About Compounding

Under federal law, there are specific conditions that must be met for pharmacists or other authorized practitioners to legally compound human drug products. The federal provision is section 503A of the Food, Drug, and Cosmetic Act (FDCA) (21 USC 353a). You can find the full text here.[1] This law defines the substances allowed in human drug compounding. Substances that do not meet the requirements of this law cannot be used in compounding. Some substances, called Category 1 bulk drug substances, are not approved for compounding. They can be used, but only if specific conditions are met as outlined in a federal enforcement discretion policy. This policy is detailed in a federal guidance document. The list of Category 1 bulk drug substances is available here. Currently, the list includes glutathione and methylcobalamin.

Federal law says that human drug compounding must follow United States Pharmacopeia (USP) standards. These standards include provisions for the quality of ingredients in compounded preparations. USP is a nonprofit organization. Its goal is to build trust in the supply of safe, quality medicines. USP standards are accepted by regulators around the world. These standards are based on rigorous science and developed by USP's Expert Committees. The standards boost patient safety. They do this by ensuring safe and quality medicines, dietary supplements, and foods.

The Board is working on regulations for pharmacies. These rules will allow them to compound with Category 1 bulk drug substances such as glutathione and methylcobalamin. The Board's proposed regulations give pharmacies a legal way to compound with these substances under state law. Right now, there is no path to do this in California.

These FAQs were developed to help people understand the issue.

Question: Do the Board's proposed regulations ban the compounding of Category 1 bulk drug substances such as glutathione and methylcobalamin?

Answer: No. The Board's proposed regulations permit compounding with substances such as glutathione and methylcobalamin. This is allowed as long as it follows federal law, federal guidance documents, national standards, and state law, including the Sherman Food, Drug, and Cosmetic Law.

Question: Can firefighters obtain glutathione for at-home inhalation therapy?

Answer: Yes. The Board has confirmed that patient-specific glutathione prescriptions are available from sources licensed to dispense medications in California.

[1] Other federal laws (i.e., section 503B of the FDCA) outline the conditions under which registered outsourcing facilities can compound human drug products.

Question: Have glutathione and methylcobalamin been approved by the FDA for injection or inhalation?

Answer: No. The FDA has not approved these substances for injection or inhalation. Rather, these substances are currently being evaluated by the FDA for possible inclusion on a list of ingredients that can legally be used in compounding.

Question: Has the FDA determined that glutathione and methylcobalamin are safe and effective when administered via injection or inhalation?

Answer: No. The FDA has not determined that these preparations are safe or effective when administered via injection or inhalation.

Question: Why is the Board making these changes to compounding requirements related to Category 1 bulk drug substances?

Answer: Compounded medications give California patients whose needs cannot be met by FDA-approved drugs access to medication that they may need. However, there are risks involved. Nonsterile to sterile compounding of Category 1 bulk drug substances can harm patient health if not done properly. The Board has conducted investigations of compounded preparations, including compounded glutathione, that resulted in harm to patients. It is the Board's goal to protect patients while balancing consumer access.

Question: The Board is aiming to align with which federal laws?

Answer: The Board is aiming to align with section 503A of the federal Food, Drug and Cosmetic Act (FDCA). Section 503A covers human drug compounding. It allows some exemptions from the FDCA[2] for drug products that meet the requirements and are compounded properly. All other parts of the FDCA still apply. This includes the rule against distributing adulterated drugs found in section 301.

The FDA has released guidance on the requirements for compounding under the provisions of section 503A. As included in the guidance, a drug product must be compounded in compliance with the United States Pharmacopeia (USP) chapters on pharmacy compounding. This guidance also includes details on violations that could lead to FDA action, such as:

> "The drug product must not consist in whole or in part of any filthy, putrid, or decomposed substance, or be prepared, packed, or held under insanitary conditions whereby it may have been contaminated with filth or whereby it may

[2] Section 503A generally provides an exemption from the following provisions of the FDCA for drug products compounded by a state-licensed pharmacist or state-licensed physician:

1) Section 501(a)(2)(B) (concerning the requirement to comply with current good manufacturing practice);
2) Section 502(f)(1) (concerning the labeling of drugs with adequate directions for use); and
3) Section 505 (concerning the new drug approval process).

> have been rendered injurious to health. (Sections 501(a)(1) and (a)(2)(A) of the FDCA.)"

Question: I was told the FDA allows for compounding with glutathione and methylcobalamin?

Answer: The FDA has not approved or authorized the compounding of these substances. The FDA has not stated that compounding with these substances is safe in every instance. The FDA has issued guidance[3] that outlines an interim policy. This policy applies when an authorized facility or individual compounds with specific bulk drug substances that FDA is currently evaluating. This would include substances like glutathione and methylcobalamin, but only under very specific conditions.[4] These conditions include that the original manufacturer and all subsequent manufacturers of the bulk drug substance are establishments that are registered under section 510 of the FDCA; that the bulk drug substance is accompanied by a valid Certificate of Analysis; and that the drug product compounded using the bulk drug substance is compounded in compliance with all other conditions of section 503A. This would include, for example, that the compound has not been produced or held under insanitary conditions.

Question: What are examples of insanitary conditions?

Answer: Under section 501(a)(2)(A) of the FDCA, a drug is deemed to be "insanitary" or adulterated "if it has been prepared, packed, or held under insanitary conditions whereby it may have been contaminated with filth, or whereby it may have been rendered injurious to health…" Drug products prepared, packed, or held under insanitary conditions could become contaminated and cause serious adverse events, including death.

The FDA released guidance that describes examples of insanitary conditions that the FDA has observed. In the guidance, the FDA explains: "FDA is issuing this guidance to help compounding facilities and state regulatory agencies understand some examples of what FDA considers to be insanitary conditions that could cause a drug product to become contaminated or rendered injurious to health. These examples are intended to help compounding facilities prevent the occurrence of these and other insanitary conditions. This guidance is also intended to help compounding facilities identify and remediate such insanitary conditions when they already exist." The guidance cites the following as an example of insanitary conditions:

> "Using active ingredients, inactive ingredients, or processing aides, that have or may have higher levels of impurities compared to compendial or pharmaceutical grade equivalents (e.g., ingredients with potentially harmful

[3] The FDA initially released this guidance in 2017. The most recent version of the guidance was released in January 2025.

[4] The FDA's interim enforcement discretion policy only applies to bulk drug substances that appear in "503A Category 1 – Bulk Drug Substances Under Evaluation" on FDA's website at https://www.fda.gov/media/94155/download.

impurities, ingredients labeled with "not for pharmaceutical use" or an equivalent statement)."

Question: If the FDA's guidance on insanitary conditions specifies that using ingredients that may have higher levels of impurities compared to compendial or pharmaceutical grade equivalents is an example of an insanitary condition, how is the Board allowing for pharmacies to compound with Category 1 bulk drug substances that may have higher levels of impurities?

Answer: The Board's proposed regulation related to compounding of Category 1 bulk drug substances includes key parts of the national standards.[5] It also requires facilities to set up a process to ensure the quality of the ingredient.

Question: Has the FDA released findings involving the use of inappropriate ingredients?

Answer: Yes, the FDA has released a number of inspection reports that cite, as part of the findings, the use of inappropriate ingredients. Below are links to a few examples.

Empower Clinic Services, LLC – Inspection dates 10/16/2023 – 12/1/2023 (Observation 3)
La Vita Compounding Pharmacy – Inspection dates 3/4/2020 – 3/11/2020 (Observation 1)
McGuff Compounding Pharmacy Services – Inspection dates 11/12/2019 – 11/22/2019 (Observation 7)

Question: Has the FDA released any other information about the use of inappropriate ingredients?

Answer: Yes, the FDA has released compounding alerts. One alert dated June 7, 2019, is called "FDA highlights concerns with using dietary ingredient glutathione to compound sterile injectables." In October 2024, FDA released information called, "FDA reminds compounders to use ingredients suitable for sterile compounding."

Question: Is the FDA considering glutathione as a substance for inclusion in federal regulations that would legally authorize compounding using glutathione?

Answer: Yes. On June 8, 2022, the Pharmacy Compounding Advisory Committee (PCAC) reviewed glutathione. They considered if it should be added to the list of bulk drug substances that may legally be used to compound drug products. This list is called

[5] Federal and state law require compounding to be performed in compliance with USP chapters on pharmacy compounding, generally USP Chapters 795, 797, 800, 825 and 1163. Most specifically related to compounding glutathione and methylcobalamin, specific provisions included in Chapter 797 related to components are relevant. As an example, Section 9.3.1 of the Chapter provides that all APIs and other components used must be evaluated for suitability for use in sterile drug preparations. Further, Section 9.3.2 provides in part that any component found to be of unacceptable quality must be promptly rejected. Section 9.3.3 also requires that compounding personnel must ascertain before use that a component is of the correct identity and appropriate quality. Any component found to be of unacceptable quality must be promptly rejected. **Note**: These conditions are similar to the guidance from the FDA related to insanitary conditions.

the 503A Bulks List.[6] The nomination included proposed dosage forms including nasal spray, inhalation preparations, and injection. Glutathione was evaluated for 24 uses:

- Skin lightening
- Cystic fibrosis
- Asthma
- Chronic obstructive pulmonary disease
- Chronic lung disease
- Oxidative stress
- Reduction of the side effects of chemotherapy
- Inhibition of chemical induced carcinogenesis
- Prevention of radiation injury
- Treatment of heavy metal poisoning (cadmium and mercury)
- Acetaminophen toxicity
- Autism spectrum disorder
- Alzheimer's disease
- Parkinson's disease
- Major depressive disorder
- Schizophrenia
- Helicobacter pylori infection
- Human immunodeficiency virus infection
- Tuberculosis
- Otitis media
- Peripheral obstructive arterial disease
- Anemia
- Diabetes
- Septic shock

Based on the information it considered, the FDA initially recommended to the PCAC that glutathione **not** be added to the 503A Bulks List.

After considering the FDA's initial recommendation, the majority of the PCAC members voted in favor of adding glutathione to the list.[7] To date, the FDA has not taken any additional action related to glutathione. Additional information is available here.

The PCAC has considered other bulk drug substances for inclusion on the 503A Bulks List. One of these was methylcobalamin, which they considered on June 9, 2021. The FDA initially advised against including methylcobalamin on the 503A Bulks List. Most PCAC

[6] The 503A Bulks List is set forth at 21 CFR 216.23(a). As part of the FDA's evaluation of substances for possible inclusion on the 503A Bulks List, the FDA must convene and consult with the PCAC. (See section 503A(c)(1) of the FDCA.) PCAC recommendations are not binding on the FDA; rather, the FDA considers the PCAC's advice but makes an independent judgment regarding whether particular substances should appear on the 503A Bulks List. (See 84 FR 4696 at p. 4704.) Substances that appear on the 503A Bulks List may legally be used in compounding. The 503A Bulks List is not the same as the 503A Category 1 list. Substances on the 503A Category 1 list (which are under evaluation by the FDA for possible inclusion on the 503A Bulks List) can only be used in compounding pursuant to the conditions set forth in the FDA's interim enforcement discretion policy.

[7] Eight members voted yes, five members voted no, and one member abstained.

members voted in favor of including it.[8] So far, the FDA has not acted further on methylcobalamin. Additional information is available here.

Question: Will the Board enforce its regulations on health care professionals other than those licensed by the Board?

Answer: No. The Board will only enforce its regulations related to compounding on its own licensees

Question: Are the Board's compounding regulations final?

Answer: No. The Board recently released a fourth modified text for a 15-day comment period. The Board will review the comments from the 15-day comment period at its meeting on March 26, 2025.

Note and Disclaimer: The above information is a plain language summary of requirements that apply to compounding, and of common questions about the Board's proposed regulations. It is not legal advice, is not a part of the rulemaking file, and is provided as general guidance only. Compounding is a complex area of pharmacy practice. Stakeholders are encouraged to read referenced provisions of state and federal law, federal guidance documents, USP national standards, and the Board's proposed regulations to gain a full understanding.

[8] Nine members voted yes and five members voted no.