U.S. FOOD & DRUG ADMINISTRATION

Quality Supply Chain Topics
2026 Annual Listening Sessions

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Office of Compounding Quality and Compliance
Office of Compliance/CDER

Flavor [✓] Appearance [✓] Fragrance [✓]

What about Safety?*

- June 1937, a drug company salesman reported a demand for the drug sulfanilamide in liquid form.
- Until then, sulfanilamide, in tablet and powder oral dosage forms, was commonly used to treat streptococcal infections.
- The drug company's chief chemist and pharmacist experimented and found that sulfanilamide dissolves in diethylene glycol or DEG (an inactive ingredient?).
- The drug company's control lab tested the mixture for flavor, appearance, and fragrance and found it satisfactory for human consumption.
- The drug company compounded a quantity of the elixir and sent shipments-633 of them--all over the country. DEG is toxic. People died. This led to enactment of drug safety requirements and the 1938 Federal Food, Drug, and Cosmetic Act (FFDCA).

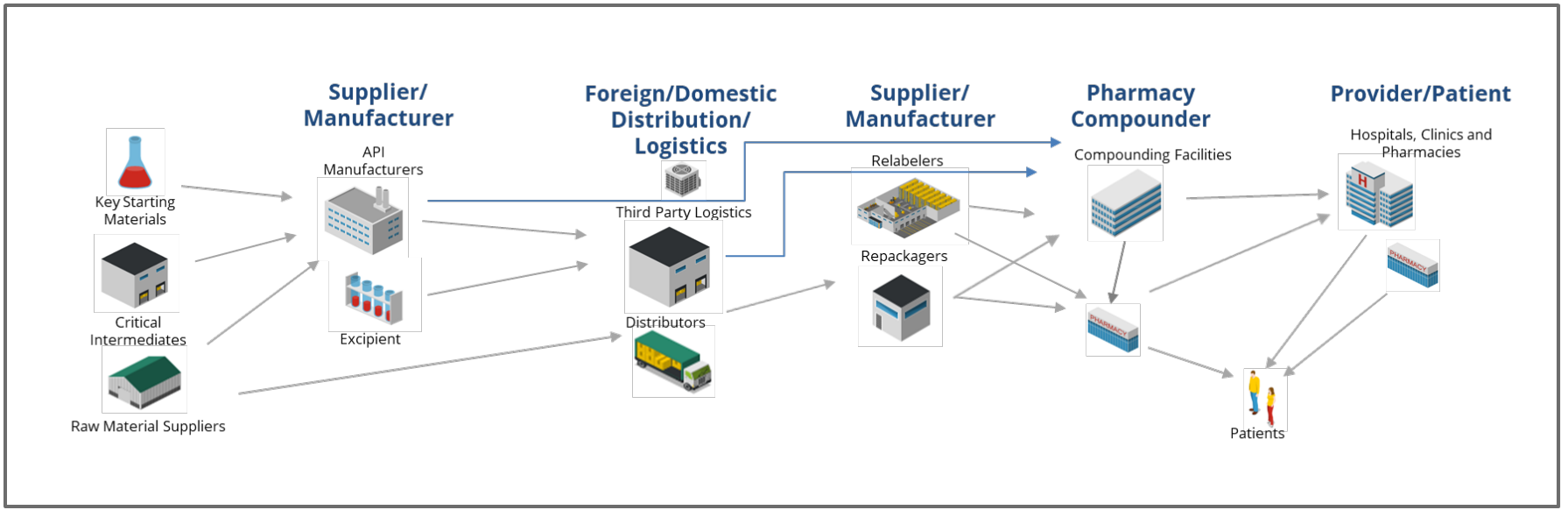
* https://www.fda.gov/files/about%20fda/published/The-Sulfanilamide-Disaster.pdf

503A & 503B Compounders

- Can the compounder determine materials quality?
- Conditions regarding bulk drug substances used in section 503A and 503B pharmacy compounding:
  - Are the active pharmaceutical ingredients (APIs) compliant with United States Pharmacopeia (USP) or National Formulary (NF) monograph standards?
  - Are the APIs sourced from FDA-registered facilities?
  - Are there valid certificates of analysis (COAs) for the APIs?
  - Are the excipients in compliance with applicable USP or NF monograph standards?

See https://www.fda.gov/drugs/human-drug-compounding/fdc-act-provisions-apply-human-drug-compounding

Compounder Supply Chain



Supply Chain, Quality, Safety

- Statutory conditions help ensure compounded drug product quality
- FFDCA exemptions for drugs compounded in accordance with Section 503A or 503B:

Provision	When compounded in accordance with Section 503A	When compounded in accordance with Section 503B
Available exemptions, if conditions are met	•Section 501(a)(2)(B) (current good manufacturing practice requirements), •Section 502(f)(1) (labeling with adequate directions for use), and •Section 505 (new drug approval requirements)	•Section 502(f)(1) (labeling with adequate directions for use), •Section 505 (new drug approval requirements), and •Section 582 (drug supply chain security requirements)

Supply Chain & Component Quality

- Know Your Bulks Suppliers*
  - Bulk Drug Substance (BDS) or Active Pharmaceutical Ingredient (API)
- Know Your Non-API Components Suppliers
  - Excipients, Inactive Ingredient, Intermediates
- Consider how other suppliers can affect the quality of the compounded drug
  - Packaging
  - Containers
  - Container closures

* See https://www.fda.gov/drugs/human-drug-compounding/fda-compounders-know-your-bulks-and-excipients-suppliers

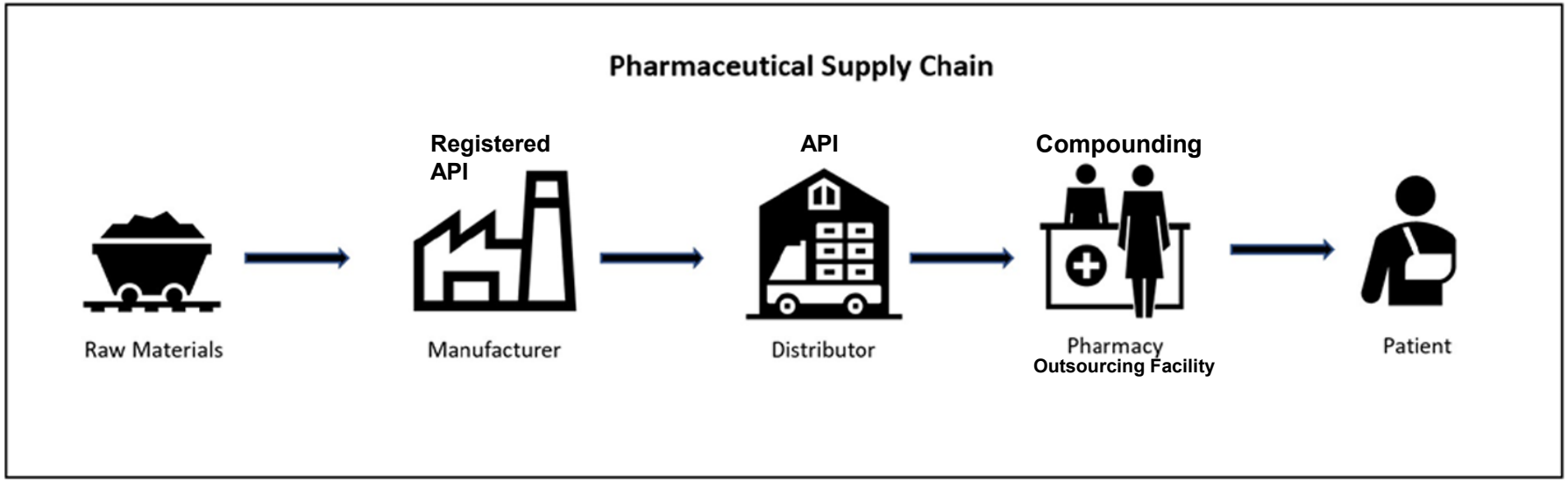
Not always a simple task

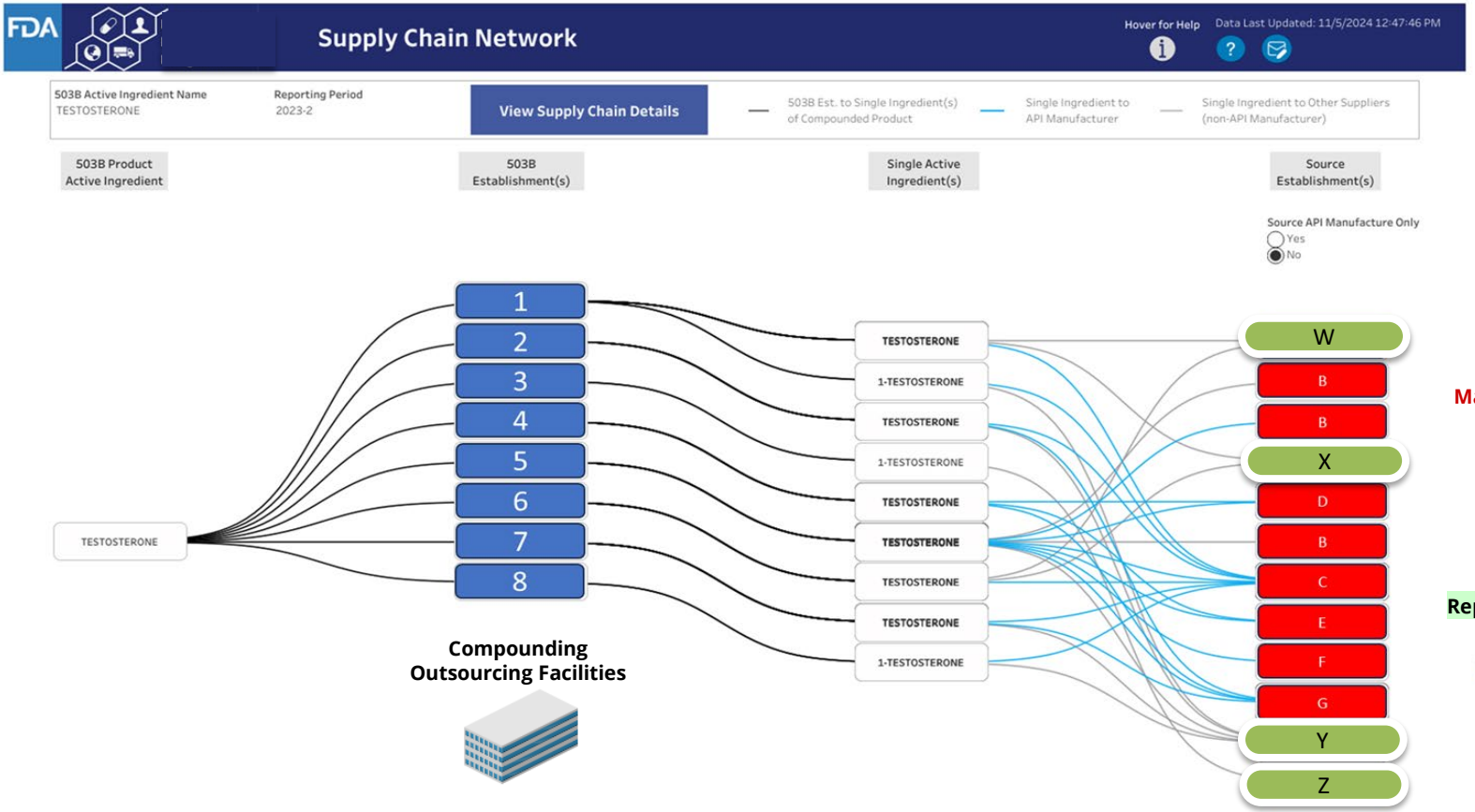
- API repackers/relabelers may further the manufacturing process
- It could be a challenge to determine the original API source or obtain the original COA in a complex supply chain
- 503A Compounding Pharmacies do not register or report to FDA drugs compounded

503B Outsourcing Facility (OF)

  - Required to submit compounded product report twice/year
  - OF Product Reports include portions of the complex API supply chain
  - CDER has analyzed compounded product report data to determine risks to the supply chain for certain single ingredient drugs including opioids & controlled substances
  - CDER found supply chains for most controlled bulk drug substances are simpler and less globalized

Compounding Supply Chain




FDA
Supply Chain Network
Hover for Help
Data Last Updated: 11/5/2024 12:47:46 PM
503B Active Ingredient Name
TESTOSTERONE
Reporting Period
2023-2
View Supply Chain Details
503B Est. to Single Ingredient(s) of Compounded Product
Single Ingredient to API Manufacturer
Single Ingredient to Other Suppliers (non-API Manufacturer)
503B Product Active Ingredient
503B Establishment(s)
Single Active Ingredient(s)
Source Establishment(s)
Source API Manufacture Only
Yes
No
TESTOSTERONE
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Compounding Outsourcing Facilities
Source API Manufacturers
API Repacker/Relabeler

Navigating the GLP-1 Landscape

Matt Lash, JD
Deputy Director
CDER Office of Compliance
Acting Director Office of Compounding Quality and Compliance

Actions Taken to Combat Illegal Unapproved and Counterfeit GLP-1s

Distinguishing “counterfeit” from “unapproved”

“Counterfeit drug”

- A drug that falsely purports to be the drug product of someone other than the actual manufacturer/distributor/processor of the product by bearing an unauthorized trademark, trade name, or other identifying mark. FDCA at 21 U.S.C. § 321(g)(2).

“Unapproved drug”

- A drug that lacks FDA approval to be distributed in the United States.
- Compounded drugs are unapproved but may be legally marketed in some circumstances.

Unapproved Glucagon-like Peptide-1 (GLP-1) Products

- Multi-faceted compliance response
- Foreign sourced API
- Compounding pharmacy and traditional manufacturing

Warning letters issued to telehealth platforms selling compounded products

FDA Actions Against Unapproved GLP-1s: Internet Pharmacy Warning Letter - Ozempen

- Ozempen.com – Warning Letter issued 6/24/24
  - “www.ozempen.com offers semaglutide drug products marketed as ‘4mg Semaglutide Pen’ and ‘8mg Semaglutide Pen.’ Your website states “Same active ingredient as Ozempic, Rybelsus and Wegovy, now more budget friendly.” While there are FDA-approved versions of semaglutide, on the market in the U.S., there are no approved drug applications pursuant to section 505 of the FD&C Act in effect for the “4mg Semaglutide Pen” and “8mg Semaglutide Pen” offered by www.ozempen.com.”

FDA Actions Against Unapproved “Research Only” GLP-1s

- Companies are selling GLP-1s as “research only chemicals,” and/or labeled “not for human use.”

- FDA can support warning letters if evidence supports that the products are intended for human use, with disease and/or structure/function claims.

- FDA has issued multiple WLs for products described as "for research only":
  - Helix Chemical Supply; US Chem Labs; Xcel Research LLC; Summit Research Peptides; Prime Vitality, Inc; Swisschems; Usapeptide.com.
  - Products marketed for “Alzheimer’s,” “weight loss,” “diabetes,” and others.

FDA Actions to Protect Against Counterfeit Drugs

- FDA takes reports of suspected counterfeits seriously and works closely with other federal agencies and the private sector to help protect the nation's drug supply.

- FDA works with industry and stakeholders to create a tighter, closed prescription drug distribution system to prevent harmful drugs from entering the supply chain, detect harmful drugs if they do enter the supply chain, and enable rapid response when such drugs are found.

Preventing imports of counterfeit drugs

- FDA works with U.S. Customs and Border Protection and focuses on areas that present the most substantial threat to our drug supply.

- FDA-regulated drugs imported into the U.S. are electronically screened to ensure imported drugs meet FDA's rigorous standards for quality, safety and effectiveness just as drugs made in the U.S. do.

- The U.S. government works with foreign regulatory counterparts, when possible, to disrupt or close illegal operations involving the production and distribution of counterfeit drugs.

FDA warns consumers not to use counterfeit Ozempic (semaglutide) found in U.S. drug supply chain

- On April 14, 2025, FDA issued a statement noting that the Agency was notified by Novo Nordisk of counterfeit Ozempic in the U.S. drug supply chain.
- FDA took rapid action and seized hundreds of units of counterfeit products.
- Statement advised wholesalers, retail pharmacies, health care practitioners and patients to check the product they have received and not distribute, use, or sell products labeled with specified lot and serial numbers (as pictured).

April 2025 Statement: https://www.fda.gov/drugs/drug-safety-and-availability/fda-warns-consumers-not-use-counterfeit-ozempic-semaglutide-found-us-drug-supply-chain

Criminal Investigations into Unapproved and Counterfeit Products

- FDA's Office of Criminal Investigations (OCI) conducts criminal investigations of illegal activities involving FDA-regulated products, working closely with the Department of Justice to prosecute those responsible for violations of the criminal laws.

- This includes activities such as cybercrime and distributing counterfeit, unapproved and misbranded drugs.

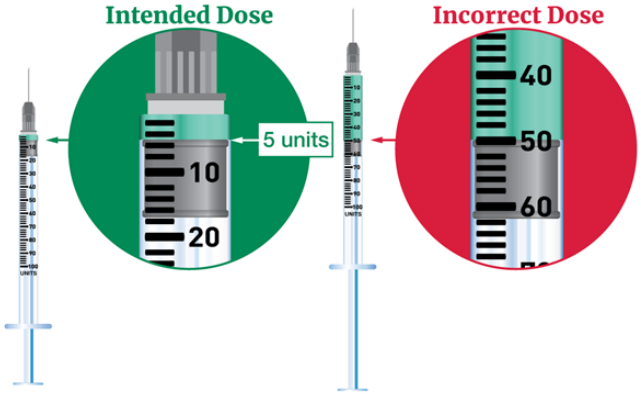
- FDA, through the Office of Compliance and OCI, continues to investigate all instances of counterfeit products, including GLP-1 products, in the supply chain, and will not hesitate to seize product, pursue criminal action, and inform the public of potential risks to the supply chain.

Compounding Risk Alert: Dosing Errors Associated with Compounded Injectable Semaglutide Products

- Alert that FDA has received reports of adverse events, some requiring hospitalization, that may be related to overdoses due to dosing errors that have resulted from:
  - Patients measuring and self-administering incorrect doses
  - Health care providers miscalculating doses

- Many of the patients lacked experience with self-injections

Figure 1. **U-100 insulin syringe with fill volume of 5 units and 50 units**



Voluntary Compliance Initiative: Listing Letters

- Targeted letters to entities that have listed ineligible bulk drug substances for human drug compounding in FDA's electronic Drug Registration and Listing System (eDRLS)
- Clarifies that compounded human drug products containing the bulk drug substance would not currently qualify for the exemptions provided under section 503A or section 503B of the FD&C Act

Conclusion

- FDA uses a multifaceted approach to address illegal unapproved and counterfeit GLP-1 Products.

- As demand for these drugs continues to increase, addressing illegal shipments of GLP-1 API intended for human use in the U.S. as well as illegal unapproved and counterfeit product will remain a top priority.

- We welcome the opportunity to hear from you during these listening sessions and in general as we seek to address this complex and evolving landscape.

U.S. FOOD & DRUG ADMINISTRATION

503A and 503B Interim Policy on Bulks Updates

2026 Annual Listening Sessions

Dorcas Ann Taylor

Acting Division Director, Division III

Office of Compounding Quality and Compliance

Office of Compliance/CDER

Statutory Framework

Section 503A (Enacted 1997 FDAMA)	Section 503B (Enacted 2013 DQSA)
Conditions under which drug products compounded by a **licensed pharmacist in a State-licensed pharmacy or Federal facility**, or by a **licensed physician**, qualify for exemptions from three requirements of the FD&C Act: (1) New drug approval requirements (section 505), (2) Labeling with adequate directions for use (section 502(f)(1)), and (3) Current good manufacturing practice (CGMP) requirements (section 501(a)(2)(B))	Conditions under which drug products compounded by or under the direct supervision of a licensed pharmacist in an **outsourcing facility** qualify for exemptions from three requirements of the FD&C Act: (1) New drug approval requirements (section 505), (2) Labeling with adequate directions for use (section 502(f)(1)), and (3) Drug supply chain security requirements (section 582). **Outsourcing facilities remain subject to CGMP requirements.**

Drug Products Compounded with BDS

Section 503A	Section 503B
• Must comply with an **applicable** United States Pharmacopeia (USP) or National Formulary (NF) **monograph**, if one exists, and the USP chapter on pharmacy compounding; • If an applicable USP/NF monograph does not exist, be a **component** of an **FDA-approved drug**; or • If such a monograph does not exist and the substance is not a component of an FDA-approved drug, appear on a **list of bulk drug substances** that can be used in compounding under section 503A developed by FDA through regulations	• Must appear on a **list** developed by FDA **of bulk drug substances** that can be used in compounding under section 503B, or • The drug compounded from the bulk drug substance must appear on FDA's **drug shortage list** at the time of compounding, distribution, and dispensing

Bulk Drug Substances

- Sections 503A(b)(1)(A) and 503B(a)(2) define a “bulk drug substance” by referencing the definition in 21 CFR 207.3(a)(4): “the same as active pharmaceutical ingredient as defined in 21 CFR 207.1”
- Active pharmaceutical ingredient is defined in 21 CFR 207.1 as “any substance that is intended for incorporation into a finished drug product and is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body,” but the term “does not include intermediates used in the synthesis of the substance”

How Entries are Added to the 503A Bulks List

- Nominations for the 503A Bulks List may be submitted to docket FDA-2015-N-3534 at https://www.regulations.gov/document?D=FDA-2015-N-3534-0001
  - The Federal Register notice associated with this link provides instructions on the information that should be submitted with a bulk drug substance nomination
- FDA evaluates substances for inclusion on this list on a rolling basis and publishes notices in the Federal Register to communicate its intentions and decisions regarding groups of substances
  - Substances nominated for the 503A Bulks List with adequate support are reviewed by FDA and presented to the Pharmacy Compounding Advisory Committee which makes a recommendation on whether to add the substance to the list, then FDA publishes a proposed rule in the Federal Register, review comments, and a final rule in the Federal Register to add or not add a substance to the list
- The 503A Bulks List is codified at 21 CFR 216.23

Current 503A Bulks List

- 503A Bulks List codified at 21 CFR § 216.23(a):

  (1) Brilliant Blue G, also known as Coomassie Brilliant Blue G-250.
  (2) Cantharidin (for topical use only).
  (3) Diphenylcyclopropenone (for topical use only).
  (4) N-acetyl-D-glucosamine (for topical use only).
  (5) Squaric acid dibutyl ester (for topical use only).
  (6) Thymol iodide (for topical use only).

Development of 503B Bulks List

- Section 503B condition: the drug is compounded in an outsourcing facility that does not compound using bulk drug substances unless --
    - the bulk drug substance appears on **a list** established by the Secretary **identifying bulk drug substances for which there is a clinical need**, or
    - the drug compounded from such bulk drug substance appears on the drug shortage list in effect under section 506E at the time of compounding, distribution, and dispensing

How Entries are Added to the 503B Bulks List

- Nominations for the 503B Bulk List may be submitted to docket FDA-2015-N-3469 at https://www.regulations.gov/document?D=FDA-2015-N-3469-0001
  - The Federal Register notice associated with this link provides instructions on the information that should be submitted with a bulk drug substance nomination
- FDA evaluates substances for inclusion on this list on a rolling basis and publishes notices in the Federal Register to communicate its intentions and decisions regarding groups of substances
  - Substances nominated for the 503B Bulks List with adequate support are reviewed by FDA, and then FDA publishes its proposal to add or not add the substance to the list in a preliminary Federal Register notice, and then FDA publishes its decision to add or not add a substance to the list in a Federal Register notice
- The 503B Bulks List is housed on FDA's website

Current 503B Bulks List

- 503B Bulks List:
  - (1) Diphenylcyclopropenone (for topical use only).
  - (2) Glycolic Acid (for topical use in concentrations up to 70% only).
  - (3) Quinacrine HCl (for oral use only).
  - (4) Squaric Acid Dibutyl Ester (for topical use only).
  - (5) Trichloroacetic Acid (for topical use only).

2017 Interim Policies for 503A and 503B Bulks

- In response to concerns about potential disruptions to patient care while FDA developed the 503A Bulks List and 503B Bulks Lists, FDA published in 2016, and revised in 2017, two guidance documents describing the conditions under which FDA did not intend to take action for compounding using certain bulk drug substances that are not eligible for use in compounding under section 503A or section 503B.
  - *Interim Policy on Compounding Using Bulk Drug Substances Under Section 503A of the Federal Food, Drug, and Cosmetic Act*
  - *Interim Policy on Compounding Using Bulk Drug Substances Under Section 503B of the Federal Food, Drug, and Cosmetic Act*

503A and 503B Interim Categories

- **Category 1: Substances nominated for the Bulks List currently under evaluation**
  - These substances may be eligible for inclusion on the 503A or 503B Bulks List, were nominated with sufficient supporting information for FDA to evaluate them, and do not appear on any other list.
  - Until the substance has been evaluated and is identified as being included or not included on the 503A or 503B Bulks List, FDA does not intend to take action when substances in Category 1 are used in compounding, provided the conditions in the relevant guidance are met.

503A and 503B Interim Categories

- **Category 2: Substances nominated for the Bulks List that raise significant safety risks**
  - These substances were nominated with sufficient supporting information to permit FDA to evaluate them, and they may be eligible for inclusion on the 503A or 503B Bulks List. However, FDA has identified significant safety risks relating to the use of these substances in compounding pending further investigation.
  - These substances are not within the scope of the policies described for the substances in Category 1.

503A and 503B Interim Categories

- **Category 3: Substances nominated for the Bulks List without adequate support**
  - These substances may be eligible for inclusion on the 503A or 503B Bulks List but were nominated with insufficient supporting information for FDA to evaluate them. These substances can be re-nominated with sufficient supporting information through a docket that FDA has established, available at FDA-2015-N-3534 (503A) and FDA-2015-N-3469-0001 (503B) via www.regulations.gov
  - These substances are not within the scope of the policies described for the substances in Category 1.

2025 Interim Policies for 503A and 503B Bulks

- On January 7, 2025, FDA published the final versions of the Interim Policy Guidance Documents and revised the policies described in the 2017 Interim Policy guidance with respect to categorization of certain substances nominated for inclusion on the 503A Bulks List and 503B Bulks List.
  - FDA ended categorization of bulk drug substances nominated on or after January 7, 2025
  - Bulk drug substances nominated before January 7, 2025, that are on Category 1 remain eligible for the enforcement discretion while FDA continues to evaluate them.
  - Bulk drug substances nominated after January 7, 2025, are not within the scope of the policy described in section III.A of the guidance and we intend to continue to evaluate such substances, provided they are nominated with sufficient supporting information. These substances will not be categorized.

Links to 503A and 503B Interim Categories

- **503A Interim Guidance Categories -**
  https://www.fda.gov/media/94155/download

- **503B Interim Guidance Categories-**
  https://www.fda.gov/media/94164/download

Compounding Quality Center of Excellence Overview
2026 Annual Listening Sessions

Meghan Murphy and Jill Hammond, Co-Directors,
Compounding Quality Center of Excellence
Office of Compounding Quality and Compliance
Office of Compliance/CDER

Compounding Quality Center *of* Excellence

Mission

Support outsourcing facilities and related stakeholders in their efforts to provide high quality drugs for patients who need them.

Quality
Build the capacity of the OF market to improve the quality of compounded drugs produced by OFs

Provider Needs
Build the capacity of the OF market to meet provider needs for high quality compounded drugs

Compounding Quality
Center *of* Excellence

FDA

Program Areas

TRAINING: provide education on CGMP and compounding policy

REGULATORY SCIENCE: examine scientific, technical questions

CONFERENCE: convene outsourcing facilities and related entities to learn about emerging trends and compounding best practices

ENGAGEMENT: consistently engage outsourcing facility and stakeholders to educate, solve problems, and build networks

RESEARCH AND ANALYSIS: conduct quantitative and qualitative research to understand outsourcing facility challenges and opportunities

Training

- Provide trainings on CGMP to educate outsourcing facility and compounding industry improve the quality of compounded drugs
- Collaboration with PDA through 4-year Cooperative Agreement
- **20K+** course completions since inception (2020)
- Tremendous positive stakeholder feedback

Upcoming Instructor-Led Trainings

Sterile Drug Compounding | March 16 – 18 | College Station, TX

Process Validation | April 13 – 16 | Virtual

Coming Soon! **Change Management | April 28 – 29 | Durham, NC**

Learn more and register!

Self-Guided Online Trainings

Our free, self-guided online courses provide an overview of key CGMP requirements and compounding policy topics.

Coming Soon! **Introduction to Visual Inspection**

Learn more and register!

Compounding Quality Center *of* Excellence

Preserve access to compounded drugs for patients and health care professionals

Improve the quality of compounded drugs

Promote patient safety

Training Program

Webinars

- Cleanroom and Cleanroom Behaviors: Why they Matter
- Inspections for Outsourcing Facilities
- What to Expect after an Inspection: 483s, Responses and Beyond
- Regulatory Framework for Human Drug Compounding
- Environmental Monitoring in Compounding

Recorded webinars are available free **on-demand.**

Instructor-led Trainings

- Cleanroom
- Data Integrity (NEW)
- Environmental Monitoring
- Investigations and Corrective and Preventive Actions (CAPA)
- Quality Management Systems
- Process Validation
- Sterile Drug Compounding
- Visual Inspection (NEW)

Offerings are available for **$249 each** throughout the year**.**

Self-Guided Online Trainings

- Airflow
- Aseptic Process Simulations (Media Fills)
- Insanitary Conditions and Sterility Assurance
- Investigations and Corrective and Preventive Actions (CAPA)
- Outsourcing Facility Guide
- Personnel Gowning in Sterile Drug Production
- Regulatory Framework for Human Drug Compounding
- Stability and Beyond Use Dates
- Sterility Testing: Common Misconceptions
- Supplier/Contractor Qualification and Management

Courses are available free **on-demand.**

For more information, visit the Compounding Quality Center of Excellence website:
www.fda.gov/drugs/human-drug-compounding/compounding-quality-center-excellence

Regulatory Science

Goals:

- Identify priority regulatory science research projects and determine needs to execute Membership – Office of Compliance, Office of Pharmaceutical Quality, Office of Regulatory Affairs/Science
- Engage in targeted scientific/lab-based research to help inform policy, regulatory, and enforcement decisions

Current projects:

- Non-sterile gowning apparel and cleaning supplies bioburden study (FDA laboratories)
- Drug product formulation toxicity study (NCTR)
- Sporicidal efficacy study (NCTR)

Additional research project ideas:

- Bulk drug substances qualification
  - Develop recommendations for 503Bs to use when qualifying API vendors and substances
- Measuring extractables and leachables considerations for container-closure systems commonly used by compounders

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Conference

Conference to engage outsourcing facilities and related stakeholders (e.g., hospitals, health systems, federal and state regulators, general public) on topics relevant to outsourcing facilities. Hybrid since 2024, virtual from 2020-2023.

Themes:

2020: Working Together for Patient Safety

2021: Culture of Quality

2022: The Shared Pursuit of Compounding Excellence

2023: Ten Years as a Regulated Outsourcing Facility Industry: Addressing Challenges to Improve Patient Care

2024: Learning and Collaborating: Driving Toward the Future of Quality

2025: Meeting Patient Needs for Quality, Safety, Integrity, and Access

99% of respondents to 2025 post-conference evaluation **strongly agreed/agreed** that they would recommend the Center of Excellence Annual Conference to a colleague.

98% of respondents to 2025 post-conference evaluation **strongly agreed/agreed** that the speakers were engaging and conveyed useful information that increased my understanding of the outsourcing facility industry.

Discussion Series

Series of virtual discussions featuring industry members and other stakeholders—less so, FDA.

Attempt to build networks across the industry through knowledge sharing.

Two different series:

- **New Outsourcing Facility Discussion Series** –for newly registered outsourcing facilities in first few years of operation
- **Quality Discussion Series -** for outsourcing facilities interested in advancing quality and will focus on topics related to quality culture and practices

Compounding Quality
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FDA

Annual Study

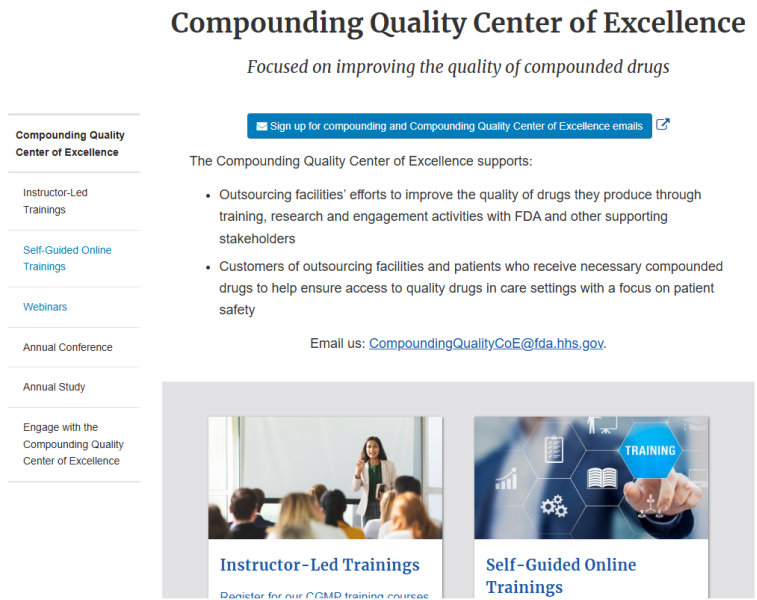
Annual research effort to better understand barriers and opportunities encountered by outsourcing facilities in major areas:

- Outsourcing facility marketplace and business viability
- Compliance with federal law (especially CGMP)
- Good quality drug production
- FDA/outsourcing facility interactions

Compounding Quality Center *of* Excellence

Visit our webpage for more information:

https://www.fda.gov/drugs/human-drug-compounding/compounding-quality-center-excellence



Stay on top of the latest events and resources!
Sign up for Compounding and Compounding Quality Center of Excellence emails.