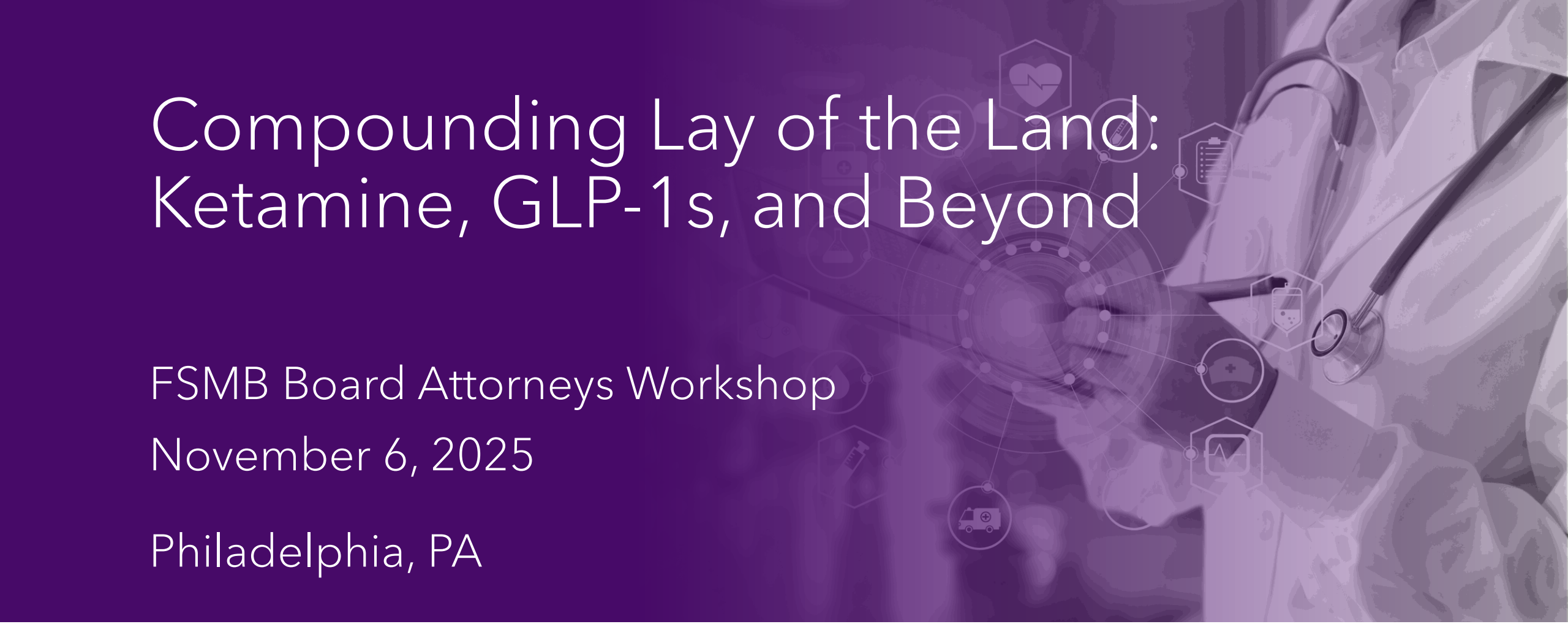
Compounding Lay of the Land: Ketamine, GLP-1s, and Beyond



FSMB Board Attorneys Workshop

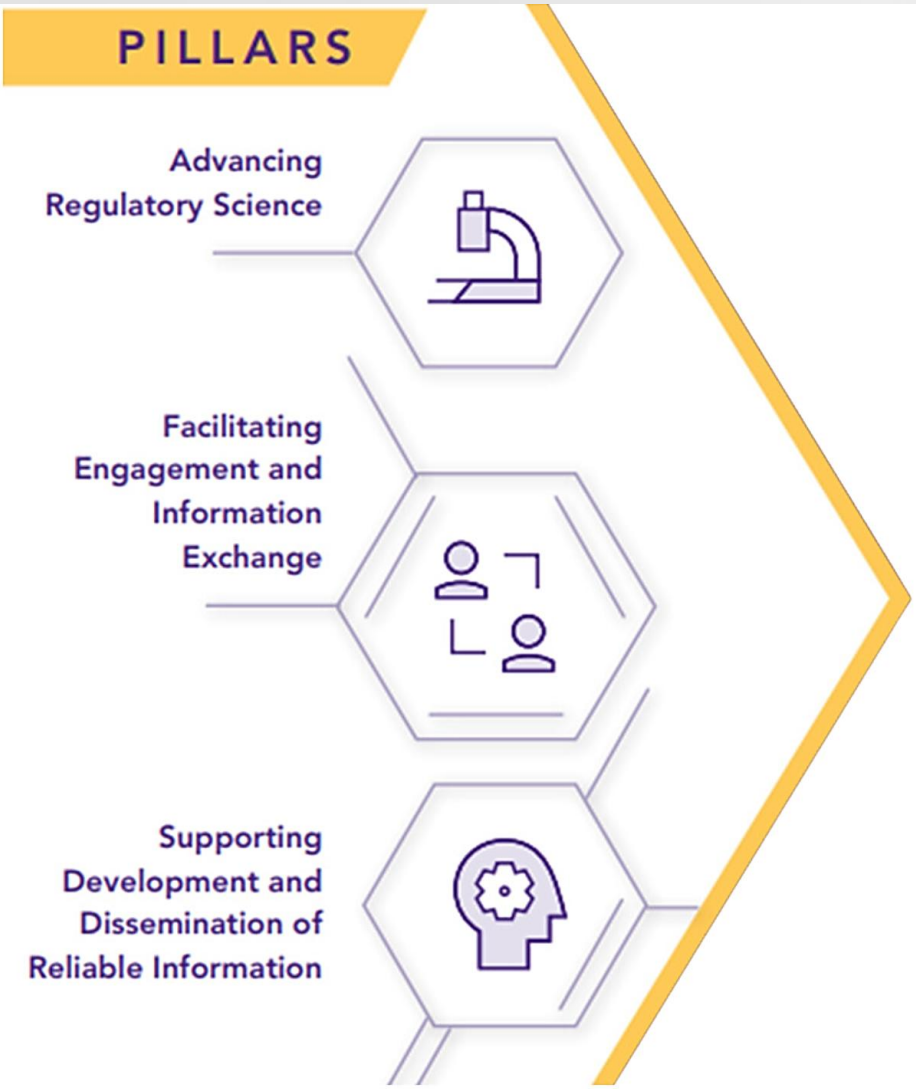
November 6, 2025

Philadelphia, PA

Susan C. Winckler, RPh, Esq
swinckler@reaganudall.org

REAGAN-UDALL FOUNDATION FOR THE FDA

About the Foundation



- Independent nonprofit organization created by US Congress in 2007 to help FDA "do more" to protect and promote the public's health by advancing innovation
- Foundation receives financial support from the US FDA and many organizations within the FDA ecosystem
- As a working Foundation, we manage a suite of programs that stimulate change: we help the FDA engage with external stakeholders and facilitate evidence generation, improve public understanding of the Agency and the products it regulates, and deliver more accessible health information to the public

NOTE: Compounded products are NOT FDA approved

Two Types of Compounding: 503A vs 503B

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	503A	503B
Compounding standards	USP 795 or USP 797	cGMP (current Good Manufacturing Practices)
Formulations	primarily oral, nasal, topical	primarily injectable
Purchasers	patients	health systems; health practices; 503A pharmacies
Prescription Requirement	yes	no, unless dispensing directly to patient
DEA registration	yes	yes
PDMP reporting	yes	no

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Compounding for GLP-1s: A Snapshot…with detail in next presentation

Timeline for GLP-1 Shortages

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End of 2022:

Shortage for semaglutide began;

Allows greater leeway for compounding

2023 – 2024:

Demand continued to increase, and shortages expanded to other GLP-1s

End of 2024 – Mid 2025:

FDA ended shortage status for GLP-1s;

Compounding rules return to status quo (need not met by commercially-available product)

Sept 2025:

FDA established a green list for imported API

FDA Communication about GLP-1s

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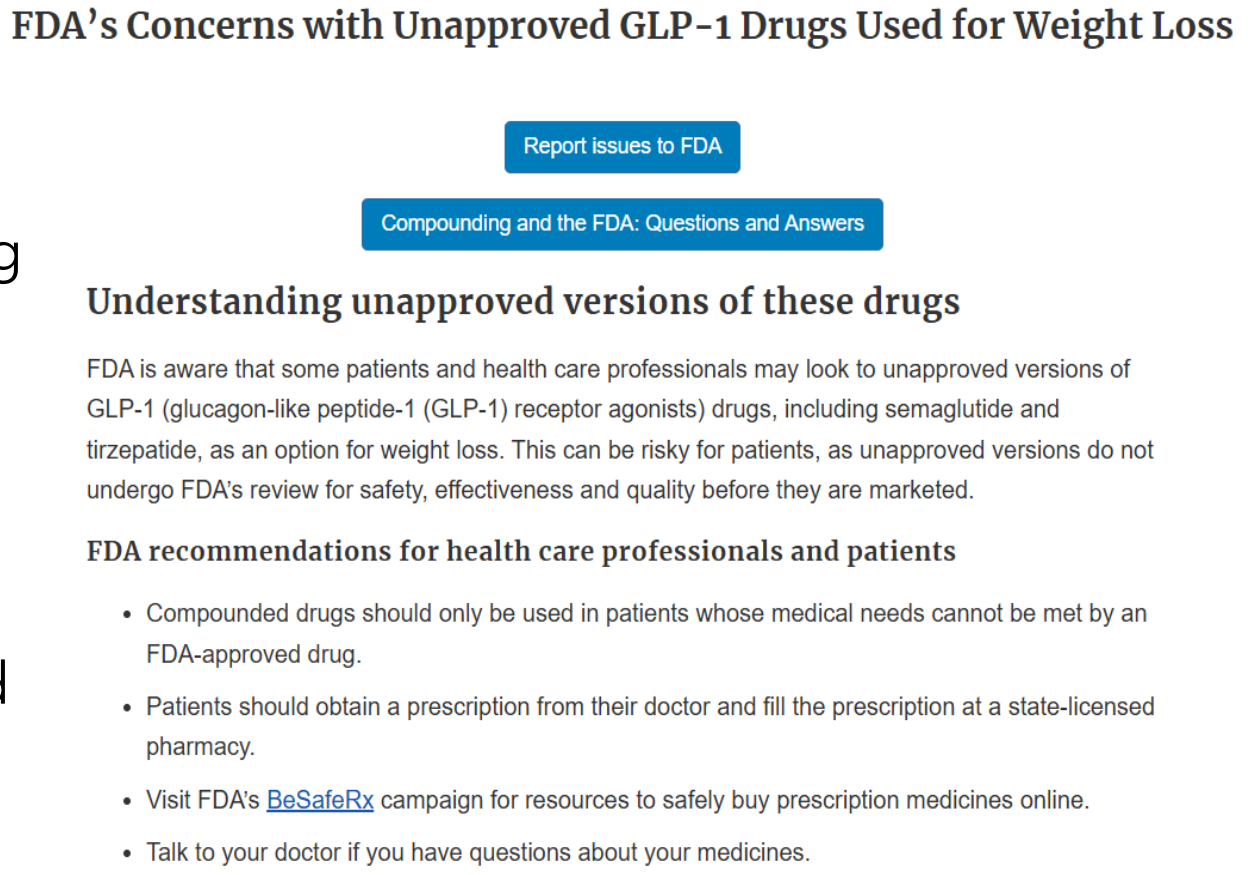
- FDA issued postmarket drug safety information in September about unapproved GLP-1s
- Shortages led to increased compounding of API from foreign sources
- Concerns about adulterated API and other quality issues
- Established a green list import alert that lists registered foreign manufacturers of GLP-1 API whose facilities and associated products appear to be in compliance with CGMP requirements



FDA's Concerns with Unapproved GLP-1 Drugs Used for Weight Loss

Report issues to FDA

Compounding and the FDA: Questions and Answers

Understanding unapproved versions of these drugs

FDA is aware that some patients and health care professionals may look to unapproved versions of GLP-1 (glucagon-like peptide-1 (GLP-1) receptor agonists) drugs, including semaglutide and tirzepatide, as an option for weight loss. This can be risky for patients, as unapproved versions do not undergo FDA's review for safety, effectiveness and quality before they are marketed.

FDA recommendations for health care professionals and patients

- Compounded drugs should only be used in patients whose medical needs cannot be met by an FDA-approved drug.
- Patients should obtain a prescription from their doctor and fill the prescription at a state-licensed pharmacy.
- Visit FDA's BeSafeRx campaign for resources to safely buy prescription medicines online.
- Talk to your doctor if you have questions about your medicines.

A Certain SuperBowl Ad: Advertising for Medical Products

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- FDA regulates prescription drug promotion
- Modern compounding marketplace is not comprised of prescription drug manufacturers or distributors
- Instead, wellness clinics, telehealth services, or med spas advertise sub-anesthetic ketamine, GLP-1s, and other prescription products

FDA Warning Letters

- In September 2025, FDA sent over 100 warning letters to manufacturers and others about direct-to-consumer advertising.
  - More than 50 to GLP-1 manufacturers and compounders
- Language like “generic versions” or “contain the same active ingredient as FDA-approved GLP-1 drugs” is false or misleading

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Emerging Therapeutic Uses of Ketamine

These activities are part of a multi-part Foundation project related to substance use disorder. The multi-part project is supported by the Food and Drug Administration (FDA) of the U.S. Department of Health and Human Services (HHS) as part of an overall award of $2,470,442 of federal funds (100% of the project). The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement, by FDA, HHS, or the U.S. Government.

The number of seizures of ketamine increased 349% from 55 in 2017 to 247 in 2022

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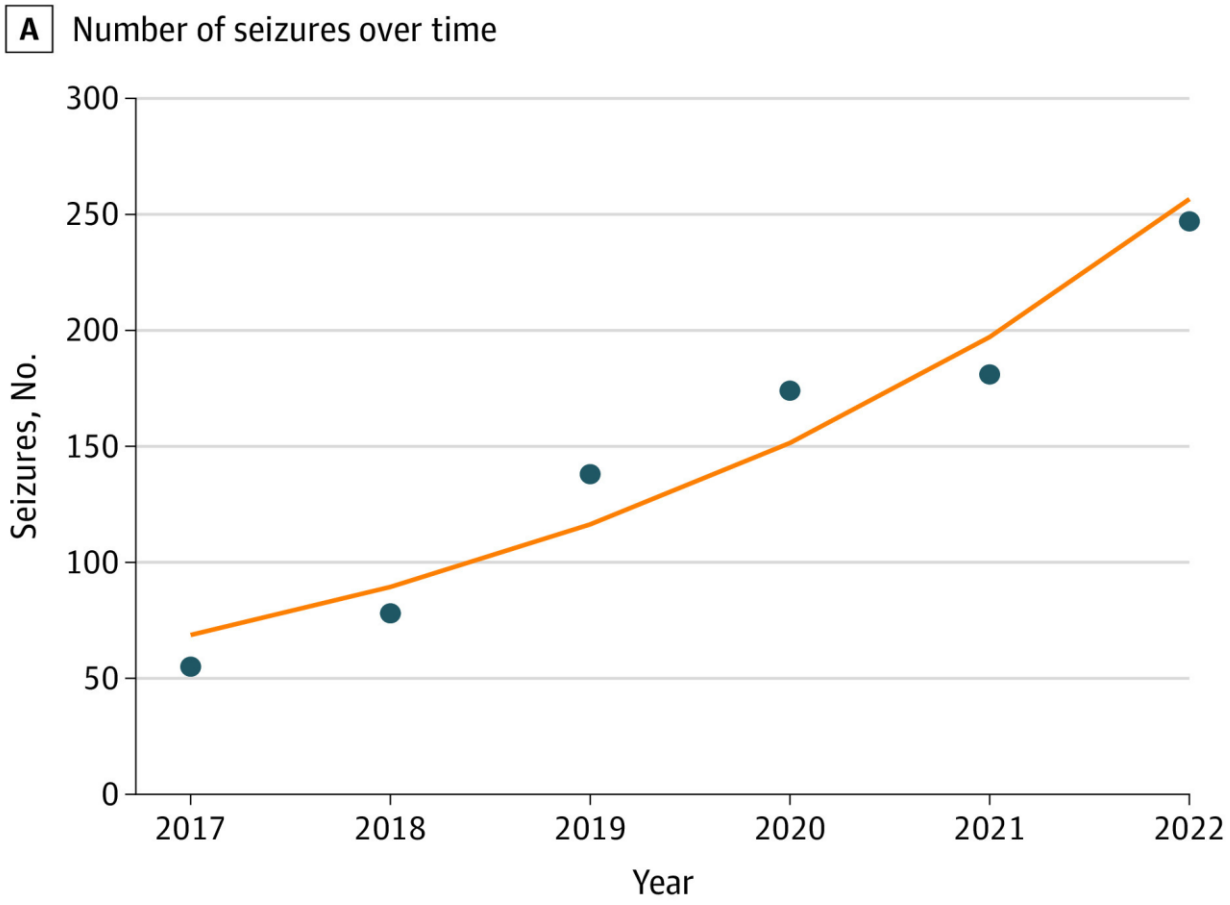
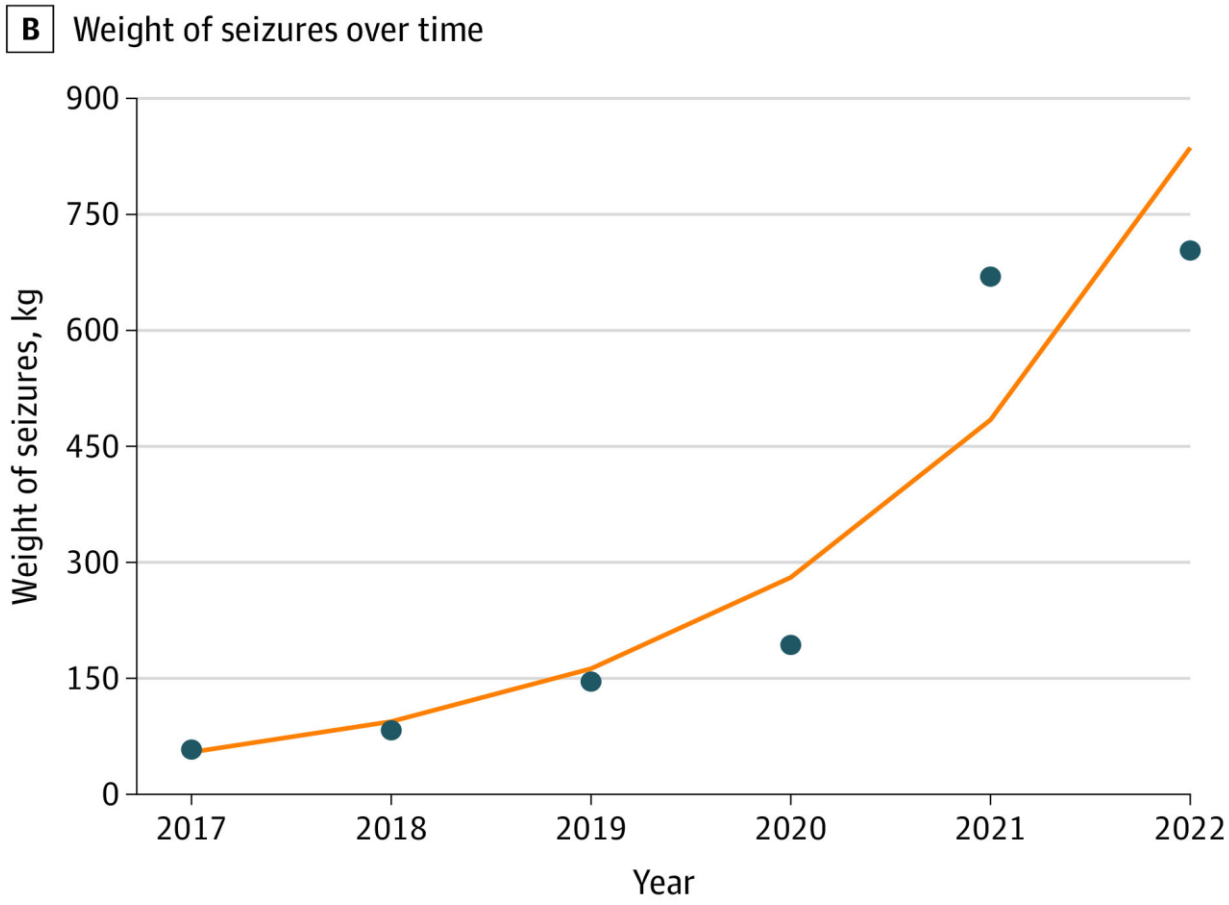
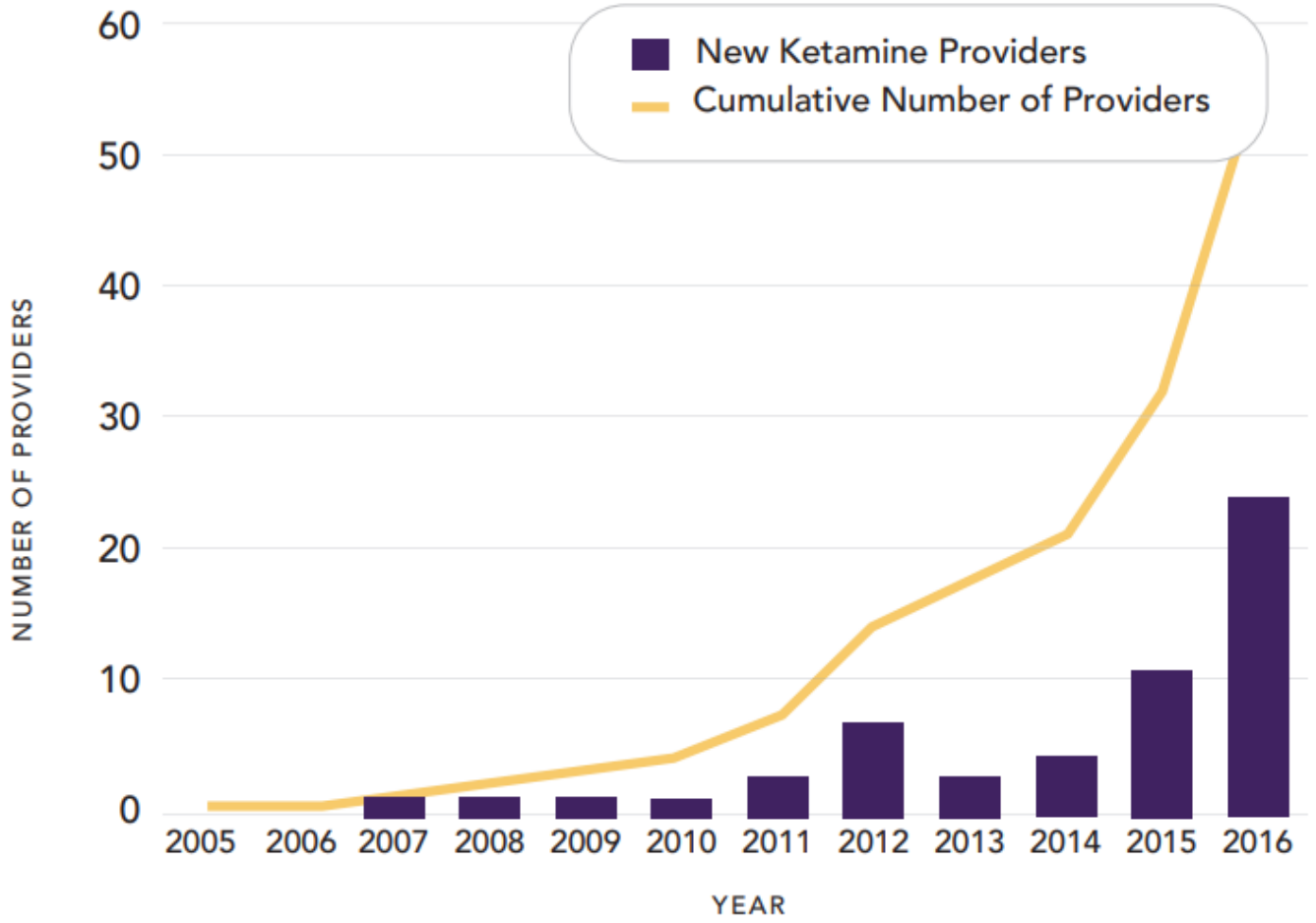




Palamar JJ, Wilkinson ST, Carr TH, Rutherford C, Cottler LB. Trends in Illicit Ketamine Seizures in the US From 2017 to 2022. *JAMA Psychiatry*. 2023;80(7):750-751. doi:10.1001/jamapsychiatry.2023.1423

Rapid Increase in Clinicians Providing Ketamine for the Treatment of Psychiatric Disorders

Indications that clinical use of ketamine is expanding alongside an increase in illicit use



Total Number of Physicians Initiating the Practice of Providing Ketamine Off Label for the Treatment of Psychiatric Disorders per Calendar Years (Bars) and Cumulative Number of Ketamine Providers Over Time (Line)

Wilkinson ST, Toprak M, Turner MS, Levine SP, Katz RB, Sanacora G. A Survey of the Clinical, Off-Label Use of Ketamine as a Treatment for Psychiatric Disorders. *Am J Psychiatry*. 2017;174(7):695-696. doi:10.1176/appi.ajp.2017.17020239

Ketamine Compounding

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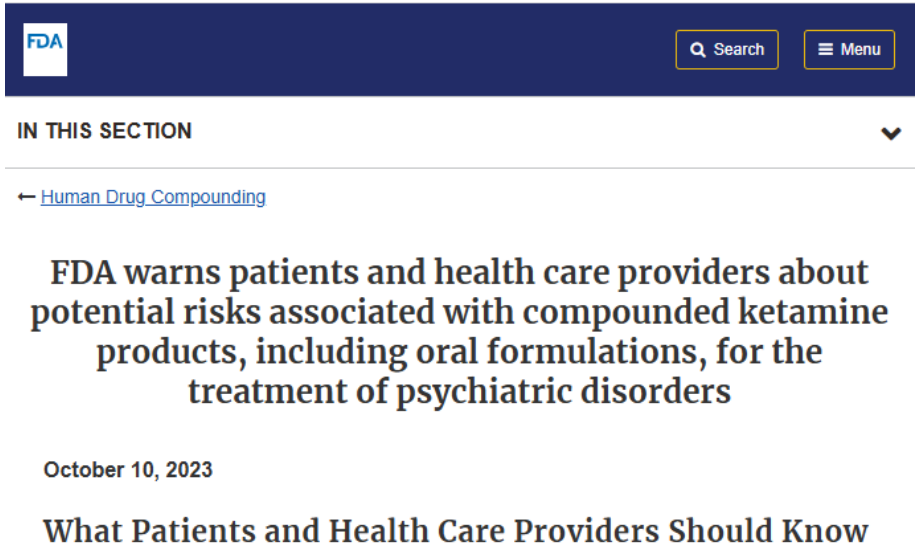
- Recent increased interest in compounded ketamine products for the treatment of psychiatric disorders
- Ketamine clinics appear to be increasing around the country
- Telehealth online offerings are readily and easily available
  - Started in 2021, per COVID controlled substance flexibilities
- Despite increase in recreational illicit use of ketamine, unclear if increase in compounded therapeutic use of ketamine



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Ketamine Compounding Landscape Assessment

Who we spoke to

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Ten conversations with ketamine compounding stakeholders

Pharmacy operators, associations, boards, API distributor

All actively engaged in ketamine compounding or oversight

Ketamine Compounding Ecosystem

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503A compounders

503B outsourcing facilities

API wholesalers

Telehealth platforms

Hospitals
Surgical centers
Clinics

Clinical investigators

Rogue online sources

IV hydration clinics
Medspa
Wellness centers

Regulators

Ketamine Compounding Ecosystem

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Consistent Themes

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- There is a clinical need for compounded ketamine
- Ensuring strong triad relationships is important (patient/prescriber/pharmacist)
- Ketamine compounding is not complex (relative to other products)
- Compounding best practices are available
- Rogue sellers undermine legitimate use
- Little or no data available about dispensing, prescribing, or compounding
    - PDMP reporting (limited interpretability, no data sharing)

Trends

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- 503A and 503B have distinct lanes re: formulations and use
- View esketamine and ketamine as very different treatment approaches because racemic and oral formulations offer personalized and convenient dosing and mitigate adverse events
- No perceived change in compounding following esketamine approval
- Pharmacists understand bioavailability challenges with oral forms
- Ketamine clinics appear to be increasing around the country
- Telehealth online offerings are readily and easily available
    - Started in 2021, per COVID controlled substance flexibilities
- Despite increase in recreational illicit use of ketamine, unclear if increase in compounded therapeutic use of ketamine

503A Compounders

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- 503A – primarily troches, sublingual, intranasal, transdermal
- Most 503A compounders offer ketamine
  - Formulations offered differ
- Alliance for Pharmacy Compounding Best Practices
- Compounders understand the pharmacokinetic and pharmacologic aspects of the different formulations and potential uses
- Used mostly for maintenance for pain, neuralgia, depression, other mental health uses
- Patients: Using ketamine as stand-alone therapy or between infusions
- Report to state PDMP, but data is reported on a molecule level
- DEA registered
- No apparent challenges to buying API

503B Outsourcing Facilities

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- 503B – primarily infusion, pre-filled syringes
- Used mostly for anesthesiology, pain, sedation
- Outsourcing Facilities Association Best Practices (not publicly shared)
- 13 outsourcing facilities reported compounding ketamine in 2024 June reporting
- 60 NDCs for compounded ketamine by 503Bs
- No PDMP reporting, not required
- DEA registered
- 503B sales to 503A, per FDA draft guidance
- Report that 503B conducts independent testing of API

API Wholesalers

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- API readily available, no problem sourcing
- Perform due diligence of new compounders before sale
- One reported 114 active formulations (recipes) for ketamine
  - Most downloaded is for topical formulation
  - New formulations are developed per literature use and per customer request
- No visibility into quantity dispensed or prescribed
- Utilization for ketamine does not appear to have changed over last few years

State Health Professional Licensing Board Conversations

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- Limited data
- PDMP data are reported by molecule (based on powder form) and are not identified by formulation, impossible to tease out formulations or use/indication
  - But, they can tell if it is compounded based on the pharmacy reporting
- No visibility in clinical administration data, just prescription data
- No sign of diversion, based on what is under their jurisdiction
- Several states have issued joint statements with Boards of pharmacy, nursing, and medicine regarding IV hydration, medspas, and wellness clinics

Telehealth & Compounder Arrangements

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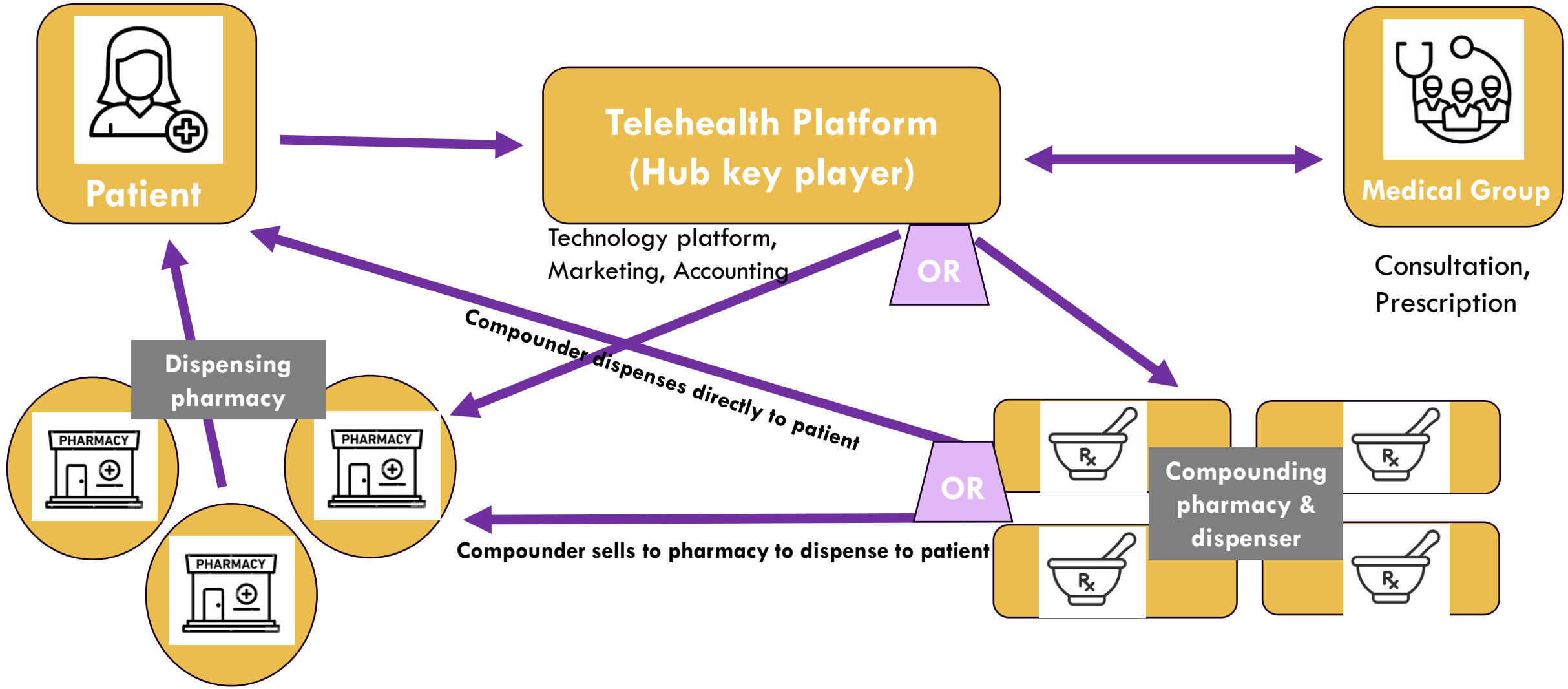
- Landscape
  - Per one accreditor: 20-30 certified telehealth merchants
    - Each contract with a few pharmacies
  - Per another accreditor: 13 platforms connected to 10 fulfillment compounding pharmacies
  - Same pharmacies servicing multiple merchants/platforms
- Pharmacies/telehealth are accredited by NABP or LegitScript to enable credit card transactions
  - Transparent and "rigorous" standards
- Complex regulatory oversight
  - State/federal/local laws – vary if shipping into or out of state
  - Different providers have different oversight Boards (e.g., medicine, pharmacy, nursing)
- Safety monitoring
  - Standard includes evaluation of how the entity monitors patient safety, such as compliance with REMS, pulse-ox safeguards, BP monitoring, companion training and registration, "welcome packets with safety info and equipment," self-attestation feedback

Telehealth Business Model



Digital Ketamine Providers

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Legitimate digital pharmacies	Rogue online sellers
Strong triad relationship (prescriber/pharmacy/patient)	Limited or no communication and feedback
Data collection/safety monitoring	Limited or no data collection or safety monitoring
Legitimate API sourcing	Unknown API sourcing
Transparent information about business	No disclosures
Accredited	Not accredited
Comply with laws/regs	Unknown compliance
Participation in associations, discussion groups	No participation
Accept credit cards	Cash only

Enforcement

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- Limited state/federal enforcement cases
  - Healthcare fraud, kickbacks, ancillary to other charges or disciplinary action
- Limited oversight at clinics/spas/wellness centers
  - Most pharmacy boards lack jurisdiction
  - Medical boards may not have investigation/inspection personnel
- Limited to “is there a valid prescription?”

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Thank you!

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Learn more about the Foundation's work related to controlled substances:

These activities are part of a multi-part Foundation project related to substance use disorder. The multi-part project is supported by the Food and Drug Administration (FDA) of the U.S. Department of Health and Human Services (HHS) as part of an overall award of $2,470,442 of federal funds (100% of the project). The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement, by FDA, HHS, or the U.S. Government.

Pharmacist's Perspective:
Implications for Compounding & Patient Safety

Michael J. Freudiger, PharmD, APh, BCPS, BCSCP
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https://www.linkedin.com/in/michaelfreudiger/

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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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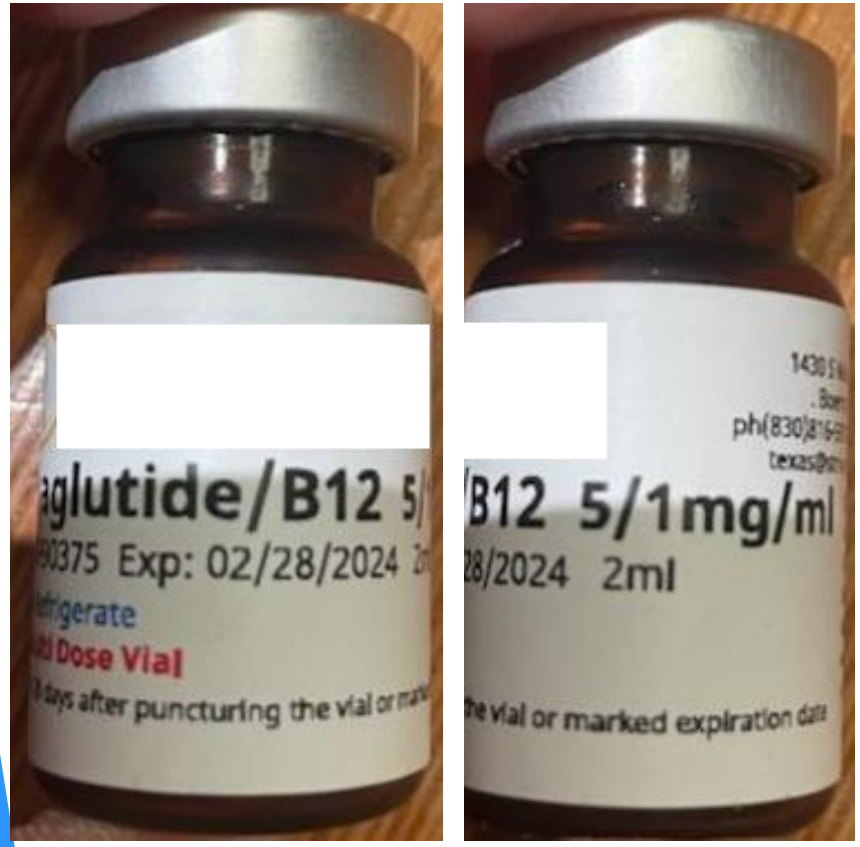
Patient Case: Semaglutide Overdose



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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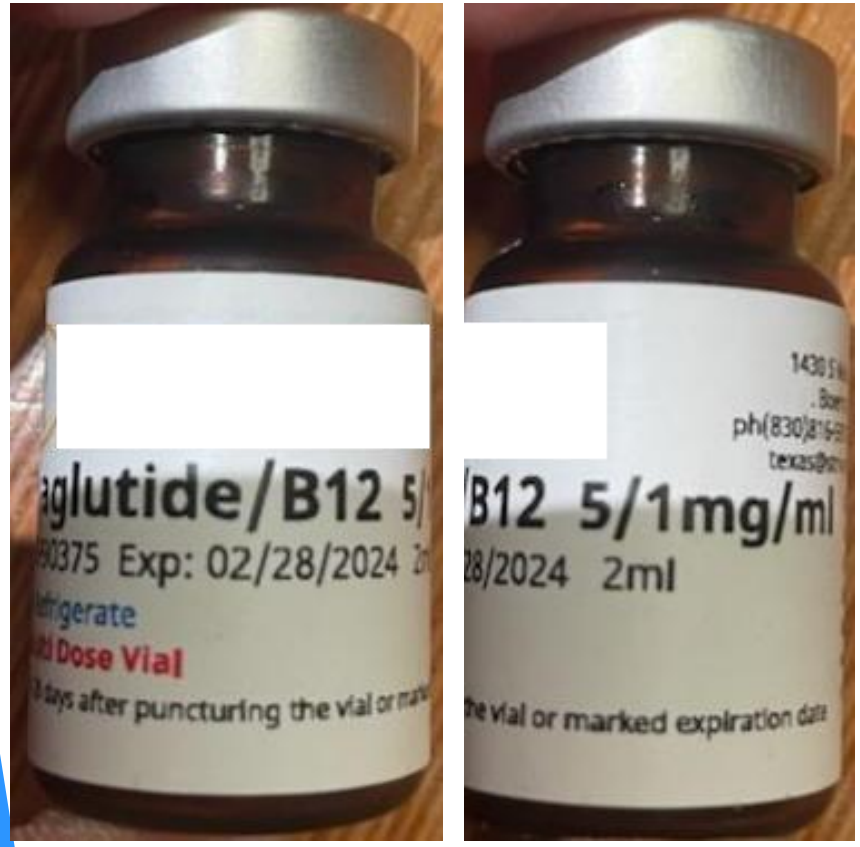
Patient Case: Semaglutide Overdose



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
  - 5 mg/mL ÷ 1.7 mg = 0.34 mL

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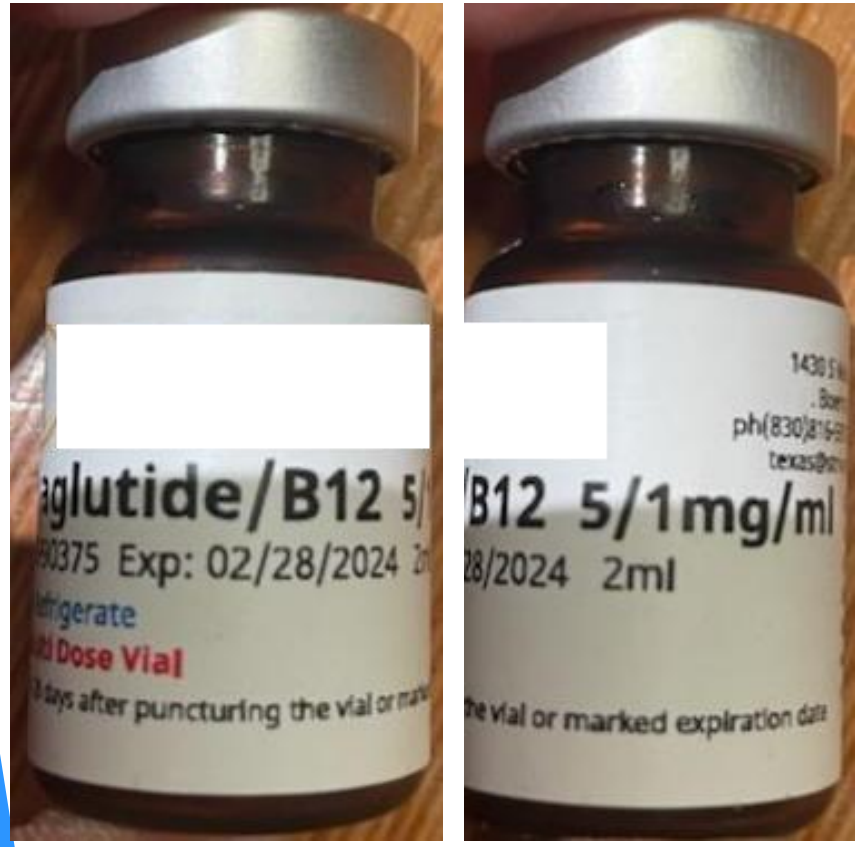
Patient Case: Semaglutide Overdose



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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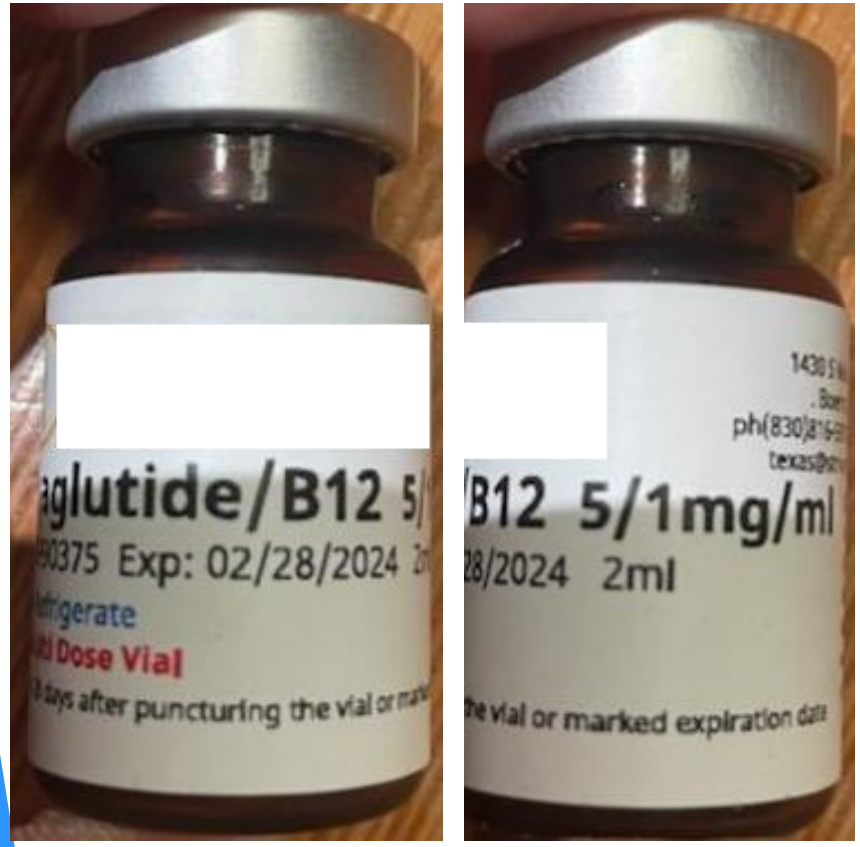
Patient Case: Semaglutide Overdose



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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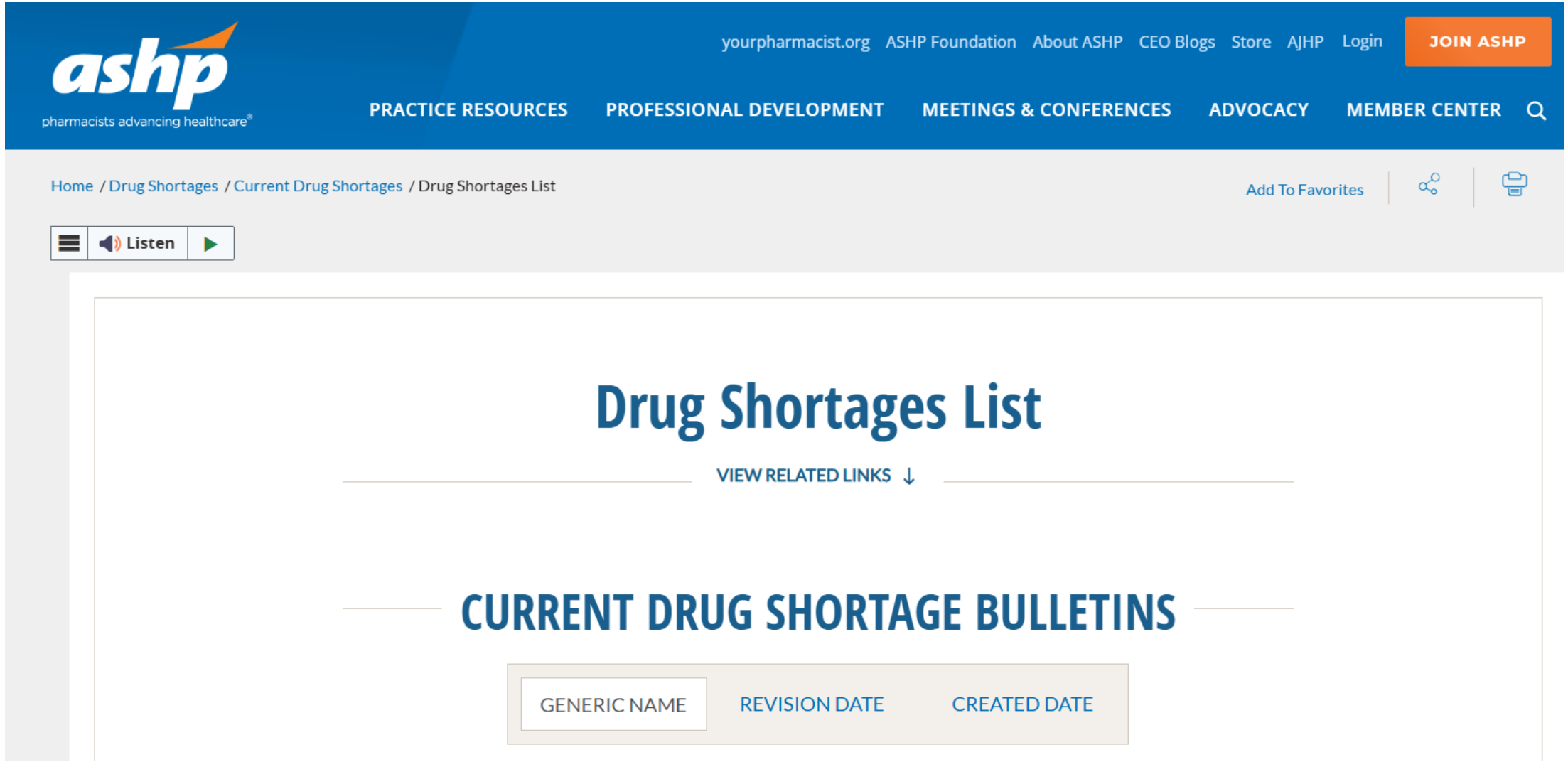
ASHP Drug Shortages List



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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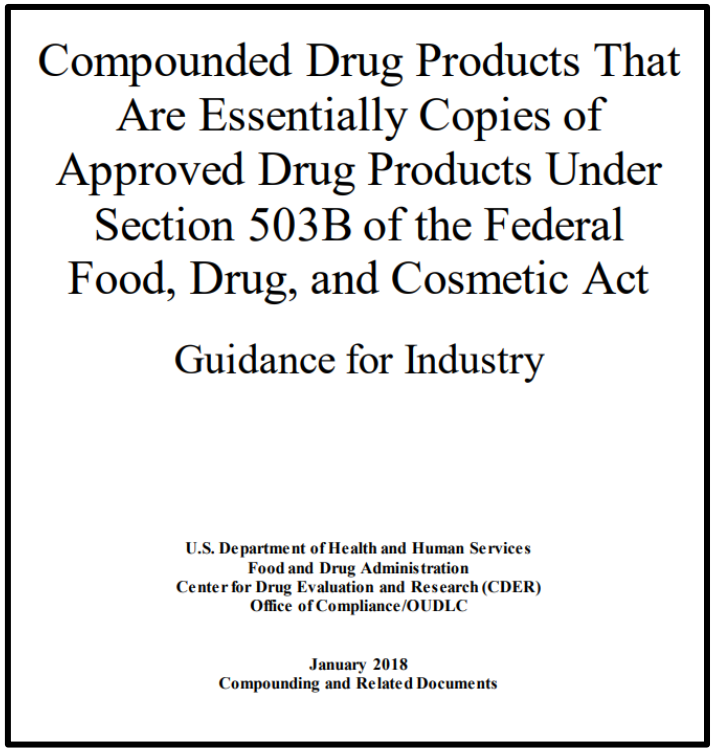
Essentially a Copy

- 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:
  - **Active ingredient(s)**
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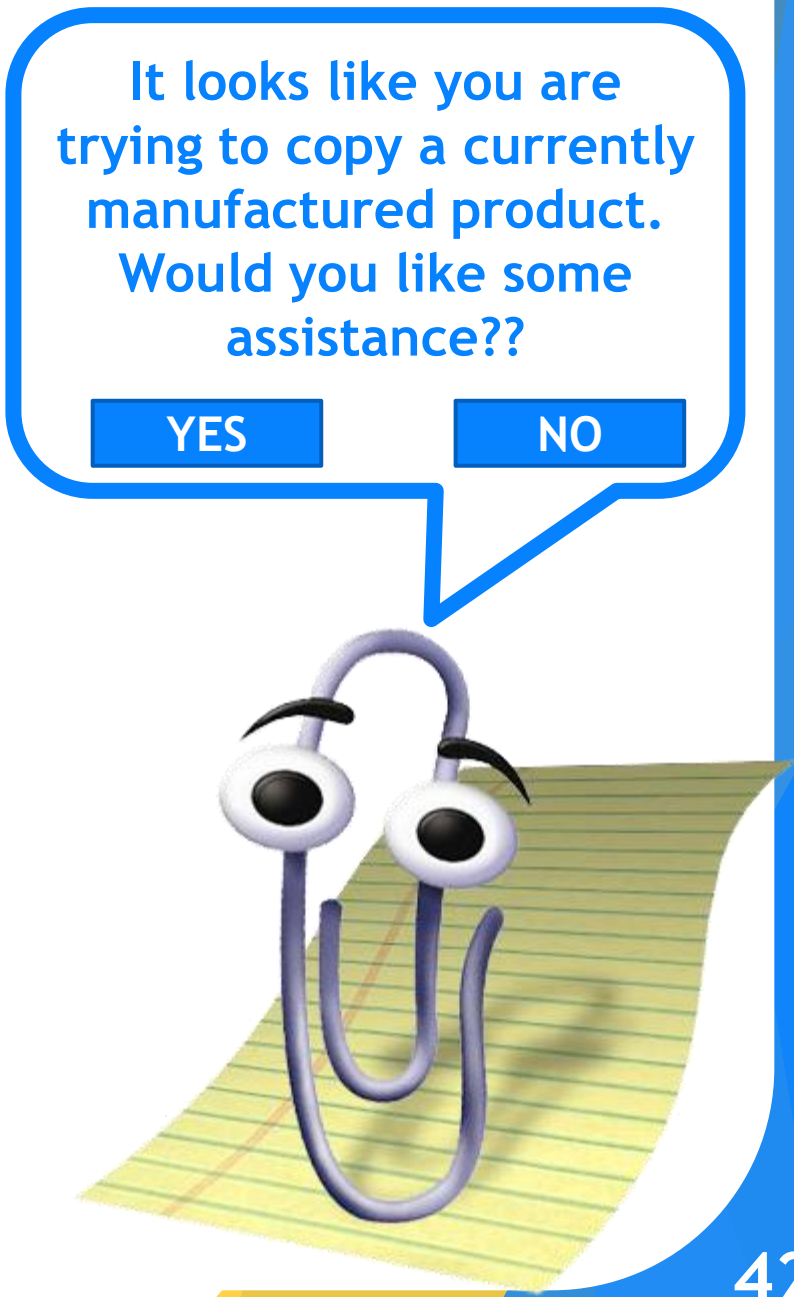

https://www.fda.gov/media/98964/download

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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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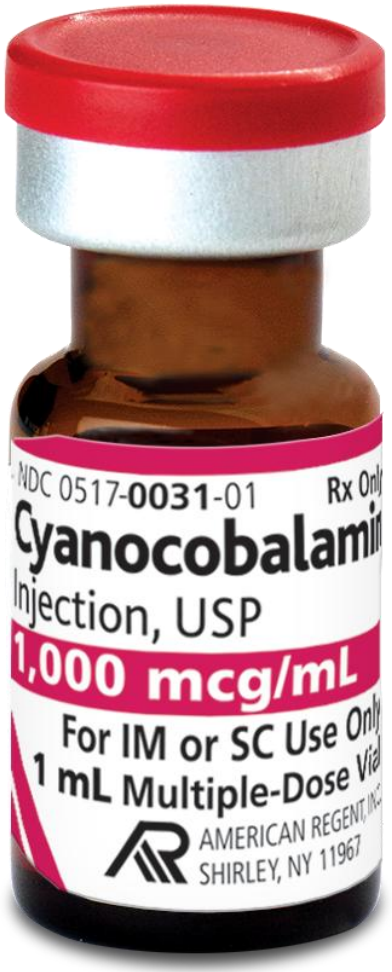
GLP-1 and Vitamin B12

Do these really need to be mixed together?



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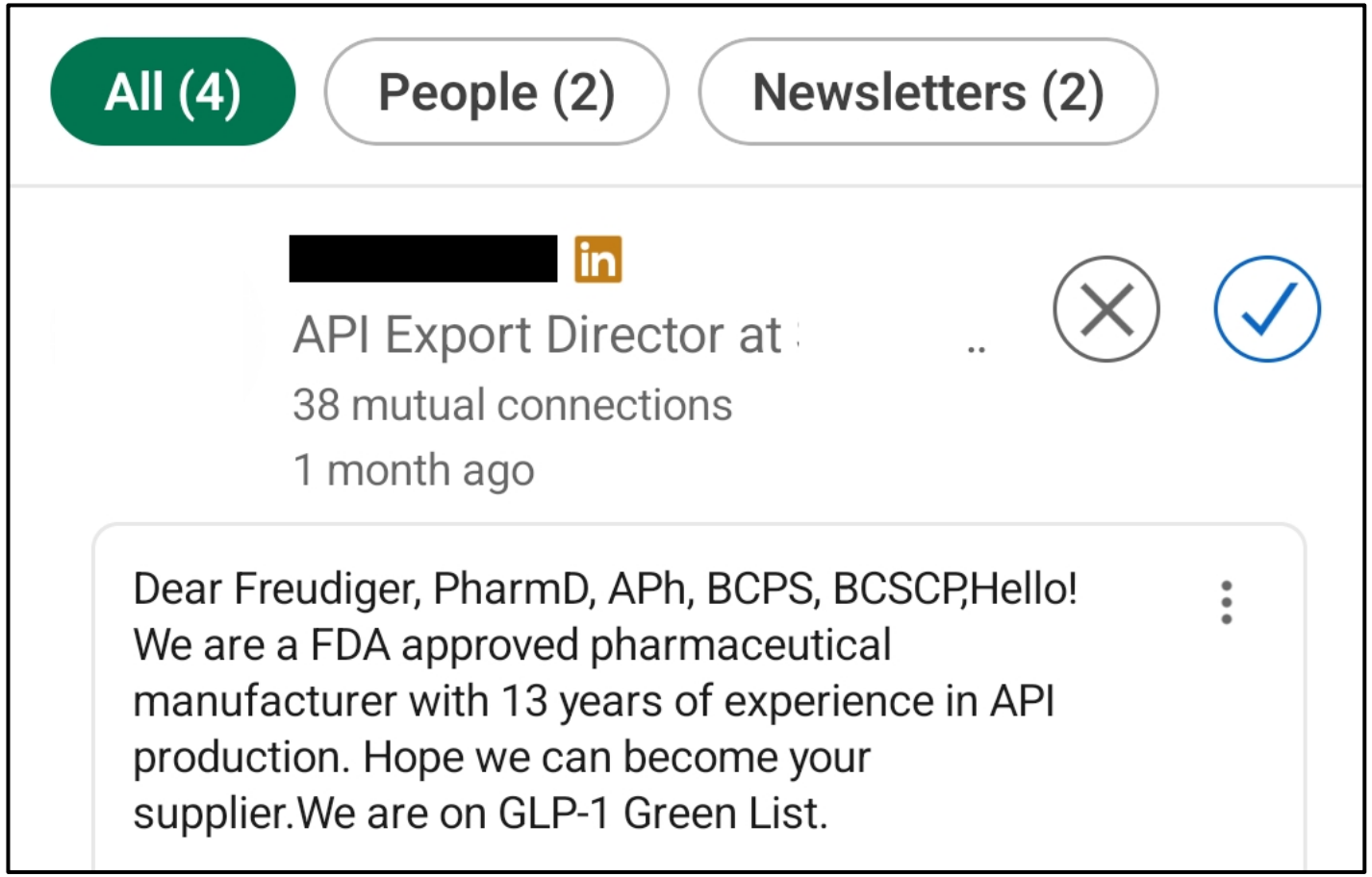
Concerns About API Sources

- 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

U.S. FOOD & DRUG ADMINISTRATION

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Import Alert 66-80

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(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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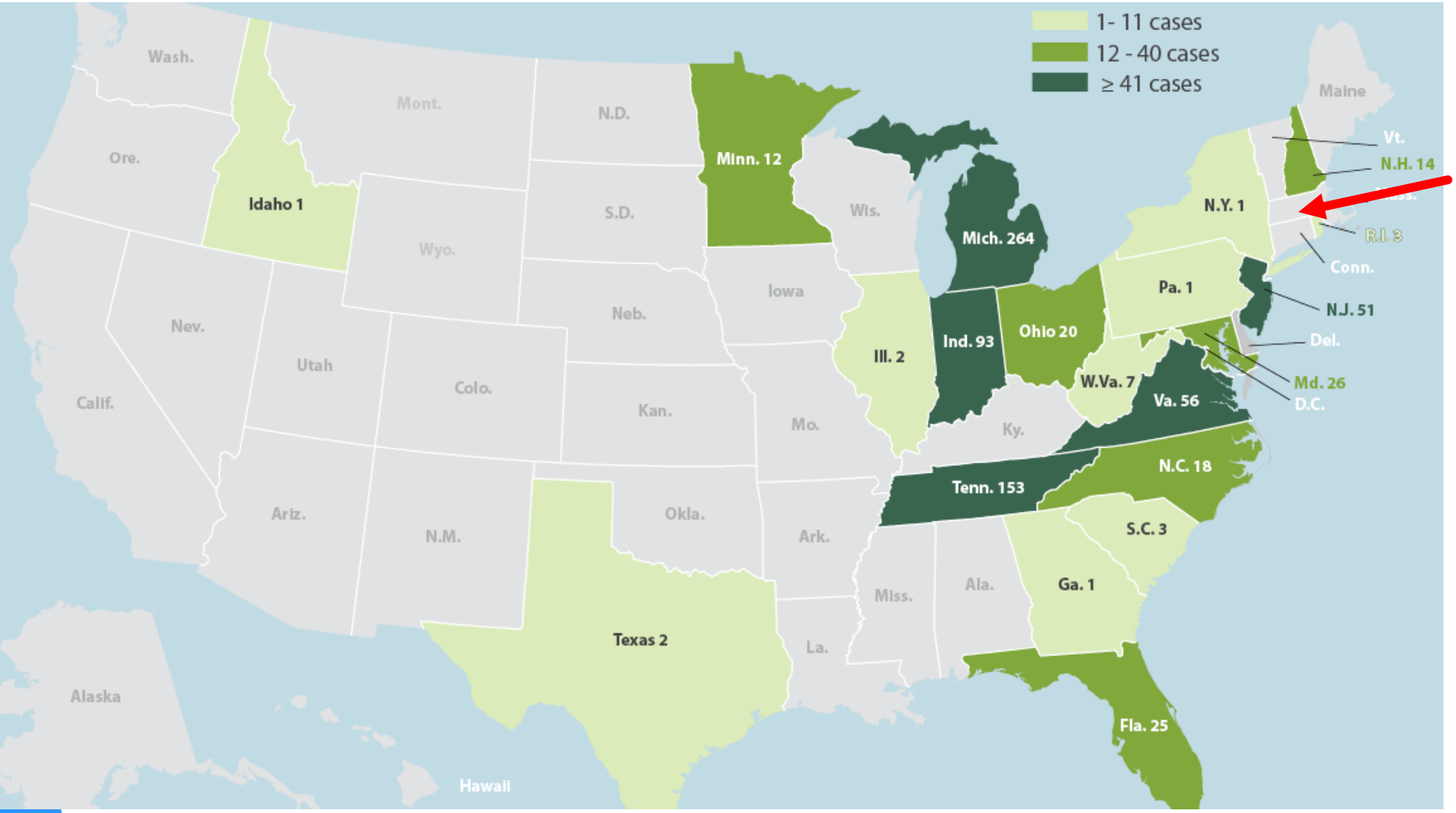
NECC Outbreak: Cases by State



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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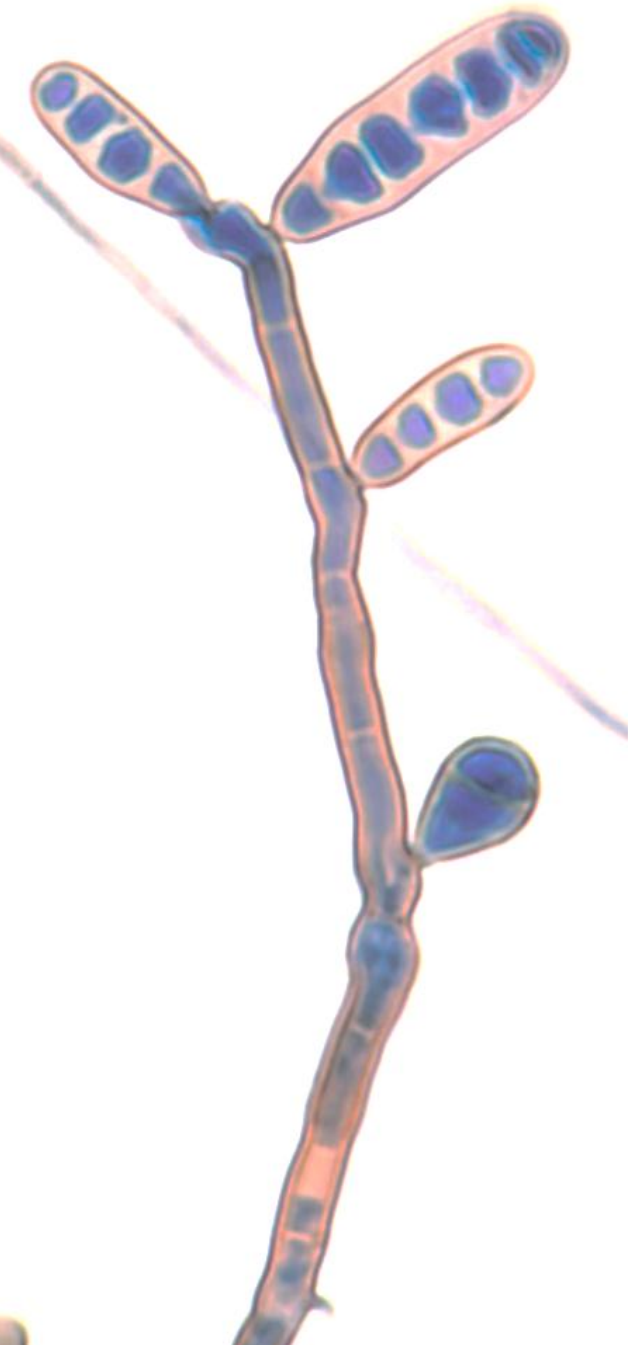

NECC: Fungal Organisms

- ***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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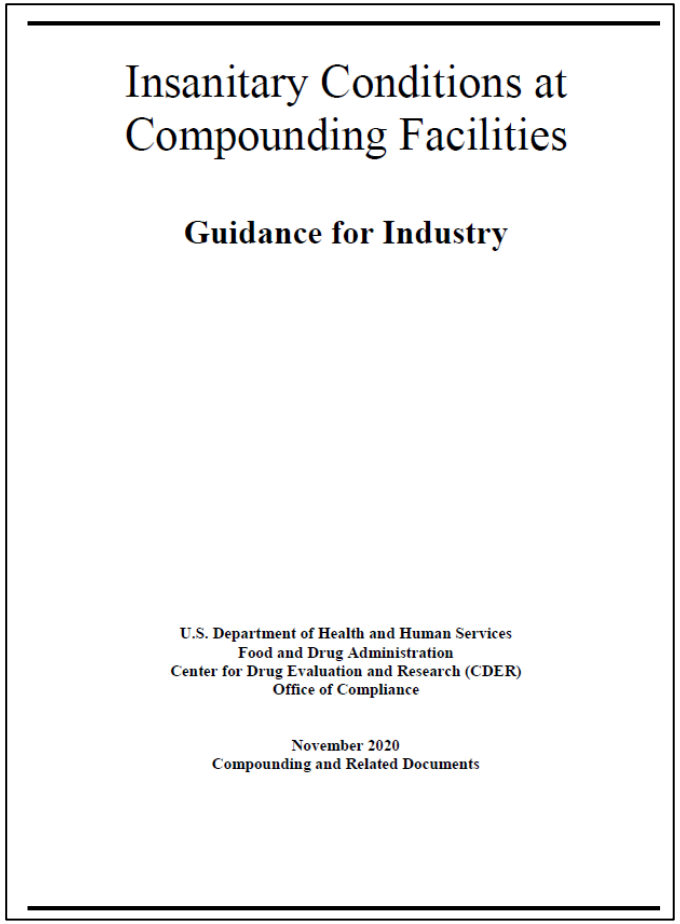
FDA Insanitary Conditions

- **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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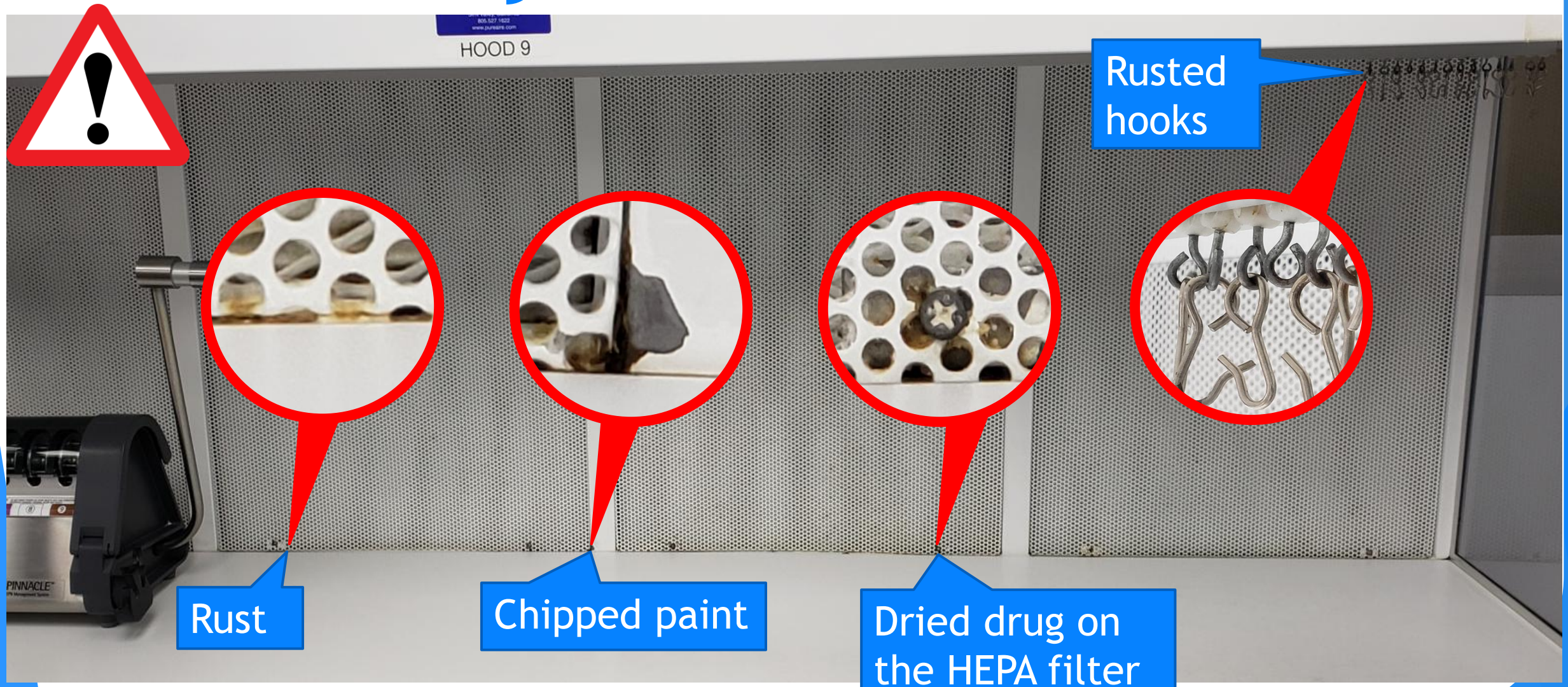
Insanitary Conditions: Hoods



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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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