IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

PUBLIC CITIZEN, INC., 1600 20th Street NW Washington, DC 20009, Plaintiff, v. FOOD AND DRUG ADMINISTRATION, 10903 New Hampshire Avenue Silver Spring, MD 20993, Defendant.	)	C.A. No. 17-1926

COMPLAINT FOR DECLARATORY AND INJUNCTIVE RELIEF

INTRODUCTION

1. Plaintiff Public Citizen brings this action pursuant to the Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. § 301 *et seq.*, and the Administrative Procedure Act (APA), 5 U.S.C. §§ 702 and 706, to compel the United States Food and Drug Administration (FDA) to act on Public Citizen's petition seeking (a) a reopening of the administrative record for the monograph for over-the-counter (OTC) oral health care drug products, (b) revision of the proposed required labeling for OTC benzocaine oral healthcare drug products to remove the infant teething indication and to include a contraindication advising against using gel and liquid benzocaine products for teething pain, and (c) a requirement for a methemoglobinemia warning label for all remaining OTC benzocaine products covered by the OTC oral health care drug monograph. Public Citizen petitioned the FDA on July 28, 2014, pursuant to the FDCA, 21 U.S.C. § 352, and 21 C.F.R. §§ 10.30 and 330.10(a)(7)(v). Although more than three years have passed since Public Citizen filed its petition, the FDA has neither granted nor denied it. Nor

has the FDA taken any of the actions that Public Citizen requested to address serious health risks. Therefore, to protect public safety and prevent needless death and injury, Public Citizen seeks a declaration that the FDA has acted unlawfully by withholding action on Public Citizen's petition and an order requiring the FDA to act on its petition.

PARTIES

2. Plaintiff Public Citizen is a non-profit, public-interest organization based in Washington, D.C., with members in every state. Since its founding in 1971, Public Citizen has worked before Congress, regulatory agencies, and in the courts to advance the interests of its members on a wide range of consumer-protection issues. Among other things, Public Citizen promotes research-based, system-wide changes in health care policy and monitors health and safety issues concerning drugs, medical devices, doctors, hospitals, and occupational health. Public Citizen and its members have been, and continue to be, injured by the FDA's failure to act on Public Citizen's petition. Furthermore, as long as the FDA does not revise its tentative final monograph and that monograph continues to state that OTC benzocaine oral health care drug products may be used for infant teething pain, and for other uses without an additional warning label, Public Citizen's members are at risk of suffering the adverse effects of these drugs, including death or the death of their children.

3. Defendant FDA is a component of the Department of Health and Human Services (HHS), an agency of the federal government. The FDA is responsible for administration of the FDCA. In particular, the FDA is responsible for regulating the labeling of OTC drugs and the classification of such as drugs as generally recognized as safe and effective. *See* 21 U.S.C. § 352; 21 C.F.R. § 330.1 *et seq.* As set forth in more detail below, the FDA has violated the law by failing to act on Public Citizen's petition requesting that the FDA (a) reopen the administrative

record for the monograph for OTC oral health care drug products, (b) revise the proposed required labeling for OTC benzocaine oral health care drug products in specific ways, and (c) require a methemoglobinemia warning label for all remaining OTC benzocaine products covered by the monograph.

JURISDICTION

4. This Court has jurisdiction pursuant to 28 U.S.C. § 1331.

FACTS

5. Benzocaine is an active ingredient commonly found in many OTC medications, including products used to relieve pain associated with teething and other mouth and throat pain.

6. OTC benzocaine oral health care drug products are drugs within the meaning of the FDCA, 21 U.S.C. § 321(g)(1).

7. The FDCA prohibits the introduction into interstate commerce of any misbranded drug. 21 U.S.C. § 331(a). A drug is deemed misbranded unless its labeling bears "adequate directions for use" and certain warnings, including "such adequate warnings against use … by children where its use may be dangerous to health … in such manner and form, as are necessary for the protection of users." *Id.* § 352(f).

8. The FDCA also prohibits the introduction into interstate commerce of any new drug without FDA approval. *Id.* § 355(a). In general, to not be considered "new," a drug must be "generally recognized" among qualified experts "as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof." *Id.* § 321(p)(1). This standard is known as "GRASE."

9. The FDA uses its regulations and monographs to spell out the conditions under which the agency recognizes certain categories of OTC drugs as GRASE and not misbranded. 21 C.F.R. § 330.1.

10. Creation of a drug monograph requires several steps, including a report from an advisory review panel and publication of a tentative final monograph, which precedes publication of the final monograph. 21 C.F.R. § 330.10.

11. On September 24, 1991, a tentative final monograph covering OTC oral health care drug products was published in the Federal Register (with minor corrections published shortly thereafter). This monograph amended a prior tentative final monograph and combined two earlier monograph processes. 56 Fed. Reg. 48302, 48402-03 (Sept. 24, 1991); *see also* 56 Fed. Reg. 65930 (Dec. 19, 1991).

12. The 1991 tentative final monograph proposed classifying benzocaine as GRASE as an OTC anesthetic/analgesic, with one proposed use as "anesthetic/analgesics for teething pain." For this use, a product label would be required to state: "For the temporary relief of sore gums due to teething in infants and children 4 months of age and older." The 1991 tentative final monograph also proposed use for the temporary relief of certain other types of mouth or throat pain. 56 Fed. Reg. at 48343, 48347.

13. The 1991 tentative final monograph did not propose that benzocaine products include any warning label regarding the risk of methemoglobinemia.

14. Methemoglobinemia is a life-threatening blood disorder that impedes the body's ability to use oxygen. Symptoms of methemoglobinemia include headache, dizziness, difficulty breathing, and altered mental state. With severe methemoglobinemia, patients may develop seizures, comas, abnormal heart rhythms, and metabolic acidosis, and may die.

15. Benzocaine is known to induce methemoglobinemia.

16. The advisory review panels that informed the 1991 tentative final monograph recognized that benzocaine could be linked to methemoglobinemia and that infants were more susceptible to the condition. 47 Fed. Reg. 22760, 22805-06 (May 25, 1982); 47 Fed. Reg. 22712, 22724 (May 25, 1982).

17. An advisory panel recommended that OTC benzocaine oral health care drug products be classified as GRASE for use "[f]or the temporary relief of sore gums due to teething in infants and children 4 months of age and older." 47 Fed. Reg. at 22740. The panel considered a methemoglobinemia warning label unnecessary. *Id.* at 22724. In making its recommendation, however, the panel did not discuss any studies of benzocaine's effectiveness that focused specifically on use in teething. Regarding safety, the panel was aware of several cases of methemoglobinemia related to high doses of benzocaine given to infants and children; none of those cases were related to teething medication.

18. The FDA has not produced a final monograph on OTC oral health care drug products.

19. Data regarding the risk of benzocaine-linked methemoglobinemia have continued to accumulate, including since the 1991 tentative final monograph. These data regard the safety of benzocaine products and are thus relevant to the FDA's final classification of benzocaine and conditions for OTC benzocaine oral health care drug products. The data include:

a. Adverse event reports submitted to the FDA and case reports published in medical journals of benzocaine-linked methemoglobinemia in children, including after the use of benzocaine gel to relieve teething pain. In 2011, the FDA reported that "[a] search of the FDA Adverse Event Reporting System (FAERS) database through March 16, 2011 identified 21 cases

of methemoglobinemia associated with the use of OTC benzocaine gel or liquid products." Ten of these cases were classified as life-threatening and fifteen of them involved children, eleven of whom were two-years-old or younger and "were administered benzocaine gel for teething pain." In 2012, the FDA reported that since 2006, "the agency ha[d] received 29 reports of benzocaine gel-related cases of methemoglobinemia. Nineteen of those cases occurred in children, and 15 of the 19 cases occurred in children under 2 years of age."

b. Adverse event reports submitted to the FDA and case reports published in medical journals of benzocaine-linked methemoglobinemia in adults. In 2011, the FDA analyzed 319 reports of methemoglobinemia associated with the use of benzocaine sprays. Of these cases, seven led to fatalities, and thirty-two were identified as life-threatening. Seventy-two of the cases, including three deaths, had been reported after 2006.

20. Between 2003 and 2014, the FDA issued multiple safety announcements related to the risk of methemoglobinemia with OTC benzocaine products. Three of those announcements addressed OTC benzocaine oral health care drug products for relief of teething pain in infants.

21. In 2012, the FDA cited the risk of benzocaine-linked methemoglobinemia in denying a drug manufacturer's petition to expand the 1991 tentative final monograph to cover additional uses of OTC benzocaine products. The FDA's denial stated that "[s]ince the publication of the [1991 tentative final monograph], additional safety concerns regarding benzocaine have been raised due to an increase in adverse event reports of methemoglobinemia associated with the use of topical benzocaine."

22. On May 12, 2014, the FDA advised drug manufacturers that the FDA would "not object" if OTC oral health care benzocaine products bore a warning label regarding the risk of

methemoglobinemia. The advisory did not, however, require the warning label. As the advisory stated, the optional warning "is outside the current label specifications in the tentative final monograph."

23. Also since 1991, the FDA has published information indicating that benzocaine gel products are not necessary or useful in relieving teething pain. A 2014 FDA notice cautioned consumers that "teething … can be treated without prescription or over-the-counter (OTC) medications." A 2014 FDA safety announcement stated that "[t]opical pain relievers and medications that are rubbed on the gums are not necessary or even useful because they wash out of the baby's mouth within minutes." This information concerns the effectiveness of benzocaine products and is thus relevant to the FDA's final classification of benzocaine and conditions for OTC benzocaine oral health care drug products.

24. On July 28, 2014, pursuant to 21 U.S.C. § 352, and 21 C.F.R. §§ 10.30 and 330.10(a)(7)(v), Public Citizen submitted to the FDA a petition asking the FDA not to classify OTC benzocaine oral healthcare drug products as GRASE for use for infant teething pain, and to require such products to include additional warnings about the risks of methemoglobinemia. The FDA assigned the petition docket no. FDA-2014-P-1256.

25. Specifically, Public Citizen requested that the FDA (a) reopen the administrative record for the monograph for OTC oral health care drug products, (b) revise the proposed required labeling for OTC benzocaine oral healthcare drug products, to remove the infant teething indication and to include a contraindication advising against using gel and liquid benzocaine products for teething pain, and (c) require a methemoglobinemia warning label for all remaining OTC benzocaine products covered by the OTC oral health care drug monograph. The petition identified specific modifications to the 1991 tentative final monograph and stated

warning label language that was modeled in part on the voluntary methemoglobinemia warning that the FDA authorized in 2014.

26. In support of its petition, Public Citizen cited the FDA's own analyses of data in the FAERS database and case reports in medical journals demonstrating that benzocaine teething gels and other benzocaine products can lead to life-threatening methemoglobinemia, even when the benzocaine product is used in accordance with its labeling. The petition also cited the lack of information regarding the effectiveness of benzocaine in relieving teething pain.

27. Since Public Citizen submitted its July 28, 2014 petition, the FDA has received multiple new reports of serious adverse reactions to benzocaine, including adverse reactions in children who were given OTC benzocaine oral health care drug products. Also, medical journals have published new case reports of patients suffering serious injury from methemoglobinemia linked to OTC benzocaine products.

28. Under agency regulations, the FDA considers a submission of new data and information as a petition to amend a monograph when that data or information is submitted after certain deadlines have passed and between the publication of a tentative final monograph and the publication of the final monograph. FDA regulations further provide that petitions to amend monographs are submitted under 21 C.F.R. § 10.30, a provision regarding citizen petitions generally. 21 C.F.R. § 330.10(a)(7)(v), (a)(12)(i).

29. FDA regulations state that the agency will respond to each citizen petition within 180 day of receipt of the petition. *Id.* § 10.30(e)(2). The response will either grant the petition, deny the petition, dismiss the petition as moot, or provide a tentative response explaining why the agency has been unable to reach a decision.

30. On or about February 2, 2016, the FDA provided an "interim" response to Public Citizen's petition, indicating that the FDA had not yet reached a decision because the petition "raises significant/complex issues requiring extensive review and analysis by Agency officials." The response also stated that the agency would respond to Public Citizen's petition "as soon as [the FDA has] reached a decision" on it.

31. Public Citizen's petition provides sufficient grounds for the FDA to reopen the administrative record for the 1991 tentative final monograph, to change the proposed labeling requirements as Public Citizen's petition requests, and to require a methemoglobinemia warning.

32. Public Citizen's petition also shows good cause to warrant consideration prior to the publication of a final monograph on OTC oral health care drug products.

33. To date, the FDA has not issued a decision on Public Citizen's petition and has not taken the requested actions to address the risks of benzocaine-linked methemoglobinemia. The FDA has failed to act despite the significant and continuing reports to the agency of methemoglobinemia linked to the use of OTC benzocaine oral health care drug products, particularly in children.

34. The FDA's decisional process is lagging unreasonably in light of the nature and extent of the public health interests addressed in the petition and harmed by the FDA's delay.

CLAIMS FOR RELIEF

35. The FDA's failure to act on Public Citizen's petition constitutes agency action unlawfully withheld or unreasonably delayed under the APA, 5 U.S.C. § 706(1).

36. The FDA's failure to act on Public Citizen's petition is arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law, under the APA, 5 U.S.C. § 706(2)(A).

WHEREFORE, Plaintiff requests that this Court

A. Declare unlawful the FDA's failure to act on Public Citizen's petition;

B. Order the FDA to issue a decision on Public Citizen's petition within 30 days of the Court's order;

C. Award Public Citizen its reasonable costs and attorney's fees under 28 U.S.C. § 2412; and

D. Grant all other appropriate relief.

Respectfully submitted,

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