediately follow the *Summary of risks and mitigations* provision to demonstrate whether specific mitigations are general and/or special controls.

(Response 29) The order in proposed § 860.234(a)(9) through (11) follows the order in which section 513(f)(2)(A)(v) of the FD&C Act discusses corresponding items. However, we believe the commenters' proposed changes make sense. Accordingly, we are revising the order of the paragraphs as follows:

- § 860.220(a)(9) *Summary of risks and mitigations*;
- § 860.220(a)(10) *Proposed special controls;* and
- § 860.220(a)(11) *Classification recommendation.*

(Comment 30) A comment supports the requirement for a summary of known or reasonably known probable risks, while another comment suggests that the De Novo request include both a summary and a discussion of the probable risks and mitigations identified through a formal risk analysis.

(Response 30) FDA agrees with the comment supporting the requirement for a De Novo request to include a summary of known or reasonably known probable risks, but FDA believes that requiring both a summary and a discussion of these probable risks and proposed mitigations is unnecessary. The De Novo request will be required to summarize probable risks to health associated with use of the device that are known or should reasonably be known to the requester and the proposed mitigations. For each mitigation measure that involves specific performance testing or labeling, the request must reference the associated section or pages of the supporting information, such as supporting protocols and/or testing data. FDA believes such information is sufficient to assist the Agency in identifying the probable risks to health and in evaluating the proposed risk mitigation measures to determine whether general controls or general and special controls can provide reasonable assurance of safety and effectiveness. Furthermore, FDA requires a related discussion demonstrating that the probable benefit to health outweighs the probable risks of the De Novo device in § 860.220(a)(14) (this final rule renumbers the proposed § 860.234(a)(14) as § 860.220(a)(14)).

(Comment 31) A comment requests that FDA revise the standards paragraph to clarify that De Novo requesters are not required to declare conformity to standards referenced in the De Novo request.

(Response 31) The standards paragraph at § 860.220(a)(12) (this final rule renumbers the proposed § 860.234(a)(12) as § 860.220(a)(12)) does not require that De Novo requesters submit a declaration of conformity to the referenced standard, so the requested clarification is not necessary. See our guidance, ''Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices'' (Ref. 11) for additional information on how to use consensus standards in premarket submissions, including information for those choosing to rely on a consensus standard in a declaration of conformity to meet a premarket submission requirement.

(Comment 32) A commenter states that the bibliography of all published reports concerning the safety or effectiveness of the device not submitted under the technical sections of the De Novo request (§ 860.220(a)(16)(i), this final rule renumbers proposed § 860.234(a)(16)(i) as § 860.220(a)(16)(i)) and the identification, discussion, and analysis of any other data, information, or report relevant to an evaluation of the safety and effectiveness of the device (§ 860.220(a)(16)(ii), this final rule renumbers proposed § 860.234(a)(16)(ii) as § 860.220(a)(16)(ii)) should be provided to FDA for consideration.

(Response 32) FDA agrees with the comment and believes that providing a bibliography of all published reports concerning the safety or effectiveness of the device not submitted under the technical sections of the De Novo request, as required by § 860.220(a)(16)(i), and the information on other data, information, or reports relevant to an evaluation of the safety and effectiveness of the device required under § 860.220(a)(16)(ii) will be useful to FDA's assessment of safety and effectiveness.

(Comment 33) A comment opposed authorizing implanted medical devices for marketing through the De Novo pathway without long-term controlled clinical trials because the commenter states patients deserve long-term safety and effectiveness data. A comment further recommends FDA require information about changes to the research protocol and statistical methodology in the summary of studies submitted in the De Novo request because the commenter states the information is important for evaluating the quality of the study.

(Response 33) FDA disagrees that long-term controlled clinical trials must be required across all implanted medical devices. In reviewing a De Novo classification request, studies other than long-term controlled clinical trials may also constitute valid scientific evidence that FDA can rely upon in making a benefit-risk determination for an implanted device, as discussed in our guidance ''Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approval and De Novo Classifications'' (Ref. 3). ''Valid scientific evidence'' is defined in section 513(a)(3) of the FD&C Act and § 860.7(c)(2). Valid scientific evidence, as discussed in § 860.7(c)(2), includes ''partially controlled studies, studies and objective trials without matched controls, well-documented case histories conducted by qualified experts, and reports of significant human experience with a marketed device.'' FDA does not believe long-term, controlled clinical studies are necessary to demonstrate that general controls or general and special controls will provide a reasonable assurance of safety and effectiveness for all implantable devices reviewed through the De Novo pathway. For example, some devices are intended to be implanted for a relatively short period of time (*e.g.,* 30 days) and then removed from the body; longer term clinical data therefore may not be needed to assess

the safety and effectiveness of these devices when used as intended.

Requiring these studies for all implantable devices is also inconsistent with FDA's least burdensome approach to medical device regulation, which is intended to eliminate unnecessary burdens that may delay the marketing of beneficial new products, while maintaining the statutory requirements for marketing authorization. As discussed in FDA's guidance, ''The Least Burdensome Provisions: Concept and Principles'' (Ref. 12), FDA typically follows a stepwise analytical process when requesting additional information to make a decision on a marketing submission to ensure the information requested reflects the least burdensome approach. FDA typically requests clinical data when analytical or nonclinical bench performance testing data, or nonclinical animal [1] and/or biocompatibility studies are insufficient, or available scientific methods are not acceptable, *e.g.,* the scientific methods are deemed unacceptable because they are not clinically validated or are not supported by a valid scientific rationale.

We do not believe any changes are necessary to address the comment's request that FDA require information about changes to the research protocol and statistical methodology. In addition to the summary of studies required under § 860.220(a)(13) (this final rule renumbers proposed § 860.234(a)(13) as § 860.220(a)(13)), the technical sections of the De Novo request must include, among other things, protocols, investigation design, results of statistical analyses, and any other appropriate information, for each clinical investigation used to support the De Novo request (§ 860.220(a)(15), this final rule renumbers proposed § 860.234(a)(15) as § 860.220(a)(15)). Therefore, the required contents of the technical section would already capture information regarding significant changes made to the protocol or to the statistical methodology that would be important for evaluating the results of the study.

(Comment 34) A few comments propose revisions to the human subject study summaries provision at § 860.220(a)(13)(ii) (this final rule renumbers proposed § 860.234(a)(13)(ii) as § 860.220(a)(13)(ii)) to require that this section of the De Novo request include a summary of ''any clinical data'' known by or reasonably available to the requester submitted in the De Novo request instead of a summary of ''each clinical investigation'' submitted in the De Novo request. The commenters suggest that the language in the proposed rule appeared to assume that the requester's only source of clinical data would be clinical investigations that the requester initiated and note that there may be other sources of clinical data, such as studies described in literature or conducted by others, or in marketing data from other countries. They also recommend limiting the information about such clinical data required in the summary to that ''known or reasonably available'' to the requester because it would clarify that when complete data are not available, they are not required.

(Response 34) FDA agrees that sources of clinical data other than clinical investigations initiated by the requester may be available to the requester; however, we do not agree that the proposed requirement for the De Novo request to include a summary of studies limits the types of clinical data that may be submitted in a De Novo request. Under § 860.220(a)(13), (this final rule renumbers proposed § 860.234(a)(13) as § 860.220(a)(13)), the De Novo request must include an abstract of any information or report described in the De Novo request under § 860.220(a)(16)(ii) (this final rule renumbers proposed § 860.234(a)(16)(ii) as § 860.220(a)(16)(ii)) and a summary of the results of technical data submitted under § 860.220(a)(15) (this final rule renumbers proposed § 860.234(a)(15) as § 860.220(a)(15)). The information required under § 860.220(a)(16)(ii) includes ''information derived from investigations other than those in the request and from commercial marketing experience.'' Therefore, clinical data derived from other sources, such as marketing experience in other countries, are among the types of data that would be summarized under § 860.220(a)(13). The particular paragraph of § 860.220(a)(13) that the commenters suggest revising sets forth additional information that summaries must discuss for those clinical investigations involving human subjects that are submitted in the De Novo request.

FDA also disagrees that it is necessary to limit the information required under § 860.220(a)(13)(ii) (this final rule renumbers proposed § 860.234(a)(13)(ii) as § 860.220(a)(13)(ii)) to that known or reasonably available to the requester. The requester should be able to provide the information required under § 860.220(a)(13)(ii) for clinical investigations submitted in the technical sections in support of the De Novo request. To the extent certain elements required for the summary of such clinical investigations are not included in the De Novo request because they are not reasonably available to the requester, the requester should address why they are not available. Therefore, we are not revising § 860.220(a)(13)(ii) in response to these comments.

(Comment 35) A comment requests FDA to qualify the requirement for a De Novo request to provide a discussion demonstrating that the data and information in the request constitute valid scientific evidence, with the phrase, ''if applicable,'' because a De Novo request for a low-risk device may present de minimis valid scientific evidence.

(Response 35) FDA disagrees with this comment. As part of the De Novo classification process, FDA must determine that the device is of low to moderate risk (21 U.S.C. 360c(f)(2)(A)(iv)). FDA relies upon valid scientific evidence in determining the safety and effectiveness of a device for purposes of classification, as explained in our response to Comment 23. Therefore, adding the phrase ''if applicable'' as the commenter suggests would not be appropriate.

As discussed in FDA's guidance, ''Factors to Consider When Making Benefit-Risk Determinations Medical Device Premarket Approval and De Novo Classifications'' (Ref. 3), FDA assesses the benefits and risks of a device that is the subject of a De Novo request to determine if general or general and special controls are sufficient to provide reasonable assurance of safety and effectiveness (see § 860.7(d)(1) and (e)(1)). While low-risk devices may not need to show as substantial a benefit to patients to have a favorable benefit-risk profile, FDA's classification determination must still be based on valid scientific evidence.

(Comment 36) A comment requests FDA to clarify that, where relevant, requirements for data and information in the technical sections in § 860.220(a)(15) (this final rule renumbers proposed § 860.234(a)(15) as § 860.220(a)(15)) may be satisfied by cross-referencing data and information submitted in satisfaction of the summary of studies provision (§ 860.220(a)(13), this final rule renumbers proposed § 860.234(a)(13) as § 860.220(a)(13)) to avoid requiring a requester to repeat information provided earlier in the De Novo request. A comment also requests that FDA remove the list of specific items that must be

[1] FDA supports the principles of the ''3Rs,'' to reduce, refine, and replace animal use in testing when feasible. We encourage sponsors to consult with us if it they wish to use a non-animal testing method they believe is suitable, adequate, validated, and feasible. We will consider if such an alternative method could be assessed for equivalency to an animal test method.

included in the summary of each clinical investigation under § 860.220(a)(13)(ii) (this final rule renumbers proposed § 860.234(a)(13)(ii) as § 860.220(a)(13)(ii)) because the commenter asserts it is unnecessarily restrictive and repetitive to require this information in the summary when the same information is also required in the technical sections of the De Novo request under § 860.220(a)(15)(iii) (this final rule renumbers proposed § 860.234(a)(15)(iii) as § 860.220(a)(15)(iii)).

(Response 36) FDA does not agree with this comment. The summary of technical data required under § 860.220(a)(13) is intended to be analogous to an executive summary of each study used to support the De Novo request and would typically include less information than that submitted in the technical sections. The information required in the technical sections (§ 860.220(a)(15)) is the more detailed and complete information regarding each study. While it may be appropriate to cross reference the information from the summary section (§ 860.220(a)(13)), FDA does not believe cross referencing the information in the summary required under § 860.220(a)(13) would be sufficient to provide all of the required technical information to support marketing authorization. Because the summary information required for clinical investigations submitted in the De Novo request may include information other than the specific items listed in § 860.220(a)(13)(ii) and because it is intended to be a higher level summary of the data in the technical sections, we do not believe the required summary is unnecessarily restrictive or repetitive.

(Comment 37) A few comments ask FDA to revise the nonclinical testing paragraph (§ 860.220(a)(15)(i), this final rule renumbers proposed (§ 860.234(a)(15)(i) as (§ 860.220(a)(15)(i)) by moving the ''as appropriate'' qualifier forward in the sentence.

(Response 37) FDA agrees that moving the words ''as appropriate'' forward in the sentence would clarify the requirement. We are revising paragraph § 860.220(a)(15)(i) accordingly.

(Comment 38) A few comments ask FDA to revise the requirements for a summary of studies and the technical sections in a De Novo request to clarify that a statement regarding compliance with part 58 is only necessary for studies that are required to comply with part 58 because the commenters state that many nonclinical studies are outside the scope of part 58 if they do not involve the use of animals or other test systems.

(Response 38) FDA agrees that some nonclinical studies that may be submitted to support a De Novo request, such as certain electromagnetic compatibility testing, are not subject to part 58. In response to these comments, FDA is revising § 860.220(a)(15)(i) (this final rule renumbers proposed § 860.234(a)(15)(i) as § 860.220(a)(15)(i)) to clarify that a statement of compliance with part 58 (or a brief statement of the reason for noncompliance) is required only for nonclinical studies subject to part 58.

(Comment 39) A comment asks FDA to revise the requirements for submitting results of clinical investigations involving human subjects (§ 860.220(a)(15)(iii), this final rule renumbers proposed § 860.234(a)(15)(iii) as § 860.220(a)(15)(iii)) to clarify that clinical investigations are not required in all cases to support the De Novo classification decision. Comments also requested revisions to this provision to clarify that some clinical investigations submitted in the De Novo request may be ongoing (*e.g.,* clinical investigations that are ongoing but for which all subjects have reached the primary endpoint). These comments also ask FDA to revise the proposed regulatory text to refer to ''records'' instead of copies of individual subject report forms because the commenters assert that many clinical investigations are carried out with validated electronic data capture systems and individual human subject forms are not used.

(Response 39) FDA agrees that clinical evidence may not always be required in a De Novo request to support a determination that general controls or general and special controls provide a reasonable assurance of safety and effectiveness of the device and device type. However, we believe no clarification is needed regarding whether a clinical investigation involving human subjects is required because that determination will be specific to the De Novo request. If the requester believes that information regarding clinical investigations required under § 860.220(a)(15)(iii) (this final rule renumbers proposed § 860.234(a)(15)(iii) as § 860.220(a)(15)(iii)), or other information required under § 860.220(a)(15)(i) (this final rule renumbers proposed § 860.234(a)(15)(i) as § 860.220(a)(15)(i)), is not applicable to its device, then the requester may include a justification for omitting that information from the De Novo request in accordance with § 860.220(c) (this final rule renumbers proposed § 860.234(c) as § 860.220(c)). If De Novo requesters have questions about the process for submission and review of a De Novo request for their device, we recommend that they consult FDA's guidance, ''De Novo Classification Process (Evaluation of Automatic Class III Designation)'' (Ref. 5) and request a meeting with FDA through the Q-submission program. Meetings between the requester and FDA allow for an open discussion and exchange of technical, scientific, and regulatory information that can help build a common understanding of FDA's initial expectations regarding clinical studies and nonclinical studies related to the De Novo request (Ref. 13).

FDA recognizes that some De Novo requests include results from clinical investigations that remain ongoing, such as a study that has a pre-specified interim analysis of safety or effectiveness data. However, FDA believes the regulatory text in § 860.220(a)(15)(iii) would already permit inclusion of such results and does not believe a revision to the regulatory text is necessary.

We also recognize that some comments raise a concern that individual subject forms are not used in many clinical investigations. While the commenters do not object to providing individual subject information for those subjects who died during a clinical investigation or who did not complete the investigation, the commenters suggest that the term ''records'' would better reflect electronic source data instead of the term ''copies of such forms.'' We agree with the comments that data capture and collection methods used in clinical investigations have evolved over time. FDA has published guidance, ''Use of Electronic Health Record Data in Clinical Investigations,'' addressing data capture in clinical investigations that do not use paper case report forms (Ref. 14). FDA interprets the term ''individual subject form,'' as used in this rule, to include the different electronic or paper formats used to capture individual subject data. Therefore, we do not believe that using the term ''record'' is necessary.

(Comment 40) A comment asks FDA to require that the technical sections of a De Novo request include a protocol and a report for all clinical investigations and laboratory studies to make the requirements for the technical sections more consistent and less confusing.

(Response 40) We agree that additional clarity regarding technical sections requirements for nonclinical studies would be helpful. Protocols and complete test reports generally are necessary to provide sufficient detail

regarding the results of a nonclinical study to permit FDA to determine whether to grant or decline the De Novo request. However, we are revising § 860.220(a)(15)(i) (this final rule renumbers proposed § 860.234(a)(15)(i) as § 860.220(a)(15)(i)) to state expressly that these materials must be provided for each nonclinical study submitted in the technical sections of the request. FDA's guidance, ''Recommended Content and Format of Non-Clinical Bench Performance Testing Information in Premarket Submissions'' (Ref. 15) discusses the information that should typically be included in test protocols and complete test reports for nonclinical bench performance testing provided in a premarket submission. We note that in cases where a requester is appropriately declaring conformity with a voluntary consensus standard that FDA has recognized pursuant to section 514(c) of the FD&C Act (21 U.S.C. 360d(c)) to meet applicable requirements, it may not be necessary to submit complete test reports with respect to those requirements. In these cases, the requester may submit a statement of omission for this information in the De Novo request in accordance with § 860.220(c). However, consistent with section 514(c)(3)(B) of the FD&C Act, FDA may request, at any time, the data or information relied on by a person to make a declaration of conformity with respect to a recognized standard. See FDA's guidance ''Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices'' (Ref. 11) for more information regarding use of declarations of conformity in premarket submissions.

FDA disagrees with modifying § 860.220(a)(15)(iii) to specifically require submission of a clinical investigation report. This provision already describes the supporting information required regarding the results of each clinical investigation, and in our experience, there can be significant variability in the types of information included in ''reports'' prepared for clinical investigations. If some or all of the information required under § 860.220(a)(15)(iii) is included in a separate clinical investigation report, the requester may include the report in its De Novo request to satisfy those requirements.

(Comment 41) A comment asks FDA to revise the ''other information'' provision (§ 860.220(a)(16), this final rule renumbers proposed § 860.234(a)(16) as § 860.220(a)(16)) to limit the information required in the bibliography of all published reports not submitted under the technical sections of the De Novo request (§ 860.220(a)(15), this final rule renumbers proposed § 860.234(a)(15) as § 860.220(a)(15)) to those ''necessary to support the safety or effectiveness of the device'' because the commenter asserts such reports should be limited to those needed to establish the device's proposed classification, its probable risk, and its probable benefit.

(Response 41) We do not agree with limiting the bibliography required under § 860.220(a)(16) to that information necessary to support the device's safety or effectiveness. Paragraph § 860.220(a)(16)(i) (this final rule renumbers proposed § 860.234(a)(16)(i) as § 860.220(a)(16)(i)) requires that the requester submit a bibliography of all adverse or supportive published reports, other than those submitted in greater detail in the technical sections of the De Novo request, that are known to or should reasonably be known to the requester and that concern the safety and effectiveness of the device. The commenter's proposed revision would eliminate the requirement to include adverse published reports that may call into question the safety or effectiveness of the device at issue. However, such adverse reports may be important to FDA's assessment of the probable benefits and risks of the device and affect the Agency's classification determination.

(Comment 42) A comment supports the requirement to provide a sample of the device, if requested by FDA (§ 860.220(a)(17), this final rule renumbers proposed § 860.234(a)(17) as § 860.220(a)(17)) because it improves transparency. Other comments request that FDA eliminate the language indicating that the Agency may ''test'' one or more of the devices because FDA has traditionally relied on testing by the manufacturer. Another commenter indicated that while providing samples may be appropriate for a high-risk device likely to be reviewed in a PMA, it is unclear that samples are necessary for devices reviewed through the De Novo pathway.

(Response 42) FDA disagrees with the comments that suggest limiting the sample requirement and agrees with the comment that the request for samples improves transparency. In many cases, FDA relies on descriptions of a device and testing performed by manufacturers to evaluate safety and effectiveness. However, there are some situations in which FDA would request a sample of a device reviewed through the De Novo pathway because FDA needs to see or test the device to understand the device and determine if general or general and special controls are sufficient to reasonably assure safety and effectiveness of the device and device type. Examples of the situations where a device sample may be requested by FDA for examination or testing include devices intended for use by a lay person that previously have been marketed for use by a physician or other experienced healthcare professional, and devices with novel, complex designs that are difficult to assess solely through written description and/or engineering drawings.

(Comment 43) A comment supports the proposed requirement that a De Novo request include ''[l]abels, labeling, and advertisements sufficient to describe the device, its intended use, and the directions for its use'' (§ 860.220(a)(18), this final rule renumbers proposed § 860.234(a)(18) as § 860.220(a)(18)) because this requirement improves transparency. Other commenters propose limiting the requirement to not include advertisements because the commenters state advertisements are outside the scope of a class I and class II device review.

(Response 43) FDA agrees that the requirement to submit labels, labeling, and advertisements improves transparency. FDA disagrees that review of advertisements is outside the scope of De Novo request review. Under the proposed provision, only labels, labeling, and advertisements ''sufficient to describe the device, its intended use, and the directions for its use'' are required, and such information is necessary to determine the device's intended use and its safety and effectiveness for the purposes of classification. See, *e.g.,* § 860.7(b)(2).

(Comment 44) A comment supports the requirement for a requester to provide a list of any required information that is omitted from the De Novo request and a justification for any omission because the commenter states it would ensure completeness of the applicant's research and pre-application evaluations.

(Response 44) FDA agrees that it is beneficial for the requester to provide a statement identifying and justifying the omission of any information required under § 860.220(a) (this final rule renumbers proposed § 860.234(a) as § 860.220(a)) and is finalizing the requirement to provide such a statement in § 860.220(c) (this final rule renumbers proposed § 860.234(c) as § 860.220(c)). However, we wish to clarify that the omissions statement is not required to be in the format of a list, as the comment suggests.

(Comment 45) A comment requests FDA to revise the requirements for incorporation of information in FDA files by reference (§ 860.220(b), this final

rule renumbers proposed § 860.234(b) as § 860.220(b)) to permit the requester to file a general authorization allowing another person to submit additional pertinent information. According to the commenter, this would allow De Novo requesters to avoid the need for case-by-case authorization.

(Response 45) FDA disagrees with this comment and believes the commenter misunderstands the circumstances in which FDA requires an authorization. The provision in § 860.220(b) addresses situations in which a De Novo request references information in FDA's files that was submitted by someone other than the requester. For FDA to consider that information as part of the De Novo request, we require a written authorization from the person originally submitting that information to FDA that authorizes the use of the information in the De Novo request. Because the authorizer determines the scope of the authorization, it can be as broad or as limited as the authorizer wants the authorization to be. The comment seems to suggest that the requester should be able to provide authorization for the De Novo request to reference information in FDA's files submitted by others, but the submitters of the data are the ones in a position to authorize references to it.

(Comment 46) A few comments request FDA to revise the requirement to update a pending De Novo request with new information from ongoing or completed studies that may reasonably affect an evaluation of the safety and effectiveness of the device as it becomes available (§ 860.220(d), this final rule renumbers proposed § 860.234(d) as § 860.220(d)) because the commenters assert FDA should allow time for data aggregation and assessment. The comments suggest that FDA should require such information as agreed upon with the De Novo requester or as specified in a protocol.

(Response 46) FDA disagrees with these comments. The comments assume incorrectly that for each ongoing or completed nonclinical and/or clinical study, there exists a protocol that has timeframes for reporting new safety and effectiveness information to FDA or an agreement specifying when new safety and effectiveness information must be submitted to update a pending De Novo request. FDA is also concerned that specifying a set time period for updating the De Novo request would be problematic because the importance of the data required to be reported may vary. For example, FDA would be particularly interested in receiving quickly information that concerns the death of a human subject. Updating a De Novo request in accordance with pre-set periods in a protocol or agreement could also result in FDA making a decision on a De Novo request without key, available safety and effectiveness information. For example, an unplanned review of the safety data could have implications on the statistical validity of a study.

I. Comments and FDA Response on Criteria for Accepting a De Novo Request

(Comment 47) A comment states the requirements in § 860.230 (this final rule renumbers proposed § 860.245 as § 860.230)) should be moved to FDA's guidance, ''Acceptance Review for De Novo Classification Requests'' (FDA draft guidance published October 30, 2017). Another comment recommends finalizing FDA's guidance, ''Acceptance Review for De Novo Classification Requests,'' concurrently with finalizing the rule.

(Response 47) FDA disagrees with this comment because FDA's requirements are based on its statutes and regulations. FDA guidance provides non-binding recommendations. Regulations are necessary because they allow the Agency to enforce the requirements therein. For this reason, we decline to remove the accepting a De Novo request requirements, including those in § 860.230, from this regulation.

FDA's ''Acceptance Review for De Novo Classification Requests'' guidance was finalized on September 9, 2019 (84 FR 47310) (Ref. 16), so the comment requesting concurrent publication is moot.

(Comment 48) A comment requests FDA to clarify that references to ''15 days'' signify calendar days because it will enhance De Novo requester planning.

(Response 48) FDA declines to clarify in the codified but confirms that it interprets ''15 days'' to mean ''15 calendar days.'' This interpretation is consistent with FDA's final guidance entitled, ''Acceptance Review for De Novo Classification Requests'' (Ref. 16), which explains that the 15 days are calendar days. It is also consistent with our interpretation of ''days'' as used in analogous regulations for PMAs and 510(k)s.

J. Comments and FDA Response on Granting or Declining a De Novo Request

(Comment 49) A comment objects to developing a new lexicon for De Novo requests (*i.e.,* grant or decline) and asks FDA to use the term ''approval'' because the commenter asserts that CDRH approves both ''De Novo devices'' and ''PMA devices'' for marketing based on a determination that they are safe and effective for their intended use.

(Response 49) We disagree with this comment. The term ''decline'' is language from section 513(f)(2) of the FD&C Act, and FDA believes the term ''grant'' is appropriate, given that section 513(f)(2) of the FD&C Act addresses a ''request for classification.'' In addition, FDA does not make identical determinations when approving a PMA or granting a De Novo request. The statutory standards for approval of a PMA include a showing of reasonable assurance that the device is safe and effective (see section 515(d) of the FD&C Act). FDA will grant a De Novo request and classify the device as either class I or class II when the request demonstrates that general controls or general and special controls are adequate to provide reasonable assurance of safety and effectiveness (see section 513(a) and (f)(2) of the FD&C Act).

(Comment 50) To be consistent with section 513(f)(2)(C) of the FD&C Act, a few comments requested that FDA revise the provision regarding publication in the **Federal Register** of the notice announcing the classification of the device to state that the publication will occur within 30 days of granting the request.

(Response 50) FDA agrees to revise § 860.260(a)(2) (this final rule renumbers proposed § 860.289(a)(2) as § 860.260(a)(2)) to reflect the statutory timeframe for publishing a notice in the **Federal Register** announcing the classification of a device under section 513(f)(2)(C) of the FD&C Act. We are revising § 860.260(a)(2) accordingly to add the phrase ''within 30 days after the issuance of an order granting the De Novo request.'' We note that the classification of a device, including any special controls, is effective on the date the order letter is issued granting the De Novo request. Once the De Novo request is granted, the device may serve as a predicate device to which another device can claim substantial equivalence. FDA places copies of such orders on its website.

(Comment 51) A comment on the proposed provisions for declining a De Novo request notes that stating FDA ''may issue written notice'' declining a request suggests there is an alternative to issuing a written notice and asks FDA to describe the alternative.

(Response 51) FDA intended to outline the grounds for which FDA may decline a De Novo request in proposed § 860.289(b) (this final rule renumbers proposed § 860.289(b) as § 860.260(c) and moves the grounds for which FDA may decline a De Novo request into

§ 860.260(c)). FDA explained in the preamble to the proposed rule that it was proposing to ''decline a De Novo request by issuing a written order to the requester'' (83 FR 63127 at 63137). However, FDA is revising paragraph § 860.260(b) and (c) accordingly to clarify this point.

(Comment 52) A comment asks FDA to delete the entire paragraph § 860.260(c) (this final rule renumbers proposed § 860.289(b) as § 860.260(c) and moves the grounds for which FDA may decline a De Novo request into § 860.260(c)) on declining a De Novo request because the commenter states the paragraph exceeds the appropriate bases for denial of a De Novo request, which the commenter identifies as the device is inappropriate for classification into class I or class II, or there is a legally marketed predicate device.

(Response 52) FDA disagrees with this comment. Section 860.260(c)) (this final rule renumbers proposed § 860.289(b) as § 860.260(b) and moves the grounds for which FDA may decline a De Novo request into § 860.260(c)) explains FDA's interpretation and implementation of the statutory grounds for declining a De Novo request, which does not rely upon only section 513(f)(2)(A)(iv) of the FD&C Act. For example, if a product is not a device within the meaning of section 201(h) of the FD&C Act or a combination product as defined at § 3.2(e) (21 CFR 3.2(e)), then FDA may decline to grant the De Novo request.

As noted in the proposed rule (83 FR 63127 at 63137), FDA generally intends to decline a De Novo request for a combination product that does not have a device primary mode of action—(see § 3.2(m)). However, a De Novo request may be appropriate, for example, for the device constituent part of such a combination product if the constituent parts of the combination product are to be distributed separately (see § 3.2(e)(3) through (4)), and the other constituent part (drug or biological product) of the combination product is to be marketed under its own, separate application (*i.e.,* abbreviated new drug application, NDA, or biologics license application).

(Comment 53) A few comments request that FDA delete the entire paragraph on declining a De Novo request because the device labeling does not comply with parts 801 and 809 (21 CFR parts 801 and 809) because the commenters state it is outside the scope of the De Novo classification process to deny classification based on the device's labeling.

(Response 53) FDA disagrees with these comments. Parts 801 and 809 are general controls, and whether the device complies with general controls is necessary to determine whether it is of low to moderate risk for the purposes of classification. FDA may decline a De Novo request if it determines that the device submitted is not of low to moderate risk, or that general controls would be inadequate to control the risk and special controls to mitigate the risks cannot be developed. Whether the device's labeling complies with the requirements in parts 801 and 809 is necessary to determine which regulatory controls are appropriate for the new device type class. The device's labeling compliance with parts 801 and 809 is also necessary to determine the device's safety and effectiveness for the purposes of classification.

(Comment 54) A comment requests FDA to revise the basis for declining a De Novo request set forth in § 860.260(c)(8) (this final rule renumbers proposed § 860.289(b)(8) as § 860.260(c)(8)) to specify that a request may only be declined when certain nonclinical studies within the scope of part 58 are not conducted in compliance with those regulations. The commenter asserts that many nonclinical studies are outside the scope of part 58.

(Response 54) FDA agrees that a De Novo request may include nonclinical studies that are not subject to part 58, as we explained in Response 38. FDA would not decline a De Novo request on the basis that a nonclinical study failed to comply with part 58, if that study did not fall within the scope of studies that are subject to part 58. However, FDA is revising § 860.260(c)(8) to make this clearer.

(Comment 55) A comment requests that FDA revise the paragraph on declining a De Novo request (§ 860.260(c)(10)(i), this final rule renumbers proposed § 860.289(b)(10)(i) as § 860.260(c)(10)(i)) because the commenter states that failure to follow a protocol is not, per se, a reason to decline a De Novo request.

(Response 55) FDA disagrees with the commenter's suggestion to revise the provision on declining a De Novo request so that it does not include failure to follow a protocol. The failure to follow a protocol may cause the resulting data to be incomplete, invalid, or otherwise unreliable, and may be a sufficient reason to decline a De Novo request. Protocols typically discuss the objectives, design, methodology, and organization of a clinical or nonclinical study. Significant deviations from a study protocol may lead to a study that, as conducted, does not produce valid scientific evidence. Alternatively, data from a study that was terminated early may not provide sufficient information to support a reasonable assurance of safety or effectiveness.

(Comment 56) A comment objects to the placement of the paragraph on determining safety and effectiveness as one of the last paragraphs in subpart D because the commenter states FDA should do both a classification determination and a determination of the device's safety and effectiveness.

(Response 56) FDA does not agree with the comment's premise that the location of the paragraph in subpart D is an indication of the paragraph's importance. The FD&C Act provides that the De Novo process is both a classification and a marketing authorization grant for the particular device (section 513(f)(2) of the FD&C Act). The classification determination and ''determination of safety and effectiveness'' are necessary to make a determination regarding the device which is the subject of the De Novo request.

K. Comments and FDA Response on Availability of the De Novo Classification Process for Combination Products

(Comment 57) A comment requests that FDA clarify that for the summary of risk and mitigations and the risk-benefit discussion required to be submitted in the De Novo request, the summary and the risk-benefit discussion should describe the incremental risk and benefits posed by a combination product because the commenter states the content requirements should reflect that the De Novo classification process is available for combination products.

(Response 57) FDA believes that inclusion of this language is unnecessary as we consider section 503(g)(3) of the FD&C Act to be clear regarding its applicability to combination products that include an approved constituent part as defined in section 503(g)(3) of the FD&C Act. In addition, the statute is clear that these considerations apply to such combination products submitted under sections 515, 510(k), and 513(f)(2) of the FD&C Act. We do not believe inclusion of this language is necessary to provide further clarity beyond what is stated in the statute. Combination products have distinct premarket review and approvability considerations arising from combining a drug, device, and/or biological product, which retain their regulatory identities when they become constituent parts of combination products. Combination products are also a separate legal category of medical products, distinct from biological products, devices, and drugs. General principles of premarket review and

regulation for combination products include application of a risk-based approach and coordination among Centers for their review and regulation. Review of combination products in a De Novo classification request would consider safety and effectiveness questions relating to the combination product as a whole, each constituent part, interactions between them, and user/patient interaction with the product.

(Comment 58) A comment asks FDA to clarify that while a De Novo request may be appropriate for the device constituent part of a combination product where the constituent parts of the combination product are distributed separately (*e.g.,* § 3.2(e)(3) through (4)), and the non-device (drug or biologic) constituent part is to be marketed under its own, separate application, the non-device constituent part must be appropriately labeled for use with the device constituent part (*i.e.,* approved at doses, concentrations, routes of administration, indications, and adequate instructions for use). The commenter notes that if the non-device constituent part is not appropriately labeled for use with the device constituent part, then FDA would cause the non-device constituent party to be adulterated or misbranded.

(Response 58) FDA does not agree that clarification is necessary. Per § 3.2(e), the labeling of the constituent parts of such ''cross-labeled'' combination products specify use only with the other approved individually specified constituent part(s), which are required to achieve the intended use, indication, or effect. The labeling for the combination product is comprised of the labeling for each constituent part.

(Comment 59) A comment requests that FDA consider ''co-packaged'' combination products (per § 3.2(e)(2)) that have a device primary mode of action as eligible for the De Novo classification process.

(Response 59) Regarding inclusion of co-packaged combination products as defined in § 3.2(e)(2) that have a device primary mode of action, FDA does not believe further clarification is warranted in the codified because § 860.260 (this final rule renumbers proposed § 860.289 as § 860.260) explains that we are using the definition of combination products in § 3.2(e)(1) through (4). Co-packaged combination products as defined in § 3.2(e)(2) that have a device primary mode of action are part of this definition and eligible for the De Novo classification process.

VI. Effective Date

This final rule will become effective 90 days after the date of publication in the **Federal Register**.

VII. Economic Analysis of Impacts

We have examined the impacts of the final rule under Executive Order 12866, Executive Order 13563, the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (Pub. L. 104–4). Executive Orders 12866 and 13563 direct us to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). We believe that this final rule is a significant regulatory action as defined by Executive Order 12866.

The Regulatory Flexibility Act requires us to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because small entities affected by this final rule would incur very low one-time costs to read and understand the rule, we certify that the final rule will not have a significant economic impact on a substantial number of small entities.

The Unfunded Mandates Reform Act of 1995 (section 202(a)) requires us to prepare a written statement, which includes an assessment of anticipated costs and benefits, before issuing ''any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation) in any one year.'' The current threshold after adjustment for inflation is $158 million, using the most current (2020) Implicit Price Deflator for the Gross Domestic Product. This final rule would not result in an expenditure in any year that meets or exceeds this amount.

The final rule will clarify the De Novo classification process for certain medical devices to obtain marketing authorization as class I or class II devices, rather than remaining automatically designated as class III devices under the FD&C Act. In addition, the final rule will clarify and create a more efficient De Novo classification process by specifying: (1) What medical devices are eligible for the De Novo classification process; (2) what information manufacturers must provide in De Novo requests; and (3) how to organize this information. By clarifying and making the process more efficient, the final rule could reduce the time and costs associated with reviewing De Novo requests. Moreover, the final rule will allow us to refuse to accept inappropriate and deficient De Novo requests and require us to protect the confidentiality of certain data and information submitted with a request until we issue an order granting the request.

Industry will incur costs to read and understand this final rule. We estimate that the annualized costs over 10 years would range from $0.01 million to $0.17 million at a 7 percent discount rate, with a primary estimate of $0.09 million. We estimate that the annualized costs over 10 years at a 3 percent discount rate would range from $0.01 million to $0.15 million, with a primary estimate of $0.08 million.

TABLE 2—SUMMARY OF BENEFITS, COSTS AND DISTRIBUTIONAL EFFECTS OF THE FINAL RULE

[$ millions]

Category	Primary estimate	Low estimate	High estimate	Units			Notes
				Year dollars	Discount rate (percent)	Period covered (years)	
Benefits:							
Annualized				2019	7	10	
Monetized $millions/year				2019	3	10	
Annualized Quantified				2019	7	10	
				2019	3	10	

TABLE 2—SUMMARY OF BENEFITS, COSTS AND DISTRIBUTIONAL EFFECTS OF THE FINAL RULE—Continued

[$ millions]

Category	Primary estimate	Low estimate	High estimate	Units			Notes
				Year dollars	Discount rate (percent)	Period covered (years)	
Qualitative	.....	.....	.....	.....	.....	.....	Clarification of the De Novo process for requesters. Potentially fewer incomplete submissions and faster introduction of medical devices.
Costs:							
Annualized Monetized $millions/year	$0.09	$0.01	$0.17	2019	7	10	
	0.08	0.01	0.15	2019	3	10	
Annualized Quantified	.....	.....	.....	2019	7	10	
				2019	3	10	
Qualitative.							
Transfers:							
Federal Annualized Monetized $millions/year.	.....	.....	.....	2019	7	10	
	.....	.....	.....	2019	3	10	
	From:			To:			
Other Annualized Monetized $millions/year.	.....	.....	.....	2019	7	10	
	.....	.....	.....	2019	3	10	
	From:			To:			

Effects:
State, Local or Tribal Government: None.
Small Business: A small one-time administrative burden of up to $300 per year on each affected small entity.
Wages: None.
Growth: None.

We have developed a comprehensive Economic Analysis of Impacts that assesses the impacts of the final rule. The full analysis of economic impacts is available in the docket for this final rule (Ref. 20) and at *https://www.fda.gov/about-fda/reports/economic-impact-analyses-fda-regulations.*

VIII. Analysis of Environmental Impact

We have determined under 21 CFR 25.34(b) and (f) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

IX. Paperwork Reduction Act of 1995

This final rule contains information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501–3521). The title, description, and respondent description of the information collection provisions are shown in the following paragraphs with an estimate of the annual reporting burden. Included in the estimate is the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing each collection of information.

Title: Medical Device De Novo Classification Process (OMB Control Number 0910–0844)—Revision.

Description: This final rule implements the medical device De Novo classification process under section 513(f)(2) of the FD&C Act, which provides a pathway for certain new types of devices to obtain marketing authorization as class I or class II devices, rather than remaining automatically designated as a class III device, which would require premarket approval under the postamendments device classification section of the FD&C Act (section 513(f)(1)).

On October 30, 2017, FDA issued a final guidance (De Novo Program guidance) (Ref. 5) to provide recommendations on the process for the submission and review of a De Novo request. The information collections associated with the guidance are approved under OMB control number 0910–0844. We provide below a revised burden estimate for the De Novo classification process as described in this final rule.

Section 860.200 (this final rule renumbers proposed § 860.201 as § 860.200) explains the purpose of the De Novo Classification regulations and provides the applicability of a De Novo request submission. Sections 860.210 and 860.220 (this final rule renumbers proposed § 860.223 and § 860.234 as § 860.210 and § 860.220) describe the format and content, respectively, of a De Novo request. Section 860.230 (this final rule renumbers proposed § 860.245 as § 860.230) describes the conditions under which FDA may refuse to accept a De Novo request. Section 860.240(b) (this final rule renumbers proposed § 860.256(b) as § 860.240(b)) provides for supplemental, amendatory, or additional information for a pending De Novo request. Section 860.250(a)(4) (this final rule renumbers proposed § 860.267(a)(4) as § 860.250(a)(4)) provides that a requester may submit a written notice to FDA that the De Novo request has been withdrawn.

Description of Respondents: Respondents to the information collection are medical device manufacturers seeking to market medical device products that have been automatically designated as class III under section 513(f)(1) of the FD&C Act.

TABLE 3—ESTIMATED ANNUAL REPORTING BURDEN [1]

Activity; 21 CFR section	Number of respondents	Number of responses per respondent	Total annual responses	Average burden per response	Total hours	Total operating and maintenance costs
De Novo request—860.200, 860.210, 860.220, 860.230, 860.240(b).	68	1	68	182	12,376	$88
Written notice of withdrawal—860.250(a)(4).	5	1	5	0.17 (10 minutes)	1	7
Total					12,377	95

[1] Numbers have been rounded.

The information collection request (ICR) previously approved for the De Novo classification process (OMB control number 0910–0844), includes separate information collections (ICs) for De Novo requests submitted under section 513(f)(2)(i) of the FD&C Act (estimated 100-hour burden per response) and those submitted under section 513(f)(2)(ii) (estimated 180-hour burden per response), with burden estimates further separated by those sent to CDRH and those sent to the Center for Biologics Evaluation and Research.

For administrative efficiency, in this ICR revision, we are consolidating the separate ICs for requests submitted under section 513(f)(2)(i) or (ii) of the FD&C Act into a single IC for all De Novo requests submitted to FDA. Therefore, this final rule simply provides a burden estimate for all De Novo requests without distinguishing between those submitted under 513(f)(2)(i) or (ii) of the FD&C Act. This estimate includes estimated burdens associated with the initial request (purpose and applicability in § 860.200), format and content (§ 860.210 and § 860.220), supplements and amendments (§ 860.240(b)), and time to ensure that all the format and content requirements are met before submission (§ 860.230). Based on our recent experience with the De Novo Program, FDA estimates that the average burden per response for a De Novo request is 182 hours. Additionally, we adjusted the estimated number of respondents based on updated data.

The estimated burden for § 860.230 includes 2 hours per response for manufacturers to review their De Novo request for compliance with the acceptance criteria listed in § 860.230 to determine if it is complete and to complete the checklists recommended in the guidance ''Acceptance Review for De Novo Classification Requests'' (Ref.16). The information collections contained in the guidance, including 2 hours for review of the De Novo request for completeness and the checklists, were approved by OMB since publication of the proposed rule.

We estimate that the average burden per response for written notice of withdrawal of a De Novo request, as described in § 860.250(a)(4), is 10 minutes (0.17 hours). The burden table in the proposed rule erroneously listed 10 hours, rather than 10 minutes, for the average burden per response. We have corrected the error. The average burden per response is based on estimates by FDA administrative and technical staff who are familiar with the requirements for submission of a De Novo request (and related materials), have consulted and advised manufacturers on submissions, and have reviewed the documentation submitted. We expect that we will receive approximately five notices of withdrawal per year. There is no change to the currently approved burden estimate for withdrawal of a De Novo request.

These adjustments resulted in a 1,647-hour increase to the previously approved total burden estimate.

We received several comments related to the proposed rule. Descriptions of the comments on the proposed rule and FDA's responses are provided in section V of this final rule. Comments and responses related to the provisions that underlie the information collection are described in the following sections: section V.B, regarding general comments; section V.D, De Novo request information disclosure; section V.F, regarding definitions; section V.G, regarding De Novo request format; section V.H, regarding De Novo request content; section V.I, regarding criteria for accepting a De Novo request; section V.J, regarding criteria for granting or declining a De Novo request; and section V.K, regarding availability of the De Novo classification process for combination products. We have not made changes to the estimated burden as a result of the comments.

The estimate of the annual reporting burden provided in the proposed rule included printing and shipping for the complete paper submission and eCopy. Under § 860.210 of the final rule, each De Novo request must be provided as a single version in electronic format. Therefore, we have adjusted the operating and maintenance cost in the final rule to include the cost of the eCopy and shipping of the eCopy.

The cost per eCopy (CDs, DVDs, and flash drives) ranges from $0.25 to $2.50 per eCopy. All forms of eCopy media cost roughly $0.22 to ship. We estimate the average cost per eCopy, plus shipping, for a De Novo request or a request for withdrawal to be $1.30 per submission.

The annual cost estimate for De Novo requests is $88 (68 submissions × $1.30) (rounded). The annual cost estimate for requests for withdrawal is $7 (5 requests × $1.30) (rounded). Therefore, we estimate the total annual operating and maintenance costs of this information collection to be $95. This is a decrease of $7,188 to the currently approved total annual operating and maintenance cost estimate.

This final rule also refers to previously approved collections of information. These collections of information are subject to review by OMB under the PRA. The collections of information in the guidance entitled ''De Novo Classification Process (Evaluation of Automatic Class III Designation)'' (Ref. 5) have been approved under OMB control number 0910–0844; the collections of information in the guidance entitled ''Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program—Guidance for Industry and Food and Drug Administration Staff'' (Ref. 13) have been approved under OMB control number 0910–0756; the collections of information in the guidances entitled ''Guidance for Industry and Food and Drug Administration Staff—User Fees

for 513(g) Requests for Information'' (Ref. 17) and ''FDA and Industry Procedures for Section 513(g) Requests for Information under the Federal Food, Drug, and Cosmetic Act—Guidance for Industry and Food and Drug Administration Staff'' (Ref. 18) have been approved under OMB control number 0910–0705; and the collections of information in the guidance entitled ''Emergency Use Authorization of Medical Products and Related Authorities'' (Ref. 19) have been approved under OMB control number 0910–0595. The collections of information in Title 21 of the Code of Federal Regulations (CFR) are approved under the following OMB control numbers: part 3 under 0910–0523; parts 50 and 56 under 0910–0130; part 54 under 0910–0396; part 58 under 0910–0119; parts 801 and 809 under 0910–0485; part 807, subpart E, under 0910–0120; part 812 under 0910–0078; part 814, subparts A through E under 0910–0231; part 814, subpart H under 0910–0332; part 820 under 0910–0073; part 860, subpart C under 0910–0138.

The information collection provisions in this final rule have been submitted to OMB for review as required by section 3507(d) of the Paperwork Reduction Act of 1995.

Before the effective date of this final rule, FDA will publish a notice in the **Federal Register** announcing OMB's decision to approve, modify, or disapprove the information collection provisions in this final rule. An Agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

X. Federalism

We have analyzed this final rule in accordance with the principles set forth in Executive Order 13132. We have determined that the rule does not contain policies that have substantial direct effects on the States, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of government. Accordingly, we conclude that the rule does not contain policies that have federalism implications as defined in the Executive order and, consequently, a federalism summary impact statement is not required.

XI. Consultation and Coordination With Indian Tribal Governments

We have analyzed this rule in accordance with the principles set forth in Executive Order 13175. We have determined that the rule does not contain policies that would have a substantial direct effect on one or more Indian Tribes, on the relationship between the Federal Government and Indian Tribes, or on the distribution of power and responsibilities between the Federal Government and Indian Tribes. Accordingly, we conclude that the rule does not contain policies that have tribal implications as defined in the Executive Order and, consequently, a tribal summary impact statement is not required.

XII. References

The following references are on display in the Dockets Management Staff (see **ADDRESSES**) and are available for viewing by interested persons between 9 a.m. and 4 p.m., Monday through Friday; they are also available electronically at *https://www.regulations.gov.* FDA has verified the website addresses, as of the date this document publishes in the **Federal Register**, but websites are subject to change over time.

1. FDA, ''Content of Premarket Submissions for Management of Cybersecurity in Medical Devices,'' available at *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/content-premarket-submissions-management-cybersecurity-medical-devices.*
2. FDA, ''Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices,'' available at *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-content-premarket-submissions-software-contained-medical-devices.*
3. FDA, ''Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approval and De Novo Classifications,'' available at *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/factors-consider-when-making-benefit-risk-determinations-medical-device-premarket-approval-and-de.*
4. FDA, ''Patient Preference Information—Voluntary Submission, Review in Premarket Approval Applications, Humanitarian Device Exemption Applications, and De Novo Requests, and Inclusion in Decision Summaries and Device Labeling,'' available at *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/patient-preference-information-voluntary-submission-review-premarket-approval-applications.*
5. FDA, ''De Novo Classification Process (Evaluation of Automatic Class III Designation),'' available at *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/de-novo-classification-process-evaluation-automatic-class-iii-designation.*
6. FDA, CDRH Patient Engagement web page, available at *https://www.fda.gov/about-fda/about-center-devices-and-radiological-health/cdrh-patient-engagement.*
7. FDA, ''Procedures for Meetings of the Medical Devices Advisory Committee,'' available at *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/procedures-meetings-medical-devices-advisory-committee.*
8. FDA, ''eCopy Program for Medical Device Submissions,'' available at *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/ecopy-program-medical-device-submissions.*
9. FDA, ''Consideration of Uncertainty in Making Benefit-Risk Determinations in Medical Device Premarket Approvals, De Novo Classifications, and Humanitarian Device Exemptions,'' available at *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/consideration-uncertainty-making-benefit-risk-determinations-medical-device-premarket-approvals-de.*
10. FDA, ''The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)],'' available at *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/510k-program-evaluating-substantial-equivalence-premarket-notifications-510k.*
11. FDA, ''Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices,'' available at *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/appropriate-use-voluntary-consensus-standards-premarket-submissions-medical-devices.*
12. FDA, ''The Least Burdensome Provisions: Concept and Principles,'' available at *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/least-burdensome-provisions-concept-and-principles.*
13. FDA, ''Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program,'' available at *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/requests-feedback-and-meetings-medical-device-submissions-q-submission-program.*
14. FDA, ''Use of Electronic Health Record Data in Clinical Investigations,'' available at *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/use-electronic-health-record-data-clinical-investigations-guidance-industry.*
15. FDA, ''Recommended Content and Format of Non-Clinical Bench Performance Testing Information in Premarket Submissions,'' available at *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/recommended-content-and-format-non-clinical-bench-performance-testing-information-premarket.*
16. FDA, ''Acceptance Review for De Novo Classification Requests,'' available at *https://www.fda.gov/regulatory-information/search-fda-guidance-*

documents/acceptance-review-de-novo-classification-requests.

17. FDA's guidance ''Guidance for Industry and Food and Drug Administration Staff—User Fees for 513(g) Requests for Information,'' available at *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/user-fees-513g-requests-information.*
18. FDA's guidance ''FDA and Industry Procedures for Section 513(g) Requests for Information under the Federal Food, Drug, and Cosmetic Act,'' available at *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/fda-and-industry-procedures-section-513g-requests-information-under-federal-food-drug-and-cosmetic.*
19. ''Emergency Use Authorization of Medical Products and Related Authorities,'' available at *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/emergency-use-authorization-medical-products-and-related-authorities.*
20. FDA's full analysis of economic impacts is available in the Docket No. FDA–2018–N–0236 for this rule and at *https://www.fda.gov/AboutFDA/Reports ManualsForms/Reports/Economic Analyses/default.htm.*

List of Subjects in 21 CFR Part 860

Administrative practice and procedure, Medical devices.

Therefore, under the Federal Food, Drug, and Cosmetic Act, and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 860 is amended as follows:

PART 860—MEDICAL DEVICE CLASSIFICATION PROCEDURES

■ 1. The authority citation for part 860 is revised to read as follows:

Authority: 21 U.S.C. 321(h), 353(g), 360c, 360d, 360e, 360i, 360j, 371, 374.

■ 2. In part 860, remove all references to ''the act'' and add in their place ''the Federal Food, Drug, and Cosmetic Act''.

■ 3. Amend § 860.1 by revising paragraph (b) to read as follows:

§ 860.1 Scope.

* * * * *

(b) This part prescribes the criteria and procedures to be used by advisory committees, including classification panels, where applicable, in making their recommendations, and by the Commissioner in making the Commissioner's determinations regarding the class of regulatory control (class I, class II, or class III) appropriate for particular devices. Supplementing the general Food and Drug Administration procedures governing advisory committees (part 14 of this chapter), this part also provides procedures for manufacturers, importers, and other interested persons to participate in proceedings to classify and reclassify devices. This part also describes the type of data required for determination of the safety and effectiveness of a device, and the circumstances under which information submitted to advisory committees, including classification panels, or to the Commissioner in connection with classification and reclassification proceedings, will be available to the public.

■ 4. Revise § 860.3 to read as follows:

§ 860.3 Definitions.

For the purposes of this part:

Class means one of the three categories of regulatory control for medical devices, defined as follows:

Class I means the class of devices that are subject only to the general controls authorized by or under sections 501 (adulteration), 502 (misbranding), 510 (registration), 516 (banned devices), 518 (notification and other remedies), 519 (records and reports), and 520 (general provisions) of the Federal Food, Drug, and Cosmetic Act. A device is in class I if:

(1) General controls are sufficient to provide reasonable assurance of the safety and effectiveness of the device, or

(2) There is insufficient information from which to determine that general controls are sufficient to provide reasonable assurance of the safety and effectiveness of the device or to establish special controls to provide such assurance, but the device is not life-supporting or life-sustaining, or for a use which is of substantial importance in preventing impairment of human health, and which does not present a potential unreasonable risk of illness or injury.

Class II means the class of devices that is or eventually will be subject to special controls. A device is in class II if general controls alone are insufficient to provide reasonable assurance of its safety and effectiveness and there is sufficient information to establish special controls, including the promulgation of performance standards, postmarket surveillance, patient registries, development and dissemination of guidelines (including guidelines for the submission of clinical data in premarket notification submissions in accordance with section 510(k) of the Federal Food, Drug, and Cosmetic Act), recommendations, and other appropriate actions as the Commissioner deems necessary to provide such assurance. For a device that is purported or represented to be for use in supporting or sustaining human life, the Commissioner shall examine and identify the special controls, if any, which are necessary to provide adequate assurance of safety and effectiveness, and describe how such controls provide such assurance.

Class III means the class of devices for which premarket approval is or will be required in accordance with section 515 of the Federal Food, Drug, and Cosmetic Act. A device is in class III if insufficient information exists to determine that general controls are sufficient to provide reasonable assurance of its safety and effectiveness, or that application of special controls described in the definition of ''*Class II*'' in this section in addition to general controls, would provide such assurance, and if, in addition, the device is life-supporting or life-sustaining, or for a use which is of substantial importance in preventing impairment of human health, or if the device presents a potential unreasonable risk of illness or injury.

Classification panel means one of the several advisory committees established by the Commissioner under section 513 of the Federal Food, Drug, and Cosmetic Act and part 14 of this chapter for the purpose of making recommendations to the Commissioner on the classification and reclassification of devices and for other purposes prescribed by the Federal Food, Drug, and Cosmetic Act or by the Commissioner.

Classification regulation means a section under parts 862 through 892 of this chapter that contains the identification (general description and intended use) and classification (class I, II or III) of a single device type or more than one related device type(s).

Commissioner means the Commissioner of Food and Drugs, Food and Drug Administration, United States Department of Health and Human Services, or the Commissioner's designee.

De Novo request means any submission under section 513(f)(2) of the Federal Food, Drug, and Cosmetic Act for a medical device, requesting classification into class I or class II, including all information submitted with or incorporated by reference therein.

FDA means the Food and Drug Administration.

General controls mean the controls authorized by or under sections 501 (adulteration), 502 (misbranding), 510 (registration, listing, and premarket notification), 516 (banned devices), 518 (notification and other remedies), 519 (records, reports, and unique device identification), and 520 (general provisions) of the Federal Food, Drug, and Cosmetic Act.

Generic type of device means a grouping of devices that do not differ significantly in purpose, design, materials, energy source, function, or any other feature related to safety and effectiveness, and for which similar regulatory controls are sufficient to provide reasonable assurance of safety and effectiveness.

Implant means a device that is placed into a surgically or naturally formed cavity of the human body. A device is regarded as an implant for the purpose of this part only if it is intended to remain implanted continuously for a period of 30 days or more, unless the Commissioner determines otherwise to protect human health.

Life-supporting or life-sustaining device means a device that is essential to, or that yields information that is essential to, the restoration or continuation of a bodily function important to the continuation of human life.

Petition means a submission seeking reclassification of a device in accordance with § 860.123.

Special controls mean the controls necessary to provide reasonable assurance of safety and effectiveness for a generic type of device that is class II. Special controls include performance standards, performance testing, postmarket surveillance, patient registries, development and dissemination of guidelines (including guidelines for the submission of clinical data in premarket notification submissions in accordance with section 510(k) of the Federal Food, Drug, and Cosmetic Act), recommendations, and other appropriate actions, as the Commissioner deems necessary to provide such assurance.

■ 5. Amend § 860.5 by adding paragraph (g) to read as follows:

§ 860.5 Confidentiality and use of data and information submitted in connection with classification and reclassification.

* * * * *

(g) Confidentiality of data and information in a De Novo file is as follows:

(1) A ''De Novo file'' includes all data and information from the requester submitted with or incorporated by reference in the De Novo request, any De Novo supplement, or any other related submission relevant to the administrative file, as defined in § 10.3(a) of this chapter. Any record in the De Novo file will be available for public disclosure in accordance with the provisions of this section and part 20 of this chapter.

(2) The existence of a De Novo file may not be disclosed by FDA before an order granting the De Novo request is issued unless it previously has been publicly disclosed or acknowledged by the De Novo requester.

(3) Before an order granting the De Novo request is issued, data or information contained in the De Novo file is not available for public disclosure, except to the extent the existence of the De Novo file is disclosable under paragraph (g)(2) of this section and such data or information has been publicly disclosed or acknowledged by the De Novo requester.

(4) After FDA issues an order granting a De Novo request, the data and information in the De Novo file that are not exempt from release under the Freedom of Information Act, 5 U.S.C. 552, are immediately available for public disclosure.

■ 6. Add subpart D, consisting of §§ 860.200 through 860.260, to read as follows:

Subpart D—De Novo Classification

Sec.
860.200 Purpose and applicability.
860.210 De Novo request format.
860.220 De Novo request content.
860.230 Accepting a De Novo request.
860.240 Procedures for review of a De Novo request.
860.250 Withdrawal of a De Novo request.
860.260 Granting or declining a De Novo request.

Subpart D—De Novo Classification

§ 860.200 Purpose and applicability.

(a) The purpose of this part is to establish an efficient, transparent, and thorough process to facilitate De Novo classification into class I or class II for devices for which there is no legally marketed device on which to base a review of substantial equivalence and which meet the definition of class I or class II as described in section 513(a)(1) of the Federal Food, Drug, and Cosmetic Act and § 860.3.

(b) De Novo requests can be submitted for a single device type:

(1) After receiving a not substantially equivalent determination in response to a premarket notification (510(k)), or

(2) If a person determines there is no legally marketed device upon which to base a determination of substantial equivalence.

§ 860.210 De Novo request format.

(a) Each De Novo request or information related to a De Novo request pursuant to this part must be formatted in accordance with this section. Each De Novo request must be provided as a single version in electronic format. These materials must:

(1)(i) For devices regulated by the Center for Devices and Radiological Health, be sent to the current address displayed on the website *https://www.fda.gov/cdrhsubmissionaddress.*

(ii) For devices regulated by the Center for Biologics Evaluation and Research, be sent to the current address displayed on the website *https://www.fda.gov/about-fda/center-biologics-evaluation-and-research-cber/regulatory-submissions-electronic-and-paper.*

(2) Be signed by the requester or an authorized representative.

(3) Be designated ''De Novo Request'' in the cover letter.

(4) Have all content used to support the request written in, or translated into, English.

§ 860.220 De Novo request content.

(a) Unless the requester justifies an omission in accordance with paragraph (c) of this section, a De Novo request must include:

(1) *Table of contents.* A table of contents that specifies the volume (if the De Novo request contains more than one volume) and page number for each item.

(2) *Administrative information.* The name, address, phone, and email address of the requester and U.S. representative, if applicable. The establishment registration number, if applicable, of the owner or operator submitting the De Novo request.

(3) *Regulatory history.* Identify any prior submissions to FDA for the device, including, but not limited to, any premarket notifications (510(k)s) submitted under part 807 of this chapter; applications for premarket approval (PMAs) submitted under part 814 of this chapter; applications for humanitarian device exemption (HDE) submitted under part 814 of this chapter; applications for investigational device exemption (IDEs) submitted under part 812 of this chapter; requests for designation (RFD) under § 3.7 of this chapter; requests for information under section 513(g) of the Federal Food, Drug, and Cosmetic Act; applications for emergency use authorization (EUA) under section 564 of the Federal Food, Drug, and Cosmetic Act; pre-submissions, or previously submitted De Novo requests; or state that there have been no prior submissions.

(4) *Device name.* The generic name of the device as well as any proprietary name or trade name.

(5) *Indications for use.* A general description of the disease or condition the device is intended to diagnose, treat, prevent, cure or mitigate, or affect the structure or function of the body, including a description of the patient

population for which the device is intended. The indications for use include all the labeled patient uses of the device, including if it is prescription or over-the-counter.

(6) *Device description.* A complete description of:

(i) The device, including, where applicable, pictorial representations, device specifications, and engineering drawings;

(ii) Each of the functional components or ingredients of the device, if the device consists of more than one physical component or ingredient;

(iii) The properties of the device relevant to the diagnosis, treatment, prevention, cure, or mitigation of a disease or condition and/or the effect of the device on the structure or function of the body;

(iv) The principles of operation of the device; and

(v) The relevant FDA assigned reference number(s) for any medical devices (such as accessories or components) that are intended to be used with the device and that are already legally marketed.

(7) *Alternative practices and procedures.* A description of existing alternative practices or procedures that are used in diagnosing, treating, preventing, curing, or mitigating the disease or condition for which the device is intended or which similarly affect the structure or function of the body and that are known or should reasonably be known to the requester.

(8) *Classification summary.* (i) For devices not the subject of a previous submission under section 510(k) of the Federal Food, Drug, and Cosmetic Act, a complete description of:

(A) The searches used to establish that no legally marketed device of the same type exists.

(B) A list of classification regulations, PMAs, HDEs, premarket notifications (510(k)s), EUAs, and/or product codes regarding devices that are potentially similar to the subject device.

(C) A rationale explaining how the device that is the subject of the De Novo request is different from the devices covered by the classification regulations, PMAs, HDEs, 510(k)s, EUAs, and/or product codes identified in paragraph (a)(8)(i)(B) of this section.

(ii) For devices which were the subject of a previous submission under section 510(k) of the Federal Food, Drug, and Cosmetic Act that were determined not substantially equivalent (NSE), the relevant 510(k) number, along with a summary of the search performed to confirm the device has not been classified or reclassified since the date the NSE order was issued by FDA pursuant to § 807.100(a) of this chapter.

(9) *Summary of risks and mitigations.* A summary of probable risks to health associated with use of the device that are known or should reasonably be known to the requester and the proposed mitigations, including general controls and, if the classification recommendation from paragraph (a)(11) of this section is class II, special controls for each risk. For each mitigation measure that involves specific performance testing or labeling, the De Novo request must provide a reference to the associated section or pages for the supporting information in the De Novo request.

(10) *Proposed special controls.* If the classification recommendation from paragraph (a)(11) of this section is class II, then the summary must include an initial draft proposal for applicable special controls and a description of how those special controls provide reasonable assurance of safety and effectiveness.

(11) *Classification recommendation.* The recommended class (I or II) must be identified and must be supported by a description of why general controls, or general and special controls, are adequate to provide reasonable assurance of safety and effectiveness.

(12) *Standards.* Reference to any published voluntary consensus standards that are relevant to any aspect of the safety or effectiveness of the device and that are known or should reasonably be known to the requester. Such standards include voluntary consensus standards whether recognized or not yet recognized under section 514(c) of the Federal Food, Drug, and Cosmetic Act. Provide adequate information to demonstrate how the device meets, or justify any deviation from, the referenced standard.

(13) *Summary of studies.* An abstract of any information or report described in the De Novo request under paragraph (a)(16)(ii) of this section and a summary of the results of technical data submitted under paragraph (a)(15) of this section. Each such study summary must include a description of the objective of the study, a description of the experimental design of the study, a brief description of how the data were collected and analyzed, and a brief description of the results, whether positive, negative, or inconclusive. This section must also include the following:

(i) A summary of each nonclinical study submitted in the De Novo request;

(ii) A summary of each clinical investigation involving human subjects submitted in the De Novo request, including a discussion of investigation design, subject selection and exclusion criteria, investigation population, investigation period, safety and effectiveness data, adverse reactions and complications, subject discontinuation, subject complaints, device failures (including unexpected software events, if applicable) and replacements, results of statistical analyses of the clinical investigations, contraindications and precautions for use of the device, and other information from the clinical investigations as appropriate. Any investigation conducted under an investigational device exemption (IDE) under part 812 of this chapter must be identified as such.

(14) *Benefit and risk considerations.* A discussion demonstrating that:

(i) The data and information in the De Novo request constitute valid scientific evidence within the meaning of § 860.7(c) and

(ii) Pursuant to § 860.7, when subject to general controls, or general and special controls, the probable benefit to health from use of the device outweighs any probable injury or illness from such use.

(15) *Technical sections.* The following technical sections, which must contain data and information in sufficient detail to permit FDA to determine whether to grant or decline the De Novo request:

(i) A section containing the results of the nonclinical studies of the device, including, as appropriate, microbiological, toxicological, immunological, biocompatibility, stress, wear, shelf life, electrical safety, electromagnetic compatibility, and other laboratory or animal tests. Information on nonclinical studies must include protocols and complete test reports for each study. For those nonclinical studies subject to part 58 of this chapter, this section must include a statement that each such study was conducted in compliance with such regulations, or, if the study was not conducted in compliance with part 58 of this chapter, a brief statement of the reason for the noncompliance.

(ii) For all devices that incorporate software, a section containing all relevant software information and testing, including, but not limited to, appropriate device hazard analysis, hardware, and system information.

(iii) A section containing results of each clinical investigation of the device involving human subjects, including clinical protocols, number of investigators and subjects per investigator, investigation design, subject selection and exclusion criteria, investigation population, investigation period, safety and effectiveness data, adverse reactions and complications,

subject discontinuation, subject complaints, device failures (including unexpected software events if applicable) and replacements, tabulations of data from all individual subject report forms and copies of such forms for each subject who died during a clinical investigation or who did not complete the investigation, results of statistical analyses of the results of the clinical investigations, contraindications, warnings, precautions, and other limiting statements relevant to the use of the device type, and any other appropriate information from the clinical investigations. Any investigation conducted under an IDE under part 812 of this chapter must be identified as such. Information on clinical investigations involving human subjects must include the following:

(A) For clinical investigations conducted in the United States, a statement with respect to each investigation that it either was conducted in compliance with the institutional review board regulations in part 56 of this chapter, or was not subject to the regulations under § 56.104 or § 56.105 of this chapter, and that it was conducted in compliance with the informed consent regulations in part 50 of this chapter; or if the investigation was not conducted in compliance with those regulations, a brief statement of the reason for the noncompliance. Failure or inability to comply with these requirements does not justify failure to provide information on a relevant clinical investigation.

(B) For clinical investigations conducted in the United States, a statement that each investigation was conducted in compliance with part 812 of this chapter concerning sponsors of clinical investigations and clinical investigators, or if the investigation was not conducted in compliance with those regulations, a brief statement of the reason for the noncompliance. Failure or inability to comply with these requirements does not justify failure to provide information on a relevant clinical investigation.

(C) For clinical investigations conducted outside the United States that are intended to support the De Novo request, the requirements under § 812.28 of this chapter apply. If any such investigation was not conducted in accordance with good clinical practice (GCP) as described in § 812.28(a) of this chapter, include either a waiver request in accordance with § 812.28(c) of this chapter or a brief statement of the reason for not conducting the investigation in accordance with GCP and a description of steps taken to ensure that the data and results are credible and accurate and that the rights, safety, and well-being of subjects have been adequately protected. Failure or inability to comply with these requirements does not justify failure to provide information on a relevant clinical investigation.

(D) A statement that each investigation has been completed per the protocol or a summary of any protocol deviations.

(E) A financial certification or disclosure statement or both as required by part 54 of this chapter.

(F) For a De Novo request that relies primarily on data from a single investigator at one investigation site, a justification showing that these data and other information are sufficient to reasonably demonstrate the safety and effectiveness of the device when subject to general controls or general and special controls, and to ensure that the results from a site are applicable to the intended population.

(G) A discussion of how the investigation data represent clinically significant results, pursuant to § 860.7(e).

(16) *Other information.* (i) A bibliography of all published reports not submitted under paragraph (a)(15) of this section, whether adverse or supportive, known to or that should reasonably be known to the requester and that concern the safety or effectiveness of the device.

(ii) An identification, discussion, and analysis of any other data, information, or report relevant to an evaluation of the safety and effectiveness of the device known to or that should reasonably be known to the requester from any source, foreign or domestic, including information derived from investigations other than those in the request and from commercial marketing experience.

(iii) Copies of such published reports or unpublished information in the possession of or reasonably obtainable by the requester, if requested by FDA.

(17) *Samples.* If requested by FDA, one or more samples of the device and its components. If it is impractical to submit a requested sample of the device, the requester must name the location at which FDA may examine and test one or more of the devices.

(18) *Labeling and advertisements.* Labels, labeling, and advertisements sufficient to describe the device, its intended use, and the directions for its use. Where applicable, photographs or engineering drawings must be supplied.

(19) *Other information.* Such other information as is necessary to determine whether general controls or general and special controls provide reasonable assurance of safety and effectiveness of the device.

(b) Pertinent information in FDA files specifically referred to by a requester may be incorporated into a De Novo request by reference. Information submitted to FDA by a person other than the requester will not be considered part of a De Novo request unless such reference is authorized in writing by the person who submitted the information.

(c) If the requester believes that certain information required under paragraph (a) of this section to be in a De Novo request is not applicable to the device that is the subject of the De Novo request, and omits any such information from the De Novo request, the requester must submit a statement that specifies the omitted information and justifies the omission. The statement must be submitted as a separate section in the De Novo request and listed in the table of contents. If the justification for the omission is not accepted by FDA, FDA will so notify the requester.

(d) The requester must update the pending De Novo request with new safety and effectiveness information learned about the device from ongoing or completed studies and investigations that may reasonably affect an evaluation of the safety or effectiveness of the device as such information becomes available.

§ 860.230 Accepting a De Novo request.

(a) The acceptance of a De Novo request means that FDA has made a threshold determination that the De Novo request contains the information necessary to permit a substantive review. Within 15 days after a De Novo request is received by FDA, FDA will notify the requester whether the De Novo request has been accepted.

(b) If FDA does not find that any of the reasons in paragraph (c)(1) of this section for refusing to accept the De Novo request apply or FDA fails to complete the acceptance review within 15 days, FDA will accept the De Novo request for review and will notify the requester. The notice will include the De Novo request reference number and the date FDA accepted the De Novo request. The date of acceptance is the date that an accepted De Novo request was received by FDA.

(c)(1) FDA may refuse to accept a De Novo request if any of the following applies:

(i) The requester has an open or pending premarket submission or reclassification petition for the device;

(ii) The De Novo request is incomplete because it does not on its face contain all the information required

under section 513(f)(2) of the Federal Food, Drug, and Cosmetic Act or does not contain each of the items required under this part, or a justification for omission of any item;

(iii) The De Novo request is not formatted as required under § 860.210;

(iv) The De Novo request is for multiple devices and those devices are of more than one type; or

(v) The requester has not responded to, or has failed to provide a rationale for not responding to, deficiencies identified by FDA in previous submissions for the same device, including those submissions described in § 860.220(a)(3).

(2) If FDA refuses to accept a De Novo request, FDA will notify the requester of the reasons for the refusal. The notice will identify the deficiencies in the De Novo request that prevent accepting and will include the De Novo request reference number.

(3) If FDA refuses to accept a De Novo request, the requester may submit the additional information necessary to comply with the requirements of section 513(f)(2) of the Federal Food, Drug, and Cosmetic Act and this part. The additional information must include the De Novo request reference number of the original submission. If the De Novo request is subsequently accepted, the date of acceptance is the date FDA receives the additional information.

§ 860.240 Procedures for review of a De Novo request.

(a) FDA will begin substantive review of a De Novo request after the De Novo request is accepted under § 860.230. Within 120 days after receipt of a De Novo request or receipt of additional information that results in the De Novo request being accepted under § 860.230, FDA will review the De Novo request and send the requester an order granting the De Novo request under § 860.260(a) or an order declining the De Novo request under 860.260(b).

(b) A requester may supplement or amend a pending De Novo request to revise existing information or provide additional information.

(1) FDA may require additional information regarding the device that is necessary for FDA to complete the review of the De Novo request.

(2) Additional information submitted to FDA must include the reference number assigned to the original De Novo request and, if submitted on the requester's own initiative, the reason for submitting the additional information.

(c) Prior to granting or declining a De Novo request, FDA may inspect relevant facilities to help determine:

(1) That clinical or nonclinical data were collected in a manner that ensures that the data accurately represents the benefits and risks of the device; or

(2) That implementation of Quality System Regulation (part 820 of this chapter) requirements, in addition to other general controls and any specified special controls, provide adequate assurance that critical and/or novel manufacturing processes produce devices that meet specifications necessary to ensure reasonable assurance of safety and effectiveness.

§ 860.250 Withdrawal of a De Novo request.

(a) FDA considers a De Novo request to have been withdrawn if:

(1) The requester fails to provide a complete response to a request for additional information pursuant to § 860.240(b)(1) within 180 days after the date FDA issues such request;

(2) The requester fails to provide a complete response to the deficiencies identified by FDA pursuant to § 860.230(c)(2) within 180 days of the date notification was issued by FDA;

(3) The requester does not permit an authorized FDA employee an opportunity to inspect the facilities, pursuant to § 860.240(c), at a reasonable time and in a reasonable manner, and to have access to copy and verify all records pertinent to the De Novo request; or

(4) The requester submits a written notice to FDA that the De Novo request has been withdrawn.

(b) If a De Novo request is withdrawn, the Agency will notify the requester. The notice will include the De Novo request reference number and the date FDA considered the De Novo request withdrawn.

§ 860.260 Granting or declining a De Novo request.

(a)(1) FDA will issue to the requester an order granting a De Novo request if none of the reasons in paragraph (c) of this section for declining the De Novo request applies.

(2) If FDA grants a De Novo request, within 30 days after the issuance of an order granting the De Novo request, FDA will publish in the **Federal Register** a notice of the classification order, including any special controls.

(b) If FDA declines a De Novo request, FDA will issue a written order to the requester.

(c) FDA may decline a De Novo request if the requester fails to follow the requirements of this part or if, upon the basis of the information submitted in the De Novo request or any other information before FDA, FDA determines:

(1) The device does not meet the criteria under section 513(a)(1) of the Federal Food, Drug, and Cosmetic Act and § 860.3 for classification into class I or II;

(2) The De Novo request contains a false statement of material fact or there is a material omission;

(3) The device's labeling does not comply with the requirements in parts 801 and 809 of this chapter, as applicable;

(4) The product described in the De Novo request does not meet the definition of a device under section 201(h) of the Federal Food, Drug, and Cosmetic Act and is not a combination product as defined at § 3.2(e) of this chapter;

(5) The device is of a type which has already been approved in existing applications for premarket approval (PMAs) submitted under part 814 of this chapter;

(6) The device is of a type that has already been classified into class I, class II, or class III;

(7) An inspection of a relevant facility under § 860.240(c) results in a determination that general or general and special controls would not provide reasonable assurance of safety and effectiveness;

(8) A nonclinical study subject to part 58 of this chapter that is described in the De Novo request, and that is essential to show there is reasonable assurance of safety, was not conducted in compliance with part 58 of this chapter and no reason for the noncompliance is provided or, if a reason is provided, the practices used in conducting the study do not support the validity of the study;

(9) A clinical investigation described in the De Novo request involving human subjects that is subject to the institutional review board regulations in part 56 of this chapter, informed consent regulations in part 50 of this chapter, or GCP described in § 812.28(a) of this chapter, was not conducted in compliance with those regulations such that the rights or safety of human subjects were not adequately protected or the supporting data were determined to be otherwise unreliable;

(10) A clinical or nonclinical study necessary to demonstrate that general controls or general and special controls provide reasonable assurance of safety and effectiveness:

(i) Has not been completed per the study protocol, or

(ii) Deficiencies related to the investigation and identified in any request for additional information under § 860.240(b)(1) have not been adequately addressed; or

(11) After a De Novo request is accepted for review under § 860.230(b), the requester makes significant unsolicited changes to the device's:

(i) Indications for use; or

(ii) Technological characteristics.

(d) An order declining a De Novo request will inform the requester of the deficiencies in the De Novo request, including each applicable ground for declining the De Novo request.

(e) FDA will use the criteria specified in § 860.7 to determine the safety and effectiveness of a device in deciding whether to grant or decline a De Novo request. FDA may use information other than that submitted by the requester in making such determination.

Dated: September 30, 2021.

Janet Woodcock,

Acting Commissioner of Food and Drugs.

[FR Doc. 2021–21677 Filed 10–4–21; 8:45 am]

BILLING CODE 4164–01–P

FEDERAL MEDIATION AND CONCILIATION SERVICE

29 CFR Part 1400

RIN 3076–AA19

Outside Employment, Business Activities, or Interests Regulation

AGENCY: Federal Mediation and Conciliation Service.

ACTION: Final rule; rescission of regulation.

SUMMARY: On August 7, 1992, the Office of Government Ethics (OGE) published a final rule entitled ''Supplemental Agency Regulations'' requiring Federal agencies creating supplemental ethics regulations to submit such regulations to OGE for concurrence and joint issuance within their regulations. In accordance with ''Supplemental Agency Regulations,'' this final rule rescinds the current Federal Mediation and Conciliation Service (FMCS) supplemental ethics regulation ''Outside employment, business activities, or interests''.

DATES: This final rule is effective October 5, 2021.

FOR FURTHER INFORMATION CONTACT: Alisa Silverman, Attorney-Advisor, Office of General Counsel, Federal Mediation and Conciliation Service, 250 E St. SW, Washington, DC 20427; Office/Fax/Mobile 202–606–5488; *asilverman@fmcs.gov*.

SUPPLEMENTARY INFORMATION:

I. Discussion

On April 13, 1968, at 33 FR 5765, the Federal Mediation and Conciliation Service (FMCS) published a final rule entitled ''Outside employment, business activities, and interests.'' This final rule implemented ethics regulations concerning outside activities.

On August 7, 1992, at 57 FR 35042, the Office of Government Ethics (OGE) published a rule ''Supplemental Agency Regulations'' requiring Federal agencies creating supplemental ethics regulations to submit such regulations to OGE for concurrence and joint issuance within title 5 of the Code of Federal Regulations.

In accordance with 5 CFR 2635.105, FMCS is working jointly with OGE to develop new supplemental agency regulations to be published by OGE within title 5 of the Code of Federal Regulations. Therefore, FMCS is issuing this final rule, which rescinds the current rule on outside employment, business activities, and interests within title 29 of the Code of Federal Regulations.

II. Final Rule

FMCS has determined that this rule is suitable for final rulemaking. The revisions to FMCS' policies and requirements surrounding outside activities are purely internal matters of agency management, as well as the agency's procedure, and practice. Accordingly, FMCS is not required to engage in a notice and comment process to issue this rule under the Administrative Procedures Act, See U.S.C. 553(a)(2), 553(b)(A). Furthermore, because this rule is procedural rather than substantive, the normal requirement of 5 U.S.C. 553(d) that a rule not be effective until at least 30 days after publication in the **Federal Register** is inapplicable. FMCS also finds good cause to provide an immediate effective date for this rule because it imposes no obligations on parties outside the Federal Government and therefore no advance notice is required to enable employers or other private parties to come into compliance.

List of Subjects in 29 CFR Part 1400

Administrative practice and procedure.

For the reasons discussed in the preamble, and under the authority 29 U.S.C. 172 of Taft Harley Act of 1947, and 5 U.S.C. 7301, FMCS amends 29 CFR chapter XII as follows:

PART 1400—STANDARDS OF CONDUCT, RESPONSIBILITIES, AND DISCIPLINE

■ 1. The authority citation for part 1400 continues to read as follows:

Authority: E.O. 11222, 30 FR 6469, 3 CFR, 1965 Supp.; 5 CFR 735.104.

§ 1400.735–12 [Removed]

■ 2. Remove § 1400.735–12.

Issued in Washington, DC.

Sarah Cudahy,

General Counsel.

[FR Doc. 2021–21716 Filed 10–4–21; 8:45 am]

BILLING CODE 6732–01–P

DEPARTMENT OF HOMELAND SECURITY

Coast Guard

33 CFR Part 117

[Docket No. USCG–2020–0647]

RIN 1625–AA09

Drawbridge Operation Regulation; New Jersey Intracoastal Waterway, Point Pleasant, NJ; Correction

AGENCY: Coast Guard, Department of Homeland Security (DHS).

ACTION: Correcting amendments.

SUMMARY: The Coast Guard published a final rule in the **Federal Register** on August 23, 2021, which was effective on September 22, 2021, announcing changes to the Route 88 (Veterans Memorial) Bridge and Route 13 (Lovelandtown) Bridge across the NJICW at Point Pleasant Canal, mile 3.0 and 3.9, respectively at Point Pleasant, NJ. The amendatory instruction within that final rule was incorrect and the changes could not be incorporated into the CFR. This correcting amendment incorporates those changes into the CFR.

DATES: The correction is effective on October 5, 2021.

ADDRESSES: To view documents mentioned in this preamble as being available in the docket, go to *https://www.regulations.gov,* type USCG–2020–0647. In the ''SEARCH'' box and click ''SEARCH.'' Click on Open Docket Folder on the line associated with this rulemaking.

FOR FURTHER INFORMATION CONTACT: If you have questions on this rule, call or email Mr. Mickey Sanders, Bridge Administration Branch, Fifth District, U.S. Coast Guard, telephone (757) 398–6587, email *Mickey.D.Sanders2@uscg.mil.*

SUPPLEMENTARY INFORMATION:

Correction

On August 23, 2021, the Coast Guard published a final rule titled ''Drawbridge Operation Regulation; New