Pharmacist's Perspective:

Implications for Compounding & Patient Safety

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Semaglutide Usual Dosing

Initiate and adjust dose using the following schedule. In patients who do not tolerate a dosage increase, consider delaying the increase for an additional 4 weeks:

Week 1 through week 4: **0.25 mg once weekly**

Week 5 through week 8: **0.5 mg once weekly**

Week 9 through week 12: **1 mg once weekly**

Week 13 through week 16: **1.7 mg once weekly**

Week 17 and thereafter (maintenance): **2.4 mg once weekly**

UpToDate Lexidrug: Semaglutide, Accessed 11/3/2025

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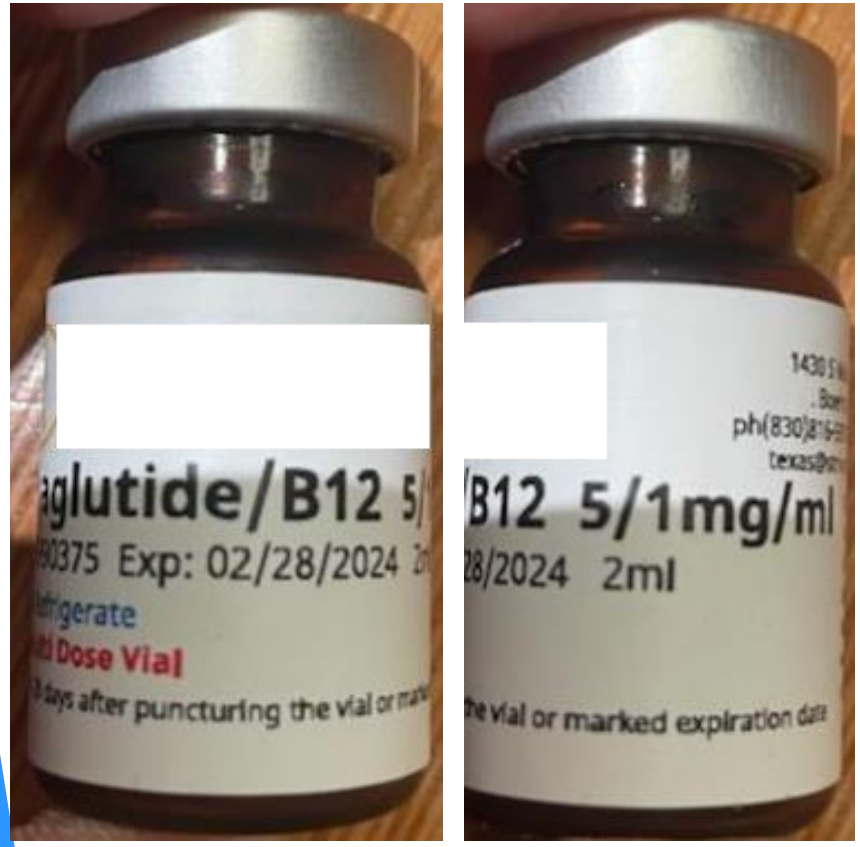
Patient Case: Semaglutide Overdose



Images: Michael Freudiger

- **Semaglutide/B12 5/1mg/mL**
- Dose: 1.7 mg per week for 6 weeks
- Syringes Supplied: 100 units/mL
- Patient drew up 1.7 mL and injected it, thinking the Semaglutide in the vial was 1 mg/mL.
- Vial Contains:
  - 5 mg/mL Semaglutide
  - 1 mg/mL Vitamin B12

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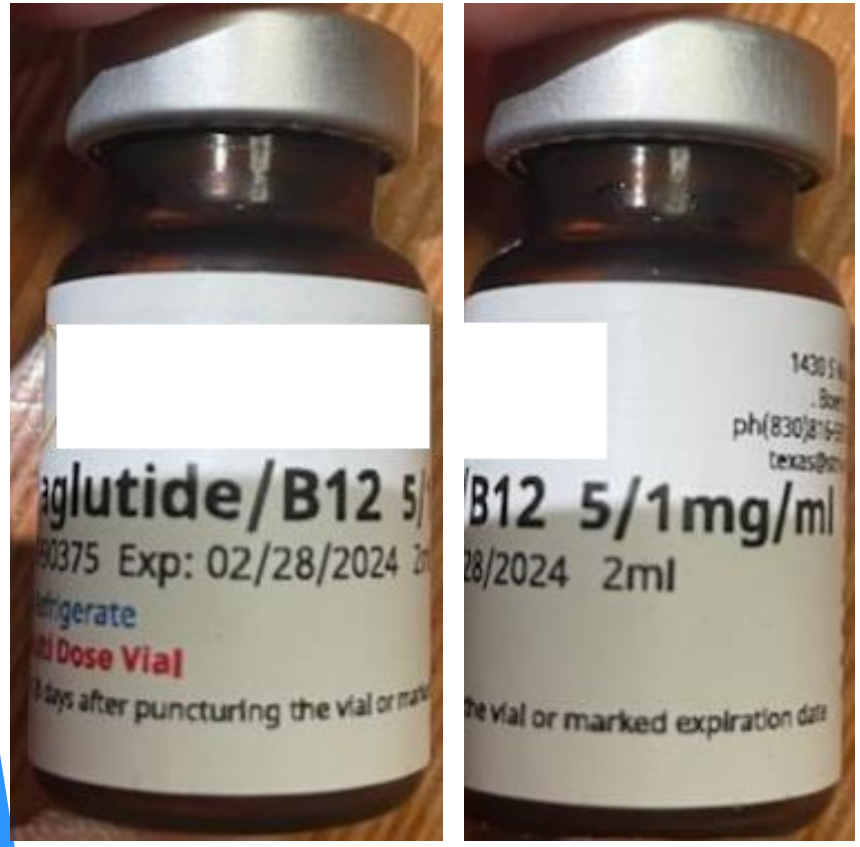
Patient Case: Semaglutide Overdose



Images: Michael Freudiger

- **Semaglutide/B12 5/1mg/mL**
- Dose: 1.7 mg per week for 6 weeks

- Correct Dosing Calculation:
  - 5 mg/mL concentration
  - 1.7 mg dose
  - 1.7 mg ÷ 5 mg/mL = 0.34 mL

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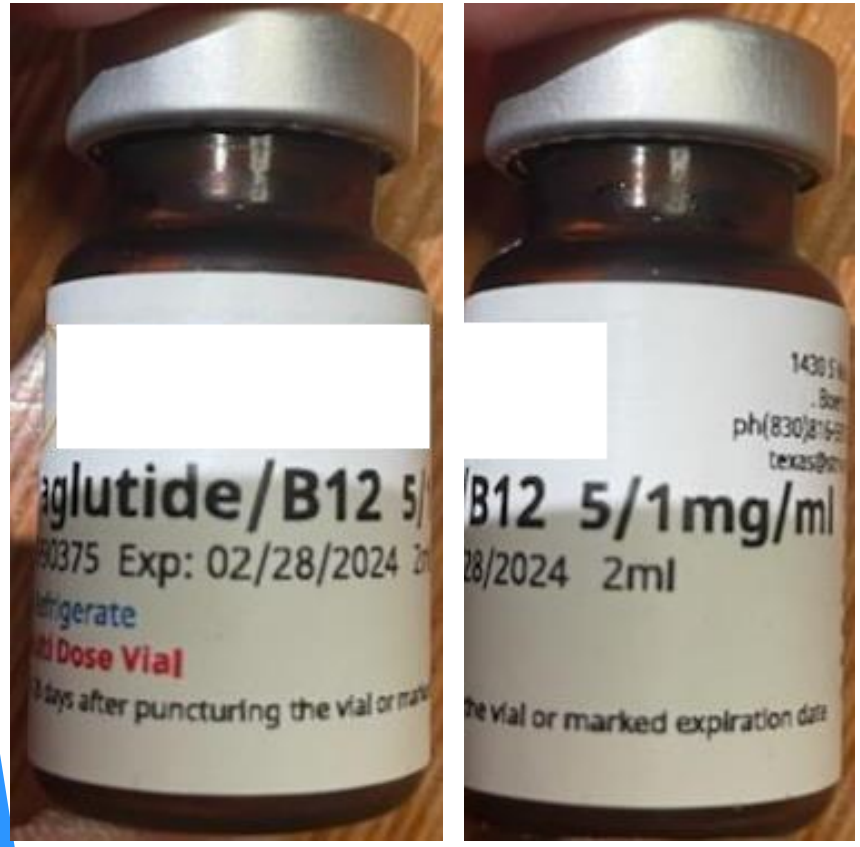
Patient Case: Semaglutide Overdose



Images: Michael Freudiger

- **Adverse Reactions:**
- **Friday** – dose injected 8 pm, woke up 2 am feeling extremely ill, vomiting multiple times over 48 hours, 7-pound weight loss over 48 hours, vomiting stopped with Zofran.
- **Sunday** – body aches and burning sensation on the trunk to extremities that only improves with hot water, then comes back, sometimes extends to fingers and toes.
- **Monday** – no appetite, persistent nausea, additional 2 pounds lost.

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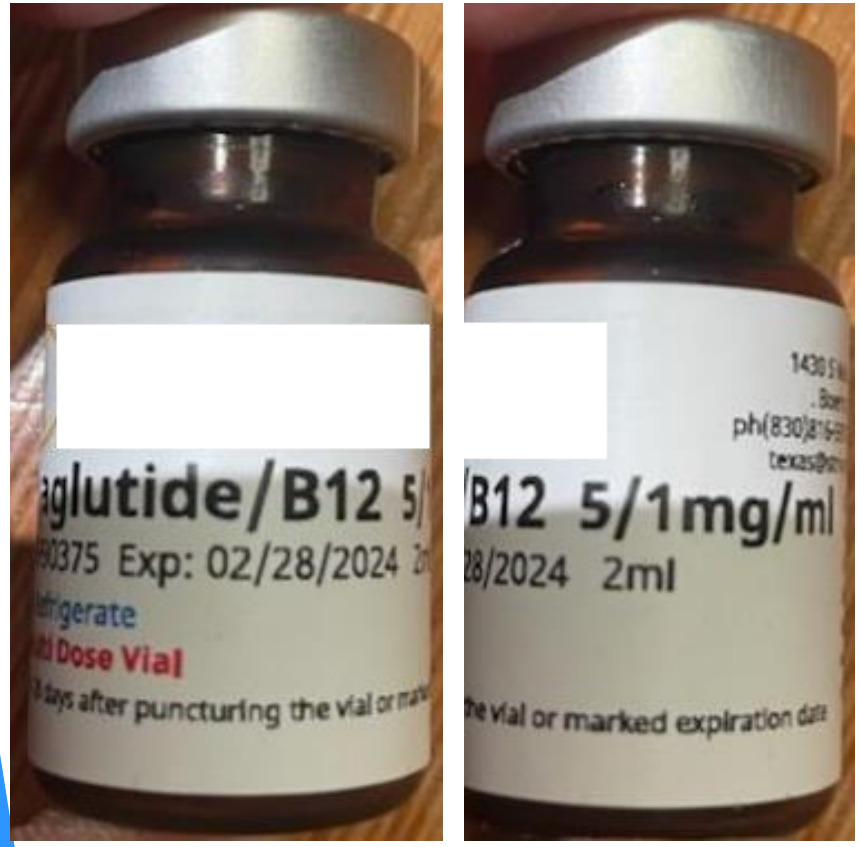
Patient Case: Semaglutide Overdose



Images: Michael Freudiger

- Patient Background:
  - Corporate Attorney
  - Husband: Army Physician

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Convenient Pens

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Phone Clinics

- Telemedicine
  - **Upside**: Increased access to physicians and medications
  - **Downside**: Patients may not be fully assessed prior to the prescription being written.
- Mail Order Pharmacy
  - **Upside**: Delivery of medications to the patient, increased access.
  - **Downside**: Patients may have no or minimal counseling to understand the use, dosing, and administration of drugs.

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GLP-1 Approvals

2005: First GLP-1, Byetta (exenatide), is approved for type 2 diabetes.
2010: Victoza (liraglutide) is approved for type 2 diabetes.
2014: Saxenda (liraglutide) is approved for weight management.
2017: Ozempic (semaglutide) is approved for type 2 diabetes.
2019: Rybelsus (semaglutide) is approved for type 2 diabetes.
2021: Wegovy (semaglutide) is approved for weight management.
2022: Mounjaro (tirzepatide) is approved for type 2 diabetes.
2023: Zepbound (tirzepatide) is approved for weight management.

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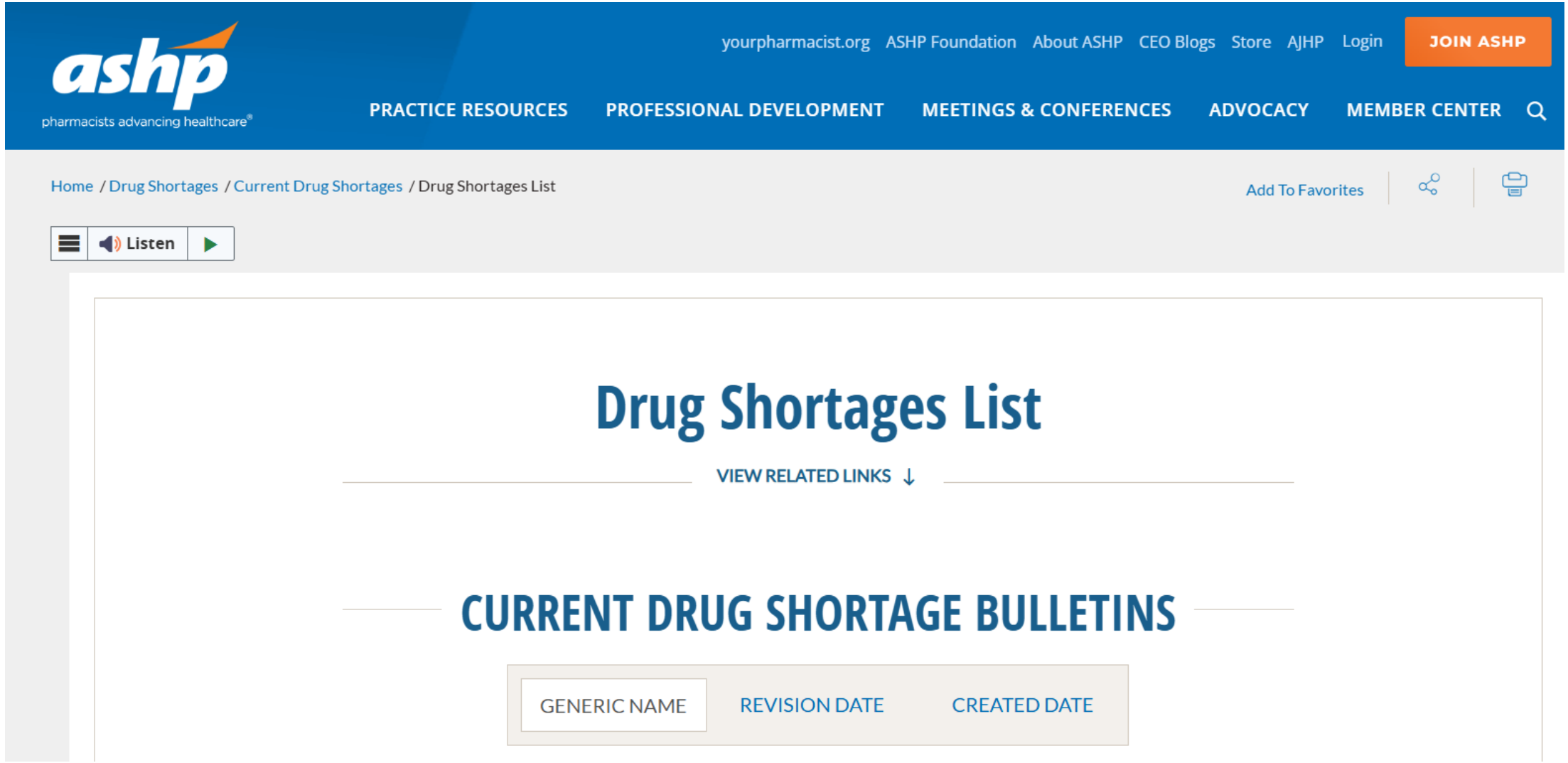
ASHP Drug Shortages List



https://www.ashp.org/drug-shortages/current-shortages/drug-shortages-list

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ASHP Drug Shortages List

	Last Update	
Timolol Ophthalmic	Sep 02, 2023	Jun 04, 2020
Tirofiban Hydrochloride Injection	Oct 25, 2019	Jun 06, 2019
Tirzepatide Injection	Apr 17, 2023	Dec 13, 2022
Tirzepatide Injection	Mar 05, 2025	Jul 20, 2023
Tobramycin Sulfate Injection	Jun 05, 2019	Sep 04, 2015
Tobramycin Sulfate Lyophilized Powder for Solution	Apr 12, 2021	Mar 2

https://www.ashp.org/drug-shortages/current-shortages/drug-shortages-list

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ASHP Drug Shortages List

	Last Update	
Secretin Injection	May 26, 2016	May 28, 2015
Selenium Injection (as Selenious Acid)	Jul 09, 2019	Apr 30, 2017
Semaglutide Injection	Mar 05, 2025	Mar 11, 2022
Sertraline Hydrochloride Oral Solution	Jun 07, 2021	Jun 04, 2020
Sertraline Oral Tablets	Mar 21, 2022	May 18, 2020
Silver Nitrate Solution	Dec 04, 2024	Sep 12, 2024

https://www.ashp.org/drug-shortages/current-shortages/drug-shortages-list

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FDA Clarifies Policies

- **[10/02/2024]** The U.S. Food and Drug Administration has determined the shortage of tirzepatide injection, a glucagon-like peptide 1 (GLP-1) medication, has been resolved. Tirzepatide injection has been in shortage since 2022 due to increased demand.
- FDA confirmed with the drug's manufacturer that their stated product availability and manufacturing capacity can meet the present and projected national demand. Patients and prescribers may still see intermittent localized supply disruptions as the products move through the supply chain from the manufacturer and distributors to local pharmacies.
- **FDA reminds compounders of the legal restrictions on making copies of FDA-approved drugs**

https://www.fda.gov/drugs/drug-safety-and-availability/fda-clarifies-policies-compounders-national-glp-1-supply-begins-stabilize

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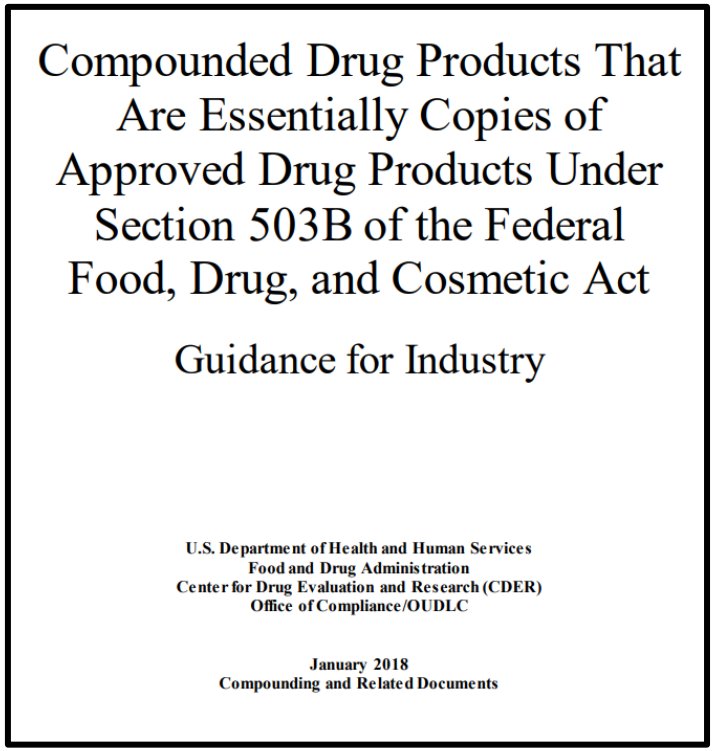
Essentially a Copy

- Sections 503A and 503B restrict the compounding of drug products that are essentially copies of commercially available (section 503A) or approved drug products (section 503B).
- FDA intends to consider a compounded drug product to be identical or nearly identical to an approved drug if the compounded drug product and the FDA-approved drug have the same:
  - **Active ingredient(s)**
  - **Route of administration**
  - **Dosage form**
  - **Dosage strength, and**
  - **Excipients**



Compounded Drug Products That Are Essentially Copies of Approved Drug Products Under Section 503B 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 and Related Documents

https://www.fda.gov/media/98964/download

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Essentially a Copy

- FDA intends to consider a compounded drug product to be identical or nearly identical to an approved drug if the compounded drug product and the FDA-approved drug have the same:
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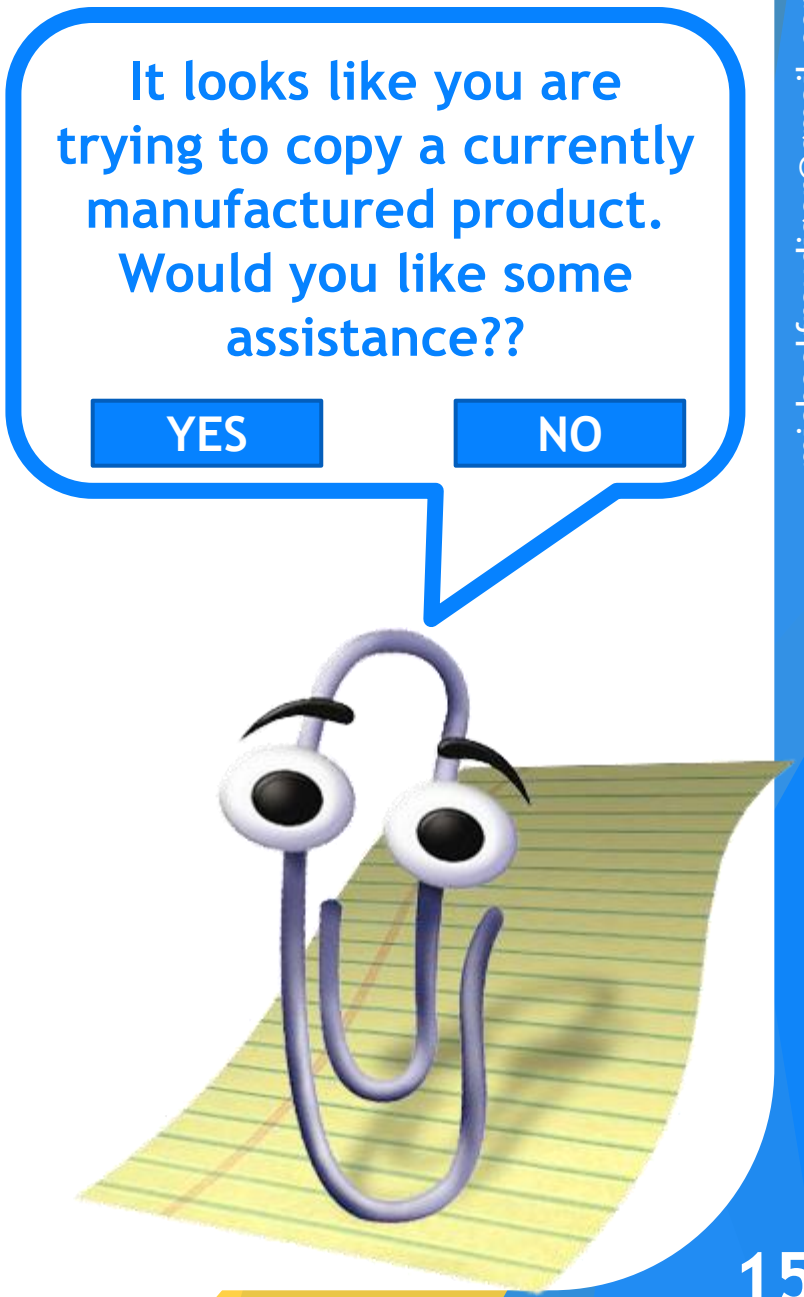

https://www.fda.gov/media/98964/download

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GLP-1 and Vitamin B12

- GLP-1 medications and vitamin B12 work together, as GLP-1s can potentially reduce the absorption of B12, leading to the use of B12 supplementation to help with energy, metabolism, and to counteract side effects like fatigue.
- While GLP-1 drugs help with blood sugar and appetite, B12 supports overall energy, nerve function, and red blood cell formation, making a combined therapy potentially beneficial for weight loss and metabolic health.
- Some research even explores conjugating B12 directly with GLP-1s to reduce side effects like nausea, notes the British Pharmacological Society.

https://taketrava.com/vitamin-b12-and-glp-1-powerful-combination/

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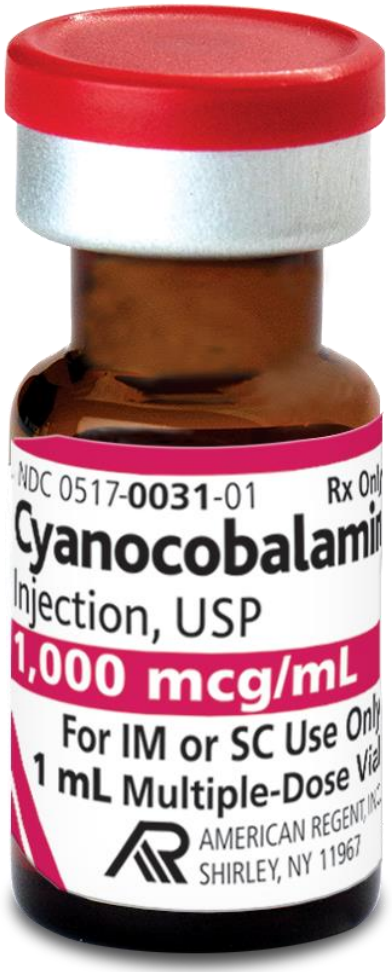
GLP-1 and Vitamin B12

Do these really need to be mixed together?



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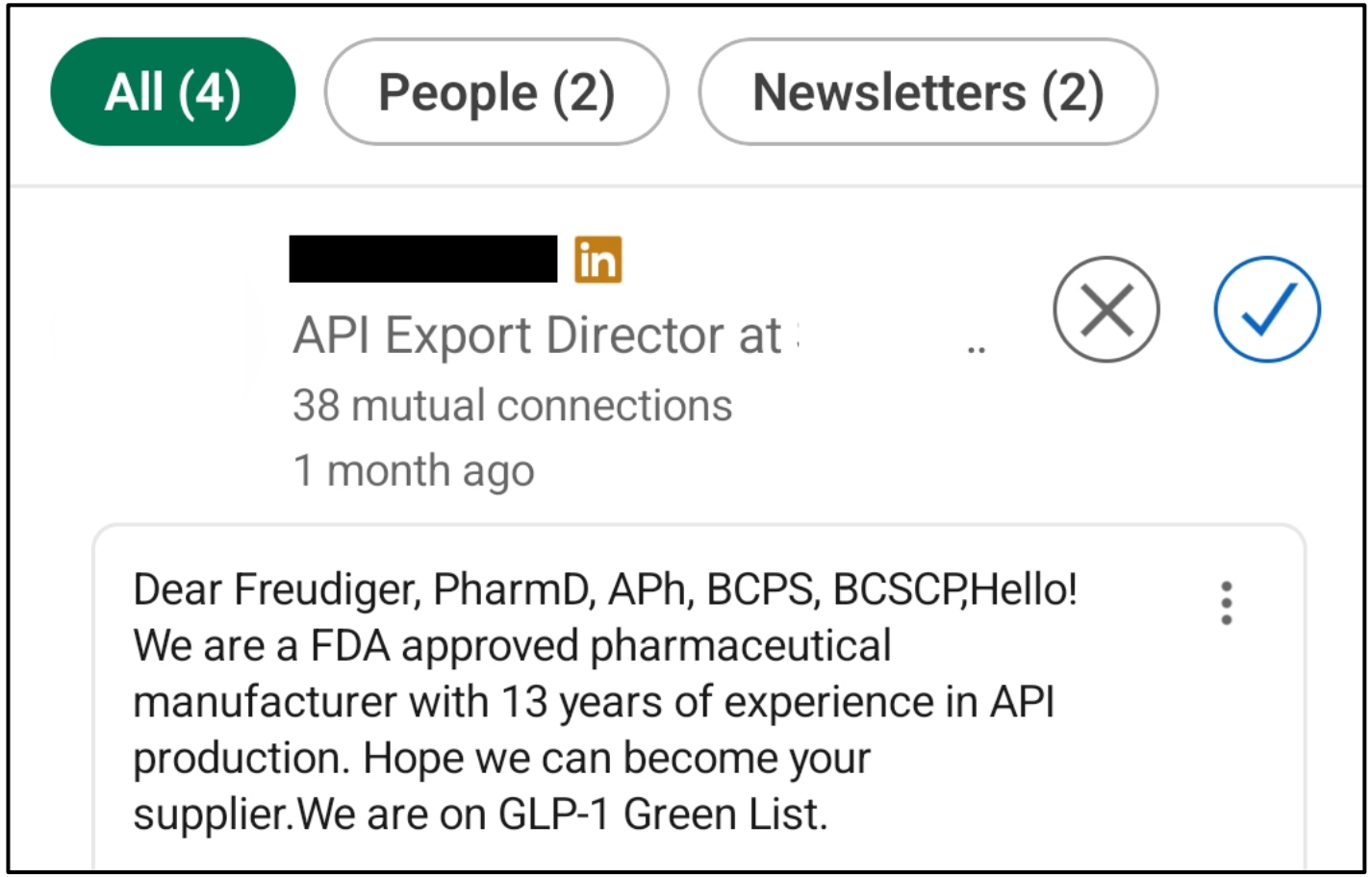
Concerns About API Sources

- Legitimate?
- Contaminants?
- Certificate of Analysis? (COA)



API = active pharmaceutical ingredient

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FDA Green List

- The agency has established a **green list import alert (66-80)** to help stop GLP-1 active pharmaceutical ingredients (APIs) that have potential quality concerns from entering the U.S. supply chain. This import alert does not apply to GLP-1 API from manufacturers that, based on an FDA inspection or other FDA evaluation, appear to be in compliance with FDA's rigorous standards for manufacturing practices.
- This action will help protect consumers from receiving poor-quality compounded drugs containing foreign-made APIs (which are also called bulk drug substances) that may be manufactured without appropriate controls to assure quality. This action does not stop the legal importation into the U.S. market of GLP-1 APIs from compliant API manufacturers, nor does it create any new limits on the legal compounding of GLP-1 drugs.

Import Alert 66-80
https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/fdas-concerns-unapproved-glp-1-drugs-used-weight-loss
https://www.fda.gov/news-events/press-announcements/fda-launches-green-list-protect-americans-illegal-imported-glp-1-drug-ingredients

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FDA Green List

Home > Import Program > Import Alerts > Imports Alerts by Number

Import Alert 66-80

SHARE TWEET LINKEDIN PIN IT EMAIL PRINT

(Note: This import alert represents the Agency's current guidance to FDA field personnel regarding the manufacturer(s) and/or products(s) at issue. It does not create or confer any rights for or on any person, and does not operate to bind FDA or the public).

Import Alert # 66-80
Published Date: 09/26/2025
Type: DWPE

Import Alert Name:

Detention Without Physical Examination of Glucagon-Like Peptide-1 (GLP-1) Receptor Agonist Bulk Drug Substances

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FDA Green List

- Only firms on this list will be permitted to import GLP-1 active pharmaceutical ingredients (“APIs”) into the United States

https://www.accessdata.fda.gov/CMS_IA/importalert_1186.html

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FDA Green List

[redacted], CHINA
61P[][]76 Liraglutide (Anti-Diabetic)
61P[][]72 Semaglutide (Anti-Diabetic)
61P[][]74 Tirzepatide (Anti-Diabetic)

[redacted], CHINA
56F[][]99 Peptide N.E.C. (Antibiotics)
61P[][]72 Semaglutide (Anti-Diabetic)
61P[][]99 Anti-Diabetic N.E.C. (Anti-Diabetic)

[redacted], CHINA
56F[][]99 Peptide N.E.C. (Antibiotics), and the importer description contains the word, Retatrutide
61P[][]76 Liraglutide (Anti-Diabetic)
61P[][]72 Semaglutide (Anti-Diabetic)
61P[][]74 Tirzepatide (Anti-Diabetic)
61P[][]99 Anti-Diabetic N.E.C. (Anti-Diabetic) and the importer description contains the word, Retatrutide

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FDA Green List

MULTIPLE COUNTRIES

- *(56 F - S 99)* Peptide N.E.C., Active Pharm Ingred/Chems for Further Manuf
- *(56 F - T 99)* Peptide N.E.C., Active Pharm Ingred/Chems for Rx Compounding
- *(56 F - R 99)* Peptide N.E.C., NonSterile Powder
- *(56 F - Z 99)* Peptide N.E.C., Sterile Powder
- *(58 H - S 06)* Dulaglutide, Active Pharm Ingred/Chems for Further Manuf
- *(58 H - T 06)* Dulaglutide, Active Pharm Ingred/Chems for Rx Compounding
- *(58 H - R 06)* Dulaglutide, NonSterile Powder
- *(58 H - Z 06)* Dulaglutide, Sterile Powder
- *(58 H - S 07)* Insulin Degludec, Active Pharm Ingred/Chems for Further Manuf

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New England Compounding Center

- September 2012
- 800 severely sick
- 76 deaths
- $200 Million Settlement
- CEO-Pharmacist → 9 years in prison

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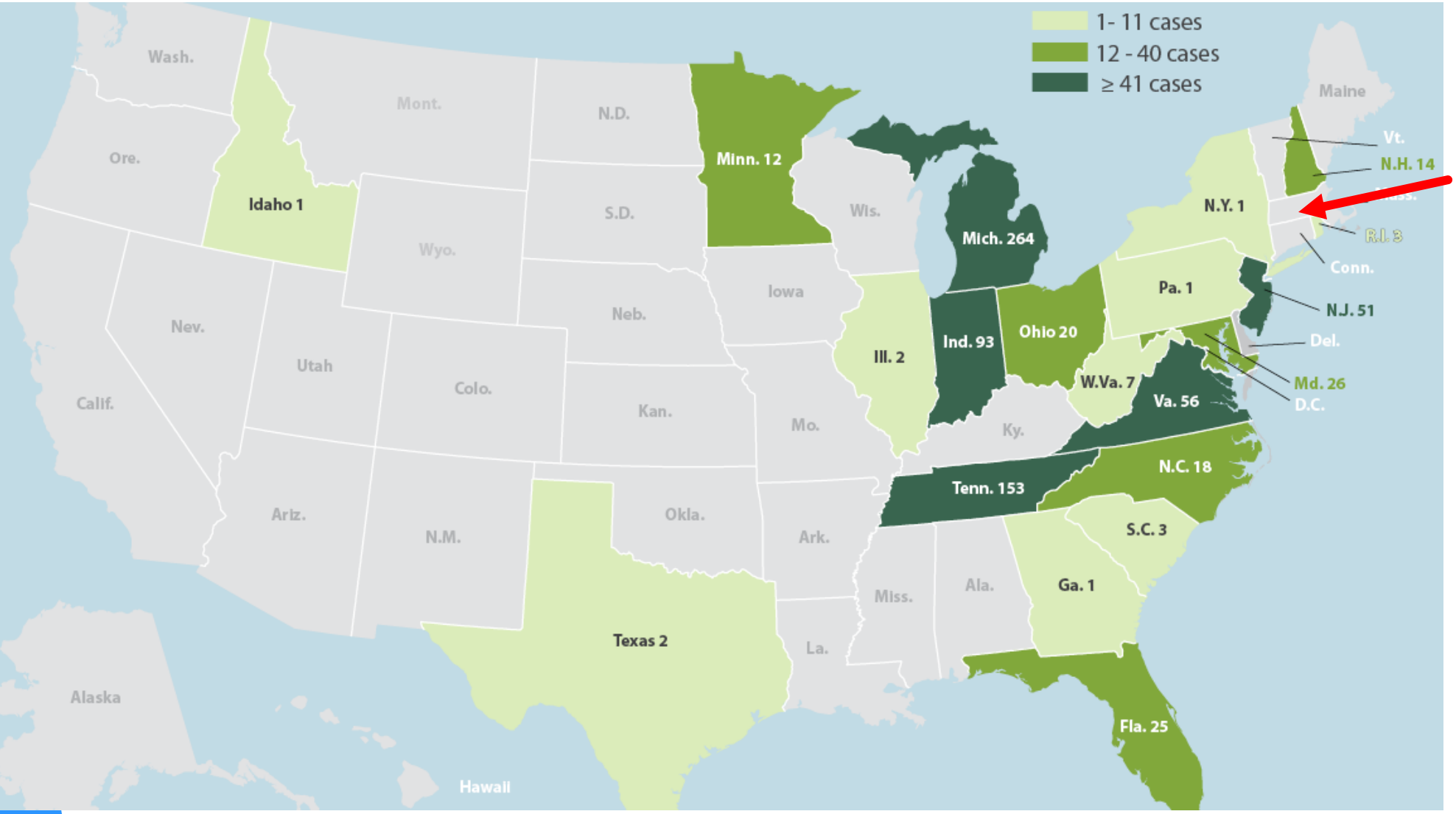
NECC Outbreak: Cases by State



New England Compounding Center 2012

Fungal Meningitis Outbreak Scandal

800 severely sick

76 deaths

What happened?

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NECC: Background

- Pharmacy was illegally manufacturing compounded “sterile” preparations rather than filling prescriptions under its license
- Products were not made in clean environment
- Multiple drugs produced by the pharmacy, mainly injections and epidurals found to be contaminated with ***Exserohilum rostratum*** (black mold)

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NECC: Fungal Organisms

- ***Exserohilum rostratum***
- *Aspergillus fumigatus*
- *Cladosporium cladosporioides*
- *Paecilomyces formosus*

https://geiselmed.dartmouth.edu/news/2013/01/04_cramer/
Image: Exserohilum rostratum

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NECC: Cerebral Spinal Fluid

https://www.cbsnews.com/news/lethal-medicine-linked-to-meningitis-outbreak-10-03-2013/

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NECC: Location

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NECC: Compounded Vials

- NECC had shipped orders of the contaminated drug without waiting for the final results of sterility testing.
- Records suggested NECC had failed to sterilize products for "even the minimum amount of time necessary to ensure sterility”

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NECC: Unsanitary Conditions

- Mats used to trap dust and dirt outside the rooms were dirty
- Sterile hoods were not properly cleaned
- Boiler was leaking next to a clean room
- Medical staff were using fake names such as "Harry Potter," "Baby Jesus," and "Chester Cheeto" to create fraudulent prescriptions for drugs

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NECC: Unsanitary Conditions

FDA INSPECTION REPORT: The firm is abutted to the rear and along the left parking area of a recycling facility that handles such materials as mattresses and plastics. On 10/2/2012, the area was observed to include large equipment (e.g. excavators and freight trucks) producing airborne particles (e.g. dust). Rooftop units serving the firm's HVAC AC systems were estimated to be located approximately 100 feet from the recycling facility.

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NECC: Environmental Sampling

Table #5: Air Sampling of ISO 7 (Class 10,000) Rooms

Alert: 5 CFU Action: 8+ CFU

Location	Result Bacteria	Result Mold	Date
Gown Room (Clean Room 1)			
Gown room	29*	1*	5/31/12
Gown room	11*	1*	6/28/12
Middle Room (Clean Room 1)			
Crimp Station	3	1	2/23/12
Prep Room (Clean Room 2)			
Prep room	0	1	5/2/12
Gown Room (Clean Room 2)			
Gown room	7*	3*	8/9/12

Note: (*) indicates result over action level

https://www.fda.gov/media/84684/download

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NECC: Environmental Sampling

Table #6: Surface and Air Sampling of ISO 5 (Class 100) Clean Room 2
No Action/Alert Levels specified by firm for ISO 5 (Class 100) areas.

Location	Sample Type	Result Bacteria	Result Mold	Date
Table 1 (near Horiz L & R hoods)	Surface	0	3	1/26/12
Table 1 (near Horiz L & R hoods)	Surface	1	1	5/2/12
Between Horiz L & Horiz R	Air	1	1	7/25/12

FDA INSPECTION REPORT: "There was no investigation conducted by the firm when levels exceeded their action limits and there was no identification of the isolates. No documented corrective actions were taken to remove the microbial contamination (bacteria and mold) from the facility."

https://www.fda.gov/media/84684/download

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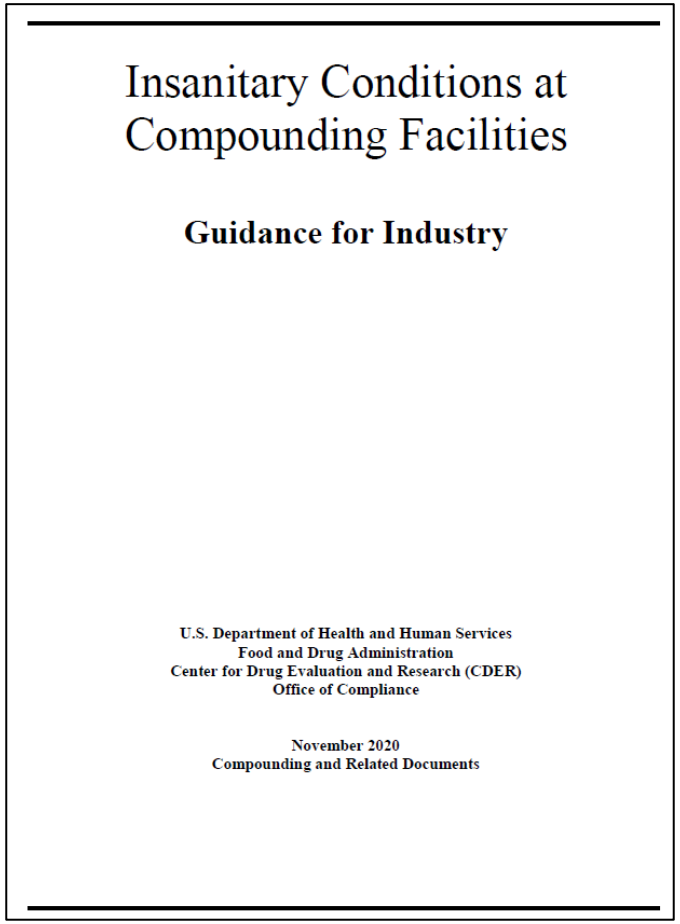
FDA Insanitary Conditions

- **BACKGROUND:** Drug products prepared, packed, or held under insanitary conditions could become contaminated and cause serious adverse events, including death.



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

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/insanitary-conditions-compounding-facilities-guidance-industry

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FDA Insanitary Conditions

- Failure to use pre-sterilized or sterilized primary containers and closures to fill sterile products
- Using a non-sterile tool to manually contact the inner surface of a sterile container
- Touching the top of an open container or bottom of a closure before adding the stopper to a vial

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/insanitary-conditions-compounding-facilities-guidance-industry

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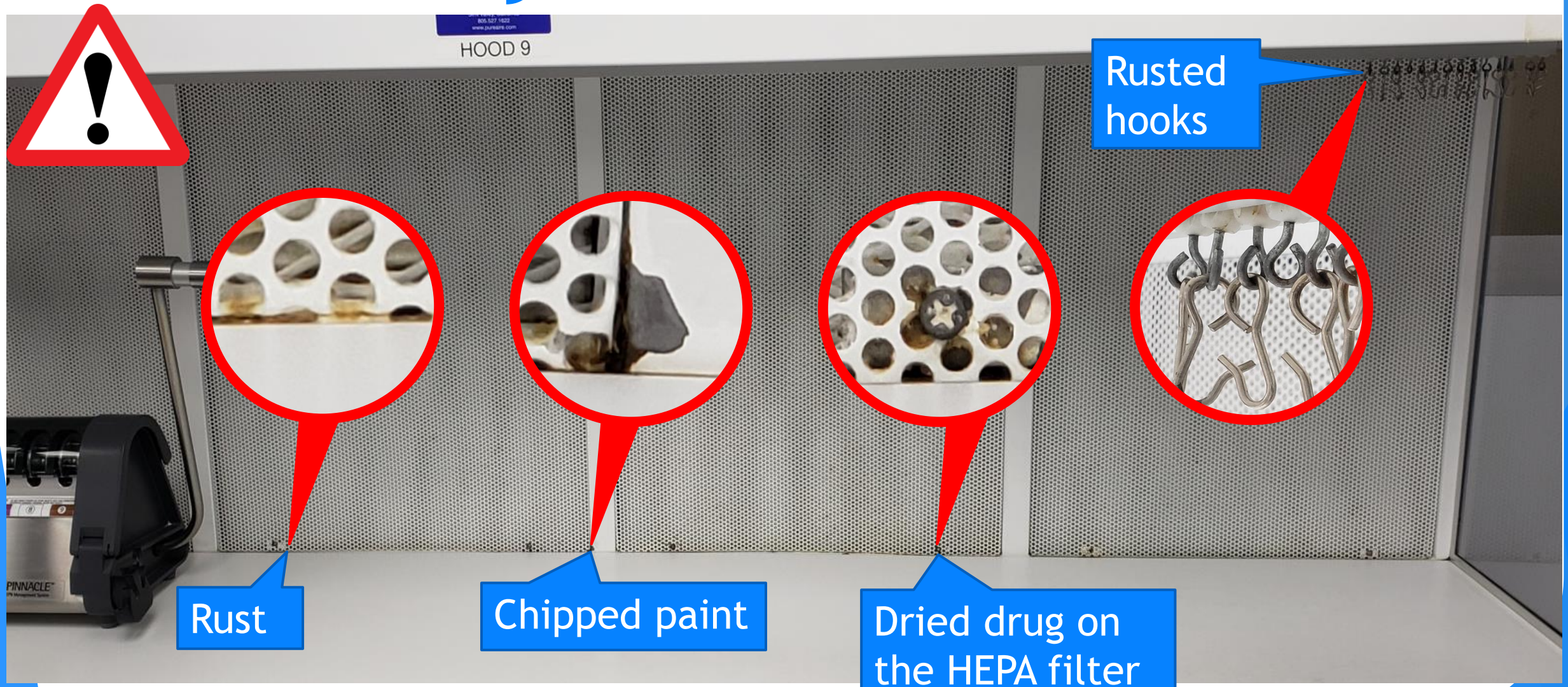
Insanitary Conditions: Hoods



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Images © Michael Freudiger

Oncology Clinic: Port Flushes

- **Outpatient oncology clinic;** compounding port flushes containing saline, heparin, vancomycin, and ceftazidime.
- **Fungal contamination:** Exophiala dermatitidis & Rhodotorula mucilaginosa
- **17 patients with a positive cultures; 2 deaths**
- Investigation Findings: failures to meet CDC infection control standards for outpatient oncology settings, failure to meet standards for sterile medication compounding and handling of hazardous drugs as outlined by USP 797 and 800 and the FDA.
- Flushes had been compounded under substandard conditions, stored in a refrigerator, and accessed daily for multiple patients over a time period of approximately **4–8 weeks** until the solution was depleted.

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Amber Vasquez et al., "Notes From the Field: Fungal Bloodstream Infections Associated With a Compounded Intravenous Medication at an Outpatient Oncology Clinic—New York City, 2016,"Morbidity and Mortality Weekly Report 65, no. 45 (2016): 1274-75, http://www.cdc.gov/mmwr/volumes/65/wr/mm6545a6.htm?s_cid=mm6545a6_w

Duke University Hospital

- Hospital compounding pharmacy; **7 patients**
- Fentanyl infusions were contaminated by **Burkholderia Cepacia** complex.
- Contamination traced to anteroom sink drain and pH probe calibration fluid from the compounding clean room.

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Moehring RW, Lewis SS, Isaacs PJ, et al. Outbreak of Bacteremia Due to Burkholderia contaminans Linked to Intravenous Fentanyl From an Institutional Compounding Pharmacy. JAMA Intern Med. 2014;174(4):606–612. doi:10.1001/jamainternmed.2013.13768

Duke University Hospital

- Investigators noted possible mechanisms for contamination from surfaces, equipment, and gloves in the compounding room:
  - Gloves were not changed between compounding steps (instead gloves were disinfected using alcohol and then used to manipulate sterile items)
  - The pH probe calibration fluid was not routinely changed
  - The pH probe was submerged into the entire volume of the preparation instead of testing small aliquots at a time.
- Staff members expressed a belief that the final filtration step would be adequate to resolve possible contamination events that occurred before this step.

Moehring RW, Lewis SS, Isaacs PJ, et al. Outbreak of Bacteremia Due to *Burkholderia contaminans* Linked to Intravenous Fentanyl From an Institutional Compounding Pharmacy. *JAMA Intern Med.* 2014;174(4):606–612. doi:10.1001/jamainternmed.2013.13768

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Questions?

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