NATURAL PRODUCTS ASSOCIATION

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Dockets Management Staff
Food and Drug Administration
5630 Fishers Lane, Rm. 1061, Rockville MD, 20852

RE: FDA-2015-N-2002-2030

Dear FDA Desk Officer

The Natural Products Association (NPA) is submitting this letter as general comment to FDA-2015-N-2002-2030 (Docket Name: Regulations Regarding Intended Uses). The NPA was founded in 1936 to promote and protect the unique values and shared interest of retailers and suppliers of natural nutritional foods and natural products, including conventional foods, medical foods, dietary supplements, and foods for special dietary use. The NPA is a non-profit 501(c)(6) association whose mission is to advocate for the rights of consumers to have access to products that will maintain and improve their health, and for the rights of retailers and suppliers to sell these products. We are the oldest and largest trade association in the natural products industry representing over 750 members account for almost 10,000 retail, manufacturing, wholesale, and distribution locations of natural products, including foods, dietary supplements, homeopathic products, and health/beauty aids. Therefore, NPA has the interest to submit comments on this topic. We thank you for the opportunity.

Background:

In September of 2015, the FDA announced a proposed rule that was intended to address when tobacco products would be regulated as drugs, devices, or a combination of products. The Family Smoking Prevention and Tobacco Control Act amended the Federal Food, Drug & Cosmetic Act (FD&C), and provides FDA with the authority to regulate tobacco products. Section 201 (rr) of the FD&C Act as amended defines the term "tobacco product" as any product made or derived from tobacco that is intended for human consumption, including any component, part, or accessory of a tobacco product except for raw materials other than tobacco used in manufacturing a component, part, or accessory of a tobacco product. The proposed rule struck the last sentence from the intended use regulations of both drugs and devices which each conveyed that, if a manufacturer knows or has noticed that it's approved drug or device is used for unapproved uses, the manufacturer must provide adequate labeling for that use, also known as the *knowledge sentence*. However, the final rule, which was published by the FDA in January of 2017, made a second change to the regulations regarding intended use.

The *knowledge sentence* has been in the regulations for years, however, the FDA's policy was to not enforce. Had the FDA chosen to enforce the provision, manufacturers who had knowledge that their drug or device was being used in an off-label manner, they would be required to include directions for that "new" use on the product's labeling and submit the labeling for FDA approval. But in the rule, the Agency stated that they would not consider the manufacturer to be intending the product for an unapproved use solely on their knowledge that

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a product could be used off-label. Thankfully, at the behest of industry, the FDA conformed the regulations so tha they were consistent with policy.

However, there was a second amendment to address feedback received in the form of comments to the federal register. In response to those comments, FDA incorporated a new sentence which stated that if the totality of the evidence establishes that a manufacturer intends a drug or device to be used for an unapproved use, the manufacturer is required to provide labeling for that use. The response from the Agency was that they were simply codifying the agency's position that, in determining a product's intended use, FDA may look to any relevant source of evidence.

This position regarding *"totality of the evidence,"* is concerning for regulated-industry. By including this language, the Agency is expanding the types of evidence that could be considered in determining intended use. This standard would give the FDA the authority to rely on non-promotional scientific exchange as evidence of intended use. This would be a major hindrance to manufacturers communicating with healthcare professionals and patients. Additionally, the Agency delayed the effective date of the rule first until March 21, 2017, then until March 19, 2018.

Intended Uses:

According to the Agency, the proposed rule is intended to "clarify an important point: that a firm's knowledge that a health care provider has prescribed or used an approved or cleared medical product for an unapproved use, standing alone, is not sufficient to establish the products intended use." The proposed rule before industry today includes:

- Deleting the last sentence from the intended use regulations for both drugs and devices (21 C.F.R. § 201.128 and 21. C.F.R. § 801.4);
- Inserts a new clause in the intended use regulations for both drugs and devices by stating "provided, however, that a firm would not be regarded as intending an unapproved new use for an [approved drug / approved or cleared device] based solely on that firm's knowledge that such [drug or device] was being prescribed or used by health care providers for such use"; and
- Adds language to the intended use regulation for both drugs and devices to include "the design or composition of the article" as possible evidence of the responsible party's intended use of the article.

The proposed rule also includes the types of evidence the Agency believes to be relevant to determining a firm's intended use of its products, including examples of evidence that, by itself, FDA believes would not be sufficient to determine a product's intended use. The types of evidence that the Agency believes would be relevant in determining a product's intended use include:

- Express and implied claims about the product that are attributable to the responsible firm.
- Product characteristics, such as medical or recreational physiologic effects for which the product is unapproved.

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- Product design or technical features, such as a device that includes software with a function or purpose not associated with approved use of the device.
- Circumstances of the sale or distribution of the product, such as a firm's repeated and proactive detailing to a health care provider whose patient population does not fall within the product's approved population.

Examples provided of evidence that, by itself, would not be sufficient to determine a product's intended use include:

- A firm will not be regarded as intending an unapproved use of an approved product based solely on that firm's knowledge that the product is being prescribed or used by health care providers for such use.
- Knowledge in combination with conduct that falls within an acknowledged FDA "safe harbor"
- Certain instances when a firm, to minimize risk to patients, shares with health care providers safety and warning information about unapproved uses of its product.
- Information contained in required corporate submissions to the Securities and Exchange Commission.
- 'Factual, Balanced, and complete' summary of clinical trial results that provides the summary solely to clinical trial participants; the summary includes relevant safety information and limitations of the study, but no conclusion about the safety or effectiveness of the unapproved product or unapproved use.

First Amendment:

While the proposed rule removed the *knowledge sentence* from the language and the Agency rejected the prior administration's inclusion of "totality of evidence," we remain concerned because the Agency rejected the argument that they should rely exclusively on a firm's claims to establish intended use, and thus rejected the argument that the 2017 rule could restrict the dissemination of truthful and non-misleading information.

By citing Wisconsin v. Mitchell, 508 U.S. 476, 489 (1993), the Agency takes the position that the government's reliance on speech as evidence of intended use under the FD&C Act does not violate the First Amendment. Additionally, the Agency cites the decision in the United States v. Caronia, 703 F.3d 149 (2d Cir.2012), because it "left open the government's ability to prove to misbrand on a theory that promotional speech provides evidence that a drug is intended for a use that is not included on the drug's FDA-approved label." NPA and our members have serious concerns with the FDA relying on a dissenting opinion.

"Intended use" is foundational in food and drug law. This is because a product's intended use can dictate whether it is subject to regulation by the FDA, and which regulatory requirements apply. Additionally, the "intended use" of the product must be consistent with the FDA-approved uses of a product. This includes when the Agency may rely on any relevant source of evidence, including express and implied claims made in product labeling or advertising, oral and written statements made by the manufacturer and its representatives, the circumstances surrounding a product's distribution, and the context in which it is sold, and most importantly, whether the manufacturer knows how its product is actually being used by healthcare providers and consumers.

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NPA and our member companies agree, the government should be able to regulate commercial speech to ensure it is not misleading or fraudulent, however, the First Amendment protects a consumer's right to hear truthful and non-misleading information. The First Amendment also protects the right of a manufacturer to utter and promulgate truthful and non-misleading information. This right is protected in a landmark case heard before the Supreme Court of the United States, *Thompson v. Western States Medical Center*. In the majority opinion issued by Justice Sandra Day O'Connor, the court held that the FDAMA's provisions amounted to unconstitutional restrictions on commercial speech. The Court reasoned that, although the speech restrictions allegedly served governmental interests in permitting drug compounding while guaranteeing that compounding was not conducted on such a scale as to undermine the drug approval process, it had not been demonstrated that the speech restrictions were not more extensive than necessary to serve such interests. The Majority opinion goes on to elaborate that "the First Amendment directs us to be especially skeptical of regulations that seek to keep people in the dark for what the government perceives to be their own good." This ruling would suggest that off-label promotion is protected speech.

Conclusion:

While the Agency has gone through extensive lengths to protect their position, NPA and our members believe the agency should refrain from the proposed rule and instead promote free speech. In the last 20 plus years, the FDA has to defend its policy position in the courts. In 1999, a case brought by the Washington Legal Foundation was heard by a federal district court which decided the FDA's policy of restricting the dissemination of medical journal articles describing off-label uses was an unconstitutional restriction of commercial speech.

In 2012, the federal Second Circuit Court of Appeals overturned the conviction of a sales representative who told a doctor about off-label uses of a prescription drug. The court held that "government can not prosecute pharmaceutical manufacturers and their representatives under the Food Drug and Cosmetic Act for speech promoting the lawful, off-label use of an FDA-approved drug."

In 2015, a U.S. district court judge in New York hand the FDA yet another blow ruling that the agency cannot bar truthful, off-label marketing without violating freedom of speech. Finally in 2011, in the case of *Sorrell v. IMS Health*, the courts ruled truth speech used in pharmaceutical marketing is entitled to the same level of First Amendment protection as other forms of commercial speech.

With these cases in mind, we respectfully encourage the agency to move ahead with FDA-2015-N-2002-2030

Thank you,

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