

# Is it a drug, device, biologic, or combination product? FDA issues final guidance on classification issues

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On September 26, 2017, the Food and Drug Administration (FDA) published a [final guidance document](#) providing further clarity on how FDA classifies a product as a drug, device, biological product, or a combination product, entitled “Classification of Products as Drugs and Devices & Additional Product Classification Issues” (Final Guidance). [See 82 FR 44802 \(Sept. 26, 2017\)](#).

The guidance combines and finalizes two draft guidance documents issued in 2011: “Classification of Products as Drugs and Devices & Additional Product Classification Issues” (Draft Classification Guidance) and “Interpretation of the Term ‘Chemical Action’ in the Definition of Device under Section 201(h) of the Federal Food, Drug, and Cosmetic Act” (Draft Chemical Action Guidance). [See our article on these draft guidances here](#). In the Final Guidance, FDA outlines general principles concerning FDA’s classification decisions and provides an overview of the request for designation (RFD) process for obtaining a formal designation of a product’s classification to determine the product’s pathway to market and the likely regulatory hurdles.

## Classification principles and examples

The Final Guidance highlights general principles regarding FDA’s approach for defining the jurisdictional line between drugs, devices, and biologics, focusing on drugs and devices. Specifically, it provides more color surrounding FDA’s current interpretation of the definitions of “device” and “drug” in the Federal Food, Drug, and Cosmetic Act (FDC Act). Without providing specific detail on the agency’s interpretation of these definitions, the guidance instead follows FDA’s recent trend of providing examples to clarify the agency’s likely approach to specific products. In preparing an RFD, FDA is suggesting that companies carefully consider the definitions and examples provided to draw analogies to their own products.

Since the majority of classification decisions hinge on an assessment of whether the product is a device or a drug, as opposed to other product types (such as biologics), the Final Guidance focuses on defining the classification principles for these two types of products. As FDA notes in the Final Guidance, all medical products inherently meet the very broad definition of a drug.

The key element to determining whether the agency will regulate a product as a device and not a drug will depend on whether the product meets the restricting language in the definition of a device in Section 201(h) of the FDC Act: “which does not achieve its primary intended purpose through chemical action within or on the body of man or other animals and which is not dependent on being metabolized for the achievement of its primary intended purpose.”

As discussed below, the Final Guidance addresses each of the elements in the first part of this phrase in greater detail, while also stating that FDA does not believe it is necessary to address at this time the second part of the device definition involving whether the product is not “dependent upon being metabolized.” FDA did not analyze this clause, because it is not at issue frequently in classification determinations. Nonetheless, the following elements of the device definition were analyzed:

- “**similar or related article:**” The first part of the device definition states that the term “means an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, **or other similar or related article** . . .” (emphasis added).
  - A device does not need to go “clank” when it hits the ground. The guidance explains that “other similar or related article” may include certain liquid, semi-liquid, gel, gas, or powder forms products, *e.g.*, gels or powders put on the skin as a barrier, gases used as space fillers, or liquids used to clean surgical instruments or contact lenses.
- “**primary intended purposes:**” A section of the device definition requires that a device “not achieve its **primary intended purposes** through chemical action within or on the body of man or other animals . . .” (emphasis added).
  - Importantly, the Final Guidance clarifies that “[a] product that has chemical action could be a device if it does not achieve its primary intended purposes through that chemical action.” Final Guidance at 6. In other words, just because a product works through some chemical activity does not render the product a drug. This is consistent with court holdings in the *Prevor* case and parallels Congress’s instruction to the agency in the 21st Century Cures Act which states that FDA may no longer determine that a combination product<sup>1</sup> has a drug primary mode of action solely because it has any sort of chemical action within or on the human body. *See Prevora v. FDA*, 895 F.Supp.2d 90, 99-101 (D.D.C. 2012); *see Prevora v. FDA*, 67 F.Supp.3d 125, 136-139 (D.D.C. 2014); 21 USC 353(g)(1)(E); *see* our client alerts regarding the 21st Century Cures Act ([here](#)) and *Prevora* ([here](#)). Although the 21st Century Cures provision addresses “primary mode of action” with respect to combination products rather than “primary intended purposes” under the device definition as explained in the Final

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<sup>1</sup> The Cures provision applies only after the agency has resolved that a product is a combination product, rather than a single entity product, for instance, where the issue is whether the single entity is a drug or device. On the other hand, the Final Guidance mainly addresses whether a product should be classified as either a drug or a device.

Guidance, the provision and the guidance are now harmonized with respect to their treatment of “chemical action” in the classification of their respective products.

Note that the Final Guidance departs considerably from the Draft Classification Guidance with respect to chemical action’s implications. Specifically, the Draft Guidance stated:

- “a 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,” and “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.” See Draft Classification Guidance at 4-5 (emphasis added).

The broader language in the draft guidance would have rendered more products as drugs. This specific issue was the subject of litigation addressing Prevor’s Diphoterine Skin Wash and may have had a significant role in the change of position to re-focus on primary intended purpose.

- “**chemical action:**” Again, one clause of the device definition requires that a device “not achieve its primary intended purposes through **chemical action** within or on the body of man . . .” (emphasis added).
  - As stated in the Final Guidance, a product exhibits “chemical action” if it “interacts at the molecular level with bodily components (*e.g.*, cells or tissues) to mediate (including promoting or inhibiting) a bodily response, or with foreign entities (*e.g.*, organisms or chemicals) so as to alter that entity’s interaction with the body.” Final Guidance at 7. This definition is slightly different from the “chemical action” definition in the Draft Chemical Action Guidance, which stated that a product exhibits “chemical action” if “through either chemical reaction or intermolecular forces or both, the product: [m]ediates a bodily response at the cellular or molecular level, or [c]ombines with or modifies an entity so as to alter that entity’s interaction with the body of man or other animals.” Draft Chemical Action Guidance at 3.
    - “**interacts at the molecular level with bodily components:**” The beginning part of the new definition of “chemical action, *i.e.*, “interacts at the molecular level” means that the interaction “occurs through either chemical reaction (*i.e.*, formation or breaking of covalent or ionic bonds), intermolecular forces (*e.g.*, electrostatic interactions), or both.” Final

Guidance at 7 n.12. And even if this interaction occurs, it must occur with “bodily components” to be considered a “chemical action.” Thus, a product’s molecules that interact *with one another* would not meet this element of the definition.

- **“to mediate (including promoting or inhibiting) a bodily response:”** FDA did not explain its thinking behind “mediate” and “bodily response,” but the examples provided in the Final Guidance suggest that binding and/or certain state changes may be exempted.
  
- From FDA’s perspective, “chemical action” would exclude the exchange of non-chemical energy, *e.g.*, electromagnetic or thermal energy, between a product and the body. Accordingly, products that achieve their primary intended purposes through thermal energy or heat transfer would not be considered to have a primary chemical mode of action and would not subject the product to regulation as a drug.
  
- **“within or on the body:”** Finally, this same exclusionary clause in the device definition requires that the product “not achieve its primary intended purposes through chemical action *within or on the body* of man or other animals . . .” (emphasis added).
  - To FDA, “within or on the body” means “inside the body or on the surface of the body,” and interpreted this to mean that chemical action that occurs *prior* to a product’s use in or on a body, would not meet this element of the definition. Final Guidance at 7. The agency also explained that a product that is not in direct contact with a user’s body, would also not satisfy the definition.

Where a product meets both the definition of a drug and a device, the key to determining classification of the product depends on whether its primary intended purpose is achieved through chemical action within or on the body of man in determining whether the product would be regulated as a device or a drug. In contrast, the Final Guidance states that where a product meets the definition of both a drug and a biologic, although no guidance is provided on the definition of biological products, these products would generally be regulated as biological products.

## The RFD process

The Final Guidance also provides an overview of the RFD process, largely consistent with information included in the FDC Act, regulations, and prior draft guidance (*see, e.g.*, 2011 guidance entitled “[How to Write a Request for Designation \(RFD\)](#)”). The Final Guidance provides further recommendations, as follows:

- **Include the good and the bad:** When a company submits an RFD to the Office of Combination Products (OCP) to obtain a classification determination, the sponsor should recommend a product classification and provide support for its position. Data should be focused on **how** the device achieves its intended purpose, and not on demonstrating that the device achieves the intended use. Submissions should include all such data and other information potentially relevant to the determination, even if it is counter to the sponsor's preferred outcome.
  
- **FDA precedent:** Of note, the Final Guidance omitted the section from the Draft Classification Guidance regarding prior agency classification determinations. This section addressed circumstances in which FDA, after reviewing an RFD, determined that the product subject to the RFD should be classified differently from how FDA previously classified product, *e.g.*, under a device classification regulation, OTC monograph, or RFD response. For instance, the draft guidance stated that if a regulation established the classification of a product (when the product consists solely of a drug, device, or biological product) or a constituent part of a combination product for the use proposed in an RFD, FDA should continue to apply the existing classification until or unless the agency changes the classification by revising the regulation. If instead FDA had made the previous determination not by regulation, but, for example, in response to a previous RFD, and the pending RFD proposed a different classification (but only for a drug or device, as opposed to a combination product), and "if current scientific understanding may potentially lead to a different classification of that product," the agency "generally" intended to refrain from providing a response and allow the sponsor's proposed classification in the RFD to be determinative. *See* Draft Classification Guidance at 7-8. According to the *Federal Register* announcing the new Final Guidance, this section was excluded because it raised complicated issues and FDA's experience in reconsidering previous determinations has been limited. Instead, the agency stated it will be evaluating these circumstances, if applicable, on a case by case basis. Nonetheless, the Final Guidance does state in a footnote that if a regulation has classified a product type, FDA would "generally" classify the product in line with the regulation. *See* Final Guidance at 4 n.10. The *Federal Register* notice, on the other hand, did leave open the possibility that a previous classification may still not be precedential, as it stated that companies may contact FDA if they have questions regarding whether a classification should be relied upon for a proposed product.
  
- **Pre-RFD process memorialized:** The Final Guidance also mentions the importance of the pre-RFD process, allowing sponsors to obtain a preliminary, non-binding classification determination or to engage in a preliminary classification discussion with FDA before filing a formal RFD. This is discussed in the agency's draft guidance issues earlier this year, entitled "[How to Prepare a Pre-Request for Designation \(Pre-RFD\)](#)."
  
- **FDA can change its mind:** The guidance explains that after OCP makes its jurisdictional determination in response to an RFD, the office may make modifications

to determinations under certain circumstances, and provides examples of possible appropriate reasons, *e.g.*, a change in a proposed indication for use or product component, or new information regarding how the product achieves its primary intended purpose.

### **Impact and conclusions**

The Final Guidance attempts to clarify FDA's thoughts regarding the classification of products. The examples provided in the document provide helpful guidance, though there is still considerable discretion left to the agency to determine the classification of a given product, with many issues still left unclear, such as what it means to "interact" and to "mediate a bodily response." Other open questions include how to determine the "primary intended purpose," which is often a question at issue in RFDs. If you have any questions about the Final Guidance and how it may affect your business or organization, please contact one of the authors of this alert or the Hogan Lovells attorney with whom you regularly work.

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