

Medical News & Perspectivesp793

Amid Reports of Infant Deaths, FTC Cracks Down on Homeopathy While FDA Investigates

The JAMA Forum.....p795

What Might an ACA Replacement Plan Look Like?

Health Agencies Updatep797

For Health Disparities, Don't Ignore the Microbiome

VHA Initiative Reduces Risky Opioid Prescribing

Public-Private Partnership Speeds Investigator Access to Cancer Drugs

Clinical Trials Updatep798

Crizanlizumab Prevents Sickle Cell Pain Crises

Listerine May Help Control Spread of Gonorrhea

Improving Shared Decision Making in Management of Dementia

News From the CDCp799

Hospital Costs for Birth Defects Reach Tens of Billions

Youths Recognize Costs of Smoking

Medical News & Perspectives

Amid Reports of Infant Deaths, FTC Cracks Down on Homeopathy While FDA Investigates

Jennifer Abbasi

Last August, an infant was rushed from her home to a hospital after seizing for about 25 minutes. Unresponsive, she began to turn blue while gasping for air. At the hospital, she was diagnosed with status epilepticus—a prolonged seizure. The child had no known medical problems or allergies but had recently been given homeopathic teething tablets for the first time. The pills—whose active ingredient is a poisonous plant called belladonna—were the only medication she had taken in the days leading up to the event.

Fortunately, the infant survived, but on September 1, her father filed a [MedWatch](#) adverse event report with the US Food and Drug Administration (FDA). That report, obtained by *JAMA* through a Freedom of Information Act request, described the life-threatening scenario.

"As a member of the Law Enforcement community," the child's father wrote in the report, "I believe that this product should be inspected to make sure that it is safe for human consumption especially for children."

The report triggered an FDA investigation, which found more than 400 reports of adverse events in infants and children associated with homeopathic teething products filed over the past 6 years. The events included additional seizures, as well as tremor, fever, shortness of breath, lethargy

and sleepiness, constipation, vomiting, agitation, and irritability.

Most alarming, however, 10 of the reported events were deaths.

On September 30, the FDA issued a [warning](#) to consumers that homeopathic teething tablets and gels may pose a risk to infants and children. The agency recommended that consumers stop using the products.

The same day as the warning, CVS Pharmacy [voluntarily removed](#) all brands of homeopathic teething products from its online and retail stores. This included its store brand product, which was cited in the adverse event report that triggered the FDA investigation. Less than 2 weeks later, Hyland's, a popular purveyor of homeopathic teething remedies, [discontinued](#) its line in the United States. The action prevented new Hyland's teething products from entering the market but did not address products already on store shelves.

In late November, Raritan Pharmaceuticals issued a voluntary [recall](#) of 3 homeopathic teething and ear relief products for infants and children—including the CVS tablets—after the FDA investigation found varying levels of belladonna in the products and recommended the recall.

"The FDA is concerned about inconsistent amounts of belladonna, a potentially toxic ingredient if present in sufficient quan-

ties, in homeopathic products," FDA press officer Lyndsay Meyer said in an email after the recall was announced.

Then, in January of this year, the FDA [announced](#) that its laboratory analysis had found elevated belladonna levels in certain homeopathic teething tablets that "far exceeded" the amount stated on the label.

Although the announcement did not specify the brand of tablets with high levels of belladonna, it stated that the agency had asked Standard Homeopathic Company, the makers of Hyland's homeopathic teething remedies, to recall its teething pills, which would remove them from stores and online retailers.

At press time, the company had not agreed to the request, according to the FDA. The agency does not have authority to force the recall, and it would not comment on possible compliance and enforcement actions.

The FDA investigation of homeopathic teething products is ongoing. According to Meyer, the agency is analyzing the products to determine whether they caused the adverse events. Other factors, such as underlying health conditions, sometimes explain these complications, she said.

How Homeopathy Could Kill

The adverse events reports—along with growing consumer popularity—have health



experts and agencies taking new notice of homeopathy, a 2-centuries-old complementary and alternative medicine system that has flown largely below the regulatory radar.

"I think there are some really substantial safety concerns, as illustrated by this warning from the FDA," said Josephine P. Briggs, MD, director of the National Center for Complementary and Integrative Health (NCCIH), part of the National Institutes of Health (NIH). "We are concerned about the regulatory issues and concerned about public safety."

According to the [American Institute of Homeopathy](#), the botanical, mineral, and animal-sourced ingredients in homeopathic medicines are selected based on the principle "let likes cure likes," the idea that a substance that triggers symptoms in a healthy person can cure a sick person who has similar symptoms.

Homeopathic teething remedies, for example, may contain belladonna, also known as deadly nightshade. According to D. Craig Hopp, PhD, program director for natural products research at NCCIH, the primary agent in belladonna is atropine, which can cause redness of the skin and dryness of the mouth and throat, as well as fever, delirium, and hallucinations.

Despite such ingredients, homeopathy should, in theory, be safe. The remedies are formulated based on the principle of "the minimum dose"—the idea that the lower the dose of the medication, the more effective it will be if prepared properly. Classic homeopathic remedies are repeatedly diluted to the point where "you end up

with almost no detectable molecules in the final solution," Briggs explained. The remedies are vigorously agitated at each stage and, according to homeopathic practitioners, the final shaken and diluted solution retains a "memory" of the original substance that exerts its effects with minimal adverse effects.

The principle of the minimum dose should at least imbue safety from adverse events, if not effectiveness. "[I]n general, the theory would suggest that homeopathic remedies are unlikely to be harmful," said Erica Sibinga, MD, associate professor of pediatrics at the Johns Hopkins School of Medicine and chair of the American Academy of Pediatrics Section on Integrative Medicine.

But problems have arisen with homeopathic remedies that may not have been properly diluted. Hyland's teething tablets were [recalled](#) in 2010, after an FDA [warning](#) following reports of serious adverse events. That time, the FDA's laboratory analysis found that the product contained inconsistent amounts of belladonna, and the adverse events reports were consistent with belladonna toxicity. The investigation also uncovered substandard manufacturing of the teething tablets. The product recall was voluntary, however, and Standard Homeopathic Company, the makers of Hyland's teething tablets, introduced a reformulated version in 2011.

According to Meyer, since 2009, the FDA has issued nearly 40 consumer warning letters for homeopathic products for a variety of reasons. That year, it advised con-

sumers to stop using 3 over-the-counter (OTC) zinc-containing [Zicam cold remedies](#) marketed as homeopathic after more than 130 reports of loss of smell associated with their use. In 2014, consumers were warned that [Pleo Homeopathic](#) products for colds, yeast infections, pain, and other conditions could contain penicillin or its derivatives, which could cause life-threatening allergic reactions. And in 2015, the FDA warned against the use of [OTC asthma products](#) labeled as homeopathic.

A Tale of 2 Agencies

"The folks in the [homeopathic] industry are always quick to point out that if you compare the adverse event rate for homeopathic products or other dietary supplements with the fact that there are tens of thousands of deaths from opioid overdoses every year, in comparison, they're actually quite safe," Hopp said.

In fact, a [systematic review and meta-analysis](#) of randomized controlled trials published in 2016 found that a similar proportion of patients experienced adverse effects after being randomized to homeopathic treatments compared with those who were randomized to receive placebos and conventional medicine.

"The difference is that people use these products with the assumption that they're safe," Hopp said of homeopathic remedies, adding that consumers are more aware of known risks with pharmaceutical products.

The use of homeopathic medicine is still relatively uncommon in the United States, but the modality is growing in popularity, making safety concerns increasingly salient. The prevalence of homeopathy use among US adults during the previous year increased from 1.8% in 2007 to 2.1% in 2012—a 15% increase—according to an [analysis](#) of National Health Interview Survey data. Between the late 1980s and 2007, the US homeopathic drug market expanded from a [multimillion dollar market](#) to a multibillion dollar industry, with consumers [paying \\$2.9 billion out of pocket](#).

Federal regulators are starting to respond. In November, the Federal Trade Commission (FTC) announced a new [enforcement policy statement](#) on marketing claims for nonprescription homeopathic drugs. The agency ruled that OTC homeopathic drug marketing must effectively communicate that evidence for health claims is lacking. Marketing mes-

sages for homeopathic products that fail to effectively convey that lack of scientific substantiation to consumers will be in violation of FTC policy.

The FDA has also taken notice. The [website](#) of the nonprofit National Center for Homeopathy states that the “safe” and “gentle” remedies are FDA regulated. Technically, the FDA does regulate homeopathic medicines as drugs under the Federal Food, Drug, and Cosmetic Act, but it has chosen to assert its authority only so far.

Importantly, although the agency does step in when safety concerns arise with an existing product, it does not require pre-market testing for safety or efficacy for OTC or prescription homeopathic medicines. According to the [FDA Compliance Policy Guide for homeopathic drugs](#), issued in 1988, as long as the active ingredients are listed in the [Homeopathic Pharmacopoeia of the United States](#), the official compendium of homeopathic standards, the remedy can be marketed without agency preapproval.

In 2015, the FDA held a public hearing to obtain information from stakeholders about the current use of homeopathic products and the agency’s regulatory framework for them. According to Meyer, the FDA is gathering information about whether to adjust the current enforcement policies to reflect the dramatic increase in the homeopathic product marketplace. “[W]e have received more than 9000 comments to the docket about homeopathy, which can take considerable time to weigh and consider,” she said.

More Than a Question of Safety

Despite its many adherents, including some in the medical profession, there’s a lack of credible research showing that homeopathy works.

“Although there are some positive studies, the conclusion of... evidence-based reviews has been that they were not necessarily the highest quality studies,” Briggs said. “Most of the studies that have been done by the modern standards of evidence-based medicine have been negative,” offering little evidence to support them as effective.

A 2007 systematic review in [Mayo Clinic Proceedings](#) found the evidence from clinical trials was not convincing enough to recommend homeopathy as prevention or treatment for any condition in children or adolescents, for example. And a 2015 evidence-based [review](#) by the Australian government that Briggs called “rigorous” concluded that “there are no health conditions for which there is reliable evidence that homeopathy is effective.”

Studying highly diluted homeopathic remedies poses inherent challenges. Homeopathy has a “plausibility problem,” Hopp said: “It goes against all of the established and known principles of pharmacology.”

He noted that designing a rigorous placebo-controlled trial to test a homeopathic remedy is fraught with methodological issues. “You can’t distinguish the quote-unquote active homeopathic preparation from a placebo preparation,” he said. “In effect, they’re both water.”

Researchers at McMaster University in Hamilton, Ontario, Canada, are launching a controversial [clinical trial](#) of homeopathic “vaccines”—known as “nosodes”—for diphtheria, pertussis, tetanus, measles, and mumps. Although the investigators have [predicted](#) negative results, which could influence regulation, critics of the study say that conducting it legitimizes quackery.

New NIH-supported research on homeopathy is unlikely to be forthcoming in the near future. According to Briggs, NCCIH has received few grant applications to study homeopathic interventions, and the institute is currently not supporting any studies on homeopathic medicine.

That could change, however, if a research proposal focused on measurable aspects of the homeopathic care paradigm, such as how the amount of time homeopathic practitioners spend with patients relates to health outcomes.

“I’m not sure everything that’s embedded in homeopathic practice is always negative,” Briggs said.

Sibinga noted that the increased use of homeopathy, even in the absence of scientific evidence, shows that patients want attention paid toward their symptoms, “even if we don’t have typical allopathic treatments for them.”

She added, “Some of the homeopathic remedies are aimed at common symptoms, like teething and colic or muscle aches, and perhaps it suggests that physicians can listen to those concerns more attentively.” ■

Note: The print version excludes source references. Please go online to [jama.com](#).

The JAMA Forum

What Might an ACA Replacement Plan Look Like?

Larry Levitt, MPP

The US House of Representatives and Senate recently took initial steps towards repealing the Affordable Care Act (ACA), passing budget resolutions that pave the way towards a “budget reconciliation” measure that can repeal major aspects of Obamacare with a 51-vote majority in the Senate.

This budget procedure allows the tax and spending elements of the ACA to

be repealed without requiring any votes from Democrats, assuming almost all Republicans—who hold 52 seats in the Senate plus the vice presidency, which serves as President of the Senate—hang together.

A [trial run](#) for this legislative approach was used in early 2016. The Republicans in Congress passed a bill that repealed the ACA’s premium subsidies and Medicaid



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