



Alliance for Natural Health USA

6931 Arlington Road, Suite 304
Bethesda, MD 20814

email: office@anh-usa.org
tel: 800.230.2762
202.803.5119
fax: 202.315.5837
www.anh-usa.org

ANH-USA is a regional office of ANH-Intl

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anhinternational.org

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

CITIZEN PETITION

Dear Sir or Madam:

The Alliance for Natural Health USA ("ANH-USA" or "Petitioner") submits this petition under the Administrative Procedure Act¹ and Title 21 of the Code of Federal Regulations, Sections 10.25 and 10.30, to request the Commission of Food and Drugs issue a regulation banning phthalates from prescription and nonprescription drugs.

I. ACTION REQUESTED

This petition requests the Commission to take the following action: issue a regulation banning the use of phthalates in all prescription and nonprescription drugs.

II. PETITIONERS

ANH-USA is a Virginia nonprofit corporation founded in 1992. ANH-USA, formerly the American Association for Health Freedom and, before that, the American Preventative Medical Association, is a membership-based organization consisting of consumers, healthcare practitioners, food and dietary supplement company members, and over 260,000 advocate members. ANH-USA focuses on the protection and promotion of information in the market concerning the actual and potential benefits of healthy foods and dietary supplements, and access to these healthy products that consumers need to maintain optimal health. By educating the general public and ANH-USA members about the benefits of a healthy diet and lifestyle, and ensuring the proper options are available, ANH-USA strives to arm consumers with the tools necessary to make informed market selections.

¹ 5 U.S.C. § 553(e) (2014).

The ultimate goal is to promote disease prevention, reduce medical intervention, and reduce of the public cost of healthcare in the United States.

II. STATEMENT OF GROUNDS

Phthalates are a group of synthetic chemicals used, for example, in vinyl flooring, adhesives, automotive plastics, and detergents.² This harsh group of chemicals is also used in both prescription and nonprescription drugs as an excipient. The negative effects of phthalates have been shown to be significant. It is widely accepted that phthalates are “endocrine disruptors” because they limit or block the body’s natural levels of estrogen, testosterone, and other hormones.³ For adult men, phthalate exposure has been linked to DNA damage in sperm and lower sperm quality.⁴ Exposure to phthalates also can cause cognitive and behavioral problems in children.⁵ More broadly studied in animals, phthalates have been proven to decrease sperm counts and reduce fertility in male and female animals, cause testicular atrophy, birth defects, small or absent reproductive organs, developmental delays, and miscarriages.⁶

Phthalates are present in people at startlingly high rates.⁷ For example, most phthalates can be found in 80% of people.⁸ Recognizing the magnitude of the problem, in 2008, Congress prohibited the use of dibutyl phthalate (DBP), di(2-ethylhexyl) phthalate (DEHP) and butyl benzyl phthalate (BBP) from children’s toys.⁹ Congress also banned, on an interim basis, three additional types of phthalates, diisononyl phthalate (DINP),

² Ctrs. for Disease Control and Prevention, *Fact Sheet: Phthalates* (available at http://www.cdc.gov/biomonitoring/phthalates_factsheet.html) (last visited June 18, 2014).

³ Food and Drug Admin. Center for Drug Evaluation and Research, *Guidance for Industry Limiting the Use of Certain Phthalates as Excipients in CDER-Regulated Products* (Dec. 2012) (hereinafter “FDA Guidance”); *Adverse Effects of Phthalates on Ovarian Response to IVF*, European Society of Human Reprod. and Embryology, *ScienceDaily* (July 8, 2013) (available at <http://www.sciencedaily.com/releases/2013/07/130708103428.htm>).

⁴ Jennifer Wietelman, *Study: Exposure to Partially Banned Phthalates Is Rising*, Health2Fit.com (Jan. 16, 2014) (available at <http://www.health2fit.com/2014/01/study-exposure-partially-banned-phthalates-rising/>).

⁵ *Id.*

⁶ FDA Guidance, p. 3-4.

⁷ John D. Meeker, et al., *Urinary Phthalates Metabolites and Their Biotransformation Products: Predictors and Temporal Variability Among Men and Women*, *J. Exposure Sci. and Environ. Epidemiology*, 22(4): 376-385 (July 2012) (“Human exposure to phthalates is widespread . . .”)

⁸ Heather Somerville, *Exposure to Harmful Chemicals in Personal Care Products and Household Goods Has Declined, Study Says*, *San Jose Mercury News* (Jan. 14, 2014) (available at http://www.mercurynews.com/business/ci_24914205/exposure-harmful-chemicals-personal-care-products-and-household).

⁹ 15 U.S.C. § 2057c(a) (2014); see also FDA Guidance, p. 2.

diisodecyl phthalate (DIDP), and di-n-octyl phthalate (DnOP), from toys that can be put in children's mouths.¹⁰

Other government agencies have acknowledged the need to address the harm caused by phthalates. The U.S. Environmental Protection Agency ("EPA") regulates DEHP in drinking water, citing potential problems with people's livers, reproductive difficulties and an increased risk of getting cancer from consuming certain amounts of DEHP.¹¹ The EPA also has multiple phthalates on the list of hazardous air pollutants under the Clean Air Act¹² and has designated eight phthalates for further analysis under the Toxic Substances Control Act of 1976 ("TSCA").¹³ Moreover, DBP and DEHP are reportable to the Toxic Release Inventory under Section 313 of the Emergency Planning and Community Right-to-Know Act,¹⁴ and multiple phthalates were included in the first group of chemicals to be screened as part of the Endocrine Disruptor Screening Program ("EDSP").¹⁵ Additionally, the European Commission identified DBP, DEHP and BBP as reproductive toxicants and has prohibited their use in cosmetics.¹⁶

Despite the magnitude of the threat to Americans from phthalates, especially from consuming the chemicals, the FDA to date has issued only nonbinding guidance ("FDA guidance") for the industry. In this guidance dated December 2012, the FDA recognized the dangers of the use of DBP and DEHP, specifically, as excipients because these phthalates have been "shown to be developmental and reproductive toxicants in laboratory animals" and "epidemiological studies suggest certain phthalates may affect reproductive and

¹⁰ 15 U.S.C. § 2057c(b)(1); *see also* U.S. Consumer Prod. Safety Comm'n, *Phthalates* (available at <https://www.cpsc.gov/en/Business--Manufacturing/Business-Education/Business-Guidance/Phthalates-Information/>) (last visited June 19, 2014).

¹¹ EPA, *Basic Info. About Di(2-ethylhexyl) Phthalate in Drinking Water* (available at http://water.epa.gov/drink/contaminants/basicinformation/di_2-ethylhexyl_phthalate.cfm) (last visited June 18, 2014).

¹² EPA, *The Clean Air Act Amendments of 1990 List of Hazardous Air Pollutants* (available at <http://www.epa.gov/ttn/atw/orig189.html> (listing DEHP, dimethyl phthalate and DBP as hazardous air pollutants) (last visited June 18, 2014).

¹³ Candace Pearson, *BPA, Phthalates Won't Be EPA Chemicals of Concern*, *Envtl. Bldg. News* (Nov. 1, 2013) (available at <http://www2.buildinggreen.com/article/bpa-phthalates-wont-be-epa-chemicals-concern>); 15 U.S.C § 2601 et seq. (2014).

¹⁴ EPA, *List of Lists: Consol. List of Chemicals Subject to the Emergency Planning and Cmty. Right-to-Know Act (EPCRA, Comprehensive Env'tl Response, Comp. and Liab. Act (CERCLA) and Section 112(r) of the Clean Air Act)* (Mar. 16, 2014) (available at http://www2.epa.gov/sites/production/files/2013-08/documents/list_of_lists.pdf).

¹⁵ EPA, *Final List of Chemicals for Initial Tier 1 Screening* (Aug. 11, 2011) (available at <http://www.epa.gov/endo/pubs/prioritysetting/finallist.html>).

¹⁶ FDA Guidance, p. 2.

developmental outcomes” in humans.¹⁷ The FDA guidance acknowledges that “safer alternatives are available.”¹⁸

Following the 2012 FDA guidance, there have been limited positive changes in the pharmaceutical industry. For instance, Prilosec and generic theophylline no longer contain phthalates.¹⁹ Nonetheless, drugs such as Asacol²⁰ and didanosine (brand name Videx),²¹ and at least 15 others,²² still contain phthalates.

However, since 2012, even more studies have shown the seriousness of the effects of phthalates. For example, exposure to certain phthalates “is associated with reduced fertility [in women] when defined as a response to IVF treatment.”²³ Additionally, the concentration of monomethyl phthalate, mono-butyl phthalate, and monobenzyl phthalate in the urine of the men correlated with approximately a 20% increase in the amount of time it took for a couple to achieve pregnancy.²⁴ Specifically pertaining to children, an association has been reported between phthalate exposure and asthma and allergic disease.²⁵ Another association affecting children has been discovered between phthalates and attention deficit disorder and learning disabilities.²⁶ Additional studies on animals have produced the conclusion that “*in utero* exposure to DEHP has cardiovascular and behavioral effects in the adult male offspring.”²⁷

It is time for the FDA to stop its avoidance tactics. One of the FDA’s general missions

¹⁷ FDA Guidance, pp. 2-3.

¹⁸ FDA Guidance, p. 4.

¹⁹ See <http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=a1b077e6-b070-43f2-a98e-380cc635419d> and <http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=038c2b07-8028-4dc4-847c-adafe1b0e81a>, respectively.

²⁰ See http://www.asacolhd.com/#important_safety_information.

²¹ See <http://aidsinfo.nih.gov/drugs/16/didanosine/0/professional>.

²² *Diethyl Phthalate* (available at <http://www.drugs.com/inactive/diethyl-phthalate-212.html>) (last visited June 18, 2014); *Dibutyl Phthalate* (available at <http://www.drugs.com/inactive/dibutyl-phthalate-428.html>) (last visited June 18, 2014).

²³ *Adverse Effects of Phthalates on Ovarian Response to IVF*, European Society of Human Reprod. and Embryology, ScienceDaily (July 8, 2013) (available at <http://www.sciencedaily.com/releases/2013/07/130708103428.htm>).

²⁴ *High Plasticizer Levels in Males Linked to Delayed Pregnancy for Female Partners* (Mar. 5, 2014) (available at <http://www.nih.gov/news/health/mar2014/nichd-05.htm>).

²⁵ Tanya Tillette, *Phthalates and Childhood Asthma: Revealing an Ass’n Through Urinary Biomarkers*, *Envtl. Health Perspectives*, 121(2): A59 (Feb. 2013).

²⁶ Vidita Chopra, et al., *Ass’n Between Phthalates and Attention Deficit Disorder and Learning Disability in U.S. Children, 6-15 Years*, *Envtl. Research*, 128: 64-69 (Jan. 2014).

²⁷ D.B. Martinez-Arguelles, et al., *Maternal In Utero Exposure to the Endocrine Disruptor di-(2-ethylhexyl) Phthalate Affects the Blood Pressure of Adult Male Offspring*, *Toxicology and Applied Pharmacology*, 266(1): 95-100 (Jan. 2013).

is to “promote the public health” and do so with regards to drugs by ensuring they are “safe and effective.”²⁸ As discussed in detail above and in the FDA’s 2012 guidance, there is irrefutable evidence that phthalates make drugs unsafe. As a result, the FDA should ban the use of phthalates in drugs, thereby reducing the “widespread exposure of the general population to phthalates” and reduce the cumulative negative effects of phthalates on the health of adults and children.²⁹

III. ENVIRONMENTAL IMPACT

Petitioner claims a categorical exclusion under 21 C.F.R. § 25.30(h) and 21 C.F.R. § 25.31.

IV. ECONOMIC IMPACT

Petitioner will, upon request of the Commissioner, submit economic impact information, in accordance with 21 C.F.R. § 10.30(b).

V. CERTIFICATION

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner that are unfavorable to the petition.

Sincerely,



Gretchen DuBeau, Esq.
Executive and Legal Director
Alliance for Natural Health USA

²⁸ 21 U.S.C. § 393(b) (2014).

²⁹ FDA Guidance, p. 2.