IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

MEDINATURA, INC., Plaintiff, v. FOOD AND DRUG ADMINISTRATION, *et al.* Defendants.	Civil Action No. 1:20-cv-02066-RDM

BRIEF OF PROPOSED *AMICUS CURIAE*
THE AMERICAN ASSOCIATION OF HOMEOPATHIC PHARMACISTS, INC.

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TABLE OF CONTENTS

TABLE OF AUTHORITIES

Other Authorities

I. INTRODUCTION

This brief *amicus curiae* is submitted by the American Association of Homeopathic Pharmacists, Inc. (AAHP or the Association), a 97-year-old year old trade association representing the principal manufacturers and marketers of homeopathic drugs in the United States. While Plaintiff MediNatura, Inc. is a member of the AAHP, this brief does not focus on the legal issues raised by the Plaintiff. Instead, the Association moved this Court for leave to file this brief because the Defendants, in their Memorandum in Support of Their Motion to Dismiss and in Opposition to Plaintiff's Motion for Preliminary Injunction (Government Memorandum), assert that they have revised their policy regarding the regulation of homeopathic drugs in response "to increasing safety concerns associated with these drugs." Government Memorandum at 1. In fact, that assertion is incorrect. There are considerable data on the safety of homeopathic drugs and the AAHP wishes to provide a summary of that data to assist the Court in its consideration of this matter. Contrary to the impression sought to be conveyed by the government, homeopathic drugs have a virtually unparalleled safety record. Similar data have been submitted to Defendant Food and Drug Administration (FDA), which has never publicly addressed those data nor explained why or how they might be incorrect. *See, e.g.*, Testimony of Michelle Dossett, M.D. Ph.D., Food and Drug Administration, Homeopathic Drug Regulation: Evaluating the Food and Drug Administration's Regulatory Framework after a Quarter Century, Transcript of Hearing, April 21, 2015 *available at* https://www.regulations.gov/document?D=FDA-2015-N-0540-2179 (hereafter, Dossett Testimony).

DISCUSSION

As has been previously been noted in this case, homeopathic drugs are generally prepared with extraordinarily low concentrations of active ingredients, often in the parts per million or parts per billion range. The level of active ingredients in many dosage-form homeopathic products is so low that they cannot be detected using ordinary laboratory equipment. Indeed, one of the main criticisms of homeopathy as a treatment modality is that there is simply not enough active ingredient present in most products to measure its presence. It is thus hard to understand how drugs with vanishingly small levels of active ingredients can cause "increasing safety concerns" and consume so much of FDA's limited resources.

Drug safety is a relative concept; no drug is completely safe or unsafe. Drugs used for the treatment of cancer can and do kill, while many drugs sold without a prescription can and do cause injuries and deaths (*E.g.*, acetaminophen was responsible for 142 fatalities in 2018, according to the 2018 Annual Report of the American Association of Poison Control Centers' National Poison Data System at 25, *available at* https://www.poison.org/~/media/files/aapcc-annual-reports/npds2018.pdf?la=en). Indeed, during clinical trials designed to test the safety and efficacy of drugs under development, many patients report experiencing adverse effects while taking placebos, rather than any active test material.

FDA does not generally make regulatory decisions based on anecdotal and unusual case reports, yet it apparently is willing to do so with regards to homeopathic medicine. FDA's stated "safety concerns" involve a few products and analyses which have not been made available publicly. Because very few drug manufacturers, homeopathic or otherwise, have the resources or stomach to fight FDA publicly, the agency's "safety concerns" are rarely challenged in a

meaningful way. Yet, in fact, there are considerable data to support the safety of homeopathic drugs.

FDA held a hearing in 2015, entitled "Homeopathic Product Regulation: Evaluating the Food and Drug Administration's Regulatory Framework after a Quarter Century." (The "quarter century" referred to the adoption in 1988 of FDA Compliance Policy Guide 400.400, Conditions under Which Homeopathic Drugs May Be Marketed.)

Michelle Dossett, M.D., Ph.D., M.P.H., then a clinical researcher at Massachusetts General Hospital and Instructor at Harvard Medical School and currently Assistant Professor at the University of California, Davis, Department of Internal Medicine, addressed the issue of the safety of homeopathic drugs during the hearing. At the request of the American Institute of Homeopathy, the professional association of homeopathic physicians (and an organization which predates the American Medical Association), Dr. Dossett reported on a number of studies which demonstrated the safety of homeopathic drugs:

1. Dantas and Rampes

In 2000, Dantas and Rampes published a systematic review of the literature from 1970-1995. Dantas F, Rampes H., *Do homeopathic medicines provoke adverse effects? A systematic review*. Br Homeopath J. 2000 Jul;89 Suppl 1:S35-8. They found 19 clinical trials with detailed information on adverse events and found a mean incidence of adverse events of 9.4 in the homeopathic groups and 6.17 in the placebo groups. The adverse events (AEs) that were described were mild and transient. For the case reports they found, few described new AEs; most described aggravations of pre-existing symptoms. The overall level of causal association was low. Some reports described products that were mislabeled as homeopathic. The mean

incidence of effects was 54.3%, and overall they were not very different from nocebo effects in phase I randomized clinical trials. Dossett Testimony at 185-186.

2. Swiss Health Technology Assessment Commission

The Dantas and Rampes study was one of several reviewed in the health technology assessment commissioned by the Swiss government to examine the safety and efficacy of homeopathy. G. Bornhoft *et al.* Effectiveness, Safety and Cost-Effectiveness of Homeopathy in general practice – Summarized Health Technology Assessment, a*vailable at* https://www.karger.com/Article/Abstract/93586. After reviewing the evidence, the authors concluded that "the use of medium and high potencies is free from toxic and unexpected organ effects." Dossett testimony at 186.

3. Jong et al.

In 2012, Jong and colleagues examined pharmacovigilance data from Germany on the use of homeopathic and anthroposophic solutions sold for injection. Jong MC, Jong MU, Baars EW, *Adverse drug reactions to anthroposophic and homeopathic solutions for injection: a systematic evaluation of German pharmacovigilance databases*, Pharmacoepidemiol Drug Saf. 2012 Dec;21(12):1295-301. The practice of injecting homeopathic medicines is far more common in Germany than in the U.S. They found that between 2000 and 2009, 303 million ampoules were sold for injection. The overall reporting rate of adverse drug reactions (ADRs) was less than 4 per 1 million ampoules sold. They concluded that, "The reporting rate of ADRs associated with anthroposophic and homeopathic solutions for injection is very low." Dossett testimony at 186-187.

4. Posadzki et al.

The senior author on this highly publicized paper, Professor Ernst, is a well-known critic of homeopathy. Posadzki P, Alotaibi A, Ernst E. Adverse effects of homeopathy: a systematic review of published case reports and case series. Int J Clin Pract. 2012 Dec;66(12):1178-88. The authors performed a systematic review of the literature from 1978 – 2010. They found a total of 1,159 case reports of adverse events from homeopathy published from 17 different countries, including the U.S. They state in their paper that, "AEs ranged from mild to severe and included 4 fatalities. The most common AEs were allergic reactions and intoxications." Upon examining the paper in further detail, Dr. Dossett found that 1,070 of the 1,159 reports are of "unspecified remedies" reported to a German poison control center. These are much like the reports from the U.S. National Poison Data System. In other words, the authors of this systematic review did not go back to verify that all of those 1,070 reports were of actual homeopathic products. Moreover, on reading the abstract for the paper they cited, one realizes that these 1,070 cases largely represent accidental ingestions by young children with limited or no side effects.

On reviewing the remaining 89 cases, Dr. Dossett found that many are again of unspecified compounds. In other words, one cannot know if they are really homeopathic medicines and, if they are, whether they are single or complex products, or have other non-homeopathic ingredients added to them. Some of the compounds ingested are reported by name and are clearly not traditional homeopathic medicines, but compounded products, some of which may contain non-homeopathic ingredients. Nearly all of the reports lack documentation of concomitant conventional medical treatments. Several of the reports included use of traditional homeopathic medicines but in dilutions which would not be available OTC in the U.S. or prescribed by any reasonable homeopathic provider. Dr. Dossett concluded that it was surprising

that a review of 32 years' worth of literature across 17 countries, many in which homeopathy is used quite widely by the general population, found little evidence for serious toxicity from homeopathic treatment. Dossett testimony at 187-189.

5. American Association of Poison Control Centers, National Poison Data System

FDA cited the 2012 Annual Report of the American Association of Poison Control Centers' National Poison Data System in the announcement for the 2015 hearing:

- "There were 10,311 reported poison exposure cases related to "Homeopathic Agents," with 8,788 of those reported cases attributed to children 5 years of age and younger."
- "Of the 10,311 reported cases, 697 required treatment in a health care facility."

These numbers may sound worrisome, but in fact are not. The 10,311 case mentions include not only exposures, but calls for general information about a drug. The number of actual single exposures is 9,704. Of this number, 8,788 exposures were in children under the age of 5. This represents 91% of single exposures. Of the 9,704 exposures, 9,343 (96 percent were unintentional. Thus, Dr. Dossett noted, the overwhelming majority of exposures in children are unintentional and likely the result of small children finding the container of homeopathic medicine, noticing its sweet taste, and deciding to ingest more of it. Of the total "cases," 697 (7 percent of exposed) were treated in a healthcare facility. That does not necessarily mean that treatment was required, but that they presented to a healthcare facility for treatment; 51 of them resulted in a moderate, major, or death outcome. That is 0.5 percent of single exposures. Even that low number may overstate the case. The American Association of Poison Control Centers, the author of the report, notes that these outcomes are associations, not necessarily causations. In other words, someone may have taken a homeopathic medicine because they were feeling unwell

and their underlying illness landed them in the hospital with a significant outcome that was completely unrelated to the homeopathic medicine taken. Moreover, Dr. Dossett noted that one cannot know what percentage of the products ingested in these cases are truly homeopathic medicines vs. other products that claim to be homeopathic on the label but also contain pharmaceutically active amounts of herbs, dietary supplements, or pharmaceuticals.

Dr. Dossett put these numbers into perspective by examining some other widely available OTC medications: adult doses of acetaminophen, ibuprofen, and dextromethorphan (a widely used cough suppressant) all used in isolation to prevent confounding with other medications.

Dr. Dossett found that the proportion of single case exposures resulting in a moderate, major, or death outcome ranged from 0.5 percent for homeopathic medicines to almost 2 percent for ibuprofen, 9 percent for acetaminophen and 12 percent for dextromethorphan. Again, these outcomes are associations, not necessarily causative. Thus, homeopathic medicines appear to have a similar if not better safety profile than these OTC counterparts.

In summary, in reviewing the research data, Dr. Dossett concluded that homeopathic medicines are safe, especially compared to other OTC products. While adverse events are reported with homeopathic medicines, the vast majority are mild and self-limited. Homeopathic OTC medications are a potentially safer option for treating self-limited conditions in patients on multiple medications, though further research in this area is recommended.

6. AAHP Serious Adverse Event Survey

In connection with the 2015 FDA hearing, the AAHP conducted a membership survey to obtain information about the number of serious adverse event reports filed with FDA. Serious adverse event (SAE) reports are the only adverse event reports required to be filed with the agency. Comments of the American Association of Homeopathic Pharmacists, Exhibit 1 (Nov.

9, 2015), Food and Drug Administration, Docket No. FDA-2015-N-0540, *available at* https://www.regulations.gov/document?D=FDA-2015-N-0540-9241.

Twenty-five of the 29 members of the AAHP responded to the survey, including all of the largest members. In calendar year 2013, a total of 82 SAEs were reported; in 2015, the number was 84. Approximately 75 percent of these SAEs were filed by one company and are believed to be due to the publicity that followed a product recall. These SAEs represent an extremely small percentage of the number of product units sold in those years (approximately 56 million in 2013 and 60 million in 2014). They represent an even smaller percentage of the number of dosage units contained in the products sold, approximately 1.8 billion in 2013 and 2 billion in 2014.

II. CONCLUSION

The available data demonstrate that homeopathic drugs are at least as safe to use by consumers as allopathic drugs and often significantly safer. FDA has not refuted these data or otherwise substantiated its concerns about supposed "increasing safety concerns associated with" homeopathic drugs, which appear to be unfounded.

Respectfully submitted,

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