

Guidance for Industry and FDA Staff: Classification of Products as Drugs and Devices & Additional Product Classification Issues

DRAFT GUIDANCE

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**U.S. Department of Health and Human Services
Food and Drug Administration
Office of Combination Products in the Office of the Commissioner (OCP)
Center for Biologics Evaluation and Research (CBER)
Center for Drug Evaluation and Research (CDER)
Center for Devices and Radiological Health (CDRH)**

June 2011

Guidance for Industry

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TABLE OF CONTENTS

GUIDANCE FOR INDUSTRY AND FDA STAFF	2
I. INTRODUCTION.....	2
II. WHAT IS THE PROCESS FOR OBTAINING A FORMAL CLASSIFICATION DETERMINATION FOR A PRODUCT?	2
III. WHAT DOES FDA CONSIDER IN DETERMINING WHETHER TO CLASSIFY A PRODUCT AS A DRUG OR A DEVICE?	3
A. Statutory Definitions.....	3
1. <i>Drug</i>	3
2. <i>Device</i>	3
B. How does the Agency interpret certain key provisions of the definition of device?	4
1. <i>How does the Agency interpret “similar or related article” in the definition of device?</i>	<i>4</i>
2. <i>How does the Agency interpret “does not achieve its primary intended purposes through chemical action within or on the body of man” in the definition of device?</i>	<i>4</i>
C. How is a product classified if it meets the definitions for both drug and device, and might also meet the definition for biological product?.....	5
IV. WHAT IS THE STATUS OF THE INTERCENTER AGREEMENTS AND PRIOR AGENCY CLASSIFICATION DETERMINATIONS?	5
A. What effect do intercenter agreements have on product jurisdiction?.....	6
B. What is the status of prior Agency classification determinations?.....	6
1. <i>What if the existing classification is established by regulation?</i>	<i>7</i>
2. <i>What if the existing classification is not established by regulation?.....</i>	<i>7</i>
V. ADDITIONAL INFORMATION.....	9

Guidance for Industry and FDA Staff¹

Classification of Products as Drugs and Devices & Additional Product Classification Issues

This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic.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

I. INTRODUCTION

FDA regularly receives requests from medical product developers concerning the classification of their products. We believe that efficient, effective regulation of such products is facilitated by providing guidance on issues frequently raised in relation to such requests. Certain issues have arisen often relating to whether a product should be classified as a drug or a device. Accordingly, this guidance focuses particularly on when a product may be classified as a drug or a device. This guidance also addresses additional issues relating to product classification, including how to obtain a formal classification determination from FDA for a medical product and the status of prior Agency determinations concerning product classification.

This guidance is organized into three substantive sections.

Section II offers guidance on the process to obtain a formal determination of whether a product is classified as a drug, device, biological product, or combination product.²

Section III provides some general concepts for making classification determinations and addresses specific issues arise in determining whether products should be classified as drugs or devices.³

¹ This guidance has been prepared by the Office of Combination Products in the Office of the Commissioner (OCP), the Center for Biologics Evaluation and Research (CBER), the Center for Drug Evaluation and Research (CDER), and the Center for Devices and Radiological Health (CDRH).

² The term “combination product” is defined in 21 CFR 3.2(e). For further information regarding the definition of combination product and the regulation of combination products, please visit the webpage for the Office of Combination Products at www.fda.gov/CombinationProducts/default.htm.

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Section IV of this document provides an overview of the status of the current intercenter jurisdictional agreements, classifications that have been made by regulation, and classifications the Agency has made for a product that does not fall within the scope of a regulation, for example, by granting a marketing authorization or in responding to a request for designation.

The Agency recommends that manufacturers contact the Office of Combination Products (OCP) to confirm the classification of any products they may wish to market if the appropriate classification appears unclear for any reason. Section V provides contact information for OCP.

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

II. WHAT IS THE PROCESS FOR OBTAINING A FORMAL CLASSIFICATION DETERMINATION FOR A PRODUCT?

If the classification of a product as a drug, device, biological product, or combination product is unclear or in dispute, a sponsor can file a request for designation (RFD) with OCP in accordance with Part 3 of Title 21 of the Code of Federal Regulations (21 CFR Part 3) to obtain a formal classification determination for the product, as provided for under section 563 of the FD&C Act (21 USC 360bbb-2). In reviewing an RFD, the Agency considers the information provided in the RFD as well as other information available to the Agency at that time. Generally, the Agency will respond in writing within sixty days of the sponsor's RFD filing, identifying the classification of the product as a drug, device, biological product, or combination product. If the Agency does not provide a written response within sixty days, the sponsor's recommendation respecting the classification of the product is considered to be the final determination. 21 USC 360bbb-2(b) and (c).

The Agency may not modify a determination made under section 563 of the classification of a product or of the component of FDA that will regulate the product, except with the written consent of the sponsor, or for public health reasons based on scientific evidence. 21 USC 360bbb-2(b) and (c). However, the determination pertains only to the product described in the designation letter. A new determination may be appropriate if there is a change in, for example, an intended use or component of the product, or if the sponsor or Agency becomes aware of additional information that reveals that the mode (or modes) of action differs from what was originally described in the RFD.

Please contact OCP if you have questions regarding whether to submit an RFD or what information to provide and issues to address in an RFD to ensure its completeness and clarity. More

³ This section generally focuses on approaches for determining whether a product will be classified as a drug or a device based on application of the statutory definitions for these two terms under sections 201(g) and 201(h) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 USC 321(g) and (h)). However, as discussed more fully in section III.C of this guidance, articles that meet these statutory definitions might also meet the statutory definition of biological product under section 351(i) of the Public Health Service Act (PHS Act) (42 USC 262(i)) and could be subject to licensure under section 351 of the PHS Act as discussed in that section. The Agency expects to revise this guidance in the future to address aspects of its approach to classifying biological products. Additionally, please note that this document does not address the regulatory status of human cells, tissues, cellular or tissue-based products, as defined in 21 CFR Part 1271.

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detailed information on the RFD process is provided in OCP's guidance *How to Write a Request for Designation (RFD)* (available at <http://www.fda.gov/CombinationProducts/default.htm>).

III. WHAT DOES FDA CONSIDER IN DETERMINING WHETHER TO CLASSIFY A PRODUCT AS A DRUG OR A DEVICE?

FDA's determination of whether to classify a product as a drug or a device will be made based on the statutory definitions of these terms set forth in sections 201(g) and 201(h) of the FD&C Act, as applied to the scientific data concerning the product that are available to FDA at the time the classification determination is made. This section presents the drug and device definitions and discusses how the Agency addresses certain interpretive issues that arise when determining whether a product should be classified as a drug or a device.

A. Statutory Definitions

1. Drug.

Section 201(g) of the FD&C Act (21 USC 321(g)) provides that the term "drug" means:

(A) articles recognized in the official United States Pharmacopoeia, official Homoeopathic Pharmacopoeia of the United States, or official National Formulary, or any supplement to any of them; and (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals; and (D) articles intended for use as a component of any articles specified in clause (A), (B), or (C). . . .

2. Device.

Section 201(h) of the FD&C Act (21 USC 321(h)) provides that the term "device" means:

... an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is--

(1) recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them,

(2) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or

(3) intended to affect the structure or any function of the body of man or other animals, and

which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes.

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B. How does the Agency interpret certain key provisions of the definition of device?

Products that meet the definition of device under section 201(h) of the FD&C Act also meet the definition of drug under section 201(g) of the FD&C Act, due to the broader scope of the drug definition. Subject to the considerations noted in section III.C regarding whether the product also meets the definition of biological product, if a product is shown to meet both the drug and device definitions, the Agency generally intends to classify the product as a device. If a product meets the drug definition, but there is uncertainty regarding whether it also meets the device definition, the Agency generally intends to classify the product as a drug (again, subject to the considerations noted in section III.C).

Consequently, medical product classification determinations often focus substantially on whether the product meets the statutory definition of device. The following discussion presents the Agency's current thinking on certain interpretive issues that arise with respect to the statutory definition of device.

1. How does the Agency interpret “similar or related article” in the definition of device?

The first clause of the device definition provides that device “means an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or *other similar or related article . . .*” (emphasis added). The issue of whether a product may be considered a “similar or related article” under this clause can arise, for example, with regard to products in liquid, semi-liquid, gel, gas, or powder form. In some circumstances, the Agency believes that such products may be appropriately considered “similar or related articles,” and may be classified as devices, so long as they also satisfy the remainder of the device definition under section 201(h) of the FD&C Act, including the chemical action exclusion discussed in section III.B.2 below. This could be the case, for example, for wound covering gels, powders or liquids put on the skin as a barrier, or gases used as space fillers.

2. How does the Agency interpret “does not achieve its primary intended purposes through chemical action within or on the body of man” in the definition of device?

A product may be classified as a device if it “does not achieve its primary intended purposes through chemical action within or on the body of man or other animals . . .”, provided the product also meets the rest of the device definition under section 201(h). Interpretation of this phrase is often at issue in classification determinations. The Agency has published a companion draft guidance, *Interpretation of the Term “Chemical Action” in the Definition of Device under Section 201(h) of the Federal Food, Drug, and Cosmetic Act*, addressing our interpretation of the term “chemical action” in section 201(h) (available at <http://www.fda.gov/CombinationProducts/default.htm>). Accordingly, this guidance does not address the interpretation of the term “chemical action.” However, the other terms of this phrase are also integral to classification determinations, and the Agency's interpretation of these terms is presented below.

First, a product that exhibits chemical action within or on the body of man may meet the device definition provided that the product “does not achieve its primary intended purposes through” such chemical action. Thus, if a product's chemical action contributes to an effect other than a primary intended purpose of the product, the product could fall within the scope of section 201(h). In contrast, a

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product that depends, even in part, on chemical action within or on the body of man to achieve any one of its primary intended purposes, would not be a device. In addition, if a product has multiple therapeutic effects, each of these would be a “primary intended purpose” of the product, and the product would not meet the device definition if it achieves any one of these primary intended purposes through chemical action within or on the body of man. Second, under this phrase, a product that “achieves its primary intended purposes through chemical action” still meets the device definition provided that the chemical action does not occur “within or on the body of man or other animals.”

C. How is a product classified if it meets the definitions for both drug and device, and might also meet the definition for biological product?

As explained in section III.B above, products that meet the device definition in section 201(h) of the FD&C Act also meet the drug definition in section 201(g) of the FD&C Act. In addition, products that meet the drug definition, or both the drug and device definitions, may also meet the definition of biological product under section 351(i) of the PHS Act (42 USC 262(i)).

Section 351(i) (as amended by the Biologics Price Competition and Innovation Act of 2009, title VII of the Patient Protection and Affordable Care Act, Pub. L. No. 111-148, § 7002 (2010)) provides that:

The term “biological product” means a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein (except any chemically synthesized polypeptide), or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings.

Some products that meet the drug definition or both the drug and device definitions, and that also meet the definition of biological product, might be classified as biological products, rather than as devices or drugs, and be subject to licensure under the PHS Act.⁴ If you have questions regarding whether a product meets the definition of biological product or how this might affect its classification, please contact OCP.

IV. WHAT IS THE STATUS OF THE INTERCENTER AGREEMENTS AND PRIOR AGENCY CLASSIFICATION DETERMINATIONS?

The Agency must classify products in accordance with the statutory definitions in the FD&C Act and the PHS Act. Sponsors often argue that their products should be classified in a certain way because products they consider similar to their product have previously been classified or regulated in a particular way. While the classification of similar products may help to inform the classification of the product at issue, we believe that a case-by-case approach based on the specific characteristics of the product, including its intended use(s), and the current state of scientific knowledge at the time the classification determination is made is necessary to ensure that products are classified properly under the applicable statutory criteria.

⁴ It bears noting that an article that meets the definition of biological product and is subject to licensure under the PHS Act is still subject to regulation under the FD&C Act as a drug or device, although drug or device marketing authorization under the FD&C Act is not required so long as the article has an approved license under the PHS Act. See 42 USC 262(j).

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A. What effect do intercenter agreements have on product jurisdiction?

CBER, CDER and CDRH have entered into intercenter agreements (agreements) to clarify certain product jurisdictional determinations. See “Intercenter Agreements” available at <http://www.fda.gov/CombinationProducts/JurisdictionalInformation/IntercenterAgreements/default.htm>. Sponsors sometimes assert that their product falls within a certain category of products identified in an agreement and should, therefore, be classified in the same manner as other products in that category. While these agreements describe the allocation of responsibility for categories of products to specific agency components, they constitute nonbinding determinations.⁵ See 21 CFR § 3.5.

In 2006, the Agency reviewed these agreements and preliminarily determined that they continued to provide helpful, nonbinding guidance. See U.S.C. § 353(g)(4)(F). The Agency proposed to continue them in effect, with the understanding that they should not be independently relied upon as the Agency's most current, complete jurisdictional statements (71 FR 56,988, Sept. 28, 2006). However, in light of current scientific understanding, we are currently reviewing the agreements to determine whether it would be appropriate to modify them or replace them with new agreements.

In the interim, we note that these agreements should be considered in light of statutory definitions and current scientific understanding. Products that might appear to fall within a category addressed in one of these agreements can only be classified consistent with other products in that category if such a classification is legally permissible in light of the specific characteristics of that particular product. In addition, to the extent that those agreements appear to support classification determinations that are inconsistent with this guidance, this guidance supersedes those agreements with respect to such classifications.

B. What is the status of prior Agency classification determinations?

In some cases, the Agency has previously addressed the classification of a product (when the product consists solely of a drug, device, or biological product) or a constituent part⁶ of a combination product that is subsequently presented in an RFD. In reviewing such an RFD, OCP may determine that, in light of current scientific understanding, the means by which such a product or constituent part achieves an intended use may warrant a different classification for that product or constituent part in the pending RFD than the Agency previously provided.⁷ The following describes the Agency's proposed approach to address these relatively rare sets of circumstances and the particular considerations they present.

⁵ The agreements and the transfer of therapeutic biological products to CDER (“Transfer of Therapeutic Biological Products to the Center for Drug Evaluation and Research,” June 30, 2003,) describe assignment for specific classes of products (available at <http://www.fda.gov/CombinationProducts/JurisdictionalInformation/ucm136265.htm>). These documents are intended to explain assignment among the relevant centers when such assignment may not be obvious, e.g., when a device might be regulated by CBER rather than CDRH or when a biological product is assigned to CDER rather than CBER.

⁶ The term “constituent part” is typically used by the Agency to refer to the distinct, regulated articles (e.g., drug and device) that constitute a combination product.

⁷ For example, this issue may arise in some instances when determining the classification of gels, liquids, semi-liquids, or powders.

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1. What if the existing classification is established by regulation?

A product (when the product consists solely of a drug, device, or biological product) or a constituent part of a combination product at issue in an RFD may fall within the scope of an existing classification issued by regulation. Such a classification might be the result, for example, of the development of a monograph for over-the-counter drugs or a device classification regulation. However, in reviewing an RFD, OCP may, for instance, determine that the product or constituent part meets the statutory definition of a device even though, for example, the ingredient(s) in the product or constituent part is included in an OTC drug monograph. Alternatively, the product or constituent part at issue in the RFD may fall within a device classification regulation for a use proposed in the RFD, but OCP may be aware of evidence indicating that the product or constituent part may achieve its primary intended purposes through chemical action within or on the body of man and therefore may not meet the device definition. In such cases, if a regulation establishes the classification of a product or constituent part of a combination product for the use proposed in the RFD, we believe it is appropriate to continue to apply that existing classification until or unless the Agency changes the classification by revising the regulation.

Accordingly, in responding to an RFD, the Agency would generally classify the product or the constituent part in the RFD in accordance with the regulation if the product or constituent part falls within the scope of that regulation. The Agency may then assess whether it would be appropriate to change the classification and, if so, will initiate notice and comment rulemaking to do so.

2. What if the existing classification is not established by regulation?

In some cases, FDA may classify a product that does not fall within the scope of an existing classification established by regulation, for example, by granting marketing authorization to the product or responding to an RFD. A product (when the product consists solely of a drug, device, or biological product) or constituent part of a combination product that is the same⁸ as that previously classified product, may later be at issue in a pending RFD.⁹

In instances where the product presented in a pending RFD appears to be a drug or device (as opposed to a combination product), if current scientific understanding may potentially lead to a different classification of that product than the Agency previously applied, the Agency generally intends to refrain from providing, within 60 days of receipt of the RFD, a “written statement” or letter of designation concerning the requested classification or component of FDA that would regulate the product pursuant to section 563 of the FD&C Act. 21 U.S.C. § 360bbb-2. As a result, in such cases, the recommendation made by the submitter concerning the classification or Agency component would be considered a final determination by FDA of such classification or component. 21 U.S.C. § 360bbb-2(c); 21 CFR § 3.8(b).

⁸ For purposes of this guidance, sameness of a product or constituent part will generally be determined based on the product’s or constituent part’s chemical or physical structure, the intended use of the product, and the mode of action by which the product or constituent part achieves its intended use.

⁹ The Agency has not developed a general policy on this issue for products or constituent parts that may meet the definition of biological product. If you have questions regarding such products, please contact OCP.

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This approach would provide consistency for certain products. This approach would also enable the Agency to re-evaluate the appropriate classification for a group of products through a public process and to determine, if necessary and appropriate, how best to administratively transfer the entire group of products.¹⁰ In this manner, the Agency intends to promote procedural regularity and predictability to relevant stakeholders.

If the product presented in a pending RFD appears to be a combination product, and the Agency has previously classified a constituent part that is the same as one of the constituent parts in the potential combination product, the Agency generally intends not to classify that constituent part in responding to the RFD if the product can be classified or assigned pursuant to section 563 without addressing the classification of that constituent part. In instances where a designation cannot be made for the product without classifying the constituent part, the Agency will evaluate what approach is appropriate for the RFD on a case- by-case basis.

FDA is currently reviewing issues, including regulatory and legal options, relating to the classification and transfer of products as appropriate that fall within the scope of this section IV.B.2. Potential regulatory and legal issues the Agency is examining include determining when it may be appropriate to: (1) exercise enforcement discretion for products subject to an existing classification; (2) transfer products by determining that a currently approved application also meets the applicable requirements for another type of approved application (e.g., determining whether an approved NDA meets the requirements for an approved PMA); or (3) withdraw the existing approval for products and require new approvals for such products under the premarket approval authorities associated with the new classification. In all events, should FDA determine that action should be taken to transfer or address the classification of any such products, such efforts would be pursued in a transparent manner consistent with applicable legal requirements.

* * *

Should it appear that reclassification and/or transfer to different Agency components may be appropriate for multiple groups of products, the Agency intends to prioritize among such groups to determine the order in which to address them. Whatever the scope and particulars of the administrative process to maximize consistency of classification among products, the Agency will be transparent and comply with all applicable legal requirements. We acknowledge that we have addressed associated regulatory and procedural issues in this section IV in general terms, and we encourage comments on our proposed approach and related issues.

¹⁰ Note, however, that FDA can classify the product or constituent part presented in the RFD in accordance with current scientific understanding and applicable statutory definitions, notwithstanding the fact such a determination may result in similar products being classified differently for some period of time. In instances where an RFD determination has led to a new classification that is different from the previous classification of the same product or constituent part, it is FDA's intention to initiate an administrative process, consistent with principles of transparency and applicable legal requirements, to resolve these differences in classification. Where appropriate, the Agency anticipates transferring products regulated under the previous classification to the appropriate agency component and regulating those products under the statutory authorities relevant for the new classification.

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V. ADDITIONAL INFORMATION

For further information on the classification of products, as devices, drugs, biological products, or combination products, please refer to OCP's webpage at <http://www.fda.gov/oc/combination> or contact OCP at:

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