Compounding Hand Sanitizer During COVID-19

ACPE UAN: 0171-9999-20-035-H07-P

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Initial Release Date: 08/18/2020
Planned Expiration Date: 08/18/2023

Objectives

1. List and describe the ingredients used in compounding hand sanitizer and their purpose.
2. Explain tips for preparation and storage of compounded hand sanitizer.
3. Recall key resources that can be utilized to find up-to-date information on compounding hand sanitizer.

Abstract

COVID-19 quickly affected the quantity of essential supplies available for both individuals and businesses, including gloves, masks and hand sanitizer. To meet the demand of these unobtainable materials, the Food and Drug Administration (FDA) released their policy for "Temporary Compounding of Certain Alcohol-Based Hand Sanitizer Products During the Public Health Emergency." Pharmacists can play a key role in compounding hand sanitizer, especially as stores, schools, and health-systems begin the process of reopening. The key ingredients, processes, and regulations are outlined here as well as resources that can be accessed as conditions change throughout this current pandemic.

Key words: compounding, COVID-19, hand sanitizer

As COVID-19 began affecting communities in South Carolina in March 2020, essential supplies such as toilet paper, surgical masks, and hand sanitizer quickly became in short supply. The Centers for Disease Control and Prevention (CDC) provided guidance for workplaces, including pharmacies, to provide hand sanitizer containing at least 60% v/v alcohol on counters for use by customers and supply a sufficient amount of soap and water or hand sanitizer for all of its staff to help contain the rapid spread of the virus.[1] Pharmacists were well positioned to help fill this gap through compounding their own hand sanitizer. From information collected world-wide, the World Health Organization (WHO) acknowledges that pharmacists are one of the main producers of the alcohol-based handrubs throughout the pandemic and encourages local production in pharmacies.[2] Local distilleries also found opportunity in changing their distribution of alcohol to local pharmacy departments to supply the hard to find key ingredient of the hand sanitizer.[3]

The Food and Drug Administration (FDA) released their policy for "Temporary Compounding of Certain Alcohol-Based Hand Sanitizer Products During the Public Health Emergency" to respond to the numerous questions it had received regarding pharmacists compounding hand sanitizer in their own work settings.[4] The guidance document continues to be updated based on best practices and responses to the effects of the pandemic and can be accessed through the FDA's website (www.fda.gov). The key ingredients used in hand sanitizer (handrub) are: 1) alcohol, 2) glycerin, 3) hydrogen peroxide and 4) sterile water.

Alcohol

The FDA recommends that the alcohol be either ethyl that is 95% ethanol by volume or greater, or isopropyl alcohol (United States Pharmacopeia (USP) grade). The FDA also requires that any ethanol must be denatured prior to its use. The process of denaturing involves the addition of chemicals that help deter ingestion and the FDA includes that the process of denaturing does not have to be done by the manufacturer. The FDA further advises that the temporary manufacture of ethanol products would be allowed for incorporation into alcohol-based hand sanitizer products.[4] This means that if a pharmacy can only procure food grade ethyl alcohol, they can denature it themselves. The preferred formula to denature alcohol is to add 1/16th avoirdupois ounce of denatonium benzoate, either as a solid or liquid form, and 1/8 gallon of tert-butyl alcohol to every 100 gallons of alcohol. Other formulations for denaturing alcohol can be found in the Alcohol and Tobacco Tax and Trade Bureau (TTB) regulations in 27 CFR part 20 and 21.[5] The CDC recommends that alcohol based hand sanitizers are at least 60% v/v ethanol or 70% v/v isopropyl alcohol, but the FDA's recommendation is consistent with the higher concentration from the World Health Organization (WHO) that includes a final concentration of 80% v/v of ethanol-based preparations and 75% v/v for isopropyl based preparations.[6,7] The higher concentrations help ensure the final concentration of the preparation will exceed those needed to inactivate viruses. These formulas with higher final alcohol concentrations account for the potential for sub-potent ingredients, evaporative loss, and margin of error. In addition, the TTB waived provisions of internal revenue law with regard to distilled spirits and allowed exemptions to permittees who wished to produce ethanol-based hand sanitizers for the increased demand during the public health emergency. Over 800 U.S. distilleries, including 10 in South Carolina, took advantage of this provision and pivoted their production of alcohol for consumption to alcohol to support the production of hand sanitizer.[8]

Glycerin

Glycerin is a key excipient in the production of hand sanitizers for its humectant qualities to prevent the drying of the preparation and improve dermal tolerance.[9] Glycerin and glycerol are synonymous and may be interchanged. This ingredient is not used to enhance viscosity and no other ingredients should be added to enhance viscosity as they may decrease the effectiveness of the final product. For preparations, glycerin is not to exceed 1.45% v/v. Some data suggests that the bactericidal efficacy of the WHO formulation may be less than formulations without glycerol.[10] There are further reports that recommend a reduction from 1.45% to 0.725%, while also increasing the alcohol concentration by 5% and prolonging the application period to 5 minutes.[11] Other emollients may be considered for skin care, but should be miscible in water and alcohol. In addition, any alternative humectants or emollients should not increase toxicity or potential allergic reactions to the user.

Hydrogen Peroxide

Hydrogen peroxide is used to inactivate contaminating bacterial spores in the solution and is not considered an active ingredient for the purpose of hand antisepsis. The product should be formulated to a final strength of 0.125% v/v hydrogen peroxide using Hydrogen Peroxide Concentrate USP, Hydrogen Peroxide Topical Solution USP, or technical grade hydrogen peroxide, ensuring that the alcohol (ethanol or isopropyl alcohol) concentration remains within the specified levels.

Sterile Water

Sterile distilled water is preferred for the preparations, but may also be in short supply throughout the pandemic. Water is considered sterile if it has been boiled and cooled, distilled or prepared by other processes that meet the specifications of Purified Water USP. It should be used as quickly as possible after it is rendered sterile.

Labeling

The FDA guidance document provides samples of labels in Appendices A-D.[4] In general, the front of the display includes the name and strength of the formulation and the volume of the product in milliliters. The drug facts label looks similar to an over the counter label with active and inactive ingredients, warnings, directions and uses, and storage information.

Materials for Preparation

In addition to reagents required for production, other materials used in the compounding would include large glass or plastic bottles, measuring cylinders, plastic or metal funnels, wooden, plastic or metal paddles for stirring, and 100-500 mL plastic bottles with leak-proof tops for dispensing.[2]

Tips for Preparing

Although colors are not necessary, they may be added to allow differentiation from other fluids. They should not add to the toxicity, promote allergy, or interfere with the efficacy of the product. Flavors and smells are discouraged to prevent accidental ingestion. The American Association of Poison Control Centers reports 11,706 hand sanitizer exposure cases from January 1, 2020 through May 17, 2020, an increase of 39% compared to the same time period in 2019. Over 7500 of these cases were in children 12 years and younger and ingestion of as little as an ounce by a small child can be fatal. Accidental alcohol poisoning can cause confusion, vomiting and drowsiness, and in severe cases, respiratory arrest and death. [12]

It is expected that compounders will still follow USP General Chapter <795> Pharmaceutical Compounding – Nonsterile Preparations, which includes trained personnel, appropriate sources of ingredients, clean and maintained equipment, Master Formulation and Compounding Records, and labels with the final concentration of ethanol or isopropyl alcohol, “For External Use Only,” and a correct Beyond-Use Date. It is recommended that the hand sanitizers be stored in packaging appropriate for liquids to prevent the evaporation of the alcohol. The final product must also be left in a liquid form; gels, foams, or aerosolized sprays are not permitted. The production and storage facilities should be air conditioned or cooled and no naked flames or smoking should be permitted. An alcoholmeter can be used to control the alcohol concentration of the final use solution. Bottles should also be monitored for signs of contamination, including particulates, discoloration, and microbe growth. These guiding statements are valid for the duration of the public health emergency as declared by the Secretary of Health and Human services (HHS) on January 31, 2020.

Key Resources

The USP created a document of recommendations from its Compounding Expert Committee that includes three formulations of hand sanitizer and appropriate ingredient substitutions.[13] It also released a Hand Sanitizer Toolkit that includes up-to-date information for compounders, other facilities like distilleries, and the USP standards for hand sanitizer ingredients, as well as a handy brochure that details the three recommended formulations.[13]

The National Alliance of State Pharmacy Associations keeps an updated webpage of the specific state actions affecting the compounding of hand sanitizer which can be accessed at the website, (https://naspa.us/resource/compounding-hand-sanitizer/).[14]

As seen in a variety of ways through the pandemic, pharmacists serve as key healthcare providers in managing and preventing the spread of the disease throughout communities. Pharmacists can leverage their unique expertise in compounding to fill gaps in the supply chain to ensure that hand sanitizer is supplied to all those who need it.

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Figures

Figure 1. Labeling for Ethyl Alcohol Formulation (for Consumer Use)[4]
Front of package:

Ethyl Alcohol Antiseptic 80% Topical Solution

Hand Sanitizer

Non-Sterile Solution

(Container volume in mL)

Figure 2. Ethyl Alcohol Drug Facts Label[4]

Drug Facts

Active ingredient[s]	***Purpose***
Alcohol 80% v/v	Antiseptic

Use[s]

Hand sanitizer to help reduce bacteria that potentially can cause disease. For use when soap and water are not available.

Warnings

For external use only. Flammable. Keep away from heat or flame

Do not use

- in children less than 2 months of age
- on open skin wounds

When using this product keep out of eyes, ears, and mouth. In case of contact with eyes, rinse eyes thoroughly with water.

Stop use and ask a doctor if irritation or rash occurs. These may be signs of a serious condition.

Keep out of reach of children. If swallowed, get medical help or contact a Poison Control Center right away.

Directions

- Place enough product on hands to cover all surfaces. Rub hands together until dry.
- Supervise children under 6 years of age when using this product to avoid swallowing.

Other information

- Store between 15-30C (59-86F)
- Avoid freezing and excessive heat above 40C (104F)

Inactive ingredients glycerin, hydrogen peroxide, purified water USP

Figure 3. Labeling for Isopropyl Alcohol Formulation (for Consumer Use)[4]
Front of Package:

Isopropyl Alcohol Antiseptic 75% Topical Solution

Hand Sanitizer

Non-Sterile Solution

(Container volume in mL)

Figure 4. Drug Facts Label[4]

Drug Facts

Active ingredient[s] ***Purpose***

Isopropyl alcohol 75% v/v..... Antiseptic

Use[s]

Hand sanitizer to help reduce bacteria that potentially can cause disease. For use when soap and water are not available.

Warnings

For external use only. Flammable. Keep away from heat or flame

Do not use

- in children less than 2 months of age
- on open skin wounds

When using this product keep out of eyes, ears, and mouth. In case of contact with eyes, rinse eyes thoroughly with water.

Stop use and ask a doctor if irritation or rash occurs. These may be signs of a serious condition.

Keep out of reach of children. If swallowed, get medical help or contact a Poison Control Center right away.

Directions

- Place enough product on hands to cover all surfaces. Rub hands together until dry.
- Supervise children under 6 years of age when using this product to avoid swallowing.

Other information

- Store between 15-30C (59-86F)
- Avoid freezing and excessive heat above 40C (104F)

Inactive ingredients glycerin, hydrogen peroxide, purified water USP

Self-Assessment Questions

1. Why must alcohol be denatured prior to its use in hand sanitizer?
    a. Increase viscosity
    b. Suspend particles
    c. Deter ingestion
    d. Prevent antimicrobial growth
2. What is the purpose of glycerin in hand sanitizer?
    a. Prevent drying out
    b. Scent
    c. Increase absorption into the skin
    d. Antibacterial
3. What should the final strength of hydrogen peroxide be in the formulation?
    a. 0.001% v/v
    b. 0.125% v/v
    c. 1.25% v/v
    d. 12.5% v/v
4. Sterile water is a key ingredient of hand sanitizer. Water can be considered “sterile” if it meets the specifications of _____.
    a. Purified Water, USP
    b. Distilled Water, USP
    c. Reverse-osmosis Water, USP
    d. Mineralized Water, USP

5. While compounding hand sanitizer, pharmacists are expected to follow _____
    a. USP <700>
    b. USP <795>
    c. USP <797>
    d. USP <800>
6. What auxiliary label would be used for hand sanitizer?
    a. “Refrigerate”
    b. “May Cause Drowsiness”
    c. “For External Use Only”
    d. “Do Not Use If Pregnant”
7. What is a possible sign of contamination of the hand sanitizer?
    a. Discoloration
    b. Creaming
    c. Phase Inversion
    d. Decrease Melting Point
8. Specific state actions affecting the compounding of hand sanitizer can be found through _____.
    a. American College of Clinical Pharmacists
    b. American Medical Association
    c. National Compounders League
    d. National Alliance of State Pharmacy Associations