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Via Electronic Submission

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

Re: Proposed Rule: Clarification of When Products Made or Derived from Tobacco Are Regulated as Drugs, Devices, or Combination Products; Amendments to Regulations Regarding "Intended Uses" (Docket No. FDA-2015-N-2002)

The following comments are submitted on behalf of the Medical Information Working Group (MIWG),[1] in response to FDA's proposed rule, "Clarification of When Products Made or Derived from Tobacco Are Regulated as Drugs, Devices, or Combination Products; Amendments to Regulations Regarding 'Intended Uses,'" published in the Federal Register on September 25, 2015, 80 Fed. Reg. 57756. Our comments are limited to that part of FDA's proposal that would revise the existing regulatory definitions of "intended use" at 21 C.F.R. §§ 201.128 & 801.4 by eliminating the knowledge prong of the definitions. We express no position on FDA's proposal with respect to the regulation of products made or derived from tobacco.

The MIWG was formed in 2006 to improve the federal regulatory framework and enforcement climate affecting manufacturer dissemination of accurate scientific information about prescription drugs, biological products, and medical devices, including information about new uses of lawfully marketed products. The MIWG and its members have made numerous submissions to FDA, including a 2013 citizen petition asking the agency to remove the knowledge prong from the intended use regulations.[2] As we have explained, the knowledge prong leads to an anomalous result—manufacturers have no real choice but to attempt to restrict the practice of medicine if they wish to avoid liability for misbranding, because it is impossible for manufacturers to avoid actual or constructive knowledge of such uses. The MIWG therefore supports the proposed amendment to the definitions of "intended use" in 21 C.F.R. §§ 201.128 and 801.4, and we thank the agency for responding to our request.

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[1] The members of the MIWG are: Allergan plc; Amgen Inc.; Bayer Healthcare Pharmaceuticals Inc.; Boehringer Ingelheim Pharmaceuticals, Inc.; Bristol-Myers Squibb Company; Eli Lilly and Company; Genentech, Inc.; GlaxoSmithKline LLC; Johnson & Johnson; Novartis Pharmaceuticals Corporation; Novo Nordisk, Inc.; Pfizer, Inc.; and Sanofi US.

[2] MIWG, Citizen Petition, Docket No. FDA-2013-P-1079 (Sept. 3, 2013), http://tinyurl.com/p6f3knt; see also MIWG, Systemic, Societal, and Legal Developments Require Changes to FDA's Regulation of Manufacturer Speech, Docket No. FDA-2013-P-1079 (Oct. 31, 2014), http://tinyurl.com/mlzzymw.

We would like to draw FDA's attention to two significant issues. First, the proposed rule does not make completely clear that "intended use" is determined solely by promotional claims. Indeed, the preamble appears to reflect FDA's reliance on non-claims-based interpretations of intended use, contrary to the relevant statutory text, legislative history, and case law. Second, the preamble states that FDA has not relied on the knowledge prong for some time, contrary to recent and ongoing enforcement actions by the Department of Justice and FDA.

I. FURTHER REVISIONS ARE NECESSARY TO RENDER THE REGULATIONS CONSISTENT WITH THE STATUTE, LEGISLATIVE HISTORY, AND CASE LAW

Even while removing from the regulations' ambit one form of evidence upon which FDA may rely in a misbranding action, the proposed rule advances an interpretation of intended use that impermissibly purports to rely on evidence beyond manufacturers' promotional claims. The preamble accompanying the proposed rule states that, in evaluating a product's intended use, "the Agency may look to 'any . . . relevant source,' including but not limited to the product's labeling, promotional claims, and advertising."[3] Thus, according to the preamble, "FDA may also take into account any circumstances surrounding the distribution of the product or the context in which it is sold."[4] To support this proposition, FDA relies on cases such as Action on Smoking and Health v. Harris,[5] and Hanson v. United States.[6] Such reliance is misplaced.

Courts have invoked the "other relevant source" language, which originated in Hanson, exclusively in cases in which there were manufacturer promotional claims.[7] As those cases make clear, a new intended use can be created only by a manufacturer's (or other seller's) claims as to that use. Indeed, "courts have always read . . . 'intended' to refer to specific marketing representations."[8] We therefore request that FDA further amend the regulations to remove the "circumstances surrounding distribution" prong of the definition, and any other language suggesting that FDA can find intended use based on non-claims evidence.

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[3] 80 Fed. Reg. at 57757 (emphasis added).

[4] Id. (citations omitted).

[5] 655 F.2d 236 (D.C. Cir. 1980).

[6] 417 F. Supp. 30 (D. Minn.), aff'd, 540 F.2d 947 (8th Cir. 1976). See also Letter from Leslie Kux, Assistant Commissioner for Policy, FDA to Alan R. Bennett and Joan McPhee, Ropes & Gray LLP, and Coleen Klasmeier and Paul Kalb, Sidley Austin LLP at 3, n.3, Docket Nos. FDA-2011-P-0512 and FDA-2013-P-1079 (June 6, 2014) (citing Harris), http://tinyurl.com/nctrobk; Letter from Margaret M. Dotzel, Assoc. Commissioner for Policy, FDA to Daniel J. Popeo & Richard A. Samp, Wash. Legal Found., at 2, n.1, 4, Docket No. 01P-0250 (Jan. 28, 2002).

[7] See United States v. Article . . . "Sudden Change," 409 F.2d 734 (2d Cir. 1969) (advertisements); United States v. Millpax, Inc., 313 F.2d 152 (7th Cir. 1963) (letters and oral representations), cert. denied, 373 U.S. 903 (1963); Nature Food Ctrs., Inc. v. United States, 310 F.2d 67 (1st Cir. 1962) (speeches at public lecture hall), cert. denied, 371 U.S. 968 (1963); V.E. Irons v. United States, 244 F.2d 34 (1st Cir. 1957).

[8] Am. Health Prods. Co. v. Hayes, 574 F. Supp. 1498, 1505 (S.D.N.Y. 1983) (emphasis added) (citations omitted).

II. ONGOING INVESTIGATIONS IMPERMISSIBLY RELY ON THE KNOWLEDGE PRONG

According to the preamble accompanying the proposed rule, "FDA has previously stated" that "the Agency would not regard a firm as intending an unapproved new use for an approved or cleared medical product based solely on the firm's knowledge that such product was being prescribed or used by doctors for such use."[9] The preamble states, further, that the proposed rule merely codifies FDA's current position.[10]

As recently as August 6, 2015, however, the Government had asserted that the "[d]efendants are mistaken" in their argument that "a manufacturer's knowledge that its device will be used for an unapproved use is wholly irrelevant to the manufacturer's legal obligations."[11] Noting that "the regulation describing intended use is clear on this topic," the government cited the portion of 21 C.F.R. § 801.4 that the proposed rule would eliminate. FDA itself has also relied on the knowledge prong in Warning Letters to manufacturers, and included a knowledge-based theory of intended use in a draft guidance in 2011.[12]

For FDA's action in issuing the proposed rule to be meaningful, it must be accompanied by prompt and fair resolution of any ongoing investigation that is premised on an interpretation of intended use that conflicts with the proposed rule. We ask FDA to work with federal prosecutors to resolve those investigations immediately and equitably, and further request that FDA take steps to make sure that enforcement letters, guidance documents, and other statements do not rely on impermissible interpretations of intended use.

III. CONCLUSION

We commend FDA for proposing revisions to the intended use regulations for drugs and medical devices to remove the language purporting to create misbranding liability based solely on a manufacturer's knowledge of the fact that its product is being used off-label. The regulations, as amended, will be more consistent with applicable law, and will begin to address untenable consequences of the current regulation, to the betterment of patient care.

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[9] 80 Fed. Reg. at 57,757.

[10] Id. at 57,756 (". . . FDA is proposing . . . to conform §§ 201.128 and 801.4 to reflect how the Agency currently applies them to drugs and devices.").

[11] Government's Opposition to Defendant's Motion for Production of Legal Instructions to Grand Jury at 13-14, United States v. Facteau, Fabian, No. 15-cr-10076 (D. Mass. Aug. 6, 2015); see also United States' Response to Defendants' Supplemental Memorandum Concerning Proposed Amendment to Regulations at 2, 6, United States v. Facteau, Fabian, No. 15-cr-10076 (D. Mass. Oct. 8, 2015).

[12] See Draft Guidance for Industry and FDA Staff: Commercially Distributed In Vitro Diagnostic Products Labeled for Research Use Only or Investigational Use Only: Frequently Asked Questions (Jun. 2011); Warning Letter to Absolute Packaging, Inc. (Sept, 9, 2010); Warning Letter to Cosmed Labs, Inc. (Aug. 3, 2010); Warning Letter to DexCom, Inc. (May 21, 2010).

Our comments emphasize, however, that the regulatory and enforcement scheme will respect statutory limitations only if FDA further revises the intended use regulatory definitions to conform them to the claims-based interpretation, as outlined in our prior submissions to the agency. We also request that both FDA and Department of Justice ensure that their regulatory and enforcement actions are consistent with the "objective" understanding of intended use.

Respectfully submitted,

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