June 9, 2025

WARNING LETTER

Boothwyn Pharmacy LLC
Attention: Arthur J. Dustman
Chief Operating Officer
221 Gale Ln
Kennett Square, PA 19348
adustman@boothwyn.com

Reference Case: 710247

Dear Mr. Dustman:

The U.S. Food and Drug Administration (FDA) inspected your facility, Boothwyn Pharmacy, located at 221 Gale Lane, Kennett Square, PA, from September 23, 2024, through October 22, 2024.[1] During the inspection, the investigators noted deficiencies in your practices for producing animal drugs and issued Form FDA 483. The inspection team also discussed the circumstances under which you produce animal drugs from bulk drug substances and distribute them, including copies of FDA-approved products and office stock (drugs dispensed without patient-specific prescriptions). You responded to the inspection in writing on November 12, 2024. We have reviewed your response. Although your response addressed the objectionable practices and conditions related to drug quality described on the Form FDA 483, your response did not specify changes to the circumstances under which you intend to produce and distribute unapproved new animal drugs from bulk drug substances. Therefore, we are not able to review the adequacy of your response with respect to the introduction into interstate commerce of unapproved new animal drugs.

For the reasons set forth below, you produce and distribute adulterated and misbranded animal drugs in violation of sections 301(a) and 301(k) of the Federal Food, Drug, and Cosmetic Act (FD&C Act).

[1] FDA completed an inspection today (June 9, 2025) at your facility which primarily focused on human drug compounding. FDA may address the findings of that inspection in future correspondence.

U.S. Food and Drug Administration
MPN 2, Room E436
12225 Wilkins Avenue
Rockville, MD 20852
www.fda.gov

A. Unapproved New Animal Drugs

You compound drugs for animals from bulk drug substance(s) (BDS). From June 24, 2024, to September 23, 2024, you filled approximately (b) (4) prescriptions or orders for animal drugs. You stated that all of your animal products are compounded using BDS.[2]

Animal drugs compounded from BDS are new animal drugs as defined in section 201(v) of the FD&C Act because they are not generally recognized as safe and effective by experts qualified by scientific training and experience to evaluate the safety and effectiveness of animal drugs. Under section 512 of the FD&C Act, to be legally distributed, a new animal drug requires an approved new animal drug application, conditionally approved new animal drug application, or a listing on the Index of Legally Marketed Unapproved New Animal Drugs for Minor Species. Compounded drugs do not go through any of these pre-market review processes. Although compounded human drugs are, under certain circumstances, exempt from the human drug approval requirement in section 505 of the FD&C Act, no comparable exemption from section 512 exists for animal drugs. As a result, your compounded drugs are unsafe under section 512(a) of the FD&C Act and adulterated under section 501(a)(5) of the FD&C Act. Distribution of adulterated animal drugs violates the FD&C Act.

In addition, the drug products you compound from BDS are intended for conditions not amenable to diagnosis and treatment by individuals who are not veterinarians. Therefore, adequate directions for use cannot be written so that a lay person can use these products safely for their intended uses. Consequently, their labeling fails to bear adequate directions for their intended uses as required under section 502(f)(1) of the FD&C Act, and as they are not exempt from this requirement by any other statutory provision or regulation, they are misbranded. Distribution of misbranded animal drugs violates the FD&C Act.

Although compounded animal drugs lack the required approval or index listing, FDA acknowledges there are some situations in which no FDA-approved or indexed drug can be used to treat an animal, and a drug compounded from BDS may be medically appropriate. FDA's Guidance for Industry (GFI) #256, "Compounding Animal Drugs from Bulk Drug Substances" identifies the circumstances under which FDA does not intend to take enforcement action against drugs compounded from BDS. The guidance also generally describes our enforcement priorities with respect to compounded animal drugs. Our priorities for enforcement include animal drugs that are intended for use in food-producing animals; copies of marketed FDA-approved or indexed drugs; or compounded without a patient-specific prescription (i.e., office stock).

Drugs Without Identified Species

You distributed compounded drugs without identifying the species of the animal patient. Your prescription log includes prescriptions for "ANIMAL," "EXOTIC," and "AVIAN" instead of a species. Documenting the animal species is critical for animal health because appropriate dosing can vary between species and critical for human health to ensure that compounded animal drugs are not intended for use in a food-producing species. Use of drugs compounded

[2] The FD&C Act permits the compounding of animal drugs made from FDA-approved animal or human drugs, provided the conditions for legal extralabel use described in the FD&C Act and FDA's extralabel use regulations are met. Sections 512(a)(4) and (5) of the FD&C Act [21 U.S.C. § 360b(a)(4) and (5)] and 21 CFR part 530.

from BDS to treat food-producing animals and free-ranging wildlife risks exposing humans to potentially harmful residues in the animals' edible tissues because these drugs have not been reviewed to determine human food safety. "Animal" does not specify the species and the other terms could encompass food producing animals, such as bison and reindeer (exotic), and chickens and turkeys (avian).

Copies of Approved or Indexed Products

FDA considers an animal drug compounded from a bulk drug substance to be a copy of an FDA-approved or indexed product if it has the same active ingredient or active moiety and is given by the same route of administration ("ROA"). In addition, FDA considers a combination drug product to be a copy if any of its active ingredients is approved in the same ROA. Compounded copies of approved or indexed animal drugs are an FDA priority for enforcement because they may expose animals to drugs produced under lesser quality controls compared to the approved/indexed products and reduce incentives for firms to seek approval or indexing of their drugs. The following examples are representative of your firm's practice of compounding copies of approved products:

- Prescription number (b) (6): Aminocaproic Acid 250 mg/mL injectable solution (100mL bottle)
  - Your compounded aminocaproic acid injectable solution is a copy of FDA-approved products (ANDA: 071192 and 070010). Your records indicate you compounded this drug because "Patient would require too many vials of the approved product" but do not explain how differences in packaging (4 vials of approved products vs 1 vial of the compounded drug) will elicit a clinical difference in the patient. A practitioner can draw from multiple FDA-approved vials to achieve the desired dose because the drug is not administered to a patient directly from the vial itself.
  - If using a compounded drug would make a clinical difference in the identified patient, it may be possible to legally compound by modifying an approved product (i.e., use an approved product as the source of active ingredients) rather than illegally compound by starting from BDS.[3] For example, your records do not explain why you did not just repackage 4 vials of the FDA-approved product into a single vial.

- Prescription number (b) (6): Clenbuterol (fixed oil) 72.5 mcg/mL apple-flavored oral suspension for a horse
  - Your compounded clenbuterol oral suspension is a copy of FDA-approved product (NADA 140973), which is available as an FDA-approved 72.5 mcg/mL oral syrup, labeled for horses. Your records indicate the reason for compounding the drug was a change in dosage form was needed to achieve patient compliance, but do not explain how the compounded drug will elicit a clinical difference in the patient considering you compounded an oral suspension and the FDA-approved product is also a liquid administered orally.
  - The term "dosage form" refers to the physical form in which a drug is administered (the approved drug is a syrup, your compounded drug is a suspension). To the extent you intended to refer to achieving patient compliance with apple flavoring, your records do not explain why your firm could not legally compound by modifying an approved product, such as by adding apple flavoring to the approved product.

[3] See 21 CFR 530.13.

- Prescription number (b) (6): Omeprazole 3.08 g/10mL apple-flavored paste for a horse (30, 10 mL syringes)
  - Your compounded omeprazole paste is a copy of FDA-approved omeprazole (NADA: 141123), which is also a paste (37% oral paste, 6.15g syringe, 2.28g of omeprazole per syringe). Your records indicate the reason for compounding the drug was "[p]rescriber request strength change needed for aggressive treatment of EGUS in sport horses. FDA approved product does not enable dosing adjustments," but this does not explain how the compounded product would elicit a clinical difference in the patient, considering that the FDA-approved drug is administered via a syringe (which allows administration of any desired dose) and is more concentrated (37% vs 30.8%) than the compounded product.
  - If using a compounded drug would make a clinical difference in the identified patient, it may be possible to legally compound by modifying an approved product (i.e., use an approved product as the source of active ingredients) rather than illegally compound by starting from BDS.[4] For example, you do not have an explanation why you did not compound the drug by diluting the approved paste to achieve a lower concentration or why you did not repack the approved paste as needed to achieve same total dose of active ingredient per syringe as the product you compounded from BDS.

Drugs Compounded Without Patient-Specific Prescriptions (Office Stock)

"Office stock" refers to compounded drugs ordered by a veterinarian without a patient-specific prescription to keep on hand in the veterinary clinic or office to administer or dispense to patients. When drugs are compounded for use as office stock, and are therefore readily available for use, the products potentially expose large numbers of animals to drugs of unproven safety, effectiveness, and quality.

You stated that you do not compound animal drugs for office stock prescriptions and that all prescriptions are patient-specific. However, in multiple cases, the volume of drugs dispensed and/or associated records show the prescriptions are more likely intended for use in more than the identified patient. In many cases, the office stock you produced was also a copy of an FDA-approved drug. The following examples are representative of your firm's practice of compounding drugs intended for use in more than the identified patient:

- Prescription number (b)(4), (b) (6): Adrenocorticotrophic Hormone (ACTH) gel 80 U/mL injectable solution for a horse (50, 10 mL vials), filled 7/10/2024
  - Your records indicate this prescription was compounded for the reason "Concentration changes to accommodate wide variations in patient size." This reason is inconsistent with a patient-specific prescription for a single horse because individual patients do not have a wide variation in size.
  - Furthermore, the quantity is inconsistent with single patient use. The highest medically-reasonable dose is 600U per horse for muscle soreness. 500 mL would treat a horse daily for 66 days, which would extend past the beyond use date of 8/24/2024 (45 days from the date filled).

- Prescription number (b)(4), (b) (6): Detomidine HCl 20 mg/mL injectable solution for a horse (6, 20 mL vials), filled 9/19/2024

[4] See 21 CFR 530.13.

- Your records indicate a compounded drug was needed instead of an approved product because "Strength changes to accommodate wide variations in patient size." This reason is inconsistent with a patient-specific prescription for a single horse because individual patients do not have a wide variation in size.
- Furthermore, the quantity is inconsistent with single patient use. The labeled dose of the FDA-approved detomidine product is 0.04 mg/kg once for sedation. Even if the patient was sedated every day, this prescription would provide enough doses for 120 days in an average sized horse (500 kg) and 60 days in a very large horse (1000 kg), in both cases extending past the beyond use date of 10/31/2024 (42 days from the date filled).

- Prescription number (b)(4), (b) (6): Estradiol Cypionate 10 mg/mL injectable solution for a horse (6, 100 mL vials), filled 7/22/2024
  - Your records indicate a compounded drug was needed instead of an approved product because "Strength changes to accommodate wide variations in patient size." This reason is inconsistent with a patient-specific prescription for a single horse because individual patients do not have a wide variation in size.
  - Furthermore, the quantity prescribed is inconsistent with single patient use. The highest medically-reasonable dose is 10 mg/horse for synchronizing ovulation for breeding once daily for 10 days. This prescription would treat a single horse for 60 breeding cycles, well beyond the beyond use date of 8/25/2024 (34 days from the date filled).

B. Drug Quality Violations

All animal drugs produced from bulk drug substances are subject to the FD&C Act's Current Good Manufacturing Practice (CGMP) requirement, section 501(a)(2)(B), and our inspection determined that you are not in compliance with that requirement. We noted that your firm sells office stock which potentially exposes large numbers of animals to drugs which do not meet the CGMP quality standard set forth by the FD&C Act. We further noted that your firm produces copies of FDA-approved products from bulk drug substances but does so without the same CGMP controls which ensure their quality. For example, unlike FDA-approved products, you fail to test the strength/potency of each batch,[5] and establish, follow and validate all aseptic procedures and sterilization processes to prevent microbial contamination.[6] Of particular concern:

- You distributed seven (7) batches of drugs with out-of-specification (OOS) bacterial endotoxin testing (BET) results[7] and you failed to keep accurate records of laboratory test results and investigations.[8] Specifically, your Pharmacist In-charge (PIC) altered multiple Certificates of Analysis (COAs) that were issued by your contract laboratory for your finished products containing glucosamine by changing failing BET results to passing results and provided them to FDA in order to "limit" FDA's investigation.[9] Your PIC also created false records of investigations which did not occur, including falsely created call logs purporting to document contact with owners about products with failing test results which stated the owner told the PIC no adverse events occurred, when no such call occurred. After FDA

[5] See 21 CFR 211.165(a).
[6] See 21 CFR 211.113(b).
[7] See 21 CFR 211.165(a),(f).
[8] See 21 CFR 211.194 and 211.192.
[9] Providing documents with falsified laboratory test data delays or limits FDA's ability to investigate the underlying quality issues and renders the drugs adulterated under FD&C Act section 501(j).

investigators discovered the falsified records, the PIC admitted he acted to "falsify" the records.

We are unable to assess the adequacy of your response because you took minimal steps to verify that no other data was altered and did not gather the real information that the PIC had falsified. For example, you did not actually complete the investigations that your PIC had falsified by calling your customers regarding the adverse events.

- Your firm distributed at least thirty-one (31) of your compounded drug products that received OOS results for BET.[10] Endotoxins are pyrogens and can cause serious adverse reactions in animals. The corrective actions included in your response do not adequately consider the root cause for your OOS results.

- You have not adequately validated your aseptic processes.[11] Your smoke studies–which are intended to show you can perform aseptic operations without putting your product at risk of contamination–showed instances where first pass air is being blocked around the vials being filled or collects and creates a vortex near your operator.[12] For example, see your smoke studies "08.16.24 PS-172 FDA" and "08.16.24 PS-169 FDA". You committed to doing new smoke studies and media fills, but we have not received any additional information indicating your corrections were made.

Use of Components (BDS) that Violate the FD&C Act

You used glucosamine as an active ingredient in sterile drugs; however, the component's COA indicated the glucosamine was "FOR NUTRACEUTICAL USE ONLY." This grade of ingredient is not acceptable for use as an active ingredient in drug products–especially in injectable drug products which must be produced in a manner that controls endotoxin levels.[13] You had numerous OOSs for endotoxins for drugs you compounded containing this component, and as described above, endotoxins can cause serious adverse reactions in animals.

You compounded drugs using glucosamine BDS, including the glucosamine discussed above, that were manufactured by establishments that are not registered with FDA as required under section 510 of the FD&C Act. All manufacturers of BDS must register with FDA to ensure they are inspected. Use of BDS from non-registered establishments presents a risk to animal patients because the BDS may not have been originally manufactured for use as a drug (i.e., with the strength, quality, and purity for medical use in or on an animal) or in accordance with CGMP for drugs. Drugs manufactured by unregistered establishments are misbranded under section 502(o) of the FD&C Act. These BDS remain misbranded when incorporated into your compounded drugs. For example:

- N-Acetyl-D -Glucosamine BDS ((b)(4) lots including (b)(4)) were manufactured by (b) (4), which is not registered with FDA as an animal drug manufacturing establishment.
- Acetyl-D -Glucosamine BDS (b)(4) lots including (b)(4) were manufactured by (b)(4) (b) (4), which is not registered with FDA as an animal drug manufacturing establishment.

[10] See 21 CFR 211.165(a),(f).
[11] See 21 CFR 211.113(b).
[12] FD&C Act section 501(a)(2)(A).
[13] Section 501(a)(2)(A). See also, 21 CFR 211.160(b), 21 CFR 211.84(d)(2).

- Acetyl-D -Glucosamine BDS (b)(4) lots including (b)(4)) were manufactured by (b) (4), which is not registered with FDA as an animal drug manufacturing establishment.

Drug establishment registrations are public information and can be viewed on FDA.gov.[14]

In your written response, you indicated that Boothwyn is a state-licensed pharmacy that is registered and practicing under the authority of the Pennsylvania Board of Pharmacy and complying with FD&C Act section 503A, when applicable, and with USP General Chapters <797> and <795>.

As described above, unlike human drugs compounded in accordance with section 503A, the FD&C Act does not exempt pharmacies that produce animal drugs from bulk drug substances from CGMP. The Act's CGMP requirement in section 501(a)(2)(B) applies to anyone who manufactures or processes animal drugs.

Conclusion

All of the animal drugs you produce from BDS violate the FD&C Act's requirements for approval/indexing, adequate directions for use, and CGMP.[15]

We do not consider your firm a low priority for enforcement action as described in GFI #256 because of the practices observed at your firm, including: filling prescriptions for unidentified species (potentially including food producing animals), compounding copies of approved products, and compounding office stock (drugs intended for use in patients not identified on the prescription).

This letter is not intended to be an all-inclusive statement of violations that may exist in connection with your products. You are responsible for investigating and determining the causes of any violations and for preventing their recurrence or the occurrence of other violations. It is your responsibility to ensure that your firm complies with all the requirements of federal law, including FDA regulations.

In addition, we offer the following comments:

- FDA recognizes that there are some circumstances in which the treating veterinarian determines that a particular patient cannot be treated with the FDA-approved product(s) and needs a compounded copy with a specific difference from the FDA-approved drug. GFI #256 recommends that pharmacies obtain a medical rationale from the treating veterinarian that explains how the prescribed compounded product makes a clinical difference for the patient. This statement should explain why the approved drug cannot be used by identifying which characteristic of the approved/indexed drug is unsuitable for the individual patient and how that characteristic is altered in the prescribed compounded drug so as to create the specified clinical difference for the individual patient. If there are multiple approved products that vary in dosage form, strength or formulation, medical rationales

[14] See FDA's "Drug Establishments Current Registration Site" page at https://www.fda.gov/drugs/drug-approvals-and-databases/drug-establishments-current-registration-site.
[15] Section 512 of the FD&C Act [21 U.S.C. § 360b], 502(f)(1) of the FD&C Act [21 U.S.C. § 352(f)(1), and section 501(a)(2)(B) of the FD&C Act [21 U.S.C. § 351(a)(2)(B)]. (See also 21 CFR parts 210 and 211.)

should address each approved product, because the compounded drug is a copy of each of them.

- While most animal patients' needs for compounded drugs can be met with patient-specific prescriptions, FDA recognizes that in some cases an animal drug is urgently needed, and the time needed to compound a drug in response to an individual patient prescription may result in animal suffering or death. FDA has reviewed information concerning certain compounded drugs veterinarians need for urgent treatment. These drugs are on the List of Bulk Drug Substances for Compounding Office Stock Drugs for Use in Nonfood-Producing Animals.[16] You have dispensed drugs containing adrenocorticotrophic hormone (ACTH), detomidine, and estradiol cypionate for use as office stock. FDA reviewed information on ACTH and did not include it on the list referenced above because there are FDA-approved drugs containing the same active ingredient, in the same or similar dosage form, that can be used as labeled in horses or FDA-approved products that can be used in an extralabel manner. As of the date of issuance of this letter, detomidine and estradiol cypionate have not been nominated for inclusion on the list, and ACTH gel is on the list of "Bulk Drug Substances Reviewed and Not Listed.

Within fifteen (15) working days of receipt, respond to this letter in writing, specifying the steps you have taken to address any violations and prevent the recurrence. Include an explanation of each step you have taken or commit to take and attach copies of related documentation. If you cannot complete all of your corrective actions within fifteen (15) working days, state the reason for the delay and your schedule for completion.

This letter notifies you of our findings and provides you with an opportunity to address them. You can find the FD&C Act through links on FDA's homepage at http://www.fda.gov. If you believe that your products are not in violation of the FD&C Act, include your reasoning and any supporting information for our consideration.

Please direct your response to CVMCompounding@fda.hhs.gov and include "Reference Case: 710247 in the subject line of your email. If you have questions regarding the contents of this letter, please contact CVMCompounding@fda.hhs.gov.

Sincerely,

CINDY L. BURNSTEEL -S

Digitally signed by CINDY L. BURNSTEEL -S
Date: 2025.06.09 14:20:47 -04'00'

Cindy L. Burnsteel, DVM
Acting Director
Division of Drug Compliance
Office of Surveillance and Compliance
Center for Veterinary Medicine
U.S. Food & Drug Administration

[16] Additionally, drugs which FDA is considering for placement on the List of Bulk Drug Substances for Compounding Office Stock Drugs for Use in Nonfood-Producing Animals, and which FDA recommends remain available during FDA's review, are found on this List of Bulk Drug Substances Currently Under Review.

CC (via email):
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