Guidance Documents Related to Compounding During COVID-19

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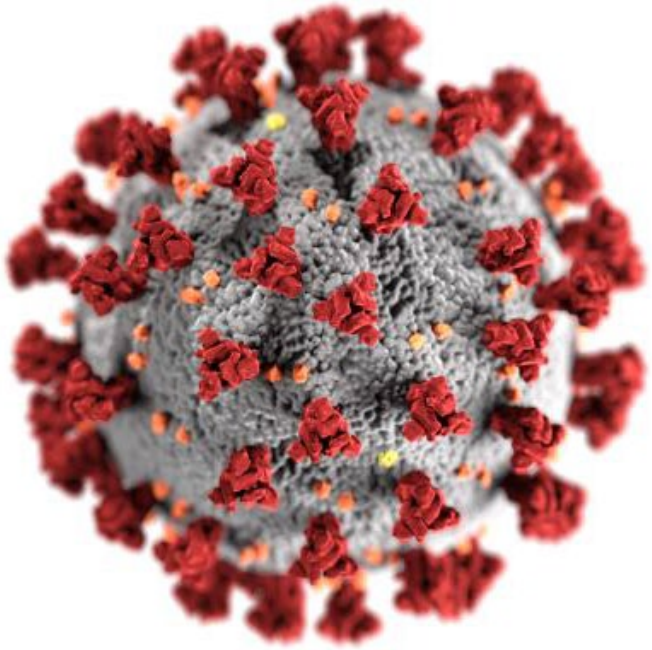
Temporary Policies related to Compounding during the COVID-19 Public Health Emergency

- Compounding of certain drugs for hospitalized patients by outsourcing facilities
- Compounding of certain drugs for hospitalized patients by pharmacy compounders not registered as outsourcing facilities
- Compounding of certain alcohol-based hand sanitizer products
- Repackaging or combining propofol drug products
- Non-standard PPE for sterile compounding by pharmacy compounders not registered as outsourcing facilities

Compounding of certain drugs for hospitalized patients during COVID-19



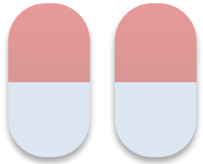
- FDA generally tries to address drug shortages by restoring supplies of FDA-approved drugs.
  - Current law also allows drug compounders to compound drugs that are in shortage in certain cases.
- In light of COVID-19, FDA developed guidance to provide additional flexibility related to drug compounding to ensure treatment options are available to hospitals that are unable to obtain FDA-approved drugs.

Compounding of certain drugs for hospitalized patients during COVID-19

- Guidance documents seek to prioritize drug supplies from certain sources.
  - Help ensure hospitals obtain FDA-approved drugs when available before seeking compounded supplies
  - Prioritize hospital sourcing from outsourcing facilities if approved drugs are not available and compounded drugs are sought

Guidance for outsourcing facilities

Temporary flexibility related to:



- "Essentially a copy" provision
  - Including a 90 day period after a product is removed from the list referenced in the guidance

- Using bulk drug substances to compound drugs that are not on FDA's drug shortage list
  - Flexibility does not include provisions related to conformance with USP standards, sourcing from FDA-registered suppliers, and receipt of certificates of analysis

- CGMP expectations related to stability studies and expiration dates

Guidance for outsourcing facilities

When the policy applies:

- Compounded drug on list on FDA's website and contains only one active ingredient
  - https://www.fda.gov/media/138276/download
- Compounded drug provided directly to hospital that has attempted and been unable to obtain adequate supplies of an FDA-approved drug product containing the same active ingredient for the same route of administration
- Weekly reporting for drug products compounded under the guidance

Guidance for outsourcing facilities

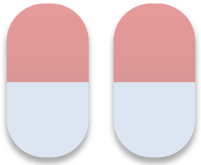
- Stability testing and expiration dates - meet the conditions described in Appendix A of the guidance except that:
  - If compounded drug is aqueous sterile solution for injection and all ingredients are readily soluble in water:
    - BUD ≤ 28 days room temperature and ≤ 42 days refrigerated when a sterility test has not been completed before release;
    - Limited stability testing initiated once aggregate batch is expected to be > 1,000 units;
    - OF uses container-closure system for which it has previous experience and data that it maintains sterility and initiates container-closure integrity testing with the first batch.

List: Products that are aqueous solutions for injection

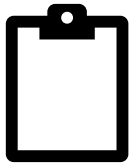
- Cisatracurium besylate
- Dexamethasone sodium phosphate
- Dexmedetomidine hydrochloride
- Epinephrine
- Etomidate
- Fentanyl citrate
- Furosemide
- Hydromorphone hydrochloride
- Ketamine hydrochloride
- Lorazepam
- Midazolam hydrochloride
- Morphine Sulfate
- Norepinephrine bitartrate
- Rocuronium bromide
- Vancomycin hydrochloride
- Vecuronium bromide

Guidance for compounding pharmacies that are not outsourcing facilities

Temporary flexibility related to:



- "essentially a copy" provision



- prescription requirement

Guidance for compounding pharmacies that are not outsourcing facilities

When the policy applies:

- Drugs on list referenced in guidance, single ingredient
- Hospital unable to obtain FDA-approved drugs or drugs from Outsourcing Facilities
- Pharmacy notifies board of pharmacy and board does not object (state in which pharmacy is located and if different, state in which hospital located)
- Mark order with hospital and COVID-19; request patients receiving drugs within one month
- Beyond use date limited
- Reporting of adverse events

Guidance on alcohol-based hand sanitizer products

Policy applies under certain circumstances, including:

- Hand sanitizer is compounded according to the following formula consistent with WHO recommendations:
  - a. Alcohol (ethanol, denatured) (formulated to 80%, volume/volume (v/v)) in an aqueous solution; **or** Isopropyl Alcohol (formulated to 75%, v/v) in an aqueous solution.,
  - b. Glycerin (glycerol) (1.45% v/v).
  - c. Hydrogen peroxide (0.125% v/v).
  - d. Sterile distilled water or boiled cold water.
- **The compounder does not add other active or inactive ingredients, such as ingredients to improve the smell or taste due to the risk of accidental ingestion in children. Different or additional ingredients may impact the quality and potency of the product.**

See guidance for additional circumstances

Methanol contamination of hand sanitizer

Update to FDA hand sanitizer guidance – August 2020

- Use of alcohol or isopropyl alcohol procured from another source rather than manufactured in-house is consistent with policy if compounders test each lot of the active ingredient for methanol content
- Compounders can use a laboratory to test (strongly recommend a lab that has been inspected by FDA and in compliance with CGMP)
- Any alcohol or IPA containing more than 630 ppm methanol is not consistent with the temporary policy and may be considered evidence of substitution and/or contamination [501(a)(2)(A) and 502(d) of FD&C Act]
- If contaminated, destroy and contact FDA

Methanol contamination of hand sanitizer

- USP: Notice of Intent to Revise Alcohol, Dehydrated Alcohol
  - Propose to add the Limit of Methanol test in the ID section of the USP Alcohol and USP Dehydrated Alcohol monographs
- Significance
  - As part of the Identification test, CGMP would require that manufacturers of drug products detect and quantify any Methanol present for each lot of Alcohol received.
  - Manufacturers of Alcohol could not deviate from the Methanol limit since this would be an aspect of identity.

COVID-19 Compounding Guidances

- Temporary Policy for Compounding of Certain Drugs for Hospitalized Patients by Outsourcing Facilities During the COVID-19 Public Health Emergency Update 5/21/2020
- Temporary Policy for Compounding of Certain Drugs for Hospitalized Patients by Pharmacy Compounders not Registered as Outsourcing Facilities During the COVID-19 Public Health Emergency Guidance for Industry Update 5/21/2020
- Temporary Policy on Repackaging or Combining Propofol Drug Products During the COVID-19 Public Health Emergency 4/22/2020
- Policy for Temporary Compounding of Certain Alcohol-Based Hand Sanitizer Products During the Public Health Emergency Update 8/7/2020
- Temporary Policy Regarding Non-Standard PPE Practices for Sterile Compounding by Pharmacy Compounders not Registered as Outsourcing Facilities During the COVID-19 Public Health Emergency Update 5/14/2020

Questions

- Hand Sanitizer Guidance: COVID-19-Hand-Sanitizers@fda.hhs.gov
- Propofol Guidance: CDER-OPQ-Inquiries@fda.hhs.gov
- Other Guidances: Compounding@fda.hhs.gov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