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FDA Clarifies "Intended Use" for Drugs, Devices, and Tobacco Products

Article By:

Vernessa T. Pollard

Michael W. Ryan

Anisa Mohanty

In its *Clarification of When Products Made or Derived From Tobacco Are Regulated as Drugs, Devices, or Combination Products; Amendments to Regulations Regarding "Intended Uses"* (Final Rule), FDA codifies its long-standing interpretation of the "knowledge" prong of its definition of "intended use." Knowledge of a product's actual use can be evidence of intended use, because claims about a product impact how FDA will regulate the product. FDA has provided guidance on intended use, which it applies to its framework for the regulation of tobacco products as well. In the Final Rule, FDA clarifies that tobacco products marketed for therapeutic purposes are subject to regulation as a drug or device separate from their counterpart "customarily marketed" tobacco products.

Knowledge and Intended Use

An article's intended use—*i.e.*, the objective intent of the individual(s) legally responsible for the labeling of the article—determines the nature and extent of the FDA's oversight of such articles. Under existing FDA regulations, "intended use" can be demonstrated by labeling claims, advertising matter or oral or written statements made on or behalf of the manufacturer. Existing regulations also state that the manufacturer's actual knowledge of the article's use for a purpose for which is it neither labeled or advertised (an unapproved or "off-label" use) may be evidence of intended use. 21 C.F.R. §§ 201.128 and 801.4. Historically, FDA relied on this provision for regulatory or information collection purposes (*e.g.*, physician labeling and safety data). In a 2015 proposed rule, FDA proposed striking the language from the regulation that allowed the agency to consider a manufacturer's knowledge of actual use as evidence of intended use.

In an apparent reversal, the Final Rule retains actual knowledge of an article's use as a relevant source of evidence of intended use and clarifies that *any* relevant source of evidence, whether direct or circumstantial, may be used to demonstrate intended use. If strictly interpreted, this language would allow FDA to take enforcement action against manufacturers for off-label promotion even if the manufacturer did not affirmatively promote or support such use. However, consistent with the

agency's historical position, the agency explicitly notes that it does not intend to bring enforcement action if the sole evidence of off-label promotion is such knowledge. The agency's clarification of this point is critical because of recent case history in which the agency predicated enforcement against speech regarding a purpose for which it is labeled or advertised ("on-label" speech) to "off-label" populations. The agency's statement seems to suggest it recognizes the inherent problem in enforcing requests for information from manufacturers on off-label uses while simultaneously prohibiting manufacturer off-label promotions or on-label promotions to off-label populations.

Intended Use of Tobacco Products

Next, in the Final Rule, in light of frequent inquiries regarding jurisdictional distinctions for products made or derived from tobacco since the passage of the Family Smoking Prevention and Tobacco Control Act of 2009, FDA also clarifies that tobacco products "marketed for therapeutic purposes" are subject to regulation as drugs, devices or combination products under Chapter V the Federal Food, Drug, and Cosmetic Act (FDCA), whereas "customarily marketed tobacco products" are subject to regulation as tobacco products under Chapter IX of the FDCA.

FDA's stated purposes for the clarification are:

- To help sponsors determine which FDA Center to consult and to which Center sponsors should make submissions in product development or postmarketing phases;
- To assist investigators in determining investigational use requirements that apply to studies when using products made or derived from tobacco for investigational use; and
- To clarify to consumers which products are intended for medical uses versus recreational or other uses.

Manufacturers making comparative claims, *i.e.*, wishing to claim a lower tobacco-related disease risk profile or lower relative risk than another tobacco product, can file a modified risk tobacco product (MRTP) application under section 911 of the FDCA. However, manufacturers wishing to claim that a medical product acts affirmatively to combat a disease or health conditions must file a New Drug Application (NDA) under section 505(b) of the FDCA or Premarket Authorization (PMA) under section 510(k) of the FDCA.

The Final Rule creates 21 C.F.R. § 1100.5, which codifies FDA's interpretation that a product made or derived from tobacco that is intended for human consumption will be regulated as a drug, device, or combination product if it is intended for therapeutic purposes, specifically:

- For use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment or prevention of disease, including use in the cure or treatment of nicotine addiction (*e.g.*, smoking cessation), relapse prevention, or relief of nicotine withdrawal symptoms ("therapeutic claims"); or
- Is intended to affect the structure or any function of the body in any way that is different from effects related to nicotine that were commonly and legally claimed in the marketing of cigarettes and smokeless tobacco products prior to March 21, 2000 (the date of the US Supreme Court's decision in *FDA v. Brown & Williamson*, 529 U.S. 120 (2000) ("structure/function claims").

Examples of structure/function claims “commonly and legally” claimed prior to *Brown & Williamson*—and therefore, which do not trigger FDA regulation as a drug, device or combination product—include:

- Satisfaction (including of addiction)
- Pleasure
- Enjoyment
- Refreshment

FDA also noted that in the absence of additional evidence of marketing pre-March 21, 2000, it will *not* consider the following claims as “commonly and legally” claimed prior to *Brown & Williamson*:

- Cessation or withdrawal relief
- Weight loss
- Maintaining memory
- Sedation
- Stimulation

The Final Rule is effective February 8, 2017.

On January 20, 2017, Reince Priebus, assistant to the president and chief of staff, issued a memorandum (Priebus memo) postponing the effective date of regulations and guidance documents that have been published in the Federal Register but not yet taken effect for 60 days from the date of the memorandum. While the Final Rule appears to be subject to the Priebus memo, the agency has not made any official statements regarding its status or delayed implementation as of this writing.

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