FDA Inspections Unwrapped: "What Every Pharmacy Owner or Manager Needs to Know"

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1

Federal Law

- 1906 Food and Drugs Act - drugs must meet the standards of strength, quality, and purity stipulated in the USP-NF
- 1938 Federal Food, Drug, and Cosmetic Act - recognizes USP-NF standards for medicines
- 1997 Food and Drug Administration Modernization Act – Amendment to FD&C - added section 503A
- 2013 Drug Quality Security Act (Short title – Compounding Quality Act) – Amendment to FD&C

2

Federal Law - DQSA

- Eliminated section concerning advertising of compounded drugs that had been found to be unconstitutional
- Added section 503B which established outsourcing facilities who are subject to CGMP requirements, and may distribute compounded drugs either pursuant to a patient-specific prescription or in response to an order from a health care provider, such as a hospital, that is not for an identified individual patient (e.g. office stock)
- Added Drug Supply Chain Security Act

3

Federal Law - FDAMA

- Lists conditions under which compounded human drug products are exempt from FDA approval prior to marketing, current good manufacturing practice (CGMP) requirements, and labeling with adequate directions for use.
- (a) In General.--Sections 501(a)(2)(B), 502(f)(1), and 505 shall not apply to a drug product if the drug product is compounded for an identified individual patient based on the unsolicited receipt of a valid prescription order or a notation, approved by the prescribing practitioner, on the prescription order that a compounded product is necessary for the identified patient, if the drug product meets the requirements of this section, and if the compounding--

Food and Drug Administration Modernization Act (FDAMA) of 1997 | FDA; accessed 2-14-25

4

Federal Law - FDAMA

- (1) is by--
- (A) a licensed pharmacist in a State licensed pharmacy or a Federal facility, or
- (B) a licensed physician, on the prescription order for such individual patient made by a licensed physician or other licensed practitioner authorized by State law to prescribe drugs; or
- (2)(A) is by a licensed pharmacist or licensed physician in limited quantities before the receipt of a valid prescription order for such individual patient; and
- (B) is based on a history of the licensed pharmacist or licensed physician receiving valid prescription orders for the compounding of the drug product, which orders have been generated solely within an established relationship between--
- (i) the licensed pharmacist or licensed physician; and
- (ii)(I) such individual patient for whom the prescription order will be provided; or
- (II) the physician or other licensed practitioner who will write such prescription order.

5

Federal Law - FDAMA

- (b) Compounded Drug.--
- (1) Licensed pharmacist and licensed physician.--A drug product may be compounded under subsection (a) if the licensed pharmacist or licensed physician--
- (A) compounds the drug product using bulk drug substances, as defined in regulations of the Secretary published at section 207.3(a)(4) of title 21 of the CFR
- (i) that--
- (I) comply with the standards of an applicable United States Pharmacopoeia or National Formulary monograph, if a monograph exists, and the United States Pharmacopoeia chapter on pharmacy compounding;
- (II) if such a monograph does not exist, are drug substances that are components of drugs approved by the Secretary; or [Page 111 STAT. 2329]
- (III) if such a monograph does not exist and the drug substance is not a component of a drug approved by the Secretary, that appear on a list developed by the Secretary through regulations issued by the Secretary under subsection (d);
- (ii) that are manufactured by an establishment that is registered under section 510 (including a foreign establishment that is registered under section 510(i)); and
- (iii) that are accompanied by valid certificates of analysis for each bulk drug substance;

Food and Drug Administration Modernization Act (FDAMA) of 1997 | FDA; accessed 2-14-25

6

Federal Law - FDAMA

- (C) does not compound a drug product that appears on a list published by the Secretary in the Federal Register of drug products that have been withdrawn or removed from the market because such drug products or components of such drug products have been found to be unsafe or not effective; and
- (D) does not compound regularly or in inordinate amounts (as defined by the Secretary) any drug products that are essentially copies of a commercially available drug product.
- (2) Definition.--For purposes of paragraph (1)(D), the term `essentially a copy of a commercially available drug product' does not include a drug product in which there is a change, made for an identified individual patient, which produces for that patient a significant difference, as determined by the prescribing practitioner, between the compounded drug and the comparable commercially available drug product.
- (3) Drug product.--A drug product may be compounded under subsection (a) only if--
- (A) such drug product is not a drug product identified by the Secretary by regulation as a drug product that presents demonstrable difficulties for compounding that reasonably demonstrate an adverse effect on the safety or effectiveness of that drug product; and

Food and Drug Administration Modernization Act (FDAMA) of 1997 | FDA; accessed 2-14-25

7

Federal Law - FDAMA

- (B) such drug product is compounded in a State--
- (i) that has entered into a memorandum of understanding with the Secretary which addresses the distribution of inordinate amounts of compounded drug products interstate and provides for appropriate investigation by a State agency of complaints relating to compounded drug products distributed outside such State; or
- (ii) that has not entered into the memorandum of understanding described in clause (i) and the licensed pharmacist, licensed pharmacy, or licensed physician distributes (or causes to be distributed) compounded drug products out of the State in which they are compounded in quantities that do not exceed 5 percent of the total prescription orders dispensed or distributed by such pharmacy or physician. [Page 111 STAT. 2330]
- The Secretary shall, in consultation with the National Association of Boards of Pharmacy, develop a standard memorandum of understanding for use by the States in complying with subparagraph (B)(i).

Food and Drug Administration Modernization Act (FDAMA) of 1997 | FDA; accessed 2-14-25

8

Federal Law - FDAMA

- (d) Regulations.--
- (1) In general.--The Secretary shall issue regulations to implement this section. Before issuing regulations to implement subsections (b)(1)(A)(i)(III), (b)(1)(C), or (b)(3)(A), the Secretary shall convene and consult an advisory committee on compounding unless the Secretary determines that the issuance of such regulations before consultation is necessary to protect the public health. The advisory committee shall include representatives from the National Association of Boards of Pharmacy, the United States Pharmacopoeia, pharmacy, physician, and consumer organizations, and other experts selected by the Secretary.
- (2) Limiting compounding.--The Secretary, in consultation with the United States Pharmacopoeia Convention, Incorporated, shall promulgate regulations identifying drug substances that may be used in compounding under subsection (b)(1)(A)(i)(III) for which a monograph does not exist or which are not components of drug products approved by the Secretary. The Secretary shall include in the regulation the criteria for such substances, which shall include historical use, reports in peer reviewed medical literature, or other criteria the Secretary may identify.

Food and Drug Administration Modernization Act (FDAMA) of 1997 | FDA; accessed 2-14-25

9

Federal Law - FDAMA

- (f) Definition.--As used in this section, the term `compounding' does not include mixing, reconstituting, or other such acts that are performed in accordance with directions contained in approved labeling provided by the product's manufacturer and other manufacturer directions consistent with that labeling.

Food and Drug Administration Modernization Act (FDAMA) of 1997 | FDA; accessed 2-14-25

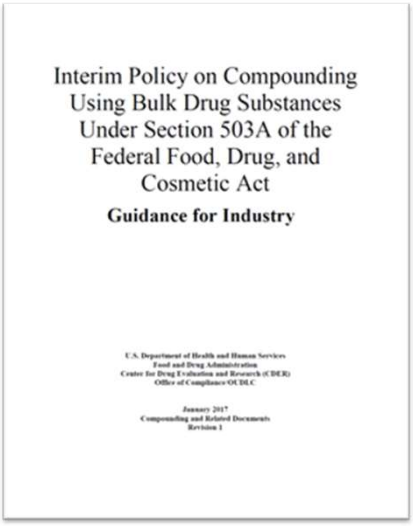
10

FDA Guidance Documents

- Contains Nonbinding Recommendations
- Represents the current thinking of the FDA on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA office responsible for this guidance as listed on the title page.
- In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word should in Agency guidances means that something is suggested or recommended, but not required.

11

FDA Food and Drug Administration


Interim Policy on Compounding Using Bulk Drug Substances Under Section 503A of the Federal Food, Drug, and Cosmetic Act

Guidance for Industry

Interim Policy on Compounding Using Bulk Drug Substances Under Section 503A of the Federal Food, Drug, and Cosmetic Act | FDA: accessed 2-14-25

12

FDA Food and Drug Administration

Meeting the definition of 503A for human use requires

- Dispensing patient-specific preparations
- APIs must meet one of the following:
  1. USP or NF
  2. Elements of FDA-approved commercial drugs (that do not appear on the FDA 'negative list' except as allowed)
  3. Appears on the bulk substance list
     - Brilliant Blue G, also known as Coomassie Brilliant Blue G-250
     - Cantharidin (for topical use only)
     - Diphenylcyclopropenone (for topical use only)
     - N-acetyl-D-glucosamine (NAG) (for topical use only)
     - Squaric acid dibutyl ester (for topical use only)
     - Thymol iodide (for topical use only)
- APIs must be manufactured in FDA-registered facility
- APIs must be accompanied by valid COA

13

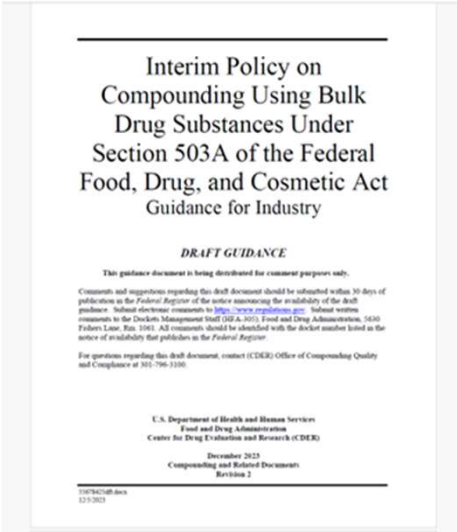
§216.24 Drug products withdrawn or removed from the market for reasons of safety or effectiveness – FDA 'Negative List' (partial list)

- Adenosine phosphate: All drug products containing adenosine phosphate.
- Adrenal cortex: All drug products containing adrenal cortex.
- Alatrofloxacin mesylate: All drug products containing alatrofloxacin mesylate.
- Aminopyrine: All drug products containing aminopyrine.
- Astemizole: All drug products containing astemizole.
- Azaribine: All drug products containing azaribine.
- Benoxaprofen: All drug products containing benoxaprofen.
- Bithionol: All drug products containing bithionol.
- Bromfenac sodium: All drug products containing bromfenac sodium (except ophthalmic solutions).
- Bromocriptine mesylate: All drug products containing bromocriptine mesylate for prevention of physiological lactation.
- Butamben: All parenteral drug products containing butamben.
- Camphorated oil: All drug products containing camphorated oil.
- Carbetapentane citrate: All oral gel drug products containing carbetapentane citrate.
- Casein, iodinated: All drug products containing iodinated casein.
- Cerivastatin sodium: All drug products containing cerivastatin sodium.
- Chloramphenicol: All oral drug products containing chloramphenicol.
- Chlorhexidine gluconate: All tinctures of chlorhexidine gluconate formulated for use as a patient preoperative skin preparation.
- Chlormadinone acetate: All drug products containing chlormadinone acetate.
- Chloroform: All drug products containing chloroform.
- Cisapride: All drug products containing cisapride

2015 Final Rule: https://www.ecfr.gov/cgi-bin/text-idx?SID=9f72be9edb31ecf7e76f977678b42878&mc=true&node=se21.4.216_124&rgn=div8
2018 Additions Https://www.federalregister.gov/documents/2018/12/11/2018-26712/list-of-drug-products-that-have-been-withdrawn-or-removed-from-the-market-for-reasons-of-safety-or

14

FDA Food and Drug Administration



Interim Policy on Compounding Using Bulk Drug Substances Under Section 503A of the Federal Food, Drug, and Cosmetic Act
Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

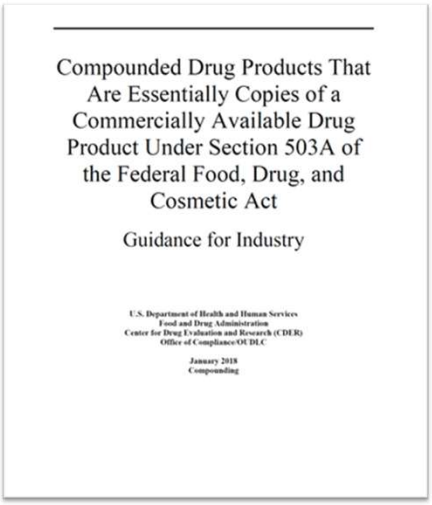
U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

December 2023
Compounding and Related Documents
Revision 2

Interim Policy on Compounding Using Bulk Drug Substances Under Section 503A of the Federal Food, Drug, and Cosmetic Act | FDA: accessed 2-14-25

15

FDA Food and Drug Administration



Compounded Drug Products That Are Essentially Copies of a Commercially Available Drug Product Under Section 503A of the Federal Food, Drug, and Cosmetic Act

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Office of Compliance/OUDLC

January 2018
Compounding

If shortage, should document on the prescription that the drug was on the FDA drug shortage list and the date the list was checked.

Compounded Drug Products That Are Essentially Copies of a Commercially Available Drug Product Under Section 503A of the Federal Food, Drug, and Cosmetic Act Guidance for Industry | FDA; 2-14-25

16

FDA Food and Drug Administration

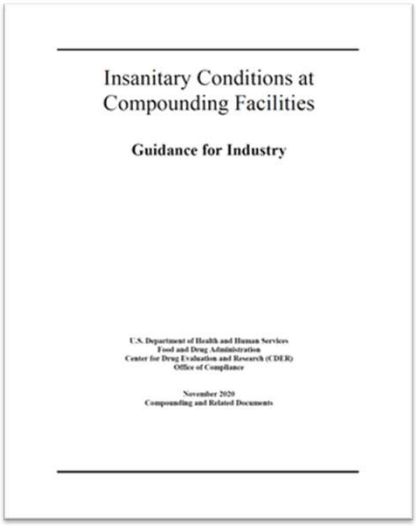
Vermin

Visible Microbial Contamination

Visible Nonmicrobial Contamination
Rust, Hair,
Glass Particles

Handling Beta-Lactam, HD, or Highly Potent Drugs without adequate controls

Adjacent construction without adequate controls


Insanitary Conditions at Compounding Facilities

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Office of Compliance

November 2020
Compounding and Related Documents

Insanitary Conditions at Compounding Facilities Guidance for Industry | FDA; accessed 2-14-25

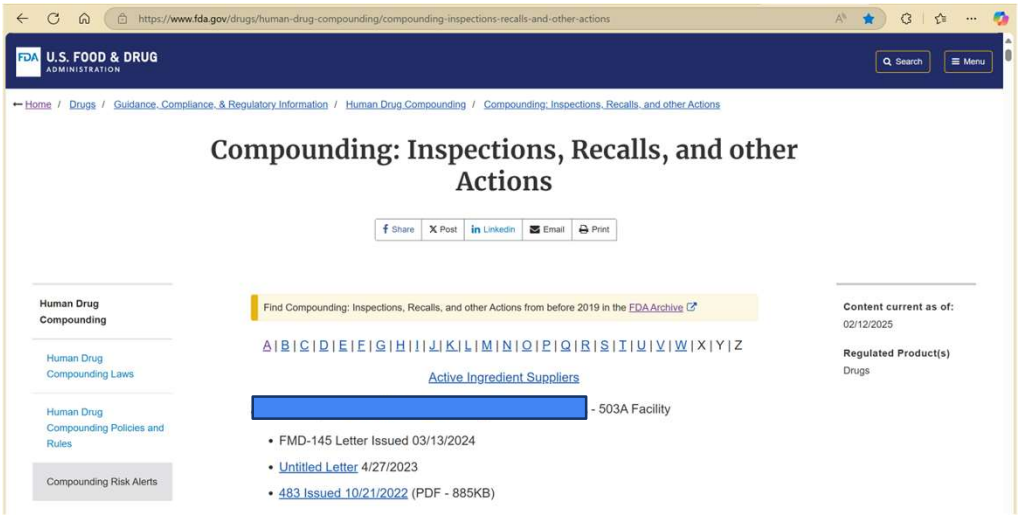
17

FDA Food and Drug Administration

Insanitary Conditions applicable to sterile compounding

- Gowning and Aseptic Practices
- Equipment/Facilities
- Sterilization
- Cleaning and Disinfection
- Other Insanitary Conditions

18



19

Animal Medicinal Drug Use Clarification Act 1994 (AMDUCA)

- § 530.13 Extralabel use
- Applies to compounding of a product from approved animal or human drugs
- Nothing in this part shall be construed as permitting compounding from bulk drugs

20

FDA Guidance Documents for Vet

- 1996 CPG 608.400
  - Revoked 2015
- 2015 GFI #230
  - Revoked 2017
- 2019 GFI #256 Draft
- 2022 GFI #256 Final

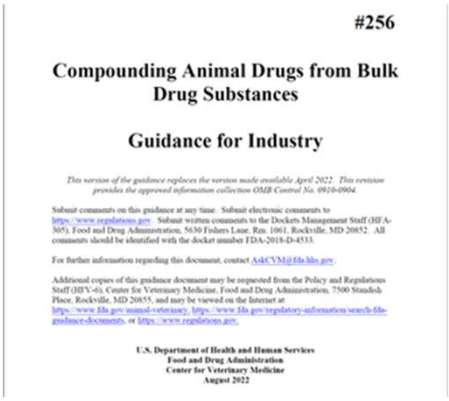
21

GFI #256 Scope

- Limits the use of animal drugs compounded from bulk drug substances to when there is no medically appropriate human or animal drug that is FDA-approved, conditionally approved, or indexed

22

FDA Food and Drug Administration



#256

Compounding Animal Drugs from Bulk Drug Substances

Guidance for Industry

This version of the guidance replaces the version made available April 2022. This revision provides the approved information collection OMB Control No. 0910-0904.

Submit comments on this guidance at any time. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number FDA-2018-D-4533.

For further information regarding this document, contact AskCVM@fda.hhs.gov.

Additional copies of this guidance document may be requested from the Policy and Regulations Staff (HFV-6), Center for Veterinary Medicine, Food and Drug Administration, 7500 Standish Place, Rockville, MD 20855, and may be viewed on the Internet at https://www.fda.gov/animal-veterinary, https://www.fda.gov/regulatory-information/search-fda-guidance-documents, or https://www.regulations.gov.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Veterinary Medicine
August 2022

Vet must document why compounding needed. Pharmacy must document why API needed. Patient-specific requires this labeling: (1) Report suspected adverse reactions to the pharmacy and to FDA using online Form FDA 1932a. (2) This is a compounded drug. Not an FDA approved or indexed drug. (3) Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

CVM GFI #256 - Compounding Animal Drugs from Bulk Drug Substances | FDA; accessed 2-14-25

23

Compounding for Nonfood-Producing Animals: Without Patient-Specific Prescriptions

- Drug is intended for use in a nonfood-producing species
- Compounded from a bulk drug substance listed on FDA's *List of Bulk Drug Substances for Compounding Office Stock Drugs for Use in Nonfood-Producing Animals*
- Label, Not for use in food-producing animals

24

DOGS, CATS, HORSES

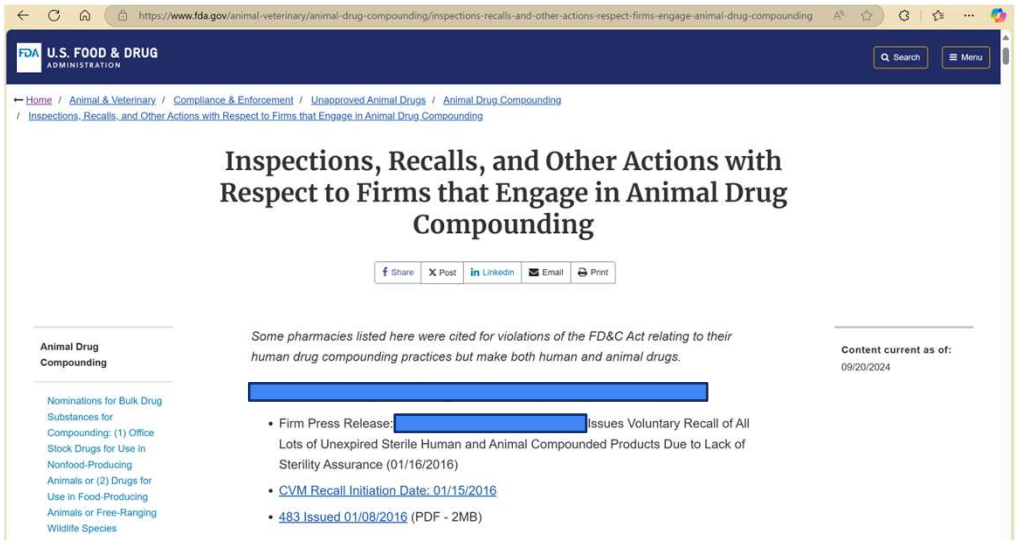
Bulk Drug Substance (BDS)	Species	Dosage form(s)	Strength/concentration
Amlodipine besylate (1/19/2023)	**dog, cat**	oral solution	1.25 mg/ml
		oral suspension	1.25 mg/ml
		capsule	0.625 mg
		tablet	0.625 mg
		mini-tab	0.625 mg
Apomorphine hydrochloride (8/11/2016)	**dog**	solution for injection	2.5 mg/ml
Chloramphenicol (2/28/2023)	**horse**	oral suspension	15 - 500 mg/ml
		oral paste	100 - 500 mg/ml
Cisapride (9/6/2016)	**cat**	tablets or capsules	2.5 and 5 mg
		oral suspension	5-10 mg/ml
Cyclosporine (9/20/2022)	**horse**	ophthalmic ointment	1-2%
Gabapentin (9/29/2023)	**dog, cat**	oral suspension	50 mg/ml
Guaifenesin (11/9/2016)	**horse**	soluble powder to be reconstituted into a solution for IV infusion with the addition of 500 ml (10%) or 1000 ml (5%) sterile diluent	50 gm
Idoxuridine (2/1/2022)	**cat**	ophthalmic ointment or solution	0.1%

25

Antidotes for Food-Producing Animals or Sedatives and Anesthetics for Free-Ranging Wildlife Species

- Compounded from a bulk drug substance listed on FDA's *List of Bulk Drug Substances for Compounding Drugs for Use in Food-Producing Animals or Free-Ranging Wildlife Species*
- Label with prescribing veterinarian-determined withdrawal time

26



27

Contact Information

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Alliance for Pharmacy Compounding
Compounding the Joy of Living

Compounding Friendly Owner Summit

28