SUMMARY OF FDA GUIDANCE ON PRODUCING ALCOHOL (ETHANOL) AND ALCOHOL-BASED HAND SANITIZER DURING THE COVIV-19 OUTBREAK
(Updated through April 6, 2020)

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I. BACKGROUND

- The Department of Health and Human Services (HHS) has determined that the COVID-19 outbreak in the United States is a **public health emergency** and the President has declared a **national emergency**.

- **Hand hygiene is an important part** of the response to COVID-19.

- The Center for Disease Control (CDC) recommends **washing hands** often with soap and water for at least 20 seconds to help prevent the spread of the infection.

- When soap and water are not readily available, the CDC recommends using an **alcohol-based hand sanitizer**, containing at least 60% alcohol.

- The U.S. Food and Drug Administration (FDA) has recognized that consumers and health care professionals are currently **having trouble obtaining alcohol-based sanitizers**.

- In response to increased demand and supply shortages, **the FDA has** announced **temporary policies** and **issued guidance documents** to:

  - **manufacture alcohol** for hand sanitizer, which is available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/temporary-policy-manufacture-alcohol-incorporation-alcohol-based-hand-sanitizer-products-during; and

  - **produce alcohol-based hand sanitizer**, which is available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-temporary-policy-preparation-certain-alcohol-based-hand-sanitizer-products-during.

- During the public health emergency, the FDA **does not intend to act** against firms that: (1) **register** with the FDA; and (2) produce alcohol or alcohol-based hand sanitizers **according to FDA recommendations, described below**.

- This document provides a **general overview and summary** of the FDA letters and guidance documents. It is not fact or case specific, and it **does not recommend any particular course of action**. The FDA documents cited herein, and the FDA website, along with any updates, **should be reviewed in consultation** with qualified professionals and/or counsel. Interested parties should also **contact the FDA directly** with questions, and for additional details and guidance.

II. FDA RECOMMENDATIONS FOR MANUFACTURING ALCOHOL (ETHANOL) FOR HAND SANITIZER

- Alcohol used as the **Active Pharmaceutical Ingredient (API)** in hand sanitizers should be **at least 94.9% ethanol by volume before denaturing**.

- The alcohol production firm **must ensure the ethanol content** in the finished API before denaturing is at **least 94.9% ethanol by volume**, or of **sufficient content to enable the finished hand sanitizer (discussed below) to meet an ethanol concentration of 80%**.

- Any **water used to adjust** the finished alcohol content **must be sterile**, e.g., by boiling, distillation, or any other process that results in water meeting the United States Pharmacopeia (USP) standards for purified water.

- Before each batch is released, **a sample batch should be tested for ethanol content** using the most accurate method of analysis available at the site, such as:

  - gas chromatography;

  - specific gravity, e.g., alcoholmeter, hydrometer, pycnometer, or gravity density meter; or

  - another test that is at least as accurate.

- The ethanol content **can be tested**:

  - **before final packaging** if the alcohol is distributed as an API to another finished-goods manufacturer; or

  - **before being used in the production process** if the alcohol production firm is also producing finished hand sanitizer.

- The alcohol **must be denatured** by the alcohol production firm or at the point of production of the finished hand sanitizer.[1] The FDA has published three **formulas for denaturing alcohol**, which include:

[1] Some distilleries have been petitioning the FDA to allow the use of undenatured alcohol (https://www.cbs19news.com/story/41964120/fda-asked-to-allow-distilleries-to-use-undenatured-alcohol-in-hand-sanitizer), but the FDA has yet to change its position.

Preferred Formula

27 CFR 21.76 Formula No. 40-B

To every 100 gallons of alcohol add:

One-sixteenth avoirdupois ounce of denatonium benzoate,[17] N.F., and 1⁄8 gallon of tert-butyl alcohol

OR

To every 100 gallons of alcohol add:

One-sixteenth avoirdupois ounce of denatonium benzoate, [18] N.F.

Alternative Formulas

27 CFR 21.75 Formula No. 40-A

To every 100 gallons of alcohol add:

One pound of sucrose octaacetate and 1⁄8 gallon of tert-butyl alcohol

OR

To every 100 gallons of alcohol add:

One pound of sucrose octaacetate

27 CFR 21.37 Formula No. 3-C

To every 100 gallons of alcohol add:

Five gallons of isopropyl alcohol

- **Denatonium benzoate** (Preferred Formula, fn. 17, 18) can be added as a solid or in liquid form, provided that the added amount is calculated on a dry basis.

- No ingredient besides **alcohol, water, and denaturants** can be added.

- If alcohol is distributed as an API to another finished-goods manufacturer, the **labeling must indicate** if the alcohol was "**denatured**" by the alcohol production firm or is "**undenatured**" when distributed to the point of production. The FDA has published **exemplary labels (attached hereto as Exhibit 1 and shown below) to be used**; however, firms regulated by the U.S. Department of Treasury, Alcohol and Tobacco Tax and Trade Bureau (TTB) should check with the TTB for additional labeling requirements:

Denatured	Undenatured
DENATURED Alcohol [insert process/denaturing compound] **Ethanol (ethyl alcohol) XX%,** **as determined by <Insert test method>** **[Insert Volume of Product in mL or Liters]** **For use in production of hand sanitizers (antiseptic hand rubs) only.** **Non-potable.** **Manufactured by:** **<Name of Manufacturer>** **<Physical Address of Manufacturing site>** **<Contact phone and email address>** **Manufacturer FDA registration number (DUNS):** **Manufactured on <Insert Date>** **Released on <Insert Date>** **Batch Number**	**UNDENATURED Alcohol** **Ethanol (ethyl alcohol) XX%,** **as determined by <Insert test method>** **[Insert Volume of Product in Milliters (mL) or Liters]** **For use in production of hand sanitizers (antiseptic hand rubs) only. Denaturing required during hand sanitizer production.** **Non-potable.** **Manufactured by:** **<Name of Manufacturer>** **<Physical Address of Manufacturing site>** **<Contact phone and email address>** **Manufacturer FDA registration number (DUNS):** **Manufactured on <Insert Date>**

- Alcohol must be prepared in **sanitary conditions** and the equipment used must be **fit for the purpose** and **well maintained**.
- **Records** should be kept to document: (1) **alcohol production;** and (2) the **verification of alcohol content** in each batch.
- Firms receiving **adverse event reports** are encouraged to **submit them to the FDA's MedWatch Adverse Event Reporting program.**

III. FDA RECOMMENDATIONS FOR MANUFACTURING HAND SANITIZER

❖ Alcohol-based hand sanitizers should be produced with **only** the following **ingredients**, and **additional ingredients are not authorized**:

Ethanol Based Sanitizer	Isopropyl Alcohol Based Sanitizer
Alcohol that is **at least 94.9% ethanol** by volume before denaturing, **or of sufficient content to enable the finished hand sanitizer to meet an ethanol concentration of 80%**; **glycerin** (glycerol)[2]; **hydrogen peroxide**[3]; and **sterile water**, e.g., by boiling, distillation, or any other process that results in water meeting the USP standards for purified water.	**Isopropyl Alcohol**; **glycerin** (glycerol)[2]**;** **hydrogen peroxide**[3]; and **Sterile water**, e.g., by boiling, distillation, or any other process that results in water meeting the USP standards for purified water.

❖ The following **formula** should be used:

- alcohol (ethanol) (80%, volume/volume (v/v)) in an aqueous solution *or* Isopropyl Alcohol (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

❖ Ethanol (if used) **must be denatured** by the alcohol production firm or at the point of production of the finished hand sanitizer.[4] The FDA has published three **formulas for denaturing alcohol**, which are listed in Section II, above.

❖ Firms must ensure that: (1) the ethanol or isopropyl alcohol **active ingredient is correct**, (2) the **correct amount of the active ingredient is used**; and, (3) **verify the alcohol content in**

[2] USP or food grade may be used.
[3] Hydrogen Peroxide Concentrate USP or Hydrogen Peroxide Topical Solution USP may be used. Technical grade hydrogen peroxide also may be used if the concentration is within that of Hydrogen Peroxide Concentrate USP or Hydrogen Peroxide Topical Solution USP.
[4] [4] Some distilleries have been petitioning the FDA to allow the use of undenatured alcohol (https://www.cbs19news.com/story/41964120/fda-asked-to-allow-distilleries-to-use-undenatured-alcohol-in-hand-sanitizer), but the FDA has yet to change its position.

samples of the finished product before each batch is released using the most accurate method of analysis available at the site, such as:

- gas chromatography;
- specific gravity, e.g., alcoholmeter, hydrometer, pycnometer, or gravity density meter; or
- another test that is at least as accurate.

- Testing for alcohol content can be performed on **in-process material** before filling containers for distribution.
- The FDA has published **exemplary product labeling** for finished hand sanitizer that should be used, is available at:https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-temporary-policy-preparation-certain-alcohol-based-hand-sanitizer-products-during, and is **attached to this summary as Exhibit 2**.
- Hand sanitizer must be prepared in **sanitary conditions** and the equipment used must be **fit for the purpose** and **well maintained**.
- Records should be kept **documenting key steps and controls** to assure each batch matches the formula developed for the product.
- Firms should have a way **to accept adverse event reports** for any products they manufacture and **submit the reports to the FDA**.

IV. REGISTRATION OF FACILITIES AND PRODUCTS

- **Prior to manufacturing and distributing alcohol as an API or finished hand sanitizer,** interested **firms must register** their facility(ies) and product(s) in the FDA Registration and Listing System at: https://www.fda.gov/drugs/guidance-compliance-regulatory-information/drug-registration-and-listing-system-drls-and-edrls.

- **Upon completion of registration and listing**, firms receive automatic confirmation from the FDA and **do not need to wait** for a further communication from the FDA before beginning to manufacture and distribute products.

V. ALTERNATIVE INGREDIENTS AND FORMULAS

- The FDA is continuing to evaluate **other** potential ingredients (e.g., denaturing agents) and formulas for alcohol as an API or finished hand sanitizer, and firms are encouraged to contact the FDA with questions at: COVID-19-hand-sanitizers@fda.hhs.gov.

EXHIBIT 1

Appendix A. Labeling for Undenatured Alcohol for Incorporation Into Alcohol-Based Hand Sanitizers (Antiseptic Hand Rubs) [15]

PRINCIPAL DISPLAY PANEL ADHERED TO EACH CONTAINER DISTRIBUTED

UNDENATURED Alcohol

Ethanol (ethyl alcohol) XX%,
as determined by <Insert test method>

[Insert Volume of Product in Milliters (mL) or Liters]

For use in production of hand sanitizers (antiseptic hand rubs) only. Denaturing required during hand sanitizer production.

Non-potable.

Manufactured by:
<Name of Manufacturer>
<Physical Address of Manufacturing site>
<Contact phone and email address>

Manufacturer FDA registration number (DUNS):

Manufactured on <Insert Date>

[15] Entities regulated by the U.S. Department of the Treasury, Alcohol and Tobacco Tax and Trade Bureau (TTB) should check with TTB for additional labeling requirements.

Appendix B. Labeling for Denatured Alcohol for Incorporation Into Alcohol-Based Hand Sanitizers (Antiseptic Hand Rubs) [16]

PRINCIPAL DISPLAY PANEL ADHERED TO EACH CONTAINER DISTRIBUTED

DENATURED Alcohol [insert process/denaturing compound]

Ethanol (ethyl alcohol) XX%,
as determined by <Insert test method>

[Insert Volume of Product in mL or Liters]

For use in production of hand sanitizers (antiseptic hand rubs) only.

Non-potable.

Manufactured by:
<Name of Manufacturer>
<Physical Address of Manufacturing site>
<Contact phone and email address>

Manufacturer FDA registration number (DUNS):

Manufactured on <Insert Date>
Released on <Insert Date>
Batch Number

[16] Entities regulated by the U.S. Department of the Treasury, Alcohol and Tobacco Tax and Trade Bureau (TTB) should check with TTB for additional labeling requirements.

EXHIBIT 2

Appendix A. Labeling for Ethyl Alcohol Formulation Consumer Use

PRINCIPAL DISPLAY PANEL (FRONT OF PACKAGE):

Alcohol Antiseptic 80%
Topical Solution

Hand Sanitizer
Non-sterile Solution

[Insert Volume of Product in mL]

DRUG FACTS LABEL

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

Appendix B. Labeling for Isopropyl Alcohol Formulation Consumer Use

PRINCIPAL DISPLAY PANEL (FRONT OF PACKAGE):

Isopropyl Alcohol Antiseptic 75% Topical Solution

Hand Sanitizer
Non-sterile Solution

[Insert Volume of Product in mL]

DRUG FACTS LABEL

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

Appendix C. Labeling for Ethyl Alcohol Formulation Health Care Personnel Handrub Use

PRINCIPAL DISPLAY PANEL (FRONT OF PACKAGE):

Alcohol Antiseptic 80%
Topical Solution

Antiseptic Hand Rub
Non-sterile Solution

[Insert Volume of Product in mL]

DRUG FACTS LABEL

Drug Facts

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

Alcohol 80% v/v..... Antiseptic

Use[s]

Health care personnel hand rub to help reduce bacteria that potentially can cause disease.

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

Appendix D. Labeling for Isopropyl Alcohol Formulation Health Care Personnel Handrub Use

PRINCIPAL DISPLAY PANEL (FRONT OF PACKAGE):

Isopropyl Alcohol Antiseptic 75% Topical Solution

Antiseptic Hand Rub
Non-sterile Solution

[Insert Volume of Product in mL]

DRUG FACTS LABEL

Drug Facts

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

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

Use[s]

Health care personnel hand rub to help reduce bacteria that potentially can cause disease.

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