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February 5, 2018

Scott Gottlieb, M.D.  
Commissioner  
Food and Drug Administration (FDA)  
Division of Dockets Management  
5630 Fishers Lane, Rm. 1061  
Rockville, MD 20852

**Docket: FDA-2015-N-2002**

*Clarification of When Products Are Made or Derived From Tobacco Are Regulated as Drugs, Devices, or Combination Products; Amendments to Regulations Regarding "Intended Uses"; Proposed Partial Delay of Effective Date*

Dear Commissioner Gottlieb,

On behalf of 40,000 general dentists, the Academy of General Dentists (AGD) is pleased to provide comments on the proposed rule: partial delay of the effective date.

The AGD agrees with the Agency's sound reasoning to delay the intended use portion of the rule [§§201.128 and 801.4] as commenters noted. The rule:

- 1) Violates the First Amendment by regulating truthful speech regarding lawful activity;
- 2) Violates the due process clause of the Fifth Amendment in that the types of evidence to be included and application are not clearly defined;
- 3) Interferes with the practice of medicine exception;
- 4) Deviates from legislative, statutory text, FDA past practices, and recent case law; and
- 5) Violates the Administrative Procedure Act (APA) by including text in the final rule that was not specified in the proposed rule.

Intended Use Regulations

As the FDA is aware, numerous entities objected to the language included in the final regulations. Subsequently, the FDA received a citizen petition<sup>1</sup> for a stay to delay

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<sup>1</sup> Citizen Petition: Sidley Austin LLP, Ropes & Gray, February 8, 2017, Petition to Stay and For Reconsideration from MIWG, PhRMA, and BIO:

<http://www.miwg.org/sites/default/files/Petition%20to%20Stay%20and%20for%20Reconsideration.pdf>



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implementation of the final rule with respect to the intended use portions of the rule and to define a new “totality of the evidence” standard.

Controversial portions of the Code of Federal Regulations are the “knowledge sentence” [§§201.128 and 801.4] (pasted in italics below).

*But if a manufacturer knows, or has knowledge or facts that would give him notice that a [drug or device] introduced into interstate commerce by him is to be used for conditions, purposes, or uses other than the ones for which he offers it, he is required to provide adequate labeling for such a drug/device which accords with such other uses to which the article is to be put.*

This sentence is problematic for a number of reasons. Manufacturers are seemingly obligated to update labeling after hearing of off-label uses from unverified sources. As such, changes in labeling would not have an evidence base and run counter to trends in medicine and dentistry that seek evidence-based practices. The knowledge sentence deviates from FDA regulations as the courts and the Agency have always found that intended use claims are those that are marketing representations specified by manufacturers.

The AGD supports deleting the “knowledge” sentence on intended uses from §§201.128 and 801.4 of the U.S. Code of Federal Regulations, Title 21.

#### Totality of Evidence Standard

In the January 9, 2017 rule, the FDA added a new standard to include the “totality of the evidence” as cited below in italics.

*And if the totality of the evidence establishes that a manufacturer objectively intends that a drug introduced into interstate commerce by him is to be used for conditions, purposes or uses other than the ones for which it is approved (if any) he is required in accordance with section 502(f) of the Federal Food, Drug, and Cosmetic Act, or, as applicable, duly promulgated regulations exempting the drug from the requirements of section 502(f)(1), to provide such drug adequate labeling that accords with such other intended uses.*

This “totality of the evidence” standard violates the Administrative Procedure Act as this language was not included in the proposed rule out for notice and comment and yet was published in the final rule. Furthermore, this new standard deviates from accepted FDA practice, case law, and again raises issues of verified vs. unverified sources being incorporated into labeled indications for a product.

The AGD supports deletion of the “totality of the evidence” standard from the final rule.



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### Generally Accepted Practices/ Standard of Care

The practice of dentistry and medicine is regulated by state laws and regulations. While the FDA recognizes the practice of medicine exception, tensions remain in efforts to protect the public's health and safety. While it is an ideal scenario to have sufficient, validated evidence for all intended uses, manufacturers make those decisions on a variety of factors, which are sometimes economic in nature.

Health care practitioners may prescribe any legally marketed product to a patient within a legitimate health care practitioner-patient relationship.<sup>2</sup> Dental professionals may use medical/dental products in the manner they deem appropriate for their patients. Health care professionals should be aware of product safety concerns and use a sound scientific basis, along with professional judgment, for off-label indications. In some instances, the off-label use of a product is considered standard of care.

### Conclusion

The AGD thanks you for this opportunity to comment on intended uses and stands ready to work with you. Should you have any questions, please do not hesitate to contact Daniel J. Buksa, JD, Associate Executive Director, Public Affairs, by phone at (312) 440-4328 or via email at [Daniel.buksa@agd.org](mailto:Daniel.buksa@agd.org).

Sincerely,

A handwritten signature in black ink that reads "Daniel J. Buksa".

Daniel J. Buksa, JD  
Associate Executive Director  
Academy of General Dentistry

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<sup>2</sup> Buckman Co. v. Plaintiffs' Legal Committee, 531 U.S. 341, 121 Supreme Court. (2001).