Antiseptic Hand Rubs in the COVID-19 Pandemic

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The opinions and information in this presentation are my own and do not reflect the views and policies of the FDA

Categories of OTC Antiseptics

- Consumer Antiseptics
  - **Rubs (leave-on products)**
    - **Hand rubs "hand sanitizer"**
    - Antiseptic hand wipes
  - Washes
    - Hand wash "antibacterial soap"
    - Antibacterial body wash
- First Aid Antiseptics
- Health Care Antiseptics
  - Health care personnel hand wash
  - **Health care personnel hand rub**
  - Surgical hand scrub
  - Surgical hand rub
  - Preoperative skin preparation
- Food Handler Antiseptics

Regulatory Pathway for Marketing Nonprescription Drugs

- New Drug Application/Abbreviated New Drug (NDA/ANDA)
  - Application submitted to FDA for premarket approval
- OTC Drug Review (OTC Monograph)
  - Marketed without an approved drug application if the drug complies with statutory and regulatory requirements
  - Began in 1972 to evaluate the safety and effectiveness of OTC drug products marketed in the United States before May 11, 1972
  - Established conditions under which an OTC drug is generally recognized as safe and effective (GRASE) in the form of OTC monographs

OTC Drug Monograph

- A “rule book” for each therapeutic category establishing conditions, such as active-ingredients, uses (indications), doses, route of administration, labeling, and testing under which an OTC drug is generally recognized as safe and effective (GRASE)
- OTC monographs cover ~ 800 active ingredients for over 1,400 different uses, authorizing over 100,000 drugs

Hand Sanitizers Under OTC Monograph Reform

- On March 27, 2020, the President signed into law H.R. 748, the "Coronavirus Aid, Relief, and Economic Security Act" (CARES Act) which modernizes the OTC drug review
- Hand Sanitizers using certain active ingredients may be marketed under Section 505G(a)(3) if they follow the 1994 Antiseptics TFM, as further amended by the 2016 Consumer Antiseptic Rub proposed rule and the 2015 Health Care Antiseptics proposed rule[1], and other applicable requirements (e.g. CGMP)
  - Alcohol (ethanol (also known as ethyl alcohol)) 60-95% v/v
  - Isopropyl alcohol 70-91.3% v/v
  - Benzalkonium chloride 0.1-0.13% v/v

[1]"Safety and Effectiveness of Consumer Antiseptic Rubs; Topical Antimicrobial Drug Products for Over-the-Counter Human Use," Final Rule, 84 FR 14847 (April 12, 2019); "Safety and Effectiveness of Health Care Antiseptics; Topical Antimicrobial Drug Products for Over-the-Counter Human Use," Final Rule, 82 FR 60474 (December 20, 2017); "Topical Antimicrobial Drug Products for Over-the-Counter Human Use; Tentative Final Monograph for Health-Care Antiseptic Drug Products," Proposed Rule, 59 FR 31402 (June 17, 1994) (1994 TFM)

Hand Sanitizers Under OTC Monograph Reform (Continued)

- Active ingredients require additional data to determine whether they are Generally Recognized as Safe and Effective (GRASE) for use in consumer hand rubs
- It is the manufacturer's responsibility to ensure their products
  - have been properly tested
  - comply with all applicable regulations
  - have inactive ingredients that are safe and suitable for use in an OTC antiseptic hand rub

Hand Sanitizer Indication and Labeling

- Indication: to help reduce bacteria that potentially can cause disease
- For use when soap and water are not available
- Examples of claims that are not permitted[1]
  - Persistence/duration of effect
  - Pathogen-specific disease claims
  - Superiority claims

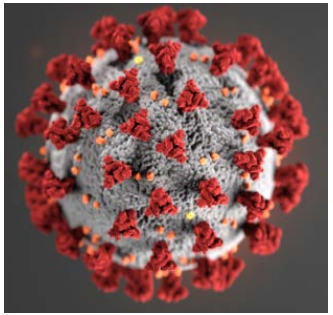
[1] Not an all-inclusive list. Claims are expected to conform to "Topical Antimicrobial Drug Products for Over-the-Counter Human Use; Tentative Final Monograph for Health-Care Antiseptic Drug Products," Proposed Rule, 59 FR 31402 (June 17, 1994)

Consumer Hand Rub Market

Prior to COVID-19[1]

- Annual dollar sales ~ $190 million
- More than 800 entities
- Most manufacturers small businesses
- Most common active ingredient ethanol (ethyl alcohol)
- All products marketed under the OTC Drug Monograph

After COVID-19



- Dramatic increase in demand
- Degree of market shortage difficult to quantitate

[1]Regulatory impact analysis, "Safety and Effectiveness of Consumer Antiseptic Rubs; Topical Antimicrobial Drug Products for Over-the-Counter Human Use," Final Rule, 84 FR 14847 (April 12, 2019)

FDA's Actions to Address Hand Sanitizer Shortage

- Issued three guidance documents outlining temporary policies to provide flexibility to help meet demand during the public health emergency
- When the public health emergency is over, FDA intends to discontinue these enforcement discretion policies and withdraw the guidances
- FDA is continually assessing needs and circumstances related to the temporary policy and will update, modify, or withdraw the policy as appropriate
  - Updated March 27, April 15, June 1, August 7, and February 10

COVID-19 Hand Sanitizer Guidances

- Compounding Guidance

  Policy for Temporary Compounding of Certain Alcohol-Based Hand Sanitizer Products During the Public Health Emergency

- Manufacturing Guidance

  Temporary Policy for Preparation of Certain Alcohol-Based Hand Sanitizer Products During the Public Health Emergency (COVID-19)

- Active Ingredient Guidance

  Temporary Policy for Manufacture of Alcohol for Incorporation Into Alcohol-Based Hand Sanitizer Products During the Public Health Emergency (COVID-19)

Terms of the Manufacturing Guidance[1]

FDA does not intend to take action against firms that prepare ABHS provided all of the conditions specified in the guidance are met

1. Uses only specified ingredients
2. Alcohol is denatured using specified formulas
3. Finished product follows WHO formula
4. Firm does not add other active or inactive ingredients
5. Firm ensures active ingredient is correct and uses correct amount (methanol and potency tests)
6. Prepared under sanitary conditions
7. Verifies alcohol content in finished product before each batch is released
8. Dosage form is an aqueous solution (no gel, foam, or aerosol spray)
9. Labeled according to guidance
10. Facility is registered with FDA Drug Registration and Listing
11. Firm has a mechanism to accept adverse event reports

[1]Temporary Policy for Preparation of Certain Alcohol-Based Hand Sanitizer Products During the Public Health Emergency (COVID-19) Guidance for Industry, March 2020, Updated February 10, 2021

Finished Hand Sanitizer Formulations Under the Guidance

- **Alcohol (ethanol) formulated to 80% v/v** in an aqueous solution
- Glycerin (glycerol) 1.45% v/v
- Hydrogen peroxide 0.125% v/v
- Sterile distilled water or boiled cold water

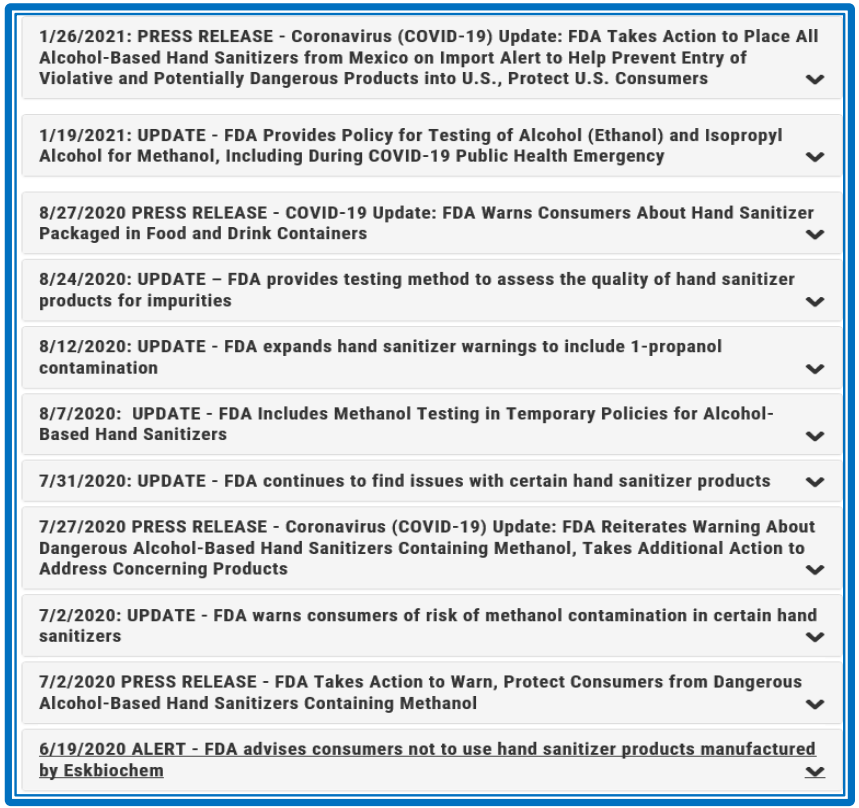
- **Isopropyl alcohol formulated to 75% v/v** in an aqueous solution
- Glycerin (glycerol) 1.45% v/v
- Hydrogen peroxide 0.125% v/v
- Sterile distilled water or boiled cold water

Impact of Hand Sanitizer Guidances

- Thousands of new firms have registered to manufacturer alcohol-based hand sanitizers and hand sanitizer active ingredients (ethanol and isopropyl alcohol)
- Many hospital systems are now able to source an adequate supply of hand sanitizers and more are available for consumer purchase
- FDA is updating the temporary guidances as needed to provide additional clarification to both increase supply and help ensure that harmful products are not on the market
- FDA appreciates the work of manufacturers, compounders, state boards of pharmacy, and the public to increase the supply of alcohol-based hand sanitizers

New and Increasing Safety Issues with Hand Sanitizers

- Accidental ingestion by young children
  - Need to denature alcohol
  - Packaging attractive to children
- Contamination
  - Methanol
  - 1-Propanol
- Subpotent and mislabeled products
- Packaging in food and drink containers
- Ocular injuries
- Flammability



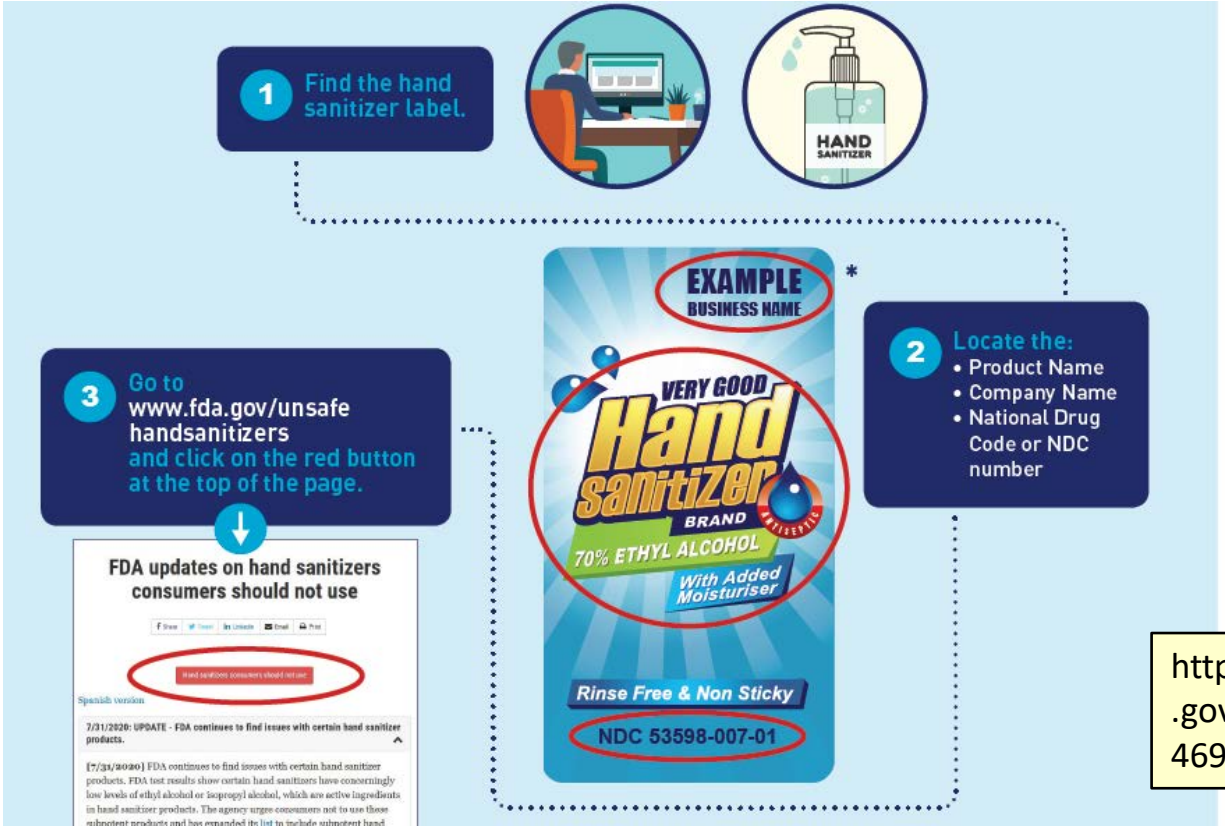
FDA's "Do Not Use" List

Allows consumers to identify a product that:

- Has been tested by FDA and found to contain methanol or 1-propanol
- Is labeled to contain methanol
- Has been tested and is found to have microbial contamination
- Is being recalled by the manufacturer or distributor
- Is subpotent, meaning it has less than the required amount of ethyl alcohol, isopropyl alcohol or benzalkonium chloride
- Is purportedly made at the same facility as products that have been tested by FDA and found to contain methanol or 1-propanol
- Is packaged in a container that resembles a food/beverage container that presents increased risk of accidental ingestion

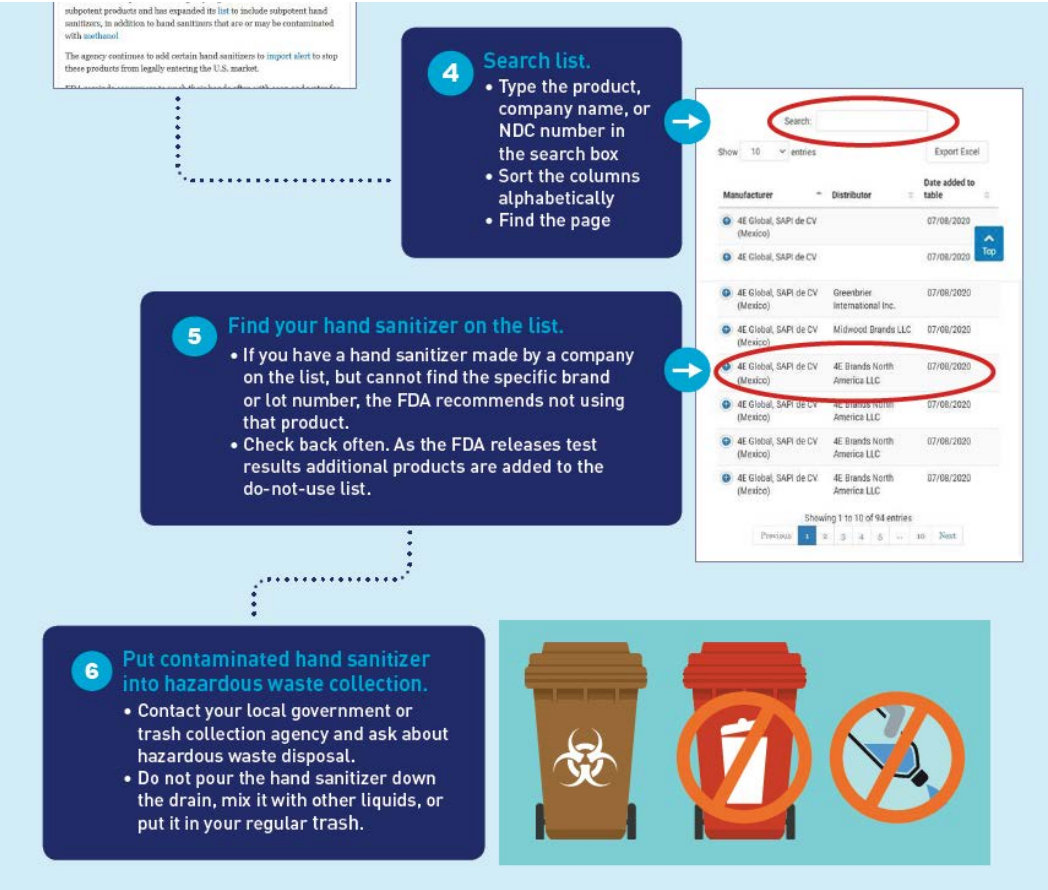
See this webpage for a full list of hand sanitizers we urge consumers not to use: https://www.fda.gov/drugs/drug-safety-and-availability/fda-updates-hand-sanitzers-methanol

How to Find Products on the List



https://www.fda.gov/media/141469/download

How to Find Products on the List (continued)



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Accidental Ingestion by Children

- Calls to National Poison Data Center increased 79% in March 2020 compared to March 2019[1]
- Many adults unaware that hand sanitizers should be kept out of children's reach[2]
- All ethyl alcohol used in hand sanitizer must contain a denaturant
- Avoid packaging in food or drink containers
- Avoid food flavors, scents, or packaging that could appeal to children

[1]McCulley L, Cheng C, Mentari E, et al. Clinical Toxicol https://doi.org/10.1080/15563650.2020.1811298

[2]Gharpure R, Hunter CM, Schnall AH, et al. Knowledge and practices regarding safe house hold cleaning and disinfection for COVID-19 prevention—United States, May 2020. MMWR Morb Mort Wkly Rep 2020;69(23);705-9.

FDA

Food?
or Drug??

https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/ashtel-studios-issues-voluntary-recall-licensed-hand-sanitizers-packaged-084-fluid-ounce-pouches-due#recall-announcement

Methanol Serious Adverse Events and Deaths

Yip L, Bixler D, Brooks DE, et al. Serious Adverse Health Events, Including Death, Associated with Ingesting Alcohol-Based Hand Sanitizers Containing Methanol — Arizona and New Mexico, May–June 2020. MMWR Morb Mortal Wkly Rep 2020;69:1070–1073. DOI: http://dx.doi.org/10.15585/mmwr.mm6932e1external icon

1-Propanol Contamination

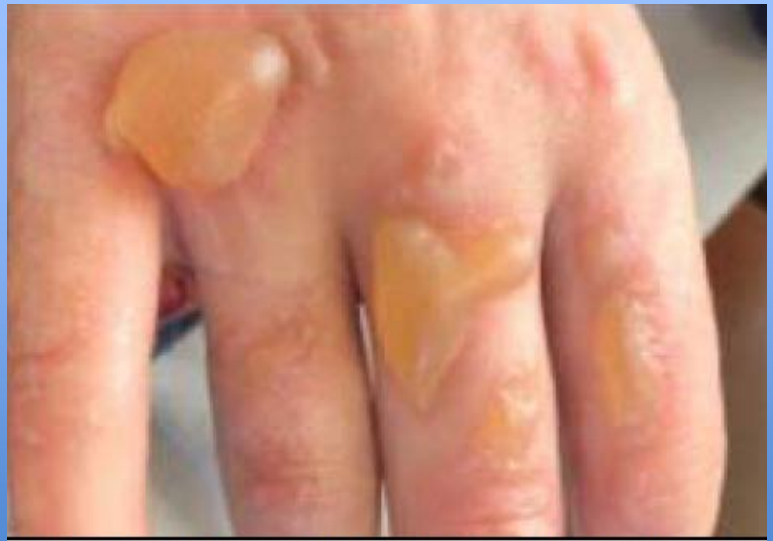
- 1-propanol is not an acceptable ingredient for hand sanitizers
- 1-propanol is not the same as 2-propanol (isopropyl alcohol/isopropanol)
- Ingestion of 1-propanol can cause central nervous system depression leading to death
- Symptoms include confusion, decreased consciousness, and slowed pulse/breathing

Ocular Exposure to Hand Sanitizers

- More frequent ocular exposures reported recently, especially in children
- Public dispensers deliver the product at the level of small children's eyes
  - Pediatric ocular exposures are occurring in public places
- Cases of corneal or conjunctival ulceration have been reported

Flammability

- FDA has advised consumers that hand sanitizer is flammable, and it should be rubbed into the hands until they feel completely dry before continuing activities that may involve heat, sparks, static electricity, or open flames
- Labels have warning about flammability
- Fires and burns associated with use of hand sanitizer have been reported
- Avoid formulations with increased risk of flammability such as aerosol sprays



Employee receives first and second-degree burns to both hands from applying hand sanitizer before touching a metal surface.

FDA Resources

- For Questions on
  - Hand sanitizers COVID-19-HandSanitizers@fda.hhs.gov
  - OTC Monograph Reform druginfo@fda.hhs.gov
  - Small business and industry assistance cdersbia@fda.hhs.gov
  - Registration and listing edrls@fda.hhs.gov
- Resources
  - Methanol and Hand sanitizers consumers should not use www.fda.gov/unsafehandsanitizers