

Before the
U.S. Food and Drug Administration

Citizens Petition to:

(1) Revoke Withdrawal of CPG 400.400;
(2) Reinstate CPG 400.400; and
(3) Cease Enforcement under
the Risk-Based Enforcement Framework
for Homeopathic Drugs, Pending
Notice and Comment Rulemaking, as
Required by 5 U.S.C. § 533(b)(c)

Division of Dockets Management-HFA303
U.S. Food and Drug Administration
5630 Fishers Lane, Room 1061,
Rockville, MD 20852

CITIZENS PETITION

This is a Citizens Petition, filed pursuant to 21 C.F.R. §§ 10.25(a), 10.30, on behalf of Alliance for Natural Health-US and Meditrend Inc. It requests that the FDA:

- (1) Revoke the Withdrawal of CPG 400.400, 84 FR 57439 (Oct. 25, 2019);
- (2) Reinstate CPG 400.400, 53 FR 21728 (June 8, 1988); and
- (3) Cease implementation of the Risk-Based Enforcement Framework for Homeopathic Drugs, 87 FR 75054 (Dec. 7, 2022),

all pending formal Notice and Comment Rulemaking as required by 5 U.S.C. § 533(b)(c).

BACKGROUND

Compliance Policy Guide 400.400 was issued in June of 1988 and described the FDA's enforcement priorities for homeopathic drugs. CPG 400.400, "Conditions Under Which Homeopathic Drugs May Be Marketed," 53 FR 21728 (June 8, 1988) (FDA, 2022). The document served as the FDA's formal enforcement posture, exempting homeopathic drug manufacturers from the federal Food Drug and Cosmetic Act's premarket approval requirements so long as they met specific conditions. To be exempt under CPG 400.400, (1) the product and its ingredients had to be listed in the Homeopathic Pharmacopoeia of the United States (HPUS), its addenda, or its supplements; (2) over-the-counter (OTC) homeopathic products were restricted solely to self-limiting conditions and symptoms amenable to self-diagnosis and treatment, rather than being used for serious diseases; (3) the label had to expressly state it was homeopathic, prominently display the ingredients, and list at least one major OTC indication for use; and (4) products had to be manufactured in compliance with Current Good Manufacturing Practice (CGMP) drug standards, including requirements for strength, quality, and purity.

Under 21 C.F.R. § 10.85, compliance policy guides "issued by FDA beginning in 1968 and codified in the Compliance Policy Guides manual" constitute advisory opinions representing the formal position of the FDA on a matter, obligating the agency to follow the CPG until it is

amended or revoked, except in unusual situations involving an immediate and significant danger to health where the Commissioner may take enforcement action contrary to the advisory opinion. 21 C.F.R. § 10.85.

In March 2015, the FDA announced a reevaluation of CPG 400.400 following the growth of the homeopathic drug industry and agency safety concerns, including reports of adverse events from homeopathic products. On October 15, 2019, the FDA formally withdrew CPG 400.400, publishing notice in the Federal Register, 84 FR 57439, effective immediately. The agency then issued a Final Guidance in December 2022, implementing a risk-based enforcement approach. Homeopathic Drug Products Guidance for FDA Staff and Industry, 2022 WL 18456898 (FDA 2022), 87 FR 75054 (Dec. 7, 2022).

The FDA's stated four grounds for withdrawal of CPG 400.400: (1) the federal Food Drug and Cosmetic Act's premarket review requirements (21 U.S.C. § 355) under which homeopathic drugs are not statutorily exempt; (2) the increase in the incidence of alleged serious adverse events arising from homeopathic drug products; (3) the continued expansion of the homeopathic industry, which increased consumer exposure; and (4) the FDA's interest in adopting a risk-based enforcement framework for homeopathic drugs.

THE PETITIONERS

Alliance for Natural Health-US. Alliance for Natural Health-US is a non-profit organization that advocates on behalf of homeopathic drug consumers and manufacturers to ensure that Americans have the greatest variety of healthcare options available to address disease. Alliance for Natural Health-US was founded in 1992 as the American Preventive Medical Association and became the Alliance for Natural Health in December 2009. Meditrend International, Inc. is a member of the Alliance for Natural Health's Corporate Leadership Circle.

Meditrend Inc. Meditrend Inc. is a manufacturer and distributor of homeopathic drugs. Founded in 1984, Meditrend has sold over 30 homeopathic drug formulations to over 5 million people predominantly over the course of its existence. See Exhibit 2: Declaration of Seneca Savage, together with the attached bank correspondence (Exhibit A), documenting Meditrend Inc.'s unsuccessful attempt to obtain financing following FDA's withdrawal of CPG 400.400.

ACTION REQUESTED

Pursuant to 21 C.F.R. § 10.30, the Petitioners request that the FDA: (1) **revoke** the Withdrawal of CPG 400.400 announced in 84 FR 57439 (Oct. 25, 2019); (2) **reinstate** CPG 400.400, "Conditions Under Which Homeopathic Drugs May Be Marketed," 53 FR 21728 (June 8, 1988); and (3) **cease** implementation of the risk-based enforcement framework adopted in Homeopathic Drug Products Guidance for FDA Staff and Industry, 87 FR 75054 (Dec. 7, 2022), all pending the conclusion of a new formal Notice and Comment Rulemaking in the Federal Register in accordance with the requirements of the Administrative Procedure Act, 5 U.S.C. § 533(b)(c).

STATEMENT OF GROUNDS

There are five justifications for the agency taking the action requested:

- (1) The FDA action to withdraw CPG 400.400 was based on isolated, unrepresentative instances of adulteration and misbranding, extant in products properly excluded from safe harbor market protection under CPG 400.400. Each instance relied upon by the agency involved products not labeled in accordance with the HPUS, not manufactured in accordance with the HPUS, not manufactured in accordance with homeopathic drug GMPs, or all three. Accordingly, the unrepresentative instances actually involved products that were not in compliance with CPG 400.400 (and indeed were not homeopathic drugs because not made in accordance with the HPUS and homeopathic GMPs);
- (2) Since before, during, and after 2019, the safety characteristic of homeopathic drugs made in accordance with the HPUS and homeopathic drug GMPs has remained static, showing no basis for the high safety risk conclusions used to justify the Withdrawal of CPG 400.400;
- (3) The FDA Withdrawal of CPG 400.400 and adoption of the risk-based enforcement framework in 87 FR 75054 (Dec. 7, 2022) failed to address, let alone take into account, the reliance interests of the regulated class, despite industry reliance on the safe harbor afforded by CPG 400.400 for a period of 31 years, a failure that is arbitrary and capricious agency action (*Encino Motorcars v. Navarro*, 579 U.S. 211, 222 (2016)).
- (4) The FDA adopted without required Notice and Comment Rulemaking a new legislative rule, its risk-based enforcement framework in 87 FR 75054 (Dec. 7, 2022), which framework can have no legal force or effect until a rulemaking is completed wherein the regulated class is given advance notice and invited to provide comment concerning the precise parameters to guide agency enforcement, the absence of which makes the new framework arbitrary and capricious under the APA, 5 U.S.C. § 533(b)(c) and void for vagueness under the Due Process Clause of the Fifth Amendment; and
- (5) The loss of a safe harbor for market entry, the absence of agency evaluation of reliance interests, the failure of the agency to engage in notice and comment rulemaking before adoption its risk-based enforcement framework, and the failure of the agency to define any parameters, let alone reasonable ones, to guide enforcement under that framework, make imperative: (a) revocation of the withdrawal of CPG 400.400; (b) reinstatement of CPG 400.400 pending completion of notice and comment rulemaking; and (c) initiation of notice and comment rulemaking to define a “safe harbor” either through reinstatement of CPG 400.400 or through provision of detailed compliance elements to make clear to the regulated class how it may avoid FDA enforcement consistent with a “risk-based enforcement” framework.

The specific factual and legal foundations for each of these five justifications is explained below and in the attached documents.

(1) The Isolated, Unrepresentative Examples of Risk Relied Upon by FDA in the Withdrawal of CPG 400.400

From the record underlying FDA's Withdrawal of CPG 400.400, FDA's own warning letters, inspection reports, product recalls, and news releases reveal that the agency's cited "safety" problems with homeopathic products do not stem from the homeopathic method itself but from isolated instances of mis-manufacture or misbranding. **See Exhibit 1** hereto which lists each of the examples relied upon by FDA as proof of the failure of CPG 400.400 to protect the public from serious risks associated with homeopathic drugs. That Exhibit reveals that the cited evidence establishes each instance of purported elevated risk to involve misbranding or mis-manufacture of the product in violation of the conditions stated in CPG 400.400. In other words, the isolated examples are not examples of homeopathic drugs that complied with CPG 400.400 and the HPUS and GMPs for homeopathic drugs. Consequently, none of the examples is representative of homeopathic drugs, indicative of homeopathic drug safety or of a homeopathic drug eligible for the CPG 400.400 "safe harbor" in the first place. In short, CPG 400.400 provides no protection from enforcement for any of the cited examples. Those cited examples are therefore inapt and not sound grounds for calling into question the validity of CPG 400.400.

The isolated instances relied upon by FDA as a justification for withdrawing CPG 400.400 involve products that do not qualify as "homeopathic" because they were not made in accordance with GMPs and the HPUS and were not, therefore, eligible for protection from enforcement under CPG 400.400. The evidence on which FDA relied repeatedly involve adverse events and enforcement actions traceable to poor quality controls, contamination, adulteration, and misbranding, not to GMP and HPUS-compliant homeopathy. Nevertheless, FDA concluded, in a *non-sequitur*, that the homeopathic method itself posed systemic danger, the result of a hasty generalization whereby FDA declared without proof of a nexus that isolated, unrepresentative instances of adulteration and misbranding are nevertheless representative of the universe of properly manufactured and HPUS-compliant homeopathic drugs, an instance of gross illogic: a general statement unqualifiedly applied to a qualified case.

Because FDA's conclusion of a lack of safety endemic to the homeopathic method is overwhelmingly contradicted by the record before it, it does not prove the existence of serious risk associated with homeopathic drugs manufactured in accordance with the HPUS and homeopathic drug GMPs. Accordingly, because both of those standards are required to be met by CPG 400.400, it does not prove the enforcement posture taken by the agency under CPG 400.400 created an environment in which products eligible for exclusion from enforcement under CPG 400.400 were responsible for serious risks of illness or injury.

FDA's own record therefore concedes that its cited "homeopathic safety" cases in fact involved products that do not meet the legal definition of homeopathy in the first place. In each instance — whether Hyland's teething tablets, Zicam's intranasal zinc, or the other cited examples — the record reveals the problem to be manufacturing noncompliance, failure to

comply with the HPUS, labeling errors, and misbranding, not the homeopathic method itself and not the parameters for safe harbor in CPG 400.400.

Reports of injury from “homeopathic” products still accounts for less than 1% of calls to Poison Control Centers, with 98% of those cases involving only minor or no adverse effects. See **American Association of Homeopathic Pharmacists, *Comments Before the U.S. Food and Drug Administration, Docket No. FDA-2015-N-0540, Homeopathic Product Regulation: Evaluating the Food and Drug Administration's Regulatory Framework After a Quarter-Century* (Nov. 9, 2015), at 126.** That statistic remains unchanged before, during, and after the 2019 Withdrawal of CPG 400.400 and belies the contention therein that homeopathic drugs pose a heightened risk of serious adverse events. See **Exhibit 1.**

(2) Before, During, and After 2019, the Safety Characteristics of Homeopathic Drugs Made in Accordance with the HPUS and Homeopathic Drug GMPs Reveal an Absence of Support for the Conclusions and Assumptions of Serious Safety Risk Used to Justify the Withdrawal of CPG 400.400

When, as here, a petitioner invokes 21 C.F.R. § 10.30 to challenge a prior FDA legislative rule¹ and demonstrates that the factual, scientific, or regulatory circumstances underlying that rule do not support the rule's continued existence, the FDA must reconsider or meaningfully explain why it ought not deviate from its prior action. The foundation for this argument lies in the APA's arbitrary-and-capricious standard, 5 U.S.C. § 706(2)(A), as

¹ A legislative rule is one that carries the force and effect of law. The Supreme Court in *Chrysler Corp. v. Brown*, 441 U.S. 281, 302-03 (1979) identified three requirements that must be met for a rule to have this status: (1) It must “affect individual rights and obligations” (which means it must “grant rights, impose obligations, or produce other significant effects on private interests,” *Batterton v. Marshall*, 648 F.2d 694, 701-02 (1980)); (2) it must be “issued by an agency pursuant to statutory authority;” and (3) it must be promulgated in conformity with the APA’s procedural requirements—chiefly, notice and comment rule-making under 5 U.S.C. § 553. If it satisfies (1) and (2) but has not been the subject of notice and comment rulemaking under the APA, it cannot have the force or effect of law. See *Chrysler Corp. v. Brown*, 441 U.S. 281, 302-03 (1979). The risk-based enforcement framework adopted by FDA is a legislative rule because it affects individual rights and obligations and produces significant effects on private interests and because it is issued by FDA under 21 U.S.C. 355.

Under the Administrative Procedure Act, 5 U.S.C. § 553, legislative (or substantive) rules are legally binding on courts, regulated parties, and the agency itself and must be promulgated through the APA's notice-and-comment rulemaking process. Non-legislative rules, by contrast, do not have binding legal effect, carry no more weight than the inherent persuasiveness of their reasoning, and are categorically exempt from notice-and-comment requirements. The APA broadly defines “rule” in 5 U.S.C. § 551(4) as “the whole or a part of an agency statement of general or particular applicability and future effect designed to implement, interpret, or prescribe law or policy or describing the organization, procedure, or practice requirements of an agency.” This broad definition encompasses both legislative and non-legislative rules. Under § 553(b) and (c), when an agency engages in rulemaking (except where exemptions apply), it must: (1) publish general notice of the proposed rule in the Federal Register, including the legal authority for the rule and its terms or subject matter; (2) give interested persons an opportunity to submit written data, views, or arguments (the “comment” phase); and (3) incorporate a concise general statement of the rule's basis and purpose in the final rule.

interpreted by the Supreme Court in *Motor Vehicle Manufacturers Ass'n of the United States, Inc. v. State Farm Mutual Automobile Insurance Co.*, 463 U.S. 29, 42 (1983), and as applied by the D.C. Circuit and district courts in the FDA-specific context.

The bedrock of any argument that the absence of changed circumstances warrants FDA reconsideration of a prior legislative rule is the APA's requirement of reasoned agency decision-making. In *Motor Vehicle Manufacturers Ass'n of the United States, Inc. v. State Farm Mutual Automobile Insurance Co.*, 463 U.S. 29, 42 (1983), the Supreme Court held that "an agency changing its course by rescinding a rule is obligated to supply a reasoned analysis for the change beyond that which may be required when an agency does not act in the first instance." Importantly, the *State Farm* Court also recognized that "the forces of change do not always or necessarily point in the direction of deregulation," and that "there is no more reason to presume that changing circumstances require the rescission of prior action, instead of a revision in or even the extension of current regulation."

Federal courts have applied the *State Farm* framework directly to FDA decisions on citizen petitions filed under 21 C.F.R. § 10.30, yielding a body of precedent squarely supporting the proposition that the absence of changed circumstances undermining a prior legislative rule warrants FDA reconsideration. *Tummino v. Torti*, 605 F.Supp.2d 519, 549 (2009) and the related decision *Tummino v. Hamburg*, 936 F.Supp.2d 162, 196 (2013) stand for the proposition that FDA departures from prior regulatory positions, untethered from changed circumstances, render citizen petition denials arbitrary and capricious. In *Tummino v. Torti*, the court vacated the FDA's denial of a citizen petition seeking over-the-counter access to the Plan B emergency contraceptive, finding that the agency had deviated in multiple respects from its own established policies—including its long history of extrapolating data from older to younger adolescents for contraceptive approvals—without identifying any changed scientific circumstances that would justify such departures. The court noted that the FDA had not identified any new data or changed conditions warranting a novel analytical approach. On remand, in *Tummino v. Hamburg*, the court again found the denial arbitrary because it "failed to offer any explanation as to why Plan B should be treated differently from other drugs so as to require numerous deviations from agency policies and practices," and "failed to acknowledge the FDA's own policy and precedent in extrapolating data from older adolescents to younger, particularly with respect to contraceptives, much less explain why the FDA failed to adhere to that precedent."

The facts presented in the attached **Exhibit 1** reveal that homeopathic drugs properly made in accordance with the HPUS and the GMPs for homeopathic formulas have an extremely low risk profile, as reflected in the AEMS/FAERS adverse-event record, causality assessment, and the accompanying scientific analysis. That circumstance is static from before 2019, during 2019, and after 2019, warranting a change in agency position to revoke the action to withdraw CPG 400.400, reinstate CPG 400.400, and conduct notice and comment rulemaking concerning the circumstances in which enforcement discretion should be exercised to avoid confusion and unnecessary injury to homeopathic manufacturers, distributors, and consumers.

(3) FDA Has Failed to Address the Reliance Interests of the Homeopathic Industry on CPG 400.400 for 31 Years, Violating the APA Arbitrary and Capricious Standard

Under the Administrative Procedure Act (APA), 5 U.S.C. § 706(2)(A), an agency that changes a longstanding rule without acknowledging and adequately addressing industry reliance interests violates the APA's arbitrarily and capricious standard. The Supreme Court has established a clear, multi-case doctrinal framework that squarely supports this conclusion. Critically, *Encino Motorcars v. Navarro*, 579 U.S. 211, 222 (2016), is directly analogous. There the Supreme Court held that a Department of Labor regulation which departed from a 33-year-old enforcement position was unlawful because the agency failed to provide adequate justification for the "decades of industry reliance" that position had generated. A rule that has been in place for 31 years presents a strong case that substantial reliance interests have developed and must be addressed. Failure to assess, weigh, or even acknowledge those reliance interests before promulgating a new rule violates the APA's reasoned decision-making requirement. FDA thus violated the APA when it revoked CPG 400.400 without assessing at all, let alone in a detailed and meaningful way, the reliance interests of the homeopathic industry.

The APA directs reviewing courts to "hold unlawful and set aside agency actions, findings, and conclusions found to be arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706. The foundational case interpreting this standard is *Motor Vehicle Manufacturers Ass'n of the United States, Inc. v. State Farm Mutual Auto. Insurance Co.*, 463 U.S. 29, 43 (1983), which held that an agency rule is arbitrary and capricious if the agency "entirely failed to consider an important aspect of the problem."

The APA's touchstone is reasoned decision-making. The agency must "examine the relevant data and articulate a satisfactory explanation for its action including a 'rational connection between the facts found and the choice made.'" *Motor Vehicle Manufacturers Association of the United States, Inc. v. State Farm Mutual Automobile Insurance Company*, 463 U.S. 29, 43 (1983).

Critically, in *F.C.C. v. Fox Television Stations, Inc.*, 556 U.S. 502, 525-16 (2009), the Supreme Court demanded that agencies provide a reasoned explanation whenever "prior policy has engendered serious reliance interests that must be taken into account." The Court confirmed that an agency may not depart from a prior policy *sub silentio*. In *Encino Motorcars, LLC v. Navarro*, 579 U.S. 211, 222 (2016), the Supreme Court directly applies this principle to a longstanding agency enforcement policy. There, the Department of Labor had maintained a position since 1978 that automotive dealership service advisors were exempt from FLSA overtime requirements. When the Department reversed course in a 2011 regulation—after 33 years—without providing a reasoned explanation for disregarding the industry's reliance interests, the Court held the regulation unlawful, arbitrary and capricious. The Court reasoned: "In explaining its changed position, an agency must also be cognizant that longstanding policies may have 'engendered serious reliance interests that must be taken into account.'" Applying this principle, the Court found that "the retail automobile and truck dealership industry had relied since 1978 on the Department's position," that "dealerships and service advisors negotiated and structured their compensation plans against this background understanding," and that this "background" required "a more reasoned explanation for its decision to depart from its existing enforcement policy." Because the Department's 2011 regulation provided "barely any explanation"—and "in particular because of decades of industry reliance on the Department's prior policy—the explanation fell short of the agency's duty to explain why it deemed it

necessary to overrule its previous position.” The Court was unequivocal: “This lack of reasoned explication for a regulation that is inconsistent with the Department's longstanding earlier position results in a rule that cannot carry the force of law.”

Department of Homeland Security v. Regents of the University of California, 140 S. Ct. 1891, 1913 (2020), further confirmed and elaborated on the reliance-interest obligation. Citing *Encino Motorcars* and *Fox Television Stations*, the Court held that when an agency changes course, as DHS did in revoking CPG 400.400, it must be cognizant that longstanding policies may have engendered serious reliance interests that must be taken into account. The Court identified a three-part duty: the agency is “required to assess whether there were reliance interests, determine whether they were significant, and weigh any such interests against competing policy concerns.”

The duration of the prior rule is not merely background context—it directly affects the magnitude of the reliance interests at stake and thus the rigor of the explanation required. *Encino Motorcars* involved a 33-year-old agency position and used the language of “decades” to describe the reliance that rendered the agency's summary explanation legally insufficient. The direct analogy to the CPG 400.400, a 31-year rule, is compelling: “decades of industry reliance” generating plans, contracts, compensation structures, and capital investments structured around the existing rule demand a meaningful accounting before the rule can be discarded. See **Exhibit 2**.

The Tenth Circuit in *American Petroleum Institute v. United States Department of Interior*, 81 F.4th 1048, 1064-65 (2023), explained: “present and continuing reliance will likely require a more detailed agency explanation than historical reliance that has faded over time.” This principle cuts strongly in favor of challengers to a 31-year rule, because the longer a rule has been in effect and the more industry continues to structure its conduct around it, the more the agency must explain before changing it. An industry that has operated under a rule for 31 years has had extensive opportunity to make long-term capital commitments, negotiate contracts, build business models, and train personnel in reliance on that regulatory environment—all of which constitute the kind of “serious reliance interests” the Supreme Court has identified as triggering enhanced obligations.

Federal circuit and district courts have consistently treated failure to address reliance interests as an independently sufficient basis for finding an APA violation. The Fifth Circuit in *BNSF Railway Co. v. Federal Railroad Administration*, 62 F.4th 905, 918 (2023), vacated a federal agency's decision to deny a railroad's waiver request, holding that the agency must “provide a reasoned explanation for the change” and “at least ‘display awareness that it is changing position[,]’” when “reliance interests have been engendered by an existing policy.” The court found that the FRA “barely articulated any basis at all” for departing from its prior approval of the same technology, and that “the paucity of reasoning is especially glaring in the face of the agency's statutory mandate.”

In *Navient Solutions, LLC v. Department of Education*, 646 F.Supp.3d 705, 719 (2022), a district court in the Fourth Circuit vacated the Department of Education's determination that Navient had improperly collected student loan subsidies, holding that the agency acted arbitrarily

and capriciously by failing to consider the company's reliance on longstanding Department guidance letters before changing course. The court emphasized that the agency had entirely neglected to analyze, or even consider, Navient's reliance on the prior guidance, and that Supreme Court precedent makes clear that the Department cannot escape its obligation to consider, weigh, and assess Navient's reliance simply by noting that the Department later concluded that its guidance was contrary to law. The court further held: "The Department was free to consider and reject these reliance interests as weak or outweighed by other policy considerations, but it must have done so during the administrative process—which the Department neglected to do." This case powerfully illustrates that an agency cannot evade the reliance-interest requirement by later claiming that the prior rule was incorrect; the agency must still account for the reliance before changing course.

(4) FDA Adopted the Risk-Based Enforcement Framework in 87 FR 75054 (Dec. 7, 2022) without Notice and Comment Rulemaking Required by 5 U.S.C. § 533(b)(c) and in Violation of the Void for Vagueness Doctrine of the Fifth Amendment Due Process Clause

In this instance, CPG 400.400 provided a safe harbor for 31 years for homeopathic drug manufacturers to enter the market. When FDA withdrew CPG 400.400 and substituted in its place a risk-based enforcement framework, it altered the rights and obligations of homeopathic drug manufacturers and sellers, by adopting what is a legislative rule without requisite notice and comment rulemaking under the Administrative Procedure Act. In revoking CPG 400.400, FDA made clear that it regarded all homeopathic drugs as illegal but would act against only those that it believed posed a risk to consumers. While FDA has implemented its risk-based enforcement framework, the guiding parameters as to what constitutes a risk FDA deems sufficient to trigger enforcement remains undisclosed by the agency and subject to the whim of individual enforcement agents. That is not only arbitrary and capricious under the APA for its failure to provide the regulated class with specific ways to modify its behavior to avoid enforcement, i.e., to define a safe harbor, it is also an action void for vagueness under the Due Process Clause of the Fifth Amendment.

The void for vagueness doctrine, as established by the Supreme Court in *Grayned v. City of Rockford*, 408 U.S. 104, 108 (1972), requires that laws satisfy two connected due process concerns: (1) "laws [must] give the person of ordinary intelligence a reasonable opportunity to know what is prohibited, so that he may act accordingly"; and (2) "laws must provide explicit standards for those who apply them" to prevent "arbitrary and discriminatory enforcement." The Supreme Court reaffirmed this standard in *FCC v. Fox Television Stations, Inc.*, 567 U.S. 239, 253 (2012), holding that "[a] conviction or punishment fails to comply with due process if the statute or regulation under which it is obtained 'fails to provide a person of ordinary intelligence fair notice of what is prohibited, or is so standardless that it authorizes or encourages seriously discriminatory enforcement.'"

In *Fox Television*, the Court found that the FCC violated due process by penalizing broadcasters for conduct that pre-existing agency policy had indicated was permissible, holding that "the Commission policy in place at the time of the broadcasts gave no notice to Fox or ABC that a fleeting expletive or a brief shot of nudity could be actionably indecent." This case

represents the paradigmatic application of the vagueness doctrine to agency enforcement—where the agency changed its enforcement interpretation without fair prior notice to regulated parties.

- (5) The loss of a safe harbor for market entry, the absence of agency evaluation of reliance interests, the failure of the agency to engage in notice and comment rulemaking before adoption its risk-based enforcement framework, and the failure of the agency to define any parameters, let alone reasonable ones, to guide enforcement under that framework, make imperative: (a) revocation of the withdrawal of CPG 400.400; (b) reinstatement of CPG 400.400 pending completion of notice and comment rulemaking; and (c) initiation of notice and comment rulemaking defining a “safe harbor” wherein homeopathic drug manufacturers and sellers may comprehend how to conform their conduct to avoid “risk-based enforcement” by FDA**

FDA has created an untenable environment for those who manufacture and consume homeopathic drugs. The regulated class, including consumers, do not, and cannot, know from day to day whether specific homeopathic drugs relied upon by the public are ones FDA deems too risky under its undefined “risk-based enforcement” framework. Agency inspections of manufacturers engaged in the production of source ingredients for homeopathic products and of homeopathic products themselves frequently involve intimidating tactics that advise the manufacturer that its homeopathic sources and drugs are not lawful and press the manufacturer to supply proof of safety in excess of that historically demanded under CPG 400.400. Under CPG 400.400, proof of compliance with the HPUS and with the GMPs for homeopathic drugs was sufficient. Currently, FDA has no defined “safe harbor” for homeopathic drugs under its risk-based enforcement framework, leaving the market and all those economic interests involved with it to guess at what FDA may or may not deem a safe homeopathic drug subject to enforcement. That, within the context of an FDA legal determination that no homeopathic drug is lawful because all are required to comply with the full requirements of the new drug approval process in 21 U.S.C. 355 et seq. See **Exhibit 2**.

Pursuant to 21 C.F.R. § 10.30, the Petitioners request that the FDA: (1) **revoke** the Withdrawal of CPG 400.400 announced in 84 FR 57439 (Oct. 25, 2019); (2) **reinstate** CPG 400.400, “Conditions Under Which Homeopathic Drugs May Be Marketed,” 53 FR 21728 (June 8, 1988); and (3) **cease** implementation of the risk-based enforcement framework adopted in Homeopathic Drug Products Guidance for FDA Staff and Industry, 87 FR 75054 (Dec. 7, 2022), until the completion of a new formal Notice and Comment Rulemaking in the Federal Register aimed at defining a “safe harbor” in accordance with the requirements of the Administrative Procedure Act, 5 U.S.C. § 533(b)(c).

In that rulemaking, the FDA should conclude that the actual evidence of injury does not support the current, essentially unbridled risk-based enforcement. Moreover, the FDA may conclude that the requirements in CPG 400.400 are necessary and sufficient to protect the public from mis-manufactured, adulterated, and misbranded homeopathic drugs. FDA could subsume CPG 400.400’s essential requirements into a redefinition of its risk-based enforcement framework where failure to satisfy the CPG 400.400 requirements would be the basis for

initiating FDA legal action against a product or manufacturer and where adherence to those requirements would be the basis for the exercise of enforcement discretion not to act against a product or manufacturer. Alternatively, FDA could define anew the parameters of its current "risk-based enforcement" framework to enable the regulated class to understand what kinds of acts or practices will trigger agency enforcement and what kinds will not.

ENVIRONMENTAL IMPACT

This petition is categorically excluded from the need for an environmental impact assessment pursuant to 21 C.F.R. § 25.30-25.34.

CERTIFICATION PURSUANT TO 21 C.F.R. § 10.30

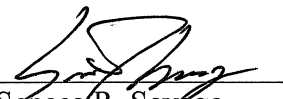
The petitioners hereby certify that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

Signature of Certifying Principals of Petitioners Alliance for Natural Health-US and Meditrend Inc.:



Dated: 09/21/2026

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Dated: 9/17/26

Seneca R. Savage,
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CONCLUSION

For the foregoing reasons, Petitioners Alliance for Natural Health-US and Meditrend Inc., by counsel, respectfully request that the FDA act without delay as requested herein.

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EXHIBIT 1

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Adverse Event Reports, Causality Assessment, and the Absence of Evidence of Significant Risk from Properly Manufactured, HPUS-Compliant, Correctly Labeled Homeopathic Drugs

This exhibit is intended to summarize the adverse-event evidence in a form suitable for regulatory and judicial review. It distinguishes adverse-event association from causation and distinguishes products that were properly manufactured, HPUS-compliant, correctly labeled, and used under the conditions formerly recognized in CPG 400.400 from products that were adulterated, mis-manufactured, misbranded, pharmacologically dosed, unlabeled, imported, used by an inappropriate route, or otherwise outside that compliance framework.

The current Exhibit contains two attachments: Attachment A is spreadsheet comprised of the complete set of records in the FDA's Adverse Event Monitoring System (AEMS) (formerly FDA Adverse Event Reporting System [FAERS]) database relating to homeopathic products, including causality analysis of data; Attachment B provides details of causality audit that has been developed from the AEMS data in Attachment A.

Executive Summary

This Exhibit addresses the scientific and empirical foundation for FDA action in response to the citizen petition. It supports three linked propositions. First, FDA's present treatment of homeopathic drugs as a class rests on an overbroad risk assessment: the adverse-event record does not establish that properly manufactured, HPUS-compliant, correctly labeled homeopathic products, used under the conditions formerly recognized in CPG 400.400, present a significant public-health risk. Second, the AEMS/FAERS record does not show that real product risk has materially changed since FDA withdrew CPG 400.400 or issued its December 2022 final guidance. Third, FDA can address the genuine risks identified in the record through a clear safe-harbor framework that distinguishes compliant low-risk products from products warranting heightened scrutiny or enforcement.

The AEMS spreadsheet reviewed for this Exhibit contains 2,068 unique case records associated with homeopathic or purportedly homeopathic products. Of those, 1,684 records are marked serious and 67 include death as an outcome. The dataset also includes 451 records listing concomitant products and substantial ambiguity in product identification, including 590 records for which the suspect product name is missing or shown only as a dash. These figures identify records that merit pharmacovigilance review; they do not establish that the products mentioned caused the reported events.

The critical scientific point is that the dataset contains adverse-event reports and associations, not causality determinations. A structured audit found zero records containing an explicit causality assessment supported by the Naranjo algorithm, RUCAM/CIOMS, Bradford Hill criteria, or equivalent formal methods. The reports therefore cannot be converted into proof of causation, much less into proof that the compliant homeopathic-drug category presents a class-wide safety risk.

The most salient product clusters are Hyland/teething products and Zicam intranasal zinc products. Those clusters are important, but they are not representative of properly manufactured, HPUS-compliant, correctly labeled homeopathic products used under CPG 400.400 conditions. The Hyland/teething cluster raises product-specific questions concerning manufacturing quality, belladonna dilution consistency, infant exposure, labeling, and lot-level controls. The Zicam cluster is best understood as a product-, route-, dose-, and pharmacologic-exposure-specific intranasal zinc problem, not as evidence that homeopathy as a modality is unsafe.

The temporal analysis likewise does not support FDA's current policy. When the data are separated into the pre-withdrawal period, the interim period after withdrawal of CPG 400.400, and the post-December 2022 final-guidance period, the same pattern persists: spontaneous association reports; concentration in product-specific, missing, ambiguous, or mixed-product records; and no formal causality assessment establishing serious harm from compliant products. The first-pass Green-candidate screen identifies no serious or death-outcome reports in any regulatory period.

The evidence therefore does not show that FDA's post-2019 and post-2022 framework has reduced a demonstrated risk from compliant homeopathic products. It shows instead that the genuine risks are targeted and identifiable: adulteration, mis-manufacture, inconsistent or excessive ingredient levels, contamination, pharmacologically active exposure inconsistent with labeling, inappropriate route of administration, vulnerable-population risk, serious-disease claims, and unresolved causally plausible serious adverse-event signals.

The current framework nevertheless creates substantial regulatory uncertainty because it does not tell responsible manufacturers what compliance measures will place a product into a predictable low-enforcement-risk category. A manufacturer may comply with HPUS standards, manufacture under CGMP, disclose ingredients and dilutions, and limit claims to appropriate OTC self-limiting conditions, yet still lack a practical safe harbor. That uncertainty can reasonably be expected to disrupt supply chains, reduce product offerings, deter investment, increase compliance costs, and diminish consumer access without a demonstrated offsetting safety benefit for compliant products.

For these reasons, this Exhibit supports either reinstatement of CPG 400.400 or adoption of an equivalent traffic-light safe-harbor framework. Green products would be presumptively lowest enforcement priority; Amber products would receive heightened scrutiny or require additional mitigation; and Red products would be enforcement priorities. Such a framework would preserve FDA's ability to act against real risks while giving responsible manufacturers clear, inspection-ready criteria for compliant, low-risk operations.

I. Background

This section provides background to the scientific and risk-assessment issues raised by the FDA's revocation of Compliance Policy Guide Sec. 400.400, 'Conditions Under Which Homeopathic Drugs May Be Marketed,'¹ and its subsequent guidance to FDA staff and industry concerning homeopathic drug products.^{1, 2} In my opinion, those materials identify several legitimate areas for regulatory

attention, but they do not establish that properly manufactured, appropriately labelled, pharmacopoeia-compliant homeopathic products are inherently unsafe.^{1, 2}

The safety concerns identified by the FDA may be grouped into six principal categories: adverse event reports; manufacturing violations; misconceptions about safety; growth of the homeopathic product market; the FDA's movement toward a risk-based enforcement approach; and concern that some consumers may rely on homeopathic products in circumstances where they should seek other medical care. Each of these subjects warrants careful scientific analysis. None, however, supports a conclusion that all homeopathic products present the same risk, or that isolated examples involving defective, adulterated, or non-compliant products may be generalized to the entire category.

A central scientific distinction is between association and causation. Adverse event reports are important pharmacovigilance signals, but they do not, by themselves, prove causation. Proper causal evaluation ordinarily requires structured assessment, including consideration of temporality, biological plausibility, dose-response, dechallenge and rechallenge where available, competing explanations, and the quality of the case evidence. Depending on the context, tools such as Bradford Hill criteria,³ the Naranjo algorithm, or ⁴ RUCAM/CIOMS methods for assessing liver toxicity,⁵ are used to assess whether an observed association is likely to be causal.

The belladonna-containing teething product episode illustrates this distinction. The FDA identified adverse event reports that it considered consistent with belladonna toxicity, but the regulatory concern centered on specific products from a specific manufacturer, where laboratory testing and inspectional findings indicated highly variable including excessive levels of belladonna alkaloids—sometimes several times greater than the amount claimed on the label—indicative of breaches in good manufacturing practices.⁶ The FDA recall notice itself, dated 2017, indicates that the recall was triggered by mislabeling.⁷

¹FDA. 84 Fed Reg 57439. Oct 25, 2019. <https://www.federalregister.gov/documents/2019/10/25/2019-23334>

²FDA. Homeopathic Drug Products: Guidance for FDA Staff and Industry. December 2022. <https://www.fda.gov/media/163755/download>

³ Hill AB. *Proc R Soc Med*. 1965;58(5):295-300. PubMed: <https://pubmed.ncbi.nlm.nih.gov/14283879/>

⁴Naranjo CA, Busto U, Sellers EM, et al. *Clin Pharmacol Ther*. 1981;30(2):239-245. PubMed: <https://pubmed.ncbi.nlm.nih.gov/7249508/>

⁵Danan G, Teschke R. *Int J Mol Sci*. 2016;17(1):14. PubMed: <https://pubmed.ncbi.nlm.nih.gov/26712744/>

⁶ FDA Notice: “Hyland's Homeopathic Teething Tablets: Questions and Answers”, December 18, 2017: <https://web.archive.org/web/20180424112207/https://www.fda.gov/ForConsumers/ConsumerUpdates/ucm230762.htm>. [Wayback Machine archive used in this citation as original link is no longer available on FDA website]

⁷ FDA Recall Notice, April 13, 2017, “Standard Homeopathic Company Issues Nationwide Recall of Hyland's Baby Teething Tablets and Hyland's Baby Nighttime Teething Tablets Due to Mislabeling”: <https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/standard-homeopathic-company-issues-nationwide-recall-hylands-baby-teething-tablets-and-hylands-baby>

According to Hyland's own explanation of its product labeling, each Hyland's Baby Teething Tablet weighs approximately 65 mg and is 'composed of 0.0003% belladonna alkaloids,' equating to roughly 0.0002 mg (200 ng) of total belladonna alkaloids per tablet. However, FDA's laboratory analysis of homeopathic teething tablets found that belladonna alkaloid content in both Hyland's and CVS-branded products was highly variable from tablet to tablet, even within the same lot. In some tested tablets, atropine levels alone ranged from about 50 to 1,100 ng per tablet, while scopolamine levels ranged from tens to hundreds of nanograms, with other tablets from the same lots below the limit of quantification. These findings indicate that certain tablets contained several-fold more belladonna alkaloids than implied by Hyland's labeling, whereas others contained substantially less, evidencing a poorly controlled manufacturing process. On this basis, FDA concluded that the products were "mislabeled" with respect to belladonna content and that homeopathic teething tablets containing belladonna posed an unnecessary risk to infants and young children.⁷

Scientific criticism of the FDA's handling of those reports has also emphasized that the reports did not provide verified proof of harm across homeopathic products generally and that plausible alternative explanations remained in many cases.⁷ Thus, even if one accepted that some cases reflected product-related toxicity, the scientific inference would be product-specific and manufacturing-specific, not category-wide.^{8,9}

The Zicam intranasal zinc products provide a second example. Significant safety concerns were associated with these products, including reports of anosmia. However, the relevant scientific concern was not that a properly prepared homeopathic product was shown to be intrinsically dangerous, but that the products delivered pharmacological quantities of zinc directly to the nasal epithelium, a route and exposure scenario supported by mechanistic toxicology concerns.^{7,8} That circumstance is more accurately understood as involving a defective or non-conforming product presentation, not a scientifically valid basis for attributing comparable risk to properly manufactured homeopathic products generally.^{10,11}

Manufacturing violations present a similar issue. For example, inadequate process controls, contamination, inconsistent ingredient levels, ingredient levels that differ significantly from labeling amounts, non-sterile manufacture of products intended for sterile use, and failure to comply with applicable manufacturing standards are genuine safety concerns. But these are all actionable manufacturing and quality violations. They are not scientific evidence that properly manufactured,

⁸ Lennihan B. *Altern Complement Ther.* 2018;24(1):19-28. doi:10.1089/act.2017.29148.ble.

⁹ FDA. Laboratory Analysis of Homeopathic Teething Tablets. <https://www.fda.gov/drugs/information-drug-class/laboratory-analysis-homeopathic-teething-tablets>

¹⁰ Davidson TM, Smith WM. *Arch Otolaryngol Head Neck Surg.* 2010;136(7):673-676. PubMed: <https://pubmed.ncbi.nlm.nih.gov/20644061/>

¹¹ FDA. FDA advises consumers not to use certain Zicam cold remedies. June 16, 2009. <https://www.fda.gov/drugs/drug-safety-and-availability/fda-advises-consumers-not-use-certain-zicam-cold-remedies>

appropriately labelled, pharmacopoeia-compliant products share the same risk profile as non-compliant products. Regulatory enforcement should distinguish between products that comply with applicable standards and products that do not.⁹

From a safety standpoint it is important to avoid the opposite errors as well. No product is made safe merely because it is described as natural, highly diluted, traditional, or homeopathic. Safety depends on, among other factors, the identity of the ingredients, their dose, chemical form, route of administration, frequency of use, intended use and population, manufacturing quality, and ingredient combinations. The FDA itself has recognized that such factors are relevant when assessing homeopathic product risk.¹² But these factors, should any apply, warrant a product-specific and risk-based assessment, not a categorical presumption that all products in the category are equally unsafe.¹³

When homeopathic products are HPUS-compliant, properly manufactured and labeled, and used in accordance with appropriate directions, the available clinical safety literature supports a favorable safety profile. For example, a systematic review and meta-analysis of randomized controlled trials of individualized homeopathic treatment found no statistically significant difference in adverse event rates between homeopathy and placebo groups, while noting that reported adverse events were generally mild.¹¹ Other reviews have similarly reported that adverse effects associated with homeopathic medicines are generally minor, transient, and comparable to placebo or are rare and mild in properly manufactured products.^{14,15,16}

The most up-to-date high-level evidence non homeopathy was undertaken by German and American scientists (Hamre *et al.*) and published in the peer reviewed journal *Systematic Reviews* in 2023.¹⁷ It is an umbrella, systematic review of meta-analyses of randomized controlled trials (RCTs) of homeopathy, plus several focused systematic reviews and a recent assessment of reporting bias. It includes 6 meta-analyses of placebo-controlled RCTs across all indications (individualized, non-individualized, and mixed). All meta-analyses showed a significant positive effect of homeopathy vs placebo when pooling all trials; one had no extractable data. When grading evidence, the authors judged the evidence for effects beyond placebo to be high quality for individualized

¹² FDA. Drug Products Labeled as Homeopathic Guidance for FDA Staff and Industry. Draft Guidance, December 2017: <https://www.fda.gov/files/drugs/published/Drug-Products-Labeled-as-Homeopathic-Guidance-for-FDA-Staff-and-Industry.pdf>.

¹³ FDA. Homeopathic Drug Products: Guidance for FDA Staff and Industry. December 2022. <https://www.fda.gov/media/163755/download>

¹⁴ Bornhoeft G, Wolf U, von Ammon K, et al. *Forsch Komplementarmed*. 2006;13 Suppl 2:19-29. PubMed: <https://pubmed.ncbi.nlm.nih.gov/16883077/>

¹⁵ Dantas F, Rampes H. *Br Homeopath J*. 2000;89 Suppl 1:S35-S38. PubMed: <https://pubmed.ncbi.nlm.nih.gov/10939781/>

¹⁶ Stub T, Musial F, Kristoffersen AA, et al. *Complement Ther Med*. 2016;26:146-163. PubMed: <https://pubmed.ncbi.nlm.nih.gov/27261996/>

¹⁷ Hamre HJ, Glockmann A, von Ammon K, Riley DS, Kiene H. Efficacy of homeopathic treatment: Systematic review of meta-analyses of randomised placebo-controlled homeopathy trials for any indication. *Syst Rev*. 2023;12(1):191. PubMed: <https://pmc.ncbi.nlm.nih.gov/articles/PMC10559431/>.

homeopathy, and moderate for non-individualized and “all homeopathy combined”. The authors concluded there is no support for the hypothesis of no difference between homeopathy and placebo overall, while emphasizing heterogeneity and methodological limitations. Regarding safety, the authors considered additional meta-analyses focusing specifically on safety and adverse events (notably by Stub *et al.* 2016¹⁸ and Stub *et al.* 2022¹⁹) and concluded that adverse effects with homeopathic treatment are generally mild to moderate and transient, and that the overall incidence of adverse effects is comparable to, or lower than, that of placebo or conventional/herbal controls, depending on the dataset.

Market growth, standing alone, is not a scientific measure of risk. Increased consumer exposure may justify greater regulatory attention, particularly to outlier products, vulnerable populations, sterile dosage forms, serious disease claims, or manufacturers with quality failures. But increased market size does not convert non-causal adverse event reports, isolated manufacturing violations, or defective product examples into proof that the whole category is unsafe.

Similarly, a risk-based enforcement approach, as proposed in FDA’s 2022 guidance, is scientifically appropriate only if it remains genuinely risk-based. Such an approach should prioritize products with plausible routes to harm, including products containing pharmacologically active levels of ingredients, products intended for vulnerable populations, products promoted for serious or life-threatening conditions, products with documented manufacturing deficiencies, products failing to comply with applicable pharmacopoeial standards, and products making false or misleading claims. It should not treat responsible manufacturers and non-compliant operators as scientifically indistinguishable.

The concern that consumers may forgo medically necessary treatment is also distinct from intrinsic product toxicity. If a product is promoted using false or misleading claims, or if it is marketed for serious conditions in a manner that may discourage appropriate medical care, that is a claims and consumer-protection issue. It does not establish that the product is chemically or toxicologically unsafe when properly manufactured, appropriately labelled, and used responsibly.

Accordingly, the background scientific principles that guide the following analysis are these: adverse event reports are signals rather than proof of causation; defective or adulterated products should not be used to characterize compliant products; manufacturing violations should be addressed as manufacturing violations; product safety depends on dose, route, formulation, quality, user population, and intended use; and a scientifically coherent regulatory approach must distinguish between generalized concern and product-specific evidence of risk.

¹⁸ Stub T, Musial F, Kristoffersen AA, Alræk T, Liu J. Adverse effects of homeopathy, what do we know? A systematic review and meta-analysis of randomized controlled trials. *Complement Ther Med.* 2016 Jun;26:146-63. PubMed: <https://pubmed.ncbi.nlm.nih.gov/27261996/>

¹⁹ Stub T, Kristoffersen AE, Overvåg G, Jong MC, Musial F, Liu J. Adverse effects in homeopathy. A systematic review and meta-analysis of observational studies. *Explore (NY).* 2022 Jan-Feb;18(1):114-128. PubMed: <https://pubmed.ncbi.nlm.nih.gov/33303386/>

This analysis does not rest on the proposition that a product category is risk-free. Rather, it rests on the principle that safety assessment must be product-specific, evidence-based, and proportionate to the actual risk presented by the product as formulated, manufactured, labelled, and used.

II. Methodological Principle: Association Is Not Causation

While regulatory safety decisions may be properly initiated by spontaneous, anecdotal adverse event reports, they should not end there. Spontaneous reports that are part of pharmacovigilance or post-marketing surveillance systems are designed precisely for this purpose: to detect possible signals. They are not in any way designed for, or capable of, establishing causation in individual cases or to measure comparative risk across products without denominator data, exposure data, narrative review, and structured adjudication using methods validated to establish direct causation.²⁰

For this reason, FDA adverse event data should be evaluated in a staged manner: first, identify possible signals; second, group signals by product, route, ingredient, dose/dilution, manufacturing status, and population; third, evaluate confounders and alternative explanations; and fourth, where possible, apply a recognized causality method. For individual adverse drug reaction cases, the Naranjo algorithm or WHO-UMC style methods may be relevant. For liver-injury cases, RUCAM/CIOMS is the accepted structured method.⁵ For broader exposure-outcome claims, Bradford Hill criteria may help assess whether the totality of evidence supports causation.²¹

The kava regulatory history illustrates the danger of converting safety signals into broad prohibitions without adequate causality analysis. European and United States authorities reacted to apparent hepatotoxicity signals involving kava products; later analyses by Teschke, Schmidt, and others emphasized confounding, product-quality differences, comedications, extraction and cultivar issues, and the importance of RUCAM-style liver-injury causality assessment.^{22,23} The German kava ban imposed in 2002 was subsequently lifted (2014) following a decision by the Cologne Administrative Court after reassessment of the benefit-risk record, finding that BfArM's ban (withdrawal of marketing authorizations) was unlawful and inappropriate.²⁴

²⁰ FDA FAERS Public Dashboard FAQ. <https://fis.fda.gov/extensions/FPD-FAQ/FPD-FAQ.html>

²¹ Hill AB. *Proc R Soc Med*. 1965;58(5):295-300. PubMed: <https://pubmed.ncbi.nlm.nih.gov/14283879/>

²² Teschke R, Fuchs J, Bahre R, et al. *J Clin Pharm Ther*. 2010;35(5):545-563. PubMed: <https://pubmed.ncbi.nlm.nih.gov/20831679/>

²³ Teschke R, Schwarzenboeck A, Hennermann KH. *Eur J Gastroenterol Hepatol*. 2008;20(12):1182-1193. PubMed: <https://pubmed.ncbi.nlm.nih.gov/18989142/>

²⁴ VG Koeln, 11 K 1367/13.

This exhibit applies the same methodological caution: alleged safety signals involving products labeled homeopathic should be assessed by product, compliance status, and causality, rather than generalized to the entire compliant class.

III. Dataset Reviewed

The following data (Table III.1) were reviewed in order to determine the likelihood that homeopathic drugs on the US market pose an unreasonable risk to human health.

Table III.1. Dataset summary

Dataset element	Finding
Source dataset	Attachment A: collation of AEMS (formerly FAERS) data on homeopathic products into spreadsheet form.
Audit summaries	Attachments B - G: causality audit summaries developed from Attachment A.
Unit of analysis	Unique AEMS case records in the AEMS dataset.
Total case records	2,068
Earliest date field used	June 26, 1998, the earliest date recorded in FAERS for an adverse event report associated with a homeopathic drug product
Pre/post cutoff used for first-pass analysis	October 25, 2019, the effective date of FDA withdrawal of CPG 400.400.
Primary date field used for pre/post counts	Latest FDA received date at time of analysis (April 15, 2026)
Primary limitation	FAERS reports are spontaneous reports/signals; AEMS/FAERS data does not provide narrative evidence sufficient to assign causality in most cases.

IV. Summary Counts

The following table provides summary information drawn from Attachment A.

Table IV.1. Summary of count data from the AEMS/FAERS dataset

Metric	Count
Total unique case records	2,068
Serious reports	1,684
Death-outcome reports	67
Reports listing concomitant products	451
Reports containing literature references	31
Reports before October 25, 2019	1,555
Reports on/after October 25, 2019	513

Explicit Naranjo causality assessment in workbook	0
Explicit RUCAM/CIOMS liver-injury assessment in workbook	0
Explicit Bradford Hill assessment in workbook	0
Rows containing formal causality terminology searched in audit	0
Hepatic/liver-related rows flagged as possible RUCAM candidates	56
Rows scoreable by RUCAM from workbook fields alone	0

Note: The audit searched for explicit terms including Naranjo, RUCAM, Roussel, CIOMS, Bradford, Hill, causal, causality, causation, probable, possible, and certain. No such formal causality assessment terms were present in the FAERS/AEMS dataset reviewed.

V. Product Clusters and Interpretation

The following table (V.1) reveals the significance of the Hyland and Zicam clusters. Once the 590 reports that do not make mention of the product name are excluded (giving a denominator of 1478 cases in total since records begun in 2006), 1137 reports were found to be related to the Hyland and Zicam clusters, this representing 77% of all records.

Table V.1. Cluster analysis of the AEMS/FAERS dataset

Product cluster	Rows	Preliminary evidentiary significance
Hyland/teething cluster	783	Product-specific cluster requiring separate analysis. Relevant issues include belladonna dilution consistency, manufacturing controls, labeling, infant population, and whether any reports contain sufficient temporal, clinical, dechallenge/rechallenge, toxicology, or alternative-cause information to support causality.
Missing suspect product name	590	Cannot be assumed to represent a compliant homeopathic product. These records require narrative/product-identity review before any regulatory inference can be made.
Zicam cluster	354	Product-specific cluster involving intranasal zinc exposure and anosmia allegations. Because route and pharmacologic zinc exposure are central, these reports should not be generalized to properly manufactured, HPUS-compliant oral/topical OTC homeopathic products.
Other named homeopathic/remedy product	161	Requires product-by-product review for HPUS status, route, dilution, labeling, and concomitant exposures.
Mixed/multi-product record; no clear homeopathic name	92	Causality cannot be assigned to a homeopathic product without additional narrative review.
Ambiguous or non-homeopathic product name with homeopathic-coded active ingredient	88	Potential coding artifact or non-homeopathic exposure; unsuitable for class-wide inference without verification.

The clear concentration of reports in a limited number of product clusters is scientifically significant. It indicates that the data should be evaluated as product- and circumstance-specific signals, not as evidence of a generalized inherent risk in the compliant homeopathic drug category.

VI. Seriousness and Outcome Categories

The following table (VI.1) shows the outcomes reported for each of the cases in the database. While 67 deaths, 288 life-threatening cases and 533 hospitalizations are reported, none of these cases have been causally associated with homeopathic products (see Section VIII).²⁵

Table VI.1. Summary data from AEMS/FAERS reports

Outcome category	Rows
Other outcomes	1,008
Hospitalized	533
Non-serious	384
Life-threatening	288
Disabled	213
Required intervention	126
Died	67
Congenital anomaly	7

Seriousness designations identify reports that should be prioritized for review. They do not establish that the product caused the event. Reports including death and serious adverse events, in particular, require review of age, baseline disease, concomitant drugs, product identity, temporal relationship, autopsy or toxicology evidence, clinical course, and alternative explanations.

VII. Temporal Stability of the AEMS/FAERS Safety Record Before and After Withdrawal of CPG 400.400

The AEMS/FAERS data were analyzed across three regulatory periods: the period before FDA withdrew CPG 400.400 on October 25, 2019; the interim period after withdrawal but before FDA issued its December 7, 2022 final guidance; and the period after the 2022 final guidance. This periodization tests whether the safety record shows a material change in real risk after FDA replaced the prior CPG framework with the current risk-based enforcement posture.

The data do not show that properly manufactured, HPUS-compliant, correctly labeled homeopathic drugs presented a heightened safety burden before the withdrawal of CPG 400.400, nor do they show that the current framework has reduced a demonstrated risk from that compliant product class. Across periods, the same evidentiary limitations persist: the records are spontaneous association reports, not causality determinations; the most salient reports remain concentrated in product-specific or ambiguous clusters; and the dataset contains no formal Naranjo, RUCAM/CIOMS, Bradford Hill, or equivalent causality assessments.

²⁵ See Attachments A and B for additional detail.

The post-final-guidance period therefore does not demonstrate a new or improved safety state attributable to the current framework. Rather, the record remains consistent with a low demonstrated risk for compliant homeopathic drugs and with the need for targeted enforcement against identifiable product risks, including adulteration, mis-manufacture, pharmacologic exposure, inappropriate route of administration, serious-disease claims, and unresolved causally plausible serious adverse-event signals.

Table VII.1. AEMS/FAERS reports by regulatory period, residual screen, and Green-candidate status

Regulatory period	All reports	Serious	Death	Residual named non-outlier	Green candidates	Green serious/death
Pre-withdrawal	1,555	1,271	36	88	6	0/0
Interim	308	235	6	29	5	0/0
Post-guidance	205	178	25	44	4	0/0

The period table shows that report counts after withdrawal and after the 2022 final guidance do not establish a materially different risk profile for compliant products. The reports remain affected by product-specific clusters, missing product names, ambiguous records, and mixed multi-product reports. Counts are therefore relevant as signal counts, not as proof that compliant homeopathic drugs caused the reported events.

Table VII.2. Product clusters by regulatory period, seriousness, and death outcome

Product cluster	Pre	Interim	Post-guidance	Total	Serious/death total
Hyland/teething	708	67	8	783	696/21
Zicam	323	14	17	354	253/0
Missing product name	361	143	86	590	437/13
Ambiguous/non-homeopathic coded	45	26	17	88	74/6
Mixed/multi-product unclear	30	29	33	92	81/17
Other named homeopathic/remedy	88	29	44	161	143/10

The cluster-adjusted analysis is important because the compliant-product risk question cannot be answered by treating Hyland/teething products, Zicam intranasal zinc products, missing product-name records, ambiguous conventional-drug records, and mixed multi-product records as though they were all properly manufactured, HPUS-compliant, correctly labeled homeopathic drugs used as directed.

The residual and first-pass green-candidate categories are conservative screening categories, not final compliance determinations. They show how few records remain once the principal product-specific, missing, ambiguous, mixed, and obvious high-risk records are separated from the compliant-product question. Notably, the first-pass Green-candidate screen identifies no serious or death-outcome reports in any regulatory period.

VIII. Causality Assessment Findings

Based on the audit and analyses (shown in Attachments A and B), the following questions were posed and subsequently interpreted.

Table VIII.1. Summary of questions raised for causality assessment of AEMS/FAERS dataset associated with homeopathic drugs

Question	Finding	Interpretation
Does the dataset contain Naranjo scores or Naranjo terminology?	No. Count = 0.	No individual adverse drug reaction causality assessment is documented in the workbook.
Does the dataset contain RUCAM, CIOMS, or Roussel terminology?	No. Count = 0.	No structured liver injury causality assessment is documented. Liver-related cases require source narratives and laboratory chronology.
Does the dataset contain Bradford Hill analysis?	No. Count = 0.	No population level causation analysis is documented. Bradford Hill could be considered only for well-defined product-outcome clusters.
Does the dataset contain adequate information to score RUCAM for liver cases?	No.	The dataset lacks the required lab chronology, dechallenge/rechallenge, risk-factor, exclusion, and concomitant-drug details.
Can FAERS rows alone prove causation?	No.	FAERS identifies reports and potential signals; it does not establish causation without additional adjudication.

IX. Recommended Classification Framework for Case-Level Review

The absence of any formal causality analysis means that it is not possible to conclude that homeopathic products have been responsible for the adverse effects with which they have been associated in the AEMS database. While FDA may use AEMS reports to prioritize inspection, investigation, product testing, warning letters, recalls, and case-specific enforcement, it is scientifically untenable to use these data to draw conclusions as to the public health risk posed by the entire class of CPG-compliant homeopathic medicines.

A reliable causality appendix should therefore begin with the highest-priority records: the 67 death-outcome cases, the 56 hepatic/liver-related cases, the Hyland/teething cluster, and the Zicam/intranasal zinc cluster. Only after narrative review should any case be classified as causal, probable, possible, indeterminate, unlikely, non-homeopathic, non-compliant, adulterated, misbranded, contaminated, or better explained by concomitant treatment/disease/misuse.

A rational approach to the categorization of cases, along with the regulatory significance of each, is provided in the table below.

Table IX.1. Summary of case-level causality assessment

Category	Definition	Regulatory significance
A. Causal or probable causal relationship to compliant product	Adequate case narrative supports causality under Naranjo, RUCAM, WHO-UMC, or other appropriate method, and the product appears properly manufactured, HPUS-compliant, correctly labeled, and used as directed.	Would be relevant to the safety of the compliant product class. None are presently identified in the workbook.
B. Causal or probable causal relationship to non-compliant product	Case supports causality, but the product appears adulterated, mis-manufactured, contaminated, mislabeled, misbranded, pharmacologically dosed, imported/unlabeled, or otherwise outside CPG/HPUS/CGMP conditions.	Supports targeted enforcement, not withdrawal of the safe harbor for compliant products.
C. Association only / insufficient information	Temporal association exists but narrative lacks key causality elements.	Cannot support class-wide risk conclusion.
D. Better explained by concomitant treatment, disease, overdose, misuse, or other factors	Alternative cause is more plausible or cannot be excluded.	Should not be attributed to compliant homeopathy.
E. Not a homeopathic product or not identifiable as one	Product identity is missing, miscoded, or inconsistent with homeopathic drug status.	Should be excluded from homeopathic-drug risk numerator unless verified.

X. Findings Concerning the Two Most Cited Product Examples

A. Hyland/Teething Products

The Hyland/teething cluster should be treated as a discrete product-quality and infant-exposure issue. FDA and the Petitioners have identified and recognized concerns involving belladonna-containing teething products, reported infant adverse events, laboratory findings of inconsistent or excessive belladonna alkaloid levels, and alleged CGMP deficiencies. If causation were established in any case, the regulatory lesson would be that adulteration, inconsistent dilution, or manufacturing failure requires enforcement. There can be no scientific or public health justification to propose—as FDA has—that all properly manufactured, HPUS-compliant, correctly labeled homeopathic drugs present significant risk.²⁶²⁷

The audit (Attachment B) found zero Naranjo, Bradford Hill, or equivalent causality determinations for these reports. The cluster should therefore be reviewed separately, with attention to product testing, lot information, infant baseline health, concurrent medications, timing, toxicology,

²⁶ Lennihan B. *Altern Complement Ther.* 2018;24(1):19-28. doi:10.1089/act.2017.29148.ble.

²⁷ FDA. Laboratory Analysis of Homeopathic Teething Tablets. <https://www.fda.gov/drugs/information-drug-class/laboratory-analysis-homeopathic-teething-tablets>

and whether reported symptoms are specific to belladonna exposure or nonspecific to pediatric illness.

B. Zicam Intranasal Zinc Products

The Zicam cluster should likewise be treated as a discrete product-route and pharmacologic exposure issue. Zicam intranasal sprays, which are non-HPUS-compliant and cannot be regarded as homeopathic given the very substantial amounts (10 mg) of zinc administered per dose, have been known since 2009 to cause significant, potentially irreversible, damage to the nasal epithelium. Intranasal zinc exposure and anosmia allegations raise different questions from highly diluted oral or topical homeopathic products used for self-limiting OTC conditions. Even if some Zicam cases are causally supported, they do not establish a generalized safety problem for products that comply with HPUS standards, correct labeling, appropriate route of administration, and CGMP requirements. The Zicam cluster was clearly associated with product-, route-, dose-, and pharmacologic-exposure-specific risk, not modality-wide risk.

XI. Peer-Reviewed Case-Report Literature Concerning Adverse Events Associated with Homeopathic or Purportedly Homeopathic Products in the United States

A targeted review of the supplied peer-reviewed case-report memorandum, the FAERS/AEMS audit materials, and targeted searches of PubMed and publisher-indexed literature identified a limited number of United States-relevant case reports, abstracts, or case-series analyses involving homeopathic or purportedly homeopathic products. The important evidentiary point is that, outside the Zicam/intranasal zinc literature, these reports generally do not apply formal Naranjo, RUCAM/CIOMS, Bradford Hill, or equivalent causality scoring. They instead use temporal association, clinical judgment, or toxicologic plausibility, often in circumstances involving product-identity uncertainty, concomitant exposures, non-compliant products, or misuse.^{28,29,30,31}

Table XI.1. Summary of adverse event case report literature associated with homeopathic products in the USA

Report / product	US relevance	Reported event	Causality method reported	Evidentiary significance
Similasan Pink Eye Relief / Belladonna-containing eye drops	US emergency-department case report.	Acute angle-closure glaucoma after use of OTC homeopathic eye drops; the patient also reported cetirizine and erythromycin ointment use shortly before presentation.	No formal Naranjo, RUCAM, or Bradford Hill causality score reported.	Potentially relevant signal for topical ophthalmic low-dilution belladonna products, but the case is a single report with confounding medication history and no structured causality score.
Ova Tosta 30C / eggshell-based homeopathic remedy	US liver-transplant case report involving product obtained through Amazon.	Acute fulminant hepatic failure requiring orthotopic liver transplantation after increased dosing of a homeopathic product.	No RUCAM/CIOMS score reported in the published case report.	A serious case that should be included as unfavorable evidence, but the absence of RUCAM, product-authentication data, contaminant analysis, and full exclusion chronology limits any class-wide inference.
pH Miracle pHour Salt	US medical-toxicology conference abstract.	Acute renal failure, caustic injury, and metabolic alkalosis after ingestion of alkaline salts in a patient with pancreatitis and alcohol-use history.	No formal Naranjo, RUCAM, or Bradford Hill score reported.	Not a conventional HPUS-compliant homeopathic drug case; more consistent with alkaline-salt ingestion/misuse and

²⁸ Zicam sources: Davidson TM, Smith WM. *Arch Otolaryngol Head Neck Surg*. 2010;136(7):673-676. PubMed: <https://pubmed.ncbi.nlm.nih.gov/20644061/>; Lim JH et al. *PLoS One*. 2009;4(10):e7647. PubMed: <https://pubmed.ncbi.nlm.nih.gov/19876403/>.

²⁹ Case-report sources: Huff ML et al. *Am J Emerg Med*. 2022;54:329.e1-329.e3. PubMed: <https://pubmed.ncbi.nlm.nih.gov/34776281/>; Goldhaber NH et al. *J Investig Med High Impact Case Rep*. 2023;11:23247096231207480. PubMed: <https://pubmed.ncbi.nlm.nih.gov/37843100/>; 2021 ACMT Annual Scientific Meeting Abstracts. *J Med Toxicol*. 2021;17:93-153. PubMed: <https://pubmed.ncbi.nlm.nih.gov/33791944/>; Reactions Weekly. 2021;1858:95. doi:10.1007/s40278-021-96813-3.

³⁰ Sarker A, Yang Y, Ramesh BP, et al. *J Am Med Inform Assoc*. 2024;31(1):57-65. PubMed: <https://pubmed.ncbi.nlm.nih.gov/37847653/>

³¹ See Attachments A and B of the present petition for additional details.

Report / product	US relevance	Reported event	Causality method reported	Evidentiary significance
				underlying disease confounding.
Unlabeled remedy mailed from Pakistan; caffeine/ephedrine/yohimbine poisoning	US pediatric toxicology case report/abstract; product source outside regulated US homeopathic-drug supply chain.	Seizures and critical illness in a young child after exploratory ingestion; GC/MS identified caffeine, theophylline/theobromine, ephedrine, and yohimbine exposure.	No formal Naranjo, RUCAM, or Bradford Hill score reported.	Strong evidence of poisoning from an unlabeled/adulterated imported product, not evidence of risk from properly manufactured, HPUS-compliant, correctly labeled homeopathic drugs.
Zicam / intranasal zinc gluconate products	US case-series/literature causality analysis involving intranasal zinc and anosmia.	Hyposmia/anosmia after intranasal zinc gluconate gel exposure.	Bradford Hill criteria were expressly applied in the published causality analysis.	Principal exception to the general absence of formal causality methods. Even if causality is accepted for intranasal zinc, the inference is product-, route-, and pharmacologic-exposure-specific.
Hyland / belladonna teething products	US regulatory cluster and peer-reviewed critique of FDA reports.	Infant adverse-event reports described by FDA as consistent with belladonna toxicity; FDA laboratory testing found non-uniform belladonna alkaloid content in tested products.	The critique did not establish formal Naranjo, RUCAM, or Bradford Hill causality for the cluster.	At most, a product-quality/manufacturing-compliance cluster requiring lot-specific and case-level review; not a class-wide demonstration of risk from compliant products.
Amazon-review pharmacovigilance analysis	US-focused signal-detection study using Amazon reviews and comparison with FAERS.	Consumer-review adverse-event signal detection for unapproved OTC homeopathic products.	No case-level Naranjo, RUCAM, or Bradford Hill adjudication of individual events.	Useful for hypothesis generation and signal detection, but not proof of causation or a substitute for case-level adjudication.

This literature review supports the same conclusion as the FAERS/AEMS audit conducted for the purpose of this petition. The peer-reviewed literature contains adverse-event signals associated with products described as homeopathic, but the available United States-relevant reports do not, with the exception of the Zicam/intranasal zinc study, provide formal causality assessment establishing that properly manufactured, HPUS-compliant, correctly labeled homeopathic drugs caused serious adverse events. The Ova Tosta liver-failure report is the most serious non-Zicam case identified and should be adjudicated using RUCAM if full clinical and product data are available. The Similasan/belladonna eye-drop case should be adjudicated using a structured adverse-drug-reaction causality method if sufficient narrative detail can be obtained. The pHour salt and Pakistan-remedy reports are better understood as non-compliant, non-HPUS, mislabeled, adulterated, imported, or non-homeopathic product events rather than evidence of inherent risk in the compliant homeopathic-drug category.

XII. Evidence from Systematic Reviews and Meta-Analyses

Systematic reviews and meta-analyses of randomized controlled trials provide the highest-level clinical evidence currently available for common or readily observable adverse effects of homeopathic treatment. They are not designed to detect extremely rare harms or harms arising from defective manufacture, adulteration, misbranding, contamination, inappropriate route of administration, or pharmacological exposure. Nevertheless, they are directly relevant to FDA's class-wide safety rationale because they assess adverse events under controlled clinical conditions in which products are administered according to trial protocols.

The most directly relevant safety-focused review is Stub et al. (2016), a systematic review and meta-analysis of randomized controlled trials examining adverse effects and homeopathic aggravations. The review identified 41 randomized trials with 6,055 participants; 28 trials reported adverse effects; and pooled data showed no statistically significant difference in the proportion of patients experiencing adverse effects during homeopathic treatment compared with placebo or conventional treatment (odds ratio 0.99; 95% confidence interval 0.86 to 1.14). Reported adverse effects were generally mild to moderate, and homeopathic aggravations were mainly mild and transient, typically on par with those of placebo arms of trials.³²

The earlier systematic review by Dantas and Rampes reached a similar conclusion. It evaluated reports of adverse effects from homeopathic medicines in English-language sources, including clinical trials and reports from regulators and manufacturers. In clinical trials, adverse effects were reported more frequently with homeopathic medicines than with placebo, but the events were generally minor and transient; the review did not identify a pattern of serious harm from appropriately used homeopathic medicines.³³

The Swiss Health Technology Assessment summary by Bornhoft et al., which evaluated effectiveness, safety, and cost-effectiveness of homeopathy in general practice, likewise concluded that homeopathic treatment appeared to have a favorable safety profile, with adverse effects uncommon and generally mild in the materials assessed.³⁴

Hamre *et al.* (2023), an umbrella systematic review of meta-analyses of randomized placebo-controlled trials of homeopathy, was primarily designed to evaluate efficacy rather than safety. Its safety relevance is therefore secondary, but important: the authors considered prior safety-focused

³² Stub T, Musial F, Kristoffersen AA, Alraek T, Liu J. Adverse effects of homeopathy, what do we know? A systematic review and meta-analysis of randomized controlled trials. *Complement Ther Med.* 2016;26:146-163. doi:10.1016/j.ctim.2016.03.013. PubMed: <https://pubmed.ncbi.nlm.nih.gov/27261996/>.

³³ Dantas F, Rampes H. Do homeopathic medicines provoke adverse effects? A systematic review. *Br Homeopath J.* 2000;89 Suppl 1:S35-S38. doi:10.1054/homp.1999.0378. PubMed: <https://pubmed.ncbi.nlm.nih.gov/10939781/>.

³⁴ Bornhoft G, Wolf U, von Ammon K, Righetti M, Maxion-Bergemann S, Baumgartner S, Thurneysen A, Matthiessen PF. Effectiveness, safety and cost-effectiveness of homeopathy in general practice - summarized health technology assessment. *Forsch Komplementmed.* 2006;13 Suppl 2:19-29. doi:10.1159/000093586. PubMed: <https://pubmed.ncbi.nlm.nih.gov/16883077/>.

systematic reviews and concluded that adverse effects associated with homeopathic treatment were generally mild to moderate and transient, with incidence comparable to placebo or lower than conventional or herbal comparators in the datasets assessed.¹⁸

Taken together, these high-level reviews support a narrow but important safety conclusion. Under controlled clinical conditions, and subject to the usual caveats about incomplete adverse-event reporting in randomized trials, homeopathic medicines do not show a signal of frequent or severe treatment-emergent adverse effects. This finding is consistent with the FAERS/AEMS causality audit: the strongest evidence does not show a scientifically established pattern of serious harm attributable to properly manufactured, HPUS-compliant, correctly labeled homeopathic drugs used according to appropriate directions.

The randomized-trial evidence should not be overstated. It cannot exclude rare serious events, detect risks from products with inconsistent dilution, contamination, unlisted ingredients, or pharmacologic dosing, or address products used in vulnerable populations outside trial protocols. Those risks warrant product-specific enforcement and case-level pharmacovigilance. But the systematic review and meta-analysis literature provides no scientific basis for treating the compliant homeopathic drug category as inherently unsafe, or for inferring that isolated events involving non-compliant or causally ambiguous products establish significant risk across the compliant class.

XIII. Absence of Evidence That the Current Risk-Based Framework Has Reduced Real Product Risk

The current record provides no empirical basis for concluding that FDA's post-2019 and post-2022 framework has reduced a demonstrated risk from properly manufactured, HPUS-compliant, correctly labeled homeopathic drugs. That is because the record does not establish that such products were presenting a significant causally supported safety risk before the withdrawal of CPG 400.400.

If the post-2019 and post-2022 framework were solving a real compliant-product safety problem, the AEMS/FAERS record would be expected to show either a prior causally supported burden from compliant products, a subsequent reduction in that burden, or both. The dataset shows neither. Instead, the report pattern remains dominated by product-specific clusters, missing product-name records, ambiguous records, mixed conventional-drug records, and records lacking the clinical narrative necessary for causality scoring.

The principal safety concerns that do appear in the record are real but targeted. They concern manufacturing quality, inconsistent ingredient levels, contamination, pharmacologically active exposure, inappropriate route of administration, vulnerable populations, serious-disease claims, unlisted ingredients, misuse, or unresolved serious signals. Those risks do not justify treating all compliant homeopathic drugs as if they present a common class-wide danger. They justify a clear enforcement system that distinguishes compliant low-risk products from products requiring heightened review or targeted enforcement.

Accordingly, the data support reconsideration of the current policy. The current framework has not been shown to improve consumer safety in relation to compliant products, while it has removed the predictable safe-harbor criteria that previously enabled responsible manufacturers to structure operations, supply chains, labeling, and quality systems around ascertainable compliance measures.

XIV. Regulatory Uncertainty Created by the Current Framework

The current risk-based enforcement framework identifies broad categories of FDA concern but does not provide the regulated class with a clear set of compliance measures that, if satisfied, will place a product into a predictable low-enforcement-risk safe harbor. A responsible manufacturer may comply with HPUS standards, manufacture under CGMP, disclose ingredients and dilutions, and limit claims to appropriate OTC self-limiting conditions, yet still remain unable to determine whether FDA will regard the product as presenting sufficient “risk” to justify enforcement.

That uncertainty is itself a regulatory harm. It affects not only the manufacturer of finished homeopathic drugs, but also contract manufacturers, suppliers of homeopathic source materials, distributors, retailers, practitioners, investors, insurers, and consumers. In the absence of an articulated safe harbor, market participants must make business decisions under the continuing threat that products historically marketed under CPG 400.400 may be treated as unlawful unapproved drugs without clear notice of what additional compliance showing would avoid that result.

Predictable consequences include supply-chain hesitation, discontinued product offerings, reduced investment, increased compliance costs, reluctance of counterparties to support the category, and diminished consumer access to long-standing homeopathic products. These consequences are disproportionate where the safety evidence does not establish a causally supported serious risk from compliant products and where the genuine safety issues can be addressed through targeted enforcement against specific product risks.

XV. A Ready-to-Implement Traffic-Light Safe-Harbor Risk-Based Enforcement Framework

FDA can preserve a genuinely risk-based approach without maintaining an indeterminate enforcement system. The scientifically proportionate approach is a transparent traffic-light framework: Green products are presumptively within a safe harbor and should be the lowest enforcement priority; Amber products require heightened scrutiny, mitigation, or additional evidence; and Red products are enforcement priorities because they present real product-specific risk or fall outside the safe harbor.

This framework is not deregulation. It directs FDA resources to the risks actually identified in the AEMS/FAERS record and peer-reviewed literature: adulteration, mis-manufacture, inconsistent or excessive ingredient levels, contamination, non-sterile products where sterility is required, pharmacologically active exposure inconsistent with homeopathic dilution principles, inappropriate route of administration, vulnerable-population risks, serious-disease claims, and causally supported serious adverse-event signals.

FDA could implement this system either by reinstating CPG 400.400 or by modifying the current risk-based framework to state precisely what compliance measures will place a product in the Green safe-harbor category and what factors will move a product into Amber or Red status.

Table XV.1. Proposed Green/Amber/Red safe-harbor enforcement framework

Tier	Status	Indicative criteria	Regulatory effect
GREEN / Tier 1 Safe harbor	Presumptively lowest enforcement priority	HPUS-listed/recognized ingredient; CGMP manufacture; correctly labeled as homeopathic; active ingredients and dilutions disclosed; OTC claims limited to self-limiting conditions; appropriate route; no unresolved plausible serious safety signal.	Manufacturer should be able to show records proving compliance and operate with minimal enforcement uncertainty.
AMBER / Tier 2 Heightened scrutiny	Not automatically enforcement priority, but requires additional review or mitigation	Low-dilution toxic substances; infant/pregnancy/immunocompromised targeting; ophthalmic, intranasal, or sterile-route issues; repeated but unadjudicated safety signals; unusual claims; unclear product identity; quality or lot-uniformity concerns.	FDA may request substantiation, testing, labeling changes, adverse-event narratives, or manufacturing evidence before deciding enforcement priority.
RED / Tier 3 Enforcement priority	Outside safe harbor or presenting real product risk	Adulteration; contamination; unlisted pharmacologically active ingredients; non-sterile products requiring sterility; ingredient level inconsistent with label; serious-disease claims; causally supported serious adverse event; refusal or failure to provide compliance records.	Targeted enforcement is scientifically proportionate and consistent with the safety concerns identified in the dataset.

Under this system, a manufacturer should be able to provide inspectors with defined records demonstrating Green status: HPUS ingredient basis; batch and lot records; CGMP documentation; identity, strength, quality, and purity controls appropriate to the product; labeling showing homeopathic status, ingredients, and dilutions; OTC self-limiting indications; route-specific quality controls; adverse-event procedures; and evidence that no unresolved plausible serious safety signal exists for the product as formulated and labeled.

Amber status should not be treated as automatic enforcement priority. It should trigger targeted FDA inquiry, manufacturer response, possible labeling revision, product testing, ingredient review, lot-uniformity review, or adverse-event narrative review. Red status should be reserved for products that are adulterated, contaminated, misbranded, mislabeled, non-sterile where sterility is required, pharmacologically dosed in a manner inconsistent with labeling, promoted for serious disease in a misleading way, or associated with serious events supported by structured causality review.

XVI. Case-Level Adjudication Procedure for Serious AEMS/FAERS Reports

The following work (see table below) is proposed, and indeed would, in the opinion of the petitioner(s), be a necessary next step, if FDA was to determine scientifically the extent to which specific homeopathic products posed a risk to public health. Without this work, FDA's determination that homeopathic drugs pose an unreasonable risk to health are entirely anecdotal and unscientific.

Table XVI.1. Summary of proposed adjudication system for serious adverse events

Priority group	Recommended review method	Purpose
67 death-outcome reports	Narrative review; Naranjo/WHO-UMC where possible; alternative-cause analysis.	Determine whether any death is plausibly attributable to a compliant homeopathic product.
56 hepatic/liver-related reports	RUCAM/CIOMS only if source narratives and laboratory chronology can be obtained.	Determine whether any liver injury is causally attributable to a product and whether product was compliant.
Hyland/teething cluster	Product-specific review; lot testing; infant clinical narratives; toxicology; Bradford Hill only if adequate cluster evidence exists.	Distinguish alleged belladonna toxicity from nonspecific infant events, confounding, and manufacturing noncompliance.
Zicam cluster	Product-route review; anosmia narrative review; mechanistic and temporal evidence; product compliance assessment.	Determine whether intranasal zinc cases are causally supported and whether they are representative of compliant homeopathic drugs.
Ambiguous/missing product-name records	Product identity verification before inclusion.	Avoid inflating the homeopathic-drug risk numerator with unverified records.

XVII. Conclusions

The adverse-event record submitted as Attachment A, together with the causality audit summarized in this Exhibit, does not establish that properly manufactured, HPUS-compliant, correctly labeled homeopathic drugs marketed under the conditions formerly recognized in CPG 400.400 present a significant public-health risk. The record consists of spontaneous adverse-event reports and product associations, not formal causality determinations.

The causality audit confirms the absence of documented Naranjo, RUCAM/CIOMS, Bradford Hill, or equivalent assessments using accepted causality methods. The most prominent report clusters are product-specific and implicate issues of manufacturing quality, product identity, route of administration, pharmacologic exposure, labeling, concomitant products, misuse, or missing data. These findings support targeted enforcement against specific risks; they do not support treating the compliant homeopathic-drug category as inherently unsafe.

The temporal record is equally important. The AEMS/FAERS data do not show that compliant homeopathic products presented a heightened causally supported safety burden before FDA withdrew CPG 400.400. Nor do they show that FDA's current post-2019 and post-2022 framework has reduced a demonstrated risk from that compliant product class. The same evidentiary pattern persists across regulatory periods: association reports, clustering in outlier or ambiguous records, and no formal causality basis for class-wide enforcement assumptions.

The current framework therefore creates a mismatch between regulatory burden and demonstrated risk. FDA has identified categories that may justify enforcement attention, including adulteration, contamination, inconsistent ingredient levels, inappropriate route of administration, pharmacologically active exposure, vulnerable populations, serious-disease claims, and unresolved causally plausible serious adverse-event signals. But those are targeted risk factors, not a scientific basis for eliminating a predictable compliance pathway for responsible manufacturers.

The practical result is regulatory uncertainty. In the absence of a clear safe harbor, manufacturers, suppliers, distributors, retailers, practitioners, investors, and consumers cannot reliably determine when a properly manufactured, HPUS-compliant, correctly labeled homeopathic product will be considered low enforcement priority. That uncertainty can disrupt supply chains, reduce consumer access, discourage investment, and remove long-standing products from the market without a corresponding showing of improved safety.

The scientifically proportionate remedy is therefore to reinstate CPG 400.400 or adopt an equivalent traffic-light safe-harbor framework. Green products should be presumptively lowest enforcement priority where manufacturers can document HPUS basis, CGMP manufacture, accurate homeopathic labeling, disclosed ingredients and dilutions, appropriate OTC self-limiting claims, appropriate route of administration, and absence of unresolved plausible serious safety signals. Amber products should receive heightened review or mitigation where risk factors exist. Red products should be enforcement priorities where adulteration, contamination, misbranding, non-sterility, pharmacologic exposure inconsistent with labeling, serious-disease claims, or causally supported serious adverse events are present.

Such an approach would preserve FDA's ability to protect the public from real product-specific risks while restoring the clarity necessary for lawful, responsible, and predictable operation of the compliant homeopathic-drug market.

ATTACHMENT A: Total AEMS (formerly FAERS) dataset associated with homeopathic drug products including causality assessment

The spreadsheet includes all available data from the AEMS system (June 26, 1996 to April 15, 2026), and these data have been interrogated based on causality criteria derived from key causality assessment systems, namely Naranjo, RUCAM and Bradford Hill.

The full spreadsheet can be downloaded from the following this [Dropbox hyperlink](#).

The dataset includes 2068 cases (i.e. rows in spreadsheet) and are shown alongside the causality audit Columns AF – AL). The columns and their respective headings are as follows:

A: Case ID
B: Suspect Product Names
C: Suspect Product Active Ingredients
D: Reason for Use
E: Reactions
F: Serious
G: Outcomes
H: Sex
I: Event Date
J: Latest FDA Received Date
K: Year
L: Case Priority
M: Patient Age
N: Patient Weight
O: Sender
P: Reporter Type
Q: Report Source
R: Concomitant Product Names
S: Latest Manufacturer Received Date
T: Initial FDA Received Date
U: Country where Event occurred
V: Reported to Manufacturer?
W: Manufacturer Control Number
X: Literature Reference
Y: Compounded Flag
Z: Latest FDA received period
AA: Event date precision
AB: Event date period
AC: Concomitant products present?
AD: Literature reference present?
AE: Product cluster

AF: Formal causality method mentioned?
AG: Formal causality term hits
AH: RUCAM hepatic-reaction candidate?
AI: Naranjo score support from workbook fields?
AJ: RUCAM score support from workbook fields?
AK: Bradford Hill row-level causality support?
AL: Preliminary interpretation

ATTACHMENT B: AEMS/FAERS DATA ANALYSIS

A. SUMMARY

FAERS Homeopathy Causality Audit - First Pass	
Input workbook	Attachment A spreadsheet
Rows / unique FAERS case IDs	2068 / 2068
Cutoff used	October 25, 2019 (FDA withdrawal of CPG 400.400) 0 of 2,068 reports contain an explicit Naranjo, RUCAM/CIOMS/Roussel, or Bradford Hill causality assessment in the available FAERS data fields.
Core finding	FAERS reports are safety signals/associations; case-level narratives and medical records are required for formal causality scoring.
Important limitation	

KPI	Count
Pre-revocation reports by Latest FDA Received Date	1555
Post-revocation/on-after reports by Latest FDA Received Date	513
Serious reports	1684
Death outcome reports	67
Reports with concomitant products listed	451
Reports with literature reference listed	31
Hepatic-reaction rows that may need RUCAM triage	56

Conclusion	The overall analysis (see below) supports the argument that the collected AEMS/FAERS data show reports associated with products coded as homeopathic, but do not themselves establish causality by accepted causality-assessment methods.
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B. COUNTS – Summary of counts from AEMS/FAERS data

Pre/post summary		
Metric	Pre	Post/on-after
All rows	1555	513
Serious rows	1271	413
Death outcome rows	36	31
Concomitant-products listed	304	147

Causality terms searched	
Term	Rows containing term
naranjo	0
rucam	0
rousseau	0
ucalf	0
cioms	0
bradford	0
hill criteria	0
causal	0
causality	0
causation	0
probable	0
possible	0
certain	0
Product clusters	
Cluster	Rows
Hyland/teething cluster	783
Missing suspect product name	590
Zicam cluster	354
Other named homeopathic/remedy product	161
Mixed/multi-product record; no clear homeopathic name	92
Ambiguous/non-homeopathic product name with homeopathic-coded active ingredient	88
Outcomes	
Outcome	Rows
Other Outcomes	1008
Hospitalized	533
Non-Serious	384

Life Threatening	288
Disabled	213
Required Intervention	126
Died	67
Congenital Anomaly	7
Top suspect product-name values	
Suspect Product Names	Rows
Baby Teething (Hyland Homeopathic)	715
[no product data given]	590
Zicam (Homeopathics)	274
Zicam Allergy Relief	35
Cold N Cough 4 Kids	23
Calms Forte 4 Kids	19
Nighttime Cold N Cough 4 Kids	15
Arnicare	14
4 Kids Complete Cold And Mucus	11
Dry Eye Relief (Homeopathics)	11
Azo Yeast Plus	10
Orajel Teething (Homeopathic)	9
Escitalopram	7
Amlodipine	7
Arnica Montana (Homeopathic)	6
Zicam Allergy Relief;Zicam Cold Remedy	6
Pink Eye Relief	4
Eliquis	4
Hylands Baby Cough Syrup	4
Coldcalm	3
Similasan For Inflammation Of The Mouth And Throat	3
Zicam Cold Remedy Rapidmelts	3
Kesimpta	3
Sambucus Nigra	3
Sambucol Cold And Flu Nasal Relief	3
Irritated Eye Relief	3
Gaba;Lyrica	3
Complete Allergy 4 Kids	3
Flomax	3
Reboost	2
Year counts	
Year	Rows
1998	1
1999	1
2000	1
2001	2

2002	1
2003	3
2004	24
2005	17
2006	25
2007	20
2008	13
2009	110
2010	147
2011	65
2012	64
2013	150
2014	157
2015	142
2016	279
2017	123
2018	98
2019	131
2020	142
2021	75
2022	73
2023	91
2024	39
2025	53
2026	21

C. CAUSALITY RUBRIC: decision-making criteria determining AEMS/FAERS data use in analysis

Method / framework	What it is for	Minimum data threshold for use in analysis	Status of analysis	Primary source (URL)
Naranjo ADR Probability Scale	Individual adverse drug reaction probability assessment.	Temporal sequence, dechallenge, rechallenge, alternative causes, dose response, prior reports, objective confirmation, and placebo/drug-level information where applicable.	No score present; not scoreable from workbook fields alone.	Naranjo et al (1981): https://pubmed.ncbi.nlm.nih.gov/7249508/
RUCAM / CIOMS / Roussel Uclaf	Structured causality assessment for suspected drug/herb-induced liver injury.	Latency; ALT/ALP/bilirubin trajectory; dechallenge course; risk factors; concomitant drugs; full non-drug liver-disease exclusion; known hepatotoxicity; rechallenge if any.	No score present; 56 hepatic-reaction rows are flagged for narrative retrieval and manual RUCAM triage.	Dana & Teschke 2016: https://www.mdpi.com/1422-0067/17/1/14
Bradford Hill viewpoints	Population-level or signal-level causal inference framework across a body of evidence.	Repeated observations, temporality, consistency, strength, specificity, biological gradient, plausibility, coherence, experiment/reversibility, analogy.	No Bradford Hill assessment present; not meaningful as a row-level FAERS score.	Bradford Hill 2005: https://pmc.ncbi.nlm.nih.gov/articles/PMC2626428/
FAERS limitation	FAERS is a postmarketing surveillance and signal-generation system.	Reports need independent causality assessment before causal claims are made.	All rows should be treated as association reports unless upgraded by narrative review.	FDA: https://fis.fda.gov/extensions/fpdwidgets/2e01da82-13fe-40e0-8c38-4da505737e36.html

D. RUCAM CANDIDATES

Case ID	Suspect Product Names	Reactions	Outcomes	Latest FDA Received Date	Event Date	Concomitant Product Names	Literature Reference	Product cluster	RUCAM status
18812254	Dextrose; Coumadin; Breo Ellipta; Metamizol; Vitamin C; Maalox Antacid; Vitamin B6; Dobutamine; Otrivin; Advair Hfa; Fragmin; Ringers And Dextrose Solution; Rocaltrol; Zocor; Trelegy Ellipta; Dexilant; Prevacid; Fosrenol; Dulcolax (Bisacodyl); Vitamin E; Anticoagulant Sodium Citrate; Tamiflu; Diprosone; Ferrlecit; Atrovent; Fiasp; Heparin Sodium In Dextrose; Aranesp; Vitamin K1; Tresiba; Novo rapid	Hyperlipidaemia; Aortic Stenosis; Anticoagulant Therapy; Chronic Obstructive Pulmonary Disease; Lower Respiratory Tract Infection; Total Lung Capacity Decreased; Incorrect Route Of Product Administration; Myasthenia Gravis; Ulcer; Blood Test Abnormal; Hypertension; Drug Hypersensitivity; Drug Therapy; Blood Creatinine Increased; Drug Ineffective; Diabetes Mellitus; Condition Aggravated; Ascites; Liver Function Test Increased; Multiple Organ Dysfunction Syndrome; Pulmonary Embolism; Bacteroides Infection; Blood Cholesterol Increased; Iron Deficiency; Aspar	Life Threatening; Other Outcomes; Congenital Anomaly; Died; Hospitalized; Disabled	10-NOV-2025	2020	Amlodipine; Disodium Hydrogen Citrate; Sodium Picosulfate; Potassium Chloride; Riboflavin 5'-Phosphate Sodium; Dobutamine; Atrovent; Warfarin; Amlodipine Maleate; Cholecalciferol; Calcitriol; Riboflavin 5'-Phosphate Sodium Anhydrous; Dobutamine Hydrochloride; Beta.- Carotene; Pyridoxine Hydrochloride; Dextrose; Simvastatin; Vitamin D; Vitamin C; Bisacodyl; Ergocalciferol	-	Other named homeopathic/remedy product	Candidate only; no RUCAM score available (in AEMS/FAERS database)

		tate Aminotransferase Increased;Pneumonia;Musculoskeletal Stiffness;Abdominal Pain;Pleural Effusion;Dry Mouth;Sepsis;Neuralgia;Hyponatraemia;Blood Uric Acid Increased;Death;Drug Intolerance;Lung Opacity;Troponin Increased;Intentional Product Misuse;Product Use In Unapproved Indication;Appendicolith;Antacid Therapy;Abdominal Distension;Dyspnoea;Nausea;Hypophosphataemia;Ventricular Fibrillation;Activated Partial Thromboplastin Time Prolonged;Oedema Peripheral;Thrombosis;Hyperphosphataemia;Sleep Disorder Therapy;Transaminases Increased;Blood Calcium Increased;End Stage Renal Disease;Vomiting;Anaemia;Stress;Gout;Cardiogenic Shock;Swelling;Off Label Use;General Physical Health						
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		Deterioration;Analgesic Therapy;Bacterial Infection;Somnolence;Appendicitis;Constipation;Sleep Disorder;Blood Phosphorus Increased							
25738899	Arsenicum Album	Drug-Induced Liver Injury;Drug Ineffective;Jaundice Cholestatic;Toxicity To Various Agents	Other Outcomes	29-AUG-2025	-	Rivaroxaban;Furosemide;Quetiapine;Amlodipine;Nitroglycerin;Pantoprazole;Carvedilol;Rosuvastatin;Allopurinol	Ferreira P, Machado V, Ramalho C, Freitas H, Oliveira N, Cabral A.. INVOLUNTARY INTOXICATION BY ARSENICUM	Other named homeopathic/remedy product	Candidate only; no RUCAM score available (in AEMS/FAERS database)

							ALBUM + CHOLESTATIC JAUNDICE IN PATIENT WITH SCABIES AND CUSHING'S SYNDROME - CLINICAL CASE.. Eur-J- Case-Rep-Intern- Med. 2019;6 (Suppl. 1):966- 967 abstr. 14		
25673817	Arsenicum Album	Jaundice Cholestatic;Drug- Induced Liver Injury;Toxicity To Various Agents;Drug Ineffective	Other Outcomes	13-AUG-2025	-	Amlodipine;Rosu vastatin;Nitrogly cerin;Rivaroxaba n;Allopurinol;Pa ntoprazole;Furos emide;Quetiapine ;Carvedilol	Ferreira P, Machado V, Ramalho C, Freitas H, Oliveira N, Cabral A.. INVOLUNTAR Y INTOXICATIO N BY ARSENICUM ALBUM + CHOLESTATIC JAUNDICE IN PATIENT WITH SCABIES AND CUSHING'S SYNDROME - CLINICAL CASE.. Eur-J- Case-Rep-Intern- Med. 2019;6 (Suppl. 1):966- 967 abstr. 14	Other named homeopathic/rem edy product	Candidate only; no RUCAM score available (in AEMS/FAERS database)
25092278	Arnica Montana (Homeopathic);Z olpidem;Symbico rt;Subutex	Foetal Exposure During Pregnancy;Drug Withdrawal Syndrome Neonatal;Jaundic e Neonatal	Hospitalized	03-AUG-2025	09-NOV-2023	-	-	Other named homeopathic/rem edy product	Candidate only; no RUCAM score available (in AEMS/FAERS database)
25278101	Leucovorin	Drug Ineffective;Hepat ic Cytolysis;Drug Interaction;Chole stasis	Other Outcomes	07-MAY-2025	07-DEC-2023	Enoxaparin	Geoffrey Strobbe.Grade 3 cytolysis in a patient with metastatic colorectal cancer consuming a mushroom	Ambiguous/non- homeopathic product name with homeopathic- coded active ingredient	Candidate only; no RUCAM score available (in AEMS/FAERS database)

							powder-based alternative therapy. Journal of Oncology Pharmacy Practice. 20-AUG-2024;31(2):329-335		
25239847	Nux Vomica; Metformin; Lantus; Arnica Montana (Homeopathic)	Hepatocellular Injury; Eosinophilic Hepatitis; Jaundice	Other Outcomes	25-APR-2025	-	-	Power S, Barritt AS. A yellow flower with jaundice power: A case of severe liver injury attributed to greater celandine. American Journal of Gastroenterology. 2023;118(10):S2289	Other named homeopathic/ready product	Candidate only; no RUCAM score available (in AEMS/FAERS database)
25120260	Arnica Montana (Homeopathic); Symbicort; Subutex; Zolpidem	Foetal Exposure During Pregnancy; Jaundice Neonatal; Drug Withdrawal Syndrome Neonatal	Hospitalized	14-APR-2025	09-NOV-2023	-	-	Other named homeopathic/ready product	Candidate only; no RUCAM score available (in AEMS/FAERS database)
25187605	Zolpidem; Subutex; Symbicort; Arnica Montana (Homeopathic)	Drug Withdrawal Syndrome Neonatal; Jaundice Neonatal; Foetal Exposure During Pregnancy	Hospitalized	11-APR-2025	09-NOV-2023	-	-	Other named homeopathic/ready product	Candidate only; no RUCAM score available (in AEMS/FAERS database)
25112331	Arnica Montana (Homeopathic); Symbicort; Zolpidem; Subutex	Jaundice Neonatal; Foetal Exposure Timing Unspecified; Foetal Exposure During Pregnancy; Drug Withdrawal Syndrome Neonatal	Hospitalized	08-APR-2025	09-NOV-2023	-	-	Other named homeopathic/ready product	Candidate only; no RUCAM score available (in AEMS/FAERS database)
25100881	Symbicort; Subutex; Arnica Montana (Homeopathic); Zolpidem	Drug Withdrawal Syndrome Neonatal; Jaundice Neonatal; Foetal Exposure During Pregnancy	Hospitalized; Other Outcomes	07-APR-2025	09-NOV-2023	-	-	Other named homeopathic/ready product	Candidate only; no RUCAM score available (in AEMS/FAERS database)

23747164	Kesimpta	Alanine Aminotransferase Increased;Aspartate Aminotransferase Increased;Nasopharyngitis;Gamma-Glutamyltransferase Increased;Hepatitis	Other Outcomes	02-MAY-2024	NOV-2023	-	-	Ambiguous/non-homeopathic product name with homeopathic-coded active ingredient	Candidate only; no RUCAM score available (in AEMS/FAERS database)
23747583	Kesimpta	Nasopharyngitis; Gamma-Glutamyltransferase Increased;Alanine Aminotransferase Increased;Hepatitis;Aspartate Aminotransferase Increased	Other Outcomes	26-APR-2024	NOV-2023	-	-	Ambiguous/non-homeopathic product name with homeopathic-coded active ingredient	Candidate only; no RUCAM score available (in AEMS/FAERS database)
23688760	Kesimpta	Hepatitis;Alanine Aminotransferase Increased;Gamma-Glutamyltransferase Increased;Aspartate Aminotransferase Increased;Nasopharyngitis	Other Outcomes	18-APR-2024	NOV-2023	-	-	Ambiguous/non-homeopathic product name with homeopathic-coded active ingredient	Candidate only; no RUCAM score available (in AEMS/FAERS database)

23734335	Erelzi;Fosamax; Otezla;Cosentyx; Imuran;Cimzia;E nbrel;Actemra;Si mponi;Humira;A rava	Joint Injury;Condition Aggravated;Arthr itis;Musculoskele tal Stiffness;Decreas ed Appetite;General Physical Health Deterioration;Fea r Of Injection;Entheso pathy;Alanine Aminotransferase Abnormal;Alanin e Aminotransferase Increased;Periphe ral Swelling;Product Use Issue;C- Reactive Protein Increased;Fatigue ;Arthropathy;Dru g Eruption;Gastroi ntestinal Disorder;Diarrho ea;Abdominal Discomfort;Bloo d Parathyroid Hormone Decreased;Pain;P anniculitis;Aspart ate Aminotransferase Increased;Granul oma;Blood Creatinine Increased;C- Reactive Protein Abnormal;Joint Swelling;Infusion Related Reaction;Red Blood Cell Sedimentation Rate Increased;Osteo myelitis;Blood Pressure Systolic Increased;Hypert ension;Mobility	Other Outcomes;Hospit alized;Disabled	12-APR-2024	-	Cannabis Sativa Flowering Top	-	Mixed/multi- product record; no clear homeopathic name	Candidate only; no RUCAM score available (in AEMS/FAERS database)
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		Decreased;Hypercalcaemia;Musculoskeletal Disorder;Arthralgia;Basal Cell Carcinoma							
23083042	-	Eye Disorder;Visual Impairment;Jaundice	Other Outcomes	18-OCT-2023	27-SEP-2023	-	-	Missing suspect product name	Candidate only; no RUCAM score available (in AEMS/FAERS database)
22993405	-	Hepatic Failure	Other Outcomes	27-SEP-2023	-	-	-	Missing suspect product name	Candidate only; no RUCAM score available (in AEMS/FAERS database)
22863842	Maalox Antacid;Dextrose;Vitamin C;Zocor;Dobutamine;Anoro Ellipta;Vitamin B6;Nicotinamide;Prevacid;Breo Ellipta;Dexilant;Novorapid;Tresiba;Vitamin E;Nph Insulin;Anticoagulant Sodium Citrate;Aranesp;Vitamin K1;Citric Acid;Ferrlecit;Picolax (Anhydrous	Somnolence;Myasthenia Gravis;Blood Phosphorus Increased;Gout;Condition Aggravated;Blood Cholesterol Increased;Blood Uric Acid Increased;Hyperlipidaemia;Product Use In Unapproved Indication;Dry Mouth	Died;Disabled;Hospitalized;Other Outcomes;Life Threatening	25-AUG-2023	-	Cholecalciferol;Beta Carotene;Colchicine;Amlodipine;Calcium Gluconate;Disodium Hydrogen Citrate;Ascorbic Acid;Vitamin C;Vitamin D	-	Mixed/multi-product record; no clear homeopathic name	Candidate only; no RUCAM score available (in AEMS/FAERS database)

	Citric Acid\Magnesium Oxide\Sodium Picosulfate);Fosrenol;Fragmin;Otrivin;Atrovent;Bismuth;Dulcolax (Bisacodyl);Coumadin								
22589808	Nicotinamide;Citric Acid;Maalox Antacid;Vitamin C;Ferrlecit;Prevacid;Fragmin;Vitamin B6;Zocor;Fosrenol;Vitamin E;Bismuth;Dexilant;Aranesp;Coumadin;Anticoagulant Sodium Citrate;Picolax (Anhydrous Citric Acid\Magnesium Oxide\Sodium Picosulfate);Tresiba;Dulcolax (Bisacodyl);Breo Ellipta;Vitamin K1;Dobutamine;Atrovent;Novorapid;Dextrose;Anoro Ellipta;Otrivin;Nph Insulin	Sepsis;General Physical Health Deterioration;Aspartate Aminotransferase Increased;Stress; Multiple Organ Dysfunction Syndrome; Ventricular Fibrillation;Aortic Stenosis;Cardiogenic Shock;End Stage Renal Disease;Hyponatraemia	Life Threatening;Hospitalized;Disabled;Other Outcomes;Died	19-JUN-2023	01-JUN-2020	Vitamin D;Vitamin C;Colchicine;Disodium Hydrogen Citrate;Ascorbic Acid;Cholecalciferol;Amlodipine; Beta Carotene;Calcium Gluconate	-	Mixed/multi-product record; no clear homeopathic name	Candidate only; no RUCAM score available (in AEMS/FAERS database)
22589803	Anticoagulant Sodium Citrate;Picolax (Anhydrous Citric Acid\Magnesium Oxide\Sodium Picosulfate);Otrivin;Aranesp;Vitamin K1;Vitamin C;Fosrenol;Coumadin;Anoro Ellipta;Prevacid;	Myasthenia Gravis;Gout;Blood Uric Acid Increased;Hyperlipidaemia;Dry Mouth;Blood Phosphorus Increased;Condition Aggravated;Blood Cholesterol Increased;Somnolence	Disabled;Hospitalized;Other Outcomes;Life Threatening;Died	19-JUN-2023	-	Amlodipine;Vitamin D;Calcium Gluconate;Disodium Hydrogen Citrate;Colchicine;Ascorbic Acid;Beta Carotene;Vitamin C;Cholecalciferol	-	Mixed/multi-product record; no clear homeopathic name	Candidate only; no RUCAM score available (in AEMS/FAERS database)

	Dexilant;Ferrelecit;Fragmin;Vitamin B6;Dobutamine;Dulcolax (Bisacodyl);Citric Acid;Breo Ellipta;Nicotinamide;Zocor;Novorapid;Tresiba;Atrovent;Dextrose;Vitamin E;Nph Insulin;Maalox Antacid;Bismuth								
21811516	Vitamin E;Fiasp;Tresiba;Fragmin;Dulcolax (Bisacodyl);Anticoagulant Sodium Citrate;Vitamin C;Prevacid;Fosrenol;Novorapid;Ferrelecit;Ascorbic Acid\Peg-3350\Potassium Chloride\Sodium (Ascorbate/Chloride/Sulfate);Atrovent;Aranesp;Vitamin K1;Dobutamine;Dextrose;Dexilant	Drug Therapy;Appendicitis;Constipation;Sepsis;Analgesic Therapy;Multiple Organ Dysfunction Syndrome;Vomiting;Ascites;Anaemia;Drug Intolerance;Sleep Disorder Therapy;Nausea;Condition Aggravated;Drug Hypersensitivity;Stress;Ventricular Fibrillation;Swelling;Iron Deficiency;Intentional Product Misuse;Hyperphosphataemia;General Physical Health Deterioration;Bacterial Infection;Abdominal Distension;Blood Cholesterol Increased;Blood Uric Acid Increased;Dyspnoea;Hypophosphataemia;Diabetes Mellitus;Thrombosis;Abdominal	Disabled;Other Outcomes;Hospitalized;Died	02-FEB-2023	2020	-	-	Mixed/multi-product record; no clear homeopathic name	Candidate only; no RUCAM score available (in AEMS/FAERS database)

		Pain;Incorrect Route Of Product Administration;Sleep Disorder;Blood Phosphorus Increased;Neuralgia;Somnolence;Cardiogenic Shock;Dry Mouth;Appendicolith;Pulmonary Embolism;Myasthenia Gravis;Death;Off Label Use;Hyponatraemia;Chronic Obstructive Pulmonary Disease							
21932663	-	Feeling Abnormal;Malaise;Heart Rate Irregular;Overdose;Near Death Experience;Liver Disorder;Palpitations;Emotional Distress;Vomiting;Angina Pectoris;Dyspnoea	Other Outcomes	31-JAN-2023	28-DEC-2022	Arnica Montana Flower	-	Missing suspect product name	Candidate only; no RUCAM score available (in AEMS/FAERS database)
21816702	Heroin;Arnica Montana (Homeopathic)	Injection Site Mass;Hepatitis C Virus Test Positive;Deep Vein Thrombosis;Abscess;Staphylococcal Bacteraemia;Blood Culture Positive;Pulmonary Infarction;Off Label Use;Drug Abuse;Lung Abscess	Hospitalized;Other Outcomes	04-JAN-2023	21-AUG-2021	-	-	Other named homeopathic/remedy product	Candidate only; no RUCAM score available (in AEMS/FAERS database)

18853128	Otrivin;Fragmin; Dextrose;Fosrenol;Dobutamine;Dexilant;Atrovent;Dulcolax (Bisacodyl);Aranesp;Ringers And Dextrose Solution;Heparin Sodium In Dextrose;Prevacid	Blood Cholesterol Increased;Ventricular Fibrillation;Abdominal Pain;Appendicitis;Nausea;Ascites;Death;Stress;Constipation;Somnolence;Incorrect Route Of Product Administration;Sepsis;Multiple Organ Dysfunction Syndrome;Hyponatraemia;General Physical Health Deterioration;Dry Mouth;Blood Uric Acid Increased;Appendicitis;Abdominal Distension;Drug Intolerance;Cardiogenic Shock;Off Label Use;Myasthenia Gravis;Blood Phosphorus Increased;Vomiting;Condition Aggravated	Died;Disabled;Other Outcomes	20-OCT-2022	05-JUN-2021	Potassium Chloride/Riboflavin 5'-Phosphate Sodium;Cholecalciferol;Disodium Hydrogen Citrate;Potassium Chloride	-	Other named homeopathic/remedy product	Candidate only; no RUCAM score available (in AEMS/FAERS database)
20405156	-	Adverse Drug Reaction;Autoimmune Hepatitis;Drug-Induced Liver Injury;Hepatitis Viral	Life Threatening;Other Outcomes;Required Intervention	30-JAN-2022	01-DEC-2018	Viiibryd;Probiotics Nos	-	Missing suspect product name	Candidate only; no RUCAM score available (in AEMS/FAERS database)
19944012	-	Hepatic Enzyme Increased	Hospitalized	12-OCT-2021	-	Tylenol	-	Missing suspect product name	Candidate only; no RUCAM score available (in AEMS/FAERS database)
19912421	-	Vomiting;Hepatic Enzyme Increased;Diarrhoea;Lethargy;Hepatic Failure	Life Threatening	02-OCT-2021	22-SEP-2021	-	-	Missing suspect product name	Candidate only; no RUCAM score available (in

									AEMS/FAERS database)
18252122	-	Decreased Appetite;Hepatic Encephalopathy; Fatigue;Toxicity To Various Agents;Ammonia Increased;Hypotension;Liver Transplant;Hepatitis;Nausea;Coagulopathy;Malaise;International Normalised Ratio Increased;Chromaturia;Multiple Sclerosis;Vomiting;Incorrect Dose Administered;Hepatic Failure	Disabled;Hospitalized;Life Threatening;Other Outcomes	09-SEP-2020	17-JUL-2020	-	-	Missing suspect product name	Candidate only; no RUCAM score available (in AEMS/FAERS database)
16439855	Keytruda	Hepatic Failure;Autoimmune Hepatitis;Pneumonitis	Died;Other Outcomes	14-OCT-2019	APR-2019	-	-	Ambiguous/non-homeopathic product name with homeopathic-coded active ingredient	Candidate only; no RUCAM score available (in AEMS/FAERS database)
16718825	-	Autoimmune Hepatitis	Other Outcomes;Required Intervention;Life Threatening;Disabled	02-JUL-2019	01-DEC-2018	Prednisone;Calcium;Probiotics Nos;Potassium Chloride;Imuran; Magnesium;Laxix;Omeprazole	-	Missing suspect product name	Candidate only; no RUCAM score available (in AEMS/FAERS database)
16206810	-	Hepatic Enzyme Increased	Non-Serious	16-APR-2019	-	-	-	Missing suspect product name	Candidate only; no RUCAM score available (in AEMS/FAERS database)
14952766	Ritalin;Lyrica;Pseudoephedrine;Fluoxetine	Intentional Overdose;Intentional Self-Injury;Suicide Attempt;Product Administration Error;Liver Function Test Abnormal;Coagulopathy	Hospitalized	30-MAY-2018	-	-	Maduemem K, Adedokun C, Umana E. Presentations and preceding factors of drug overdose amongst adolescents admitted to a large regional hospital. Irish Medical Journal	Mixed/multi-product record; no clear homeopathic name	Candidate only; no RUCAM score available (in AEMS/FAERS database)

							2018;111 (4):731.		
14528246	Questran;Medorrhinum;Envarsus Xr;Myfortic;Singulair	Hepatic Cytolysis;Transaminases Increased	Other Outcomes	14-FEB-2018	28-NOV-2017	-	-	Mixed/multi-product record; no clear homeopathic name	Candidate only; no RUCAM score available (in AEMS/FAERS database)
13875872	-	Nausea;White Blood Cell Count Decreased;Headache;Vomiting;Hepatic Enzyme Increased;Pyrexia	Hospitalized	11-AUG-2017	14-JUL-2017	-	-	Missing suspect product name	Candidate only; no RUCAM score available (in AEMS/FAERS database)
13416719	Arnica Montana (Homeopathic);Lyrica;Nexium;Alendronate;Oxycontin;Dafalgan	Hepatocellular Injury	Hospitalized	07-APR-2017	19-JAN-2017	Enoxaparin Sodium;Calcium\Cholecalciferol; Movicol;Solu-Medrol;Magnesium Aspartate Hydrochloride;Sodium Picosulfate	-	Other named homeopathic/remedy product	Candidate only; no RUCAM score available (in AEMS/FAERS database)
13410698	Nexium;Dafalgan;Oxycontin;Arnica Montana (Homeopathic);Opioid;Lyrica	Hepatocellular Injury	Hospitalized	06-APR-2017	19-JAN-2017	Movicol;Enoxaparin Sodium;Magnesium Aspartate Hydrochloride;Sodium Picosulfate;Solu-Medrol;Cerave;Calcium\Cholecalciferol	-	Other named homeopathic/remedy product	Candidate only; no RUCAM score available (in AEMS/FAERS database)
12346381	-	Hepatitis	Other Outcomes	06-MAY-2016	05-APR-2016	-	-	Missing suspect product name	Candidate only; no RUCAM score available (in AEMS/FAERS database)
12200633	Spigelia Anthelmia;Mag Phos 6x	Nausea;Tremor;Falls;Liver Disorder;Abdominal Pain Upper;Infection	Other Outcomes;Hospitalized	22-MAR-2016	-	-	-	Other named homeopathic/remedy product	Candidate only; no RUCAM score available (in AEMS/FAERS database)

12187924	-	Abdominal Distension; Liver Transplant; Abdominal Pain; Viral Infection; Hepatic Encephalopathy; Acute Hepatic Failure	Other Outcomes; Hospitalized	16-MAR-2016	04-DEC-2014	-	-	Missing suspect product name	Candidate only; no RUCAM score available (in AEMS/FAERS database)
11757348	Nauzelin; Cymbalta; Gaba	Hepatic Function Abnormal; Product Quality Issue	Non-Serious	20-NOV-2015	OCT-2015	Clotiazepam; Gabap	-	Mixed/multi-product record; no clear homeopathic name	Candidate only; no RUCAM score available (in AEMS/FAERS database)
11467611	-	Fatigue; Nausea; Vomiting; Blood Bilirubin Increased; Decreased Appetite; Hepatic Enzyme Increased; Aspartate Aminotransferase Increased; Blood Alkaline Phosphatase Increased; Alanine Aminotransferase Increased	Non-Serious	04-SEP-2015	08-MAY-2014	-	-	Missing suspect product name	Candidate only; no RUCAM score available (in AEMS/FAERS database)
10831023	Zicam (Homeopathics); Humira	Stomatitis; Alopecia; Hot Flush; Hepatic Enzyme Increased	Non-Serious	19-FEB-2015	2003	Vitamin D Nos; Calcium; Omega-3 Fatty Acids; Vitamin C; Vitamins; Glucosamine	-	Zicam cluster	Candidate only; no RUCAM score available (in AEMS/FAERS database)
10597840	Concerta	Transaminases Increased	Hospitalized	28-JAN-2015	-	-	-	Ambiguous/non-homeopathic product name with homeopathic-coded active ingredient	Candidate only; no RUCAM score available (in AEMS/FAERS database)
10547399	Calms Forte 4 Kids	Middle Insomnia; Anxiety; Nocturia; Energy Increased; Poor Quality Sleep; Liver Function Test Increased; Renal	Other Outcomes	23-OCT-2014	01-OCT-2014	Pantoprazole	-	Hyland/teething cluster	Candidate only; no RUCAM score available (in AEMS/FAERS database)

		Function Test Abnormal							
10542954	Calms Forte 4 Kids	Creatinine Renal Clearance Increased;Renal Impairment;Liver Function Test Increased;Anxiety;Nocturia;Poor Quality Sleep	Other Outcomes	23-OCT-2014	01-OCT-2014	Pantoprazole	-	Hyland/teething cluster	Candidate only; no RUCAM score available (in AEMS/FAERS database)
10483841	-	Hepatic Failure;Rash;Influenza Like Illness;Syncope;Eosinophilia	Hospitalized;Required Intervention	30-SEP-2014	15-APR-2012	Vitamins	-	Missing suspect product name	Candidate only; no RUCAM score available (in AEMS/FAERS database)
9761074	Xyrem;Zicam (Homeopathics)	Allergy To Animal;Nasal Discomfort;Blood Cholesterol Increased;Sleep Apnoea Syndrome	Other Outcomes	12-DEC-2013	OCT-2013	Fenofibrate	-	Zicam cluster	Candidate only; no RUCAM score available (in AEMS/FAERS database)
9586824	-	White Blood Cell Count Increased;Pyrexia;Hepatic Enzyme Increased;Weight Decreased	Hospitalized	01-OCT-2013	28-AUG-2013	-	-	Missing suspect product name	Candidate only; no RUCAM score available (in AEMS/FAERS database)
9321957	Temodal	Hepatitis;Jaundice	Hospitalized	18-JUL-2013	27-APR-2013	-	-	Ambiguous/non-homeopathic product name with homeopathic-coded active ingredient	Candidate only; no RUCAM score available (in AEMS/FAERS database)
9282675	Baby Teething (Hyland Homeopathic)	Dry Skin;Flushing;Product Quality Issue;Nasopharyngitis;Agitation;Abnormal Behaviour;Seizure;Hepatomegaly	Other Outcomes;Life Threatening	19-APR-2013	25-NOV-2010	-	-	Hyland/teething cluster	Candidate only; no RUCAM score available (in AEMS/FAERS database)
9275455	-	Infection;Hepatic Cirrhosis;Autoimmune Disorder	Other Outcomes	22-MAR-2013	28-FEB-2013	-	-	Missing suspect product name	Candidate only; no RUCAM score available (in AEMS/FAERS database)

8873081	Drainage Milieu	Liver Function Test Increased;Convulsive Threshold Lowered;Self-Injurious Ideation;Generalised Tonic-Clonic Seizure;Mental Disorder;Hypona traemia	Life Threatening	26-OCT-2012	06-AUG-2012	-	-	Ambiguous/non-homeopathic product name with homeopathic-coded active ingredient	Candidate only; no RUCAM score available (in AEMS/FAERS database)
8679781	Augentropfen Nr. 2	Product Delivery Mechanism Issue;Eye Injury;Ocular Hyperaemia	Other Outcomes	03-JUL-2012	07-JUN-2012	-	-	Other named homeopathic/remedy product	Candidate only; no RUCAM score available (in AEMS/FAERS database)
8659766	Cataract Care	Eye Discharge;Visual Impairment;Vitreous Floaters;Jaundice ;Purulence;Ocular Icterus	Other Outcomes	25-JUN-2012	-	-	-	Other named homeopathic/remedy product	Candidate only; no RUCAM score available (in AEMS/FAERS database)
8118209	-	Alanine Aminotransferase Increased;Gamma-Glutamyltransferase Increased;Aspartate Aminotransferase Increased	Other Outcomes	30-AUG-2011	14-AUG-2011	-	-	Missing suspect product name	Candidate only; no RUCAM score available (in AEMS/FAERS database)
7723951	Baby Teething (Hyland Homeopathic)	Abnormal Behaviour;Hepatomegaly;Dry Skin;Product Quality Issue;Nasopharyngitis;Agitation;Flushing;Hyperaesthesia;Seizure	Other Outcomes;Hospitalized	23-NOV-2010	19-OCT-2010	-	-	Hyland/teething cluster	Candidate only; no RUCAM score available (in AEMS/FAERS database)
5959658	Rocephin	Hepatitis Fulminant	Died	12-JAN-2006	21-FEB-2005	-	-	Ambiguous/non-homeopathic product name with homeopathic-coded active ingredient	Candidate only; no RUCAM score available (in AEMS/FAERS database)

E. ANALYSIS OF DEATH OUTCOMES

Case ID	Suspect Product Names	Reactions	Outcomes	Latest FDA Received Date	Event Date	Concomitant Product Names	Literature Reference	Product cluster	Causality status
21684576	Otrivin;Anticoagulant Sodium Citrate;Moviprep;Vitamin B6;Prevnar 13;Vitamin E;Fragmin;Ferrelcit;Dulcolax (Bisacodyl);Ascorbic Acid\Peg-3350\Potassium Chloride\Sodium (Ascorbate/Chloride/Sulfate);Vitamin K1;Dextrose;Novorapid;Osimetrol;Trelegy Ellipta;Citric Acid;Nicotinamide;Ringers And Dextrose Solution;Nucala;Heparin Sodium In Dextrose;Nasonex;Bacteriostatic Sodium Chloride	Appendicitis; Activated Partial Thromboplastin Time Prolonged; Musculoskeletal Stiffness; Ascites; Abdominal Pain; Drug Ineffective; Appendicolith; Sepsis; Nausea; Diabetes Mellitus; Constipation; Off Label Use; Thrombosis; Pleural Effusion; Swelling; Drug Hypersensitivity; Stress; Multiple Organ Dysfunction Syndrome; Condition Aggravated; Blood Test Abnormal; Death; Benign Prostatic Hyperplasia; Somnolence; Bronchopulmon	Other Outcomes; Disabled; Died; Hospitalized; Congenital Anomaly; Life Threatening	15-APR-2026	2020	Riboflavin 5'-Phosphate Sodium; Folic Acid; Potassium Chloride; Bismuth Subnitrate; Hydromorphone; Fiber Therapy (Calcium Polycarbophil); Disodium Hydrogen Citrate; Warfarin; Umeclidinium; Diprosone; Simvastatin; Vitamin D Nos; Amlodipine; Triglycerides, Unspecified Length; Vasopressin; Fish Oil; Iodine; Potassium Chloride\Riboflavin 5'-Phosphate Sodium	-	Other named homeopathic/ remedy product	Association report only; no formal causality score in workbook

		ary Aspergillosis Allergic;Hype rtension;Pulm onary Embolism;Inc orrect Route Of Product Administratio n;Cardiogenic Shock;Upper Respiratory Tract Infection;End Stage Renal Disease;Asthe nia;Malignant Melanoma Stage 0;Dry Mouth;Drug Intolerance;M yasthenia Gravis;Aortic Stenosis;Pneu monia;Chroni c Obstructive Pulmonary Disease;Inapp ropriate Schedule Of Product Administratio n;General Physical Health Deterioration; Gout;Aspirati on;Intentional Product Misuse;Haem optysis;Conge nital Hiatus							
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		Hernia;Sleep Disorder;Ana emia;Blood Phosphorus Increased;Ve ntricular Fibrillation;B acteroides Infection;Vo miting;Ulcer							
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18812254	Dextrose; Coumadin; Breo Ellipta; Metamizol; Vitamin C; Maalox Antacid; Vitamin B6; Dobutamine; Otrivin; Advair Hfa; Fragmin; Ringers And Dextrose Solution; Rocaltrol; Zocor; Trelegy Ellipta; Dexilant; Prevacid; Fosrenol; Dulcolax (Bisacodyl); Vitamin E; Anticoagulant Sodium Citrate; Tamiflu; Diprosone; Ferrlecit; Atrovent; Fiasp; Heparin Sodium In Dextrose; Aranesp; Vitamin K1; Tresiba; Noverapid	Hyperlipidaemia; Aortic Stenosis; Anti coagulant Therapy; Chronic Obstructive Pulmonary Disease; Lower Respiratory Tract Infection; Total Lung Capacity Decreased; Incorrect Route Of Product Administration; Myasthenia Gravis; Ulcer; Blood Test Abnormal; Hypertension; Drug Hypersensitivity; Drug Therapy; Blood Creatinine Increased; Drug Ineffective; Diabetes Mellitus; Condition Aggravated; Ascites; Liver Function Test Increased; Multiple Organ Dysfunction Syndrome; Pulmonary	Life Threatening; Other Outcomes; Congenital Anomaly; Died; Hospitalized; Disabled	10-NOV-2025	2020	Amlodipine; Disodium Hydrogen Citrate; Sodium Picosulfate; Potassium Chloride; Riboflavin 5'-Phosphate Sodium; Dobutamine; Atrovent; Warfarin; Amlodipine Maleate; Cholecalciferol; Calcitriol; Riboflavin 5'-Phosphate Sodium Anhydrous; Dobutamine Hydrochloride; Beta.-Carotene; Pyridoxine Hydrochloride; Dextrose; Simvastatin; Vitamin C; Bisacodyl; Ergocalciferol	-	Other named homeopathic/ remedy product	Association report only; no formal causality score in workbook
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		Embolism;Ba cteroides Infection;Blo od Cholesterol Increased;Iro n Deficiency;A spartate Aminotransfe rase Increased;Pne umonia;Musc uloskeletal Stiffness;Abd ominal Pain;Pleural Effusion;Dry Mouth;Sepsis ;Neuralgia;Hy ponatraemia; Blood Uric Acid Increased;Dea th;Drug Intolerance;L ung Opacity;Trop onin Increased;Inte ntional Product Misuse;Produ ct Use In Unapproved Indication;Ap pendicolith;A ntacid Therapy;Abd ominal Distension;D yspnoea;Naus							
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		ea;Hypophosphataemia;Ventricular Fibrillation;Activated Partial Thromboplastin Time Prolonged;Oedema Peripheral;Thrombosis;Hyperphosphataemia;Sleep Disorder Therapy;Transaminases Increased;Blood Calcium Increased;End Stage Renal Disease;Vomiting;Anaemia;Stress;Gout;Cardiogenic Shock;Swelling;Off Label Use;General Physical Health Deterioration;Analgesic Therapy;Bacterial Infection;Somnolence;Appendicitis;Constipation;Sleep Disorder;Blood Phosphorus Increased							
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24916065	-	Completed Suicide	Died	03-FEB-2025	2023	-	Gummin DD, Mowry JB, Beuhler MC, Spyker DA, Rivers LJ, Feldman R, et al.. 2023 Annual Report of the National Poison Data System (NPDS) from America's Poison Centers: 41st Annual Report. Clinical Toxicology. 2024;1-235	Missing suspect product name	Association report only; no formal causality score in workbook
23729155	Sambucus Nigra;Hydrocodone Bitartrate And Acetaminophen	Cardiac Arrest;Intentional Product Misuse;Respiratory Arrest	Other Outcomes;Died	10-APR-2024	-	-	Gummin DD, Mowry JB, Beuhler MC, Spyker DA, Rivers LJ, Feldman R, Brown K, Pham NPT, Bronstein AC, DesLauriers C. 2022 Annual Report of the National Poison Data System (NPDS) from America's Poison Centers: 40th	Other named homeopathic/remedy product	Association report only; no formal causality score in workbook

							Annual Report. Clinical Toxicology. 2023 Dec 12;61 (10):717-939. doi:https://doi.org/10.1080/15563650.2023.2268981		
23527762	Magnesium Sulfate In Dextrose	Death;Off Label Use	Died	15-FEB-2024	-	-	Literature Article	Ambiguous/non-homeopathic product name with homeopathic-coded active ingredient	Association report only; no formal causality score in workbook
23449766	Hydrocodone Bitartrate And Acetaminophen;Vitamin B12;Sambucus Nigra	Cardio-Respiratory Arrest;Intentional Product Misuse	Died	29-JAN-2024	2022	-	Gummin DD, Mowry JB, Beuhler MC, Spyker DA, Rivers LJ, Feldman R, et al.. 2022 Annual Report of the National Poison Data System (NPDS) from America's Poison Centers: 40th Annual Report. Clinical Toxicology. 2023;61 (10):717-939	Other named homeopathic/remedy product	Association report only; no formal causality score in workbook

23446129	Sambucus Nigra	Intentional Product Misuse; Toxicity To Various Agents	Hospitalized; Died	26-JAN-2024	-	-	-	Other named homeopathic/ remedy product	Association report only; no formal causality score in workbook
23385632	Sambucus Nigra	Intentional Product Misuse; Cardio-Respiratory Arrest	Hospitalized; Other Outcomes; Died	16-JAN-2024	2022	-	Gummin DD, Mowry JB, Beuhler MC, Spyker DA, Rivers LJ, Feldman R, Brown K, Pham NPT, Bronstein AC, DesLauriers C.. 2022 Annual Report of the National Poison Data System (NPDS) from America's Poison Centers: 40th Annual Report. Clinical Toxicology. 2023;61(10):717-939	Other named homeopathic/ remedy product	Association report only; no formal causality score in workbook

23396501	Vitamins Nos	Toxicity To Various Agents;Product Use Issue	Died;Hospitalized	12-JAN-2024	-	-	David D. Gummin, James B. Mowry, Michael C. Beuhler, Daniel A. Spyker, Laura J. Rivers, Ryan Feldman, Kaitlyn Brown, Nathaniel P.T. Pham, Alvin C. Bronstein and Carol DesLauriers. 2022 Annual Report of the National Poison Data System® (NPDS) from America's Poison Centers® : 40th Annual Report. Clinical Toxicology. 2023;61:10:7 17-939	Ambiguous/non-homeopathic product name with homeopathic-coded active ingredient	Association report only; no formal causality score in workbook
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23328672	-	Death	Died;Hospitalized	21-DEC-2023	-	-	Gummin D, Mowry J, Beuhler M, Spyker D, Rivers L, Feldman R, Brown K, Pham N, Bronstein A, DesLauriers C. 2022 Annual Report of the National Poison Data System (NPDS) from America's Poison Centers: 40th Annual Report.. Clinical Toxicology. 2023 DEC 12;61(10):717-939. doi:10.1080/15563650.2023.2268981	Missing suspect product name	Association report only; no formal causality score in workbook
23098459	Zocor;Prevacid;Maalox Antacid;Nicotinamide;Anticoagulant Sodium Citrate;Picolax (Anhydrous Citric Acid\Magnesium Oxide\Sodium	Dyspnoea;Anaemia;Neuralgia;Incorrect Route Of Product Administration;Bacterial Infection;Diabetes Mellitus;Swelling	Other Outcomes;Life Threatening; Hospitalized; Died;Disabled	23-OCT-2023	01-JUN-2020	Beta Carotene;Colchicine;Cholecalciferol;Vitamin D;Vitamin C;Disodium Hydrogen Citrate;Amlodipine	-	Mixed/multi-product record; no clear homeopathic name	Association report only; no formal causality score in workbook

	m Picosulfate);T resiba;Dobuta mine;Dulcola x (Bisacodyl);N ovorapid;Frag min;Dexilant; Vitamin B6;Vitamin C;Vitamin K1;Otrivin;Bi smuth;Ferrlec it;Anoro Ellipta;Arane sp;Atrovent;C itric Acid;Coumad in;Vitamin E;Fosrenol;N ph Insulin;Dextr ose								
23096989	Dexilant;Citric Acid;Tresiba; Ferrlecit;Dob utamine;Maal ox Antacid;Fosre nol;Anoro Ellipta;Dextro se;Fragmin;V itamin B6;Bismuth; Vitamin E;Otrivin;Ant icoagulant Sodium Citrate;Picola x (Anhydrous Citric	Thrombosis;I ntentional Product Misuse;Off Label Use;Drug Hypersensitiv ity;Sleep Disorder;Dru g Intolerance;A ctivated Partial Thromboplast in Time Prolonged	Disabled;Die d;Other Outcomes;Ho spitalized;Lif e Threatening	23-OCT-2023	-	Vitamin D;Vitamin C;Disodium Hydrogen Citrate;Amlo dipine;Cholec alciferol;Colc hicine;Beta Carotene	-	Mixed/multi- product record; no clear homeopathic name	Association report only; no formal causality score in workbook

	Acid\Magnesium Oxide\Sodium Picosulfate); Atrovent;Zocor;Novorapid; Vitamin C;Aranesp;Cumadin;Dulcolax (Bisacodyl);Nph Insulin;Nicotinamide;Prevacid								
22871828	Breo Ellipta;Dextrose;Fragmin;Atrovent;Maalox Antacid;Tresiba;Prevacid;Nicotinamide;Bismuth;Novorapid;Dobutamine;Picolax (Anhydrous Citric Acid\Magnesium Oxide\Sodium Picosulfate); Dexilant;Dulcolax (Bisacodyl);Vitamin C;Nph Insulin;Citric Acid;Aranesp;Vitamin B6;Fosrenol;	Constipation; Ulcer;Vomiting;Abdominal Pain;Troponin Increased;Appendicolith;Ascites;Nausea; Bacteroides Infection;Abdominal Distension;Appendicitis	Died;Hospitalized;Disabled;Other Outcomes	28-AUG-2023	01-JUN-2020	Vitamin D;Colchicine; Beta Carotene;Cholecalciferol;Disodium Hydrogen Citrate;Amlodipine	-	Mixed/multi-product record; no clear homeopathic name	Association report only; no formal causality score in workbook

	Zocor;Ferrlec it;Vitamin E;Anoro Ellipta;Vitami n K1;Anticoagu lant Sodium Citrate;Otrivi n								
22864041	Fosrenol;Vita min E;Nph Insulin;Dulco lax (Bisacodyl);A noro Ellipta;Fragm in;Citric Acid;Vitamin B6;Dexilant; Coumadin;At rovent;Nicoti namide;Otrivi n;Dobutamine ;Zocor;Picola x (Anhydrous Citric Acid\Magnesi um Oxide\Sodiu m Picosulfate); Dextrose;Maa lox Antacid;Aran esp;Novorapi d;Anticoagula nt Sodium Citrate;Tresib a;Prevacid;Fe rrlecit;Vitami n C;Bismuth	Thrombosis; Activated Partial Thromboplast in Time Prolonged;Of f Label Use;Drug Hypersensitiv ity;Intentional Product Misuse;Drug Intolerance;Sl eep Disorder	Disabled;Hos pitalized;Died ;Other Outcomes;Lif e Threatening	25-AUG- 2023	-	Disodium Hydrogen Citrate;Vitam in D;Amlodipin e;Beta Carotene;Cho lecalciferol;C olchicine;Vita min C	-	Mixed/multi- product record; no clear homeopathic name	Association report only; no formal causality score in workbook

22863842	Maalox Antacid;Dextrose;Vitamin C;Zocor;Dobutamine;Anoro Ellipta;Vitamin B6;Nicotinamide;Prevacid;Breo Ellipta;Dexilant;Novorapid;Tresiba;Vitamin E;Nph Insulin;Anticoagulant Sodium Citrate;Aranesp;Vitamin K1;Citric Acid;Ferrlecit;Picolax (Anhydrous Citric Acid\Magnesium Oxide\Sodium Picosulfate);Fosrenol;Fragmin;Otrivin;Atrovent;Bismuth;Dulcolax (Bisacodyl);C oumadin	Somnolence; Myasthenia Gravis;Blood Phosphorus Increased;Gout;Condition Aggravated;Blood Cholesterol Increased;Blood Uric Acid Increased;Hyperlipidaemia;Product Use In Unapproved Indication;Dry Mouth	Died;Disabled;Hospitalized;Other Outcomes;Life Threatening	25-AUG-2023	-	Cholecalciferol;Beta Carotene;Colchicine;Amlodipine;Calcium Gluconate;Disodium Hydrogen Citrate;Ascorbic Acid;Vitamin C;Vitamin D	-	Mixed/multi-product record; no clear homeopathic name	Association report only; no formal causality score in workbook
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22863709	Prevacid;Bismuth;Dextrose;Maalox Antacid;Aranesp;Fragmin;Citric Acid;Dobutamine;Nicotinamide;Atrovent;Vitamin C;Vitamin K1;Vitamin E;Picolax (Anhydrous Citric Acid\Magnesium Oxide\Sodium Picosulfate);Otrivin;Fosrenol;Anticoagulant Sodium Citrate;Vitamin B6;Ferrlecit;Coumadin;Breo Ellipta;Novorapid;Anoro Ellipta;Tresiba;Dulcolax (Bisacodyl);Zinc;Nph Insulin;Dextilant	Iron Deficiency;Hypertension;Hyperphosphataemia;Chronic Obstructive Pulmonary Disease;Death;Pulmonary Embolism;Hypophosphataemia	Disabled;Life Threatening;Died;Other Outcomes;Hospitalized	25-AUG-2023	-	Disodium Hydrogen Citrate;Vitamin D;Cholecalciferol;Colchicine;Calcium Gluconate;Amlodipine;Beta Carotene	-	Mixed/multi-product record; no clear homeopathic name	Association report only; no formal causality score in workbook
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22862359	Dexilant; Coumadin; Vitamin E; Dextrose; Vitamin C; Tresiba; Fosrenol; Picolax (Anhydrous Citric Acid/Magnesium Oxide/Sodium Picosulfate); Dulcolax (Bisacodyl); Fragmin; Otrivin; Novorapid; Prevacid; Atrovent; Maalox Antacid; Nph Insulin; Anticoagulant Sodium Citrate; Zocor; Citric Acid; Ferrlecit; Vitamin K1; Bismuth; Nicotinamide; Vitamin B6; Aranesp; Dobutamine; Anoro Ellipta	Bacterial Infection; Incorrect Route Of Product Administration; Diabetes Mellitus; Swelling; Neuralgia; Dyspnoea; Anaemia	Hospitalized; Other Outcomes; Disabled; Died; Life Threatening	24-AUG-2023	01-JUN-2020	Colchicine; Vitamin D; Vitamin C; Cholecalciferol; Beta Carotene; Amlodipine; Disodium Hydrogen Citrate	-	Mixed/multi-product record; no clear homeopathic name	Association report only; no formal causality score in workbook
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20233220	Fosrenol;Nov orapid;Otrivin ;Ferrlecit;Tres iba;Fragmin; Bismuth;Citric Acid;Zocor;Anticoagulant Sodium Citrate;Breo Ellipta;Maalox Antacid;Anoro Ellipta;Dexilant;Dextrose;Nph Insulin;Arane sp;Vitamin C;Picolax (Anhydrous Citric Acid\Magnesium Oxide\Sodium Picosulfate); Vitamin K1;Atrovent; Dobutamine; Prevacid;Dulcolax (Bisacodyl);Vitamin B6;Nicotinamide;Vitamin E	Troponin Increased;Bacteroides Infection;Appendicitis;Constipation;Abdominal Pain;Abdominal Distension;Vomiting;Ulcer;Appendicolith;Ascites;Nausea	Other Outcomes;Disabled;Hospitalized;Died;Life Threatening	24-AUG-2023	01-JUN-2020	Cholecalciferol;Vitamin C;Colchicine; Amlodipine; Disodium Hydrogen Citrate;Vitamin D;Beta Carotene	-	Mixed/multi-product record; no clear homeopathic name	Association report only; no formal causality score in workbook
16699669	Standardized Bermuda Grass Pollen;Johnson Grass Pollen;Tree	Cardiopulmonary Failure;Drug Ineffective;Coma	Died;Hospitalized	30-JUL-2023	2015	Advair Hfa	-	Mixed/multi-product record; no clear homeopathic name	Association report only; no formal causality score in workbook

	Pollen;Dog Epithelia								
22589797	Anoro Ellipta;Fosrenol;Nph Insulin;Vitamin B6;Fragmin;Ferrelecit;Zocor;Coumadin;Otrivin;Dobutamine;Dulcolax (Bisacodyl);Picolax (Anhydrous Citric Acid\Magnesium Oxide\Sodium Picosulfate);Citric Acid;Nicotinamide;Novorpid;Maalox Antacid;Tresiba;Atrovent;Dextrose;Vitamin K1;Prevacid;Vitamin E;Anticoagulant Sodium Citrate;Aranesp;Vitamin C;Dexilant;Bismuth	Thrombosis; Off Label Use;Sleep Disorder;Drug Intolerance;Drug Hypersensitivity;Activated Partial Thromboplastin Time Prolonged;Intentional Product Misuse	Hospitalized; Disabled;Died;Other Outcomes;Life Threatening	26-JUN-2023	-	Vitamin C;Beta Carotene;Colchicine;Disodium Hydrogen Citrate;Vitamin D;Cholecalciferol;Amlodipine	-	Mixed/multi-product record; no clear homeopathic name	Association report only; no formal causality score in workbook

22541977	Vitamin E; Vitamin B6; Coumadin; Citric Acid; Ferlecit; Dexilant; Atrivent; Vitamin C; Bismuth; Norovorapid; Prevacid; Picolax (Anhydrous Citric Acid/Magnesium Oxide/Sodium Picosulfate); Anoro Ellipta; Anticoagulant Sodium Citrate; Nph Insulin; Otrivin; Dulcolax (Bisacodyl); Dextrose; Zocor; Vitamin K1; Dobutamine; Aranesp; Fosrenol; Fragmin; Nicotinamide; Maalox Antacid; Treiba	Swelling; Anemia; Neuralgia; Dyspnoea; Incorrect Route Of Product Administration; Bacterial Infection; Diabetes Mellitus	Died; Life Threatening; Disabled; Hospitalized; Other Outcomes	26-JUN-2023	01-JUN-2020	Colchicine; Disodium Hydrogen Citrate; Amlodipine; Beta Carotene; Vitamin D; Vitamin C; Cholecalciferol	-	Mixed/multi-product record; no clear homeopathic name	Association report only; no formal causality score in workbook
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22589802	Novorapid;Zocor;Fosrenol;Nicotinamide;Coumadin;Atrovent;Bismuth;Anticoagulant Sodium Citrate;Prevacid;Fragmin;Otrivin;Tresiba;Nph Insulin;Maalox Antacid;Dextrose;Vitamin C;Dulcolax (Bisacodyl);Ferrelcit;Vitamin B6;Citric Acid;Aranesp;Dexilant;Breo Ellipta;Picolax (Anhydrous Citric Acid\Magnesium Oxide\Sodium Picosulfate);Vitamin K1;Dobutamine;Anoro Ellipta;Vitamin E	Pulmonary Embolism;Chronic Obstructive Pulmonary Disease;Death;Hypertension;Iron Deficiency;Hypophosphataemia;Hyperphosphataemia	Hospitalized; Disabled; Died; Life Threatening; Other Outcomes	23-JUN-2023	-	Disodium Hydrogen Citrate;Vitamin C;Beta Carotene;Amlodipine;Ascorbic Acid;Calcium Gluconate;Colchicine;Vitamin D;Cholecalciferol	-	Mixed/multi-product record; no clear homeopathic name	Association report only; no formal causality score in workbook
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22589808	Nicotinamide; Citric Acid; Maalox Antacid; Vitamin C; Ferrlecit; Prevacid; Fragma; Vitamin B6; Zocor; Fosrenol; Vitamin E; Bismuth; Dexilant; Aranesp; Coumadin; Anticoagulant Sodium Citrate; Picolax (Anhydrous Citric Acid\Magnesium Oxide\Sodium Picosulfate); Tiresiba; Dulcolax (Bisacodyl); Breo Ellipta; Vitamin K1; Dobutamine; Atrovent; Novorapid; Dextrose; Anoro Ellipta; Otrivin; Nph Insulin	Sepsis; General Physical Health Deterioration; Aspartate Aminotransferase Increased; Stress; Multiple Organ Dysfunction Syndrome; Ventricular Fibrillation; Aortic Stenosis; Cardiogenic Shock; End Stage Renal Disease; Hypo natraemia	Life Threatening; Hospitalized; Disabled; Other Outcomes; Died	19-JUN-2023	01-JUN-2020	Vitamin D; Vitamin C; Colchicine; Disodium Hydrogen Citrate; Ascorbic Acid; Cholecalciferol; Amlodipine; Beta Carotene; Calcium Gluconate	-	Mixed/multi-product record; no clear homeopathic name	Association report only; no formal causality score in workbook
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22589803	Anticoagulant Sodium Citrate;Picola x (Anhydrous Citric Acid\Magnesi um Oxide\Sodiu m Picosulfate); Otrivin;Arane sp;Vitamin K1;Vitamin C;Fosrenol;C oumadin;Ano ro Ellipta;Prevac id;Dexilant;F errlecit;Fragm in;Vitamin B6;Dobutami ne;Dulcolax (Bisacodyl);C itric Acid;Breo Ellipta;Nicoti namide;Zocor ;Novorapid;T resiba;Atrove nt;Dextrose;V itamin E;Nph Insulin;Maalo x Antacid;Bism uth	Myasthenia Gravis;Gout; Blood Uric Acid Increased;Hy perlipidaemia ;Dry Mouth;Blood Phosphorus Increased;Co ndition Aggravated;B lood Cholesterol Increased;So mnolence	Disabled;Hos pitalized;Othe r Outcomes;Lif e Threatening; Died	19-JUN-2023	-	Amlodipine; Vitamin D;Calcium Gluconate;Di sodium Hydrogen Citrate;Colchi cine;Ascorbic Acid;Beta Carotene;Vita min C;Cholecalcif erol	-	Mixed/multi- product record; no clear homeopathic name	Association report only; no formal causality score in workbook
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21811516	Vitamin E;Fiasp;Tresiba;Fragmin;Dulcolax (Bisacodyl);Anticoagulant Sodium Citrate;Vitamin C;Prevacid;Fosrenol;Novorapid;Ferrlecit;Ascorbic Acid\Peg-3350\Potassium Chloride\Sodium (Ascorbate/Chloride/Sulfate);Atrovent;Aranesp;Vitamin K1;Dobutamine;Dextrose;Dexilant	Drug Therapy;Appendicitis;Constipation;Sepsis;Analgesic Therapy;Multiple Organ Dysfunction Syndrome;Vomiting;Ascites;Anaemia;Drug Intolerance;Sleep Disorder Therapy;Nausea;Condition Aggravated;Drug Hypersensitivity;Stress;Ventricular Fibrillation;Swelling;Iron Deficiency;Intentional Product Misuse;Hyperphosphataemia;General Physical Health Deterioration;Bacterial Infection;Abdominal Distension;Blood Cholesterol Increased;Blood Uric Acid Increased;Dyspnoea;Hypop	Disabled;Other Outcomes;Hospitalized;Died	02-FEB-2023	2020	-	-	Mixed/multi-product record; no clear homeopathic name	Association report only; no formal causality score in workbook
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		hosphataemia ;Diabetes Mellitus;Thro mbosis;Abdo minal Pain;Incorrect Route Of Product Administratio n;Sleep Disorder;Bloo d Phosphorus Increased;Ne uralgia;Somn olence;Cardio genic Shock;Dry Mouth;Appen dicolith;Pulm onary Embolism;M yasthenia Gravis;Death; Off Label Use;Hyponatr aemia;Chroni c Obstructive Pulmonary Disease							
18853128	Otrivin;Frag min;Dextrose; Fosrenol;Dob utamine;Dexil ant;Atrovent; Dulcolax (Bisacodyl);A ranesp;Ringer s And Dextrose Solution;Hep arin Sodium In	Blood Cholesterol Increased;Ve ntricular Fibrillation;A bdominal Pain;Appendi colith;Nausea ;Ascites;Deat h;Stress;Cons tipation;Somn olence;Incorr ect Route Of	Died;Disable d;Other Outcomes	20-OCT-2022	05-JUN-2021	Potassium Chloride\Ribo flavin 5'- Phosphate Sodium;Chol ecalciferol;Di sodium Hydrogen Citrate;Potass ium Chloride	-	Other named homeopathic/ remedy product	Association report only; no formal causality score in workbook

	Dextrose;Prev acid	Product Administration;Sepsis;Multiple Organ Dysfunction Syndrome;Hyponatraemia;General Physical Health Deterioration;Dry Mouth;Blood Uric Acid Increased;Appendicitis;Abdominal Distension;Drug Intolerance;Cardiogenic Shock;Off Label Use;Myasthenia Gravis;Blood Phosphorus Increased;Vomiting;Condition Aggravated							
21346474	-	Cerebrovascular Accident;Blood Viscosity Decreased	Died	17-SEP-2022	2022	Xarelto	-	Missing suspect product name	Association report only; no formal causality score in workbook
19252226	-	Shock;Unresponsive To Stimuli;Pain	Died	12-MAY-2021	20-JUN-2012	Morphine	-	Missing suspect product name	Association report only; no formal causality

									score in workbook
19072017	Arnica Montana 30c	Overdose;Gait Inability;Confusional State;Renal Failure;Asthenia;Delirium;Poisoning;Somnolence;Feeling Cold;Organ Failure;Diarrhoea;Fatigue	Hospitalized;Died;Other Outcomes	07-MAY-2021	MAR-2021	Vitamins	-	Other named homeopathic/remedy product	Association report only; no formal causality score in workbook
17359209	-	Toxicity To Various Agents;Substance Abuse;Chemical Poisoning	Other Outcomes;Died	30-OCT-2020	-	-	-	Missing suspect product name	Association report only; no formal causality score in workbook
18168748	-	Product Quality Issue;Heart Rate Increased;Feeling Abnormal;Product Use In Unapproved Indication;Middle Insomnia;Near Death Experience;Fatigue	Died;Other Outcomes	18-AUG-2020	-	-	-	Missing suspect product name	Association report only; no formal causality score in workbook
16439855	Keytruda	Hepatic Failure;Autoimmune Hepatitis;Pneumonitis	Died;Other Outcomes	14-OCT-2019	APR-2019	-	-	Ambiguous/non-homeopathic product name with	Association report only; no formal causality

								homeopathic-coded active ingredient	score in workbook
16850182	-	Myocardial Infarction;Product Use In Unapproved Indication	Died	06-SEP-2019	22-MAR-2018	-	-	Missing suspect product name	Association report only; no formal causality score in workbook
16179116	-	Therapy Cessation;Polymenorrhoea; Paraesthesia; Coordination Abnormal;Hair Colour Changes	Other Outcomes;Died	07-MAR-2019	-	-	-	Missing suspect product name	Association report only; no formal causality score in workbook
15551248	-	Toxicity To Various Agents;Chemical Poisoning;Substance Abuse	Died;Other Outcomes	25-OCT-2018	-	-	-	Missing suspect product name	Association report only; no formal causality score in workbook
13841182	Baby Teething (Hyland Homeopathic)	Death	Died	07-AUG-2017	2016	-	-	Hyland/teething cluster	Association report only; no formal causality score in workbook
13805153	Baby Teething (Hyland Homeopathic)	Death Of Relative;Injury	Died	28-JUL-2017	2015	-	-	Hyland/teething cluster	Association report only; no formal causality score in workbook
13532975	Baby Teething (Hyland Homeopathic)	Death	Died	10-MAY-2017	-	-	-	Hyland/teething cluster	Association report only; no formal causality score in workbook

13423877	Childrens Tylenol	Death	Died	10-APR-2017	19-JAN-2014	-	-	Other named homeopathic/ remedy product	Association report only; no formal causality score in workbook
12964213	Baby Teething (Hyland Homeopathic)	Asphyxia; Seizure	Other Outcomes; Died	22-NOV-2016	JUN-2016	-	-	Hyland/teething cluster	Association report only; no formal causality score in workbook
12950114	Insomnia Relief	Mental Disorder; Myocardial Infarction	Disabled; Died; Hospitalized	16-NOV-2016	-	-	-	Other named homeopathic/ remedy product	Association report only; no formal causality score in workbook
12870543	Baby Teething (Hyland Homeopathic)	Death	Died	20-OCT-2016	11-MAR-2014	-	-	Hyland/teething cluster	Association report only; no formal causality score in workbook
12864950	Baby Teething (Hyland Homeopathic)	Meningitis Pneumococcal; Sepsis	Died	19-OCT-2016	05-MAY-2005	-	-	Hyland/teething cluster	Association report only; no formal causality score in workbook
12853871	Baby Teething (Hyland Homeopathic)	Cardiac Failure	Died	17-OCT-2016	-	Vitamins	-	Hyland/teething cluster	Association report only; no formal causality score in workbook
12818734	Baby Teething (Hyland Homeopathic)	Vomiting; Respiratory Arrest; Seizure; Fall	Died	06-OCT-2016	17-SEP-2016	-	-	Hyland/teething cluster	Association report only; no formal causality score in workbook

11603004	-	Death	Died	05-OCT-2015	SEP-2015	-	-	Missing suspect product name	Association report only; no formal causality score in workbook
11538824	-	Tooth Abscess;Malaise;Anaphylactic Shock	Died	22-SEP-2015	15-OCT-2014	Probiotics Nos;Xanax;Coreg	-	Missing suspect product name	Association report only; no formal causality score in workbook
10882167	Baby Teething (Hyland Homeopathic)	Agitation;Vomiting	Died	26-FEB-2015	09-JUL-2014	-	-	Hyland/teething cluster	Association report only; no formal causality score in workbook
10723317	Baby Teething (Hyland Homeopathic)	Wrong Technique In Product Usage Process;Vomiting	Died	14-JAN-2015	09-JUL-2014	-	-	Hyland/teething cluster	Association report only; no formal causality score in workbook
10061973	Humira	Completed Suicide	Died	22-MAY-2014	MAR-2014	-	-	Ambiguous/non-homeopathic product name with homeopathic-coded active ingredient	Association report only; no formal causality score in workbook
9820308	Baby Teething (Hyland Homeopathic)	Cardio-Respiratory Arrest;Death; Body Temperature Increased	Died	13-JAN-2014	02-DEC-2013	-	-	Hyland/teething cluster	Association report only; no formal causality score in workbook
9681215	Xenadrine Efx;Seroquel; Campral;Vitamin	Toxicity To Various Agents;Antipsychotic Drug	Died	11-NOV-2013	-	-	-	Mixed/multi-product record; no clear	Association report only; no formal causality

	B1;Wellbutrin XL;Vitamin D Nos	Level Above Therapeutic; Drug Interaction						homeopathic name	score in workbook
9563705	-	Death	Died	18-SEP-2013	20-AUG-2013	-	-	Missing suspect product name	Association report only; no formal causality score in workbook
9379392	Baby Teething (Hyland Homeopathic)	Unresponsive To Stimuli;Lethargy;Fatigue;Pulse Absent	Died	19-APR-2013	17-JUN-2010	-	-	Hyland/teething cluster	Association report only; no formal causality score in workbook
9026575	Baby Teething (Hyland Homeopathic)	Product Quality Issue	Life Threatening; Died	14-DEC-2012	17-OCT-2012	-	-	Hyland/teething cluster	Association report only; no formal causality score in workbook
8901822	Baby Teething (Hyland Homeopathic)	Product Quality Issue	Died	06-NOV-2012	18-OCT-2012	-	-	Hyland/teething cluster	Association report only; no formal causality score in workbook
8901821	Baby Teething (Hyland Homeopathic)	Product Quality Issue	Died	06-NOV-2012	18-OCT-2012	-	-	Hyland/teething cluster	Association report only; no formal causality score in workbook
8475966	Baby Teething (Hyland Homeopathic)	Product Quality Issue;Staring; Irritability;Pyrexia;Hypopnoea	Life Threatening; Other Outcomes;Hospitalized;Congenital Anomaly;Died;Required	26-MAR-2012	20-MAR-2012	-	-	Hyland/teething cluster	Association report only; no formal causality score in workbook

			Intervention; Disabled						
9282683	Baby Teething (Hyland Homeopathic)	Lethargy;Som nolence;Unre sponsive To Stimuli;Pulse Absent;Fatigu e;Abnormal Behaviour	Died	02-FEB-2011	17-JUN-2010	-	-	Hyland/teethi ng cluster	Association report only; no formal causality score in workbook
7774911	-	Sudden Infant Death Syndrome	Died	03-JAN-2011	12-NOV- 2010	-	-	Missing suspect product name	Association report only; no formal causality score in workbook
7763555	Baby Teething (Hyland Homeopathic)	Lethargy;Pers onality Change;Unres ponsive To Stimuli;Fatig ue;Pulse Absent	Died	17-DEC-2010	17-JUN-2010	-	-	Hyland/teethi ng cluster	Association report only; no formal causality score in workbook
7756528	Baby Teething (Hyland Homeopathic)	Toxicity To Various Agents;Circul atory Collapse;Ner vous System Disorder;Prod uct Quality Issue;Seizure	Died	10-DEC-2010	15-APR-2010	-	-	Hyland/teethi ng cluster	Association report only; no formal causality score in workbook
7744127	Baby Teething (Hyland Homeopathic)	Respiratory Arrest	Died	03-DEC-2010	17-OCT-2010	-	-	Hyland/teethi ng cluster	Association report only; no formal causality score in workbook
9282659	Baby Teething (Hyland Homeopathic)	Skin Discolouratio n;Sudden Infant Death	Died;Life Threatening	30-NOV- 2010	16-SEP-2007	-	-	Hyland/teethi ng cluster	Association report only; no formal causality

		Syndrome;Pyrexia;Petit Mal Epilepsy;Seizure							score in workbook
7183306	Vaccinium Macrocarpon Fruit Juice	Haematoma;Pulmonary Hypoplasia;Foetal Disorder;Maternal Drugs Affecting Foetus;Infection;Oligohydramnios;Abortion Induced;Amniotic Cavity Disorder;Amniotic Fluid Volume Decreased	Died;Congenital Anomaly	22-FEB-2010	21-SEP-2009	Ipecac;Pulsatilla;Opium;Sus Scrofa Placenta;Phosphorus;Vaccinium Macrocarpon Fruit Juice;Hamamelis Virginiana Leaf	-	Ambiguous/non-homeopathic product name with homeopathic-coded active ingredient	Association report only; no formal causality score in workbook
6439188	Sedatif Pc;Risperdal	Chills;Death;Feeling Cold;Fatigue;Drug Ineffective;Altered State Of Consciousness;Hunger;Abnormal Behaviour;Oculogyric Crisis;Tremor;Social Avoidant Behaviour;Pyrexia;Polydipsia;Bronchitis;Pulmonary Oedema	Died	30-JAN-2008	01-JUL-2007	Acetaminophen;Amoxicillin	-	Mixed/multi-product record; no clear homeopathic name	Association report only; no formal causality score in workbook

5959658	Rocephin	Hepatitis Fulminant	Died	12-JAN-2006	21-FEB-2005	-	-	Ambiguous/n on- homeopathic product name with homeopathic- coded active ingredient	Association report only; no formal causality score in workbook
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DECLARATION OF SENECA R. SAVAGE, PRESIDENT OF MEDITREND, INC.

I, Seneca R. Savage, declare under penalty of perjury under the laws of the United States that the following is true and correct:

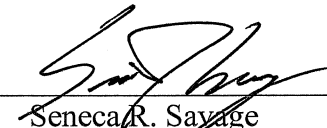
1. I am over 18 years of age and am competent to testify to the facts set out in this declaration. I make this declaration based on my personal knowledge and my experience as President of Meditrend, Inc.
2. Meditrend, Inc. is a homeopathic drug company based in Albuquerque, New Mexico. The company has been in business since 1984. For more than forty years, Meditrend has developed and distributed innovative health products, including over-the-counter products marketed as homeopathic drugs in the United States. Meditrend's products are manufactured through contract manufacturers. Meditrend markets nationwide over 45 different homeopathic formulations.
3. From 1988 until FDA revoked Compliance Policy Guide 400.400 in 2019, Meditrend relied on that guidance as the practical roadmap for doing business lawfully in the homeopathic drug market. We understood that, if Meditrend and its contract manufacturers and suppliers followed the conditions in CPG 400.400, Meditrend could make and market homeopathic drug products without being treated by FDA as selling unapproved new drugs (under 21 U.S.C. 333).
4. On that basis, Meditrend built its compliance practices around CPG 400.400. We expected our contract manufacturers and suppliers to do the same. We have only employed manufacturers that we know complied with the FDA's requirements, including those specified in CPG 400.400.
5. In my experience, Meditrend was not unusual in relying on CPG 400.400. The guidance was widely understood throughout the homeopathic products industry as the standard that allowed responsible companies to plan, manufacture, source ingredients, label products, and sell products with reasonable confidence. It gave companies, suppliers, contract manufacturers, retailers, and investors a clear set of expectations.
6. Meditrend's primary capital investor also relied on CPG 400.400. That investor's financial support was conditioned on Meditrend operating within the CPG 400.400 framework.
7. Since FDA revoked CPG 400.400, Meditrend has found it much more difficult to obtain outside financial support. The commercial lender we have approached has refused to consider a commercial loan after learning that FDA revoked CPG 400.400 and now takes

the position that homeopathic drug products are not legally marketed unless approved as new drugs by FDA. See Exhibit A.

8. The revocation has also affected the supply chain. Several companies that previously manufactured or supplied source ingredients for homeopathic products have reduced the availability of those ingredients or stopped making them altogether. This change followed FDA's revocation of CPG 400.400 and the uncertainty created by FDA's current position.
9. One of Meditrend's contract manufacturers experienced a routine FDA inspection after the revocation of CPG 400.400. During that inspection, FDA inspectors advised that the homeopathic products being manufactured were not compliant with the law because they had not been approved as new drugs. As a result, that manufacturer has largely discontinued production of those products. And, within 24 hours of the inspection, the manufacturer ordered us to remove all of our existing packaged inventory (54 pallets) from the manufacturer's facility. That same manufacturer disallowed Meditrend from that day forward from ever storing any of its homeopathic products at the manufacturer's facility.
10. Before the revocation, source-ingredient suppliers and contract manufacturers were willing to support Meditrend's homeopathic products because CPG 400.400 gave them a defined compliance pathway. After the revocation, that certainty largely disappeared.
11. During the 31 years in which CPG 400.400 was in place, Meditrend created more than 45 homeopathic formulations. We were able to market those products because manufacturers, labelers, suppliers, retailers, and investors could look to CPG 400.400 as a clear compliance framework.
12. That changed after October 25, 2019, when FDA revoked CPG 400.400 and replaced it with a risk-based enforcement approach that does not provide a clear safe harbor. The result for Meditrend has been uncertainty at every level of the business: ingredient sourcing, manufacturing, financing, retail relationships, investment, and long-term planning.
13. After the revocation, Meditrend's principal capital investor no longer wished to invest in the company on the same basis.
14. Meditrend has also had difficulty obtaining reliable production sources for certain essential ingredients, including antigens used in Meditrend's homeopathic allergy formulations. The loss of certainty has also made it difficult to secure investment for brand updates, additional personnel, and expansion of Meditrend's formulations to a wider national market.

15. As a practical matter, Meditrend cannot confidently continue making and expanding its more than 45 homeopathic formulations unless the uncertainty created by the revocation of CPG 400.400 is eliminated.
16. Meditrend has lost commitments from contract manufacturers to obtain source ingredients that are essential to Meditrend's formulations and to future contract manufacturing. In particular, Meditrend's main contract manufacturer has not been able to meet the ingredient-acquisition and validation-testing expectations now being applied to essential ingredients under pharmaceutical drug GMP requirements, as applied to Meditrend's homeopathic products.
17. Meditrend has also incurred substantial legal costs and management time because of the revocation of CPG 400.400. Legal fees have exceeded \$75,000, and Meditrend's principals have spent countless hours addressing the effects of FDA's policy change.
18. Despite these challenges, Meditrend's business history shows that there is continuing consumer demand for its products but slow growth since CPG 400.400 was revoked. Meditrend's gross annual income grew 48% between 2018 and 2019. After revocation of CPG 400.400, Meditrend's annual income growth began to decline from \$3,041,557 in 2019 to only \$3,414,917 in 2020. In the 6 years prior to 2019 (2014 – 2019), Meditrend's average annual growth rate was 16.63% per year. In the 6 years following CPG 400.400 revocation in 2019 (2020-2025), Meditrend's average annual growth rate declined to 1.86% per year. Revenues have experienced modest growth year after year since FDA's 2019 revocation of CPG 400.400.
19. If FDA reinstates CPG 400.400, or adopts an equivalent clear safe-harbor framework for compliant homeopathic products, Meditrend would be able to operate with greater confidence. Meditrend would seek to hire additional people, update and rebrand its product line, expand production, and make its formulations more widely available. Meditrend would experience a higher percentage rate of revenue growth year after year as a result.

Executed on: 9/23/26



Seneca R. Sayage



Date: 09/15/26

Dear Mr. Savage,

After careful consideration of your \$500,000 loan request for Meditrend, Inc., we must regretfully inform you that we are unable to accommodate your request at this time.

The decision to deny this credit is based on the current industry concerns surrounding homeopathic medicine (particularly the withdrawal of CPG 400.400) and income trend inconsistency.

If your industry and financial circumstances change in the future, please do not hesitate to reapply.

Thank you for choosing UMB Bank.

Travis Lewis

Vice President / Relationship Officer I
Small Business Banking Dept

UMB Bank

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