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

Guidance for Industry

March 2020

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U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

Pharmaceutical Quality/Manufacturing Standards (CGMP)/
Over-the-Counter (OTC)

Preface

Public Comment

This guidance is being issued to address the Coronavirus Disease 2019 (COVID-19) public health emergency. This is being implemented without prior public comment because FDA has determined that prior public participation for this guidance is not feasible or appropriate (see section 701(h)(1)(C)(i) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) and 21 CFR 10.115(g)(2)). This guidance document is being implemented immediately, but it remains subject to comment in accordance with the Agency's good guidance practices.

Comments may be submitted at any time for Agency consideration. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. Submit electronic comments to <https://www.regulations.gov>. All comments should be identified with the docket number FDA-2020-D-1106 and complete title of the guidance in the request.

Additional Copies

Additional copies are available from the FDA web page titled "COVID-19-Related Guidance Documents for Industry, FDA Staff, and Other Stakeholders," *available at* <https://www.fda.gov/emergency-preparedness-and-response/mcm-issues/coronavirus-disease-2019-covid-19>, and from the FDA web page "[Hand Sanitizers | Covid-19](http://wcms-internet.fda.gov/drugs/coronavirus-covid-19-drugs/hand-sanitizers-covid-19)" *available at*: <http://wcms-internet.fda.gov/drugs/coronavirus-covid-19-drugs/hand-sanitizers-covid-19>. You may also send an e-mail request to druginfo@fda.hhs.gov to receive a copy of the guidance. Please include the document number FDA-2020-D-1106 and complete title of the guidance in the request.

Questions

For questions regarding this document, contact FDA at: COVID-19-Hand-Sanitizers@fda.hhs.gov.

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Temporary Policy for Manufacture of Alcohol for Incorporation Into Alcohol-Based Hand Sanitizer Products During the Public Health Emergency (COVID-19) Guidance for Industry¹

This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA office responsible for this guidance as listed on the title page.

I. INTRODUCTION

The Food and Drug Administration (FDA or Agency) plays a critical role in protecting the United States from emerging infectious diseases, such as the Coronavirus Disease 2019 (COVID-19) pandemic. FDA is committed to providing timely guidance to support continuity and response efforts to this pandemic.

FDA is issuing this guidance in response to a number of queries from entities that are not currently registered drug manufacturers that would like to produce alcohol² for incorporation into alcohol-based hand sanitizers. This policy does not extend to other types of active ingredients for incorporation into alcohol-based hand sanitizers, such as isopropyl alcohol.³

The Agency is issuing this guidance to communicate its policy for the temporary manufacture of ethanol products by firms that manufacture alcohol for incorporation into alcohol-based hand sanitizer products under the circumstances described in this guidance (alcohol production firms) for the duration of the public health emergency declared by the Secretary of Health and Human Services (HHS) on January 31, 2020.⁴ At such time when the public health emergency is over, as declared by the Secretary, FDA intends to discontinue this enforcement discretion policy and withdraw this guidance.

¹ This guidance has been prepared by the Center for Drug Evaluation and Research at the Food and Drug Administration.

² *Alcohol* is defined as ethanol (ethyl alcohol) in the United States Pharmacopeia and National Formulary (USP-NF) and as ethyl alcohol in the Food Chemical Codex, and as used in this guidance. These monographs establish test methods and acceptance criteria for identity and purity. The definition of *alcohol* does not include isopropyl alcohol.

³ Isopropyl alcohol is manufactured by different chemical processes and is therefore not discussed in this guidance.

⁴ The HHS Public Health Emergency Declaration is available at <https://www.phe.gov/emergency/news/healthactions/phe/Pages/2019-nCoV.aspx>.

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Given this public health emergency, this guidance is being implemented without prior public comment because FDA has determined that prior public participation for this guidance is not feasible or appropriate (see section 701(h)(1)(C)(i) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. § 371(h)(1)(C)(i) and 21 CFR § 10.115(g)(2)). This guidance document is being implemented immediately, but it remains subject to comment in accordance with the Agency's good guidance practices.

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

There is currently an outbreak of respiratory disease caused by a novel coronavirus that was first detected in Wuhan City, Hubei Province, China, and that has now spread globally, including the United States. The virus has been named "SARS-CoV-2" and the disease it causes has been named "Coronavirus Disease 2019" (COVID-19). SARS-CoV-2 has demonstrated the capability to rapidly spread, leading to significant impacts on healthcare systems and causing societal disruption. The potential public health threat posed by COVID-19 is high, both globally and to the United States. On January 31, 2020, the Secretary of HHS declared a public health emergency related to COVID-19 and mobilized the Operating Divisions of HHS.⁵ In addition, on March 13, 2020, the President declared a national emergency in response to COVID-19.⁶

We understand that some consumers and health care professionals are currently experiencing difficulties accessing alcohol-based hand sanitizers. We are also aware of reports that some consumers are producing hand sanitizers for personal use in their homes; the Agency lacks verifiable information on the methods being used to prepare such products and whether they are safe for use on human skin. To enhance the availability of hand sanitizer products, FDA has issued a guidance for industry entitled *Policy for Temporary Compounding of Certain Alcohol-Based Hand Sanitizer Products During the Public Health Emergency* (March 2020) (compounding guidance) that describes the Agency's policy for the temporary compounding of certain alcohol-based hand sanitizer products by pharmacists in State-licensed pharmacies or Federal facilities and registered outsourcing facilities.⁷ FDA has also issued a guidance for industry entitled *Temporary Policy for Preparation of Certain Alcohol-Based Hand Sanitizer*

⁵ Secretary of Health and Human Services Alex M. Azar, Determination that a Public Health Emergency Exists. (Jan. 31, 2020), available at <https://www.phe.gov/emergency/news/healthactions/phe/Pages/2019-nCoV.aspx>.

⁶ Proclamation on Declaring a National Emergency Concerning the Novel Coronavirus Disease (COVID-19) Outbreak (Mar. 13, 2020), available at <https://www.whitehouse.gov/presidential-actions/proclamation-declaring-national-emergency-concerning-novel-coronavirus-disease-covid-19-outbreak/>.

⁷ The compounding guidance is available at <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/policy-temporary-compounding-certain-alcohol-based-hand-sanitizer-products-during-public-health>. We update guidances periodically. For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/regulatory-information/search-fda-guidance-documents>.

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Products During the Public Health Emergency (COVID-19) (March 2020) that describes the Agency's temporary policy for preparation of certain alcohol-based hand sanitizer products by firms that register as over-the-counter (OTC) drug manufacturers to prepare alcohol-based hand sanitizers.⁸

III. DISCUSSION

In response to the demand for alcohol-based hand sanitizers and their active ingredient, alcohol, certain entities that are not currently regulated by FDA as drug manufacturers have requested guidance on the preparation and distribution of alcohol for incorporation into hand sanitizer products for the public's use.

Because of the public health emergency posed by COVID-19, FDA does not intend to take action against alcohol production firms⁹ that manufacture alcohol (i.e., ethanol or ethyl alcohol) for use as the active pharmaceutical ingredient (API) in alcohol-based hand sanitizers for consumer use and for use as health care personnel hand rubs for the duration of the public health emergency declared by the Secretary of HHS on January 31, 2020, provided the following circumstances are present:

1. To meet component quality requirements for hand sanitizer production, the alcohol manufactured as an API is not less than 94.9% ethanol by volume.^{10,11}
2. Any water used to adjust the finished ethanol content in the alcohol API is sterile (e.g., by boiling, distillation, or other process that results in water that meets the specifications for Purified Water USP). Water is used as quickly as possible after it is rendered sterile or purified.

Additional Considerations for Alcohol (Ethanol):

Alcohol (ethanol) manufacturer for use in hand sanitizers is derived from distillation or fermentation processes typically used for consumable goods. Alcohol derived from synthetic processes is used only if it meets USP or FCC grade.

Ethanol produced in facilities normally producing fuel or technical grade may be considered for use if the ethanol is produced from fermentation and distillation as would

⁸ This guidance 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>.

⁹ Specifically, FDA does not intend to take action against alcohol production firms for the duration of the public health emergency declared by the Secretary of HHS on January 31, 2020, for violations of sections 501(a)(2)(B), 501(b), 502(f)(1), 505, or 582 of the FD&C Act (21 U.S.C. 351(a)(2)(B), 351(b), 352(f)(1), 355, and 360eee-1).

¹⁰ This is consistent with the United States Pharmacopoeia (USP) and Food Chemical Codex (FCC) grade requirements for purity. Lower ethanol content alcohol falls within this policy so long as it is labeled accordingly and the content is sufficient to enable the finished hand sanitizer to meet the ethanol concentration of 80% v/v.

¹¹ Alcohol (ethanol) used for this purpose is derived from distillation or fermentation processes typically used for consumable goods. Alcohol derived from synthetic processes is used only if it meets USP or FCC grade.

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be typically used for consumable goods, and no other additives or other chemicals have been added to the ethanol. Further, special caution should be taken to ensure any other chemicals on site are not introduced into the ethanol either intentionally or via cross contamination. Because of the potential for the presence of potentially harmful impurities due to the processing approach, fuel or technical grade ethanol should only be used if it meets USP or FCC grade requirements and the ethanol has been screened for any other potentially harmful impurities not specified in the USP or FCC requirements.¹²

Ingredients that are described as only meeting American Chemical Society (ACS) grade standards should generally not be used in in hand sanitizers. The chemical standards that have been established by ACS for reagents are not designed to determine the suitability of a chemical for human use. For example, the ACS monographs for ethanol do not include any impurity specifications. Where an ingredient is described as meeting both ACS grade and the other standard(s) cited in this section (e.g., USP or FCC grade), use of that ingredient is consistent with this policy.¹³

3. The alcohol (ethanol) is denatured either by the alcohol producer or at the point of production of the finished hand sanitizer product. Alcohol and Tobacco Tax and Trade Bureau regulations in 27 CFR part 20 and 21 provide a number of formulas for denaturing alcohol. Formulas for use in hand sanitizers are included in Appendix C of this document and include:¹⁴
 - a. Formula 40A or 40B with or without the tert-butyl alcohol
 - b. Formula 3C (isopropyl alcohol).¹⁵

Denaturing is critical because there have been reports of adverse events, including deaths, from unintentional ingestion of hand sanitizer, particularly in young children.¹⁶ The alcohol should be denatured at either (1) the point of production by the alcohol

¹² If a firm wants to use or supply a fuel or technical grade ethanol that does not meet USP or FCC requirements, submit information on the ethanol with regard to the levels of impurities listed in the USP monograph as well as any other potentially harmful impurities that may be present given the manufacturing environment to COVID-19-Hand-Sanitizers@fda.hhs.gov with “ETHANOL DATA” in the subject line for FDA’s assessment regarding the use of the ethanol under this policy.

¹³ If a firm wants to use ethanol that is described only as ACS grade, submit relevant information on the ethanol’s concentration and impurity profile to COVID-19-Hand-Sanitizers@fda.hhs.gov with “ETHANOL DATA” in the subject line for FDA’s assessment regarding the use of the ethanol under this policy.

¹⁴ FDA is continuing to evaluate other potential formulas for denaturing, and will update Appendix C as we conduct that analysis. Firms who wish to use different denaturants (bitterants) should contact FDA at COVID-19-hand-sanitizers@fda.hhs.gov.

¹⁵ Using technical grade isopropyl alcohol that meets the requirements of 27 CFR 21.113 as a denaturant is consistent with this policy.

¹⁶ Every month, there are hundreds of calls to Poison Control centers for unintentional ingestion of hand sanitizer. As indicated from data provided by the American Association of Poison Control Centers (AAPCC), in March 2020 (during the COVID-19 pandemic), calls to Poison Control centers related to hand sanitizer increased by 79% compared to March of 2019. The majority of these calls were for unintentional exposures in children 5 years of age and younger.

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production firm or (2) the point of manufacture or compounding of the hand sanitizer, with the alcohol intended for incorporation into a finished product labeled accurately as “denatured” or “undenatured” accordingly.

Beyond alcohol, water, and denaturants (if added at the point of production), the alcohol production firm does not add other ingredients. Different or additional ingredients in the API may impact the quality and potency of the finished hand sanitizer product, and may increase the risk of accidental ingestion in children.

4. The alcohol production firm ensures the ethanol content in the finished API before being denatured is at least 94.9% by volume¹⁷ (see United States Pharmacopeia National Formulary [USP-NF] or Food Chemical Codex [FCC]). If the alcohol is to be distributed to another firm for producing the hand sanitizer, it is labeled with the ethanol content determined by an appropriate test so that the hand sanitizer can be reliably produced at the intended labeled strength. A simple record should be used to document key steps and controls.
5. The alcohol is prepared under sanitary conditions and equipment used is well maintained and fit for this purpose.¹⁸
6. The alcohol production firm uses the most accurate method of analysis available at the site for verification of ethanol content in a sample before each batch is released for distribution or for use in producing the hand sanitizer. Methods can include gas chromatography (GC), specific gravity (e.g., alcoholmeter, hydrometer, pycnometer, or gravity density meter), or another test that is at least as accurate. The sample tested can be from the final API before packaging (if distributed as an API) or before actual use in producing the hand sanitizer.
7. The alcohol API, if distributed to other producers, is labeled consistent with the attached labeling in Appendices A and B (Labeling for Undenatured/Denatured Alcohol to be used for incorporation into hand sanitizers).
8. Alcohol production firms register their facility and list these products in the FDA Drug Registration and Listing System (DRLS, <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 FDA and do not need to wait for further communication from FDA before they begin to manufacture and distribute these products. FDA relies on registration and listing information to help manage drug shortages, monitor safety issues that may arise with product distributed to the public, and manage product recalls, among other important FDA public safety activities. Our help desk is standing by to assist with facilitating this process and can be contacted by sending an email to: edrls@fda.hhs.gov.

¹⁷ Or of sufficient content to enable the finished hand sanitizer to meet the ethanol concentration of 80% v/v.

¹⁸ Facilities must prevent insanitary conditions under section 501(a)(2)(A) of the FD&C Act (21 U.S.C. 351(a)(2)(A)).

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If alcohol production firms receive adverse event reports, they are encouraged to submit them to FDA's [MedWatch Adverse Event Reporting](#) program:

- Complete and submit the report [online](#); or
- Download and complete the [form](#), then submit it via fax at 1-800-FDA-0178.

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Appendix A. Labeling for Undenatured Alcohol for Incorporation Into Alcohol-Based Hand Sanitizers (Antiseptic Hand Rubs) ¹⁹

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 Milliliters (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>

¹⁹ 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.

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Appendix B. Labeling for Denatured Alcohol for Incorporation Into Alcohol-Based Hand Sanitizers (Antiseptic Hand Rubs) ²⁰

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

²⁰ 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.

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Appendix C. Formulas That May Be Used To Denature Alcohol Before It Is Used in Alcohol Based Hand Sanitizers (Antiseptic Hand Rubs)

Preferred Formula

27 CFR 21.76 Formula No. 40-B

To every 100 gallons of alcohol add:

One-sixteenth avoirdupois ounce of denatonium benzoate,²¹ 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,²² 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 alcohol²³

²¹ Denatonium benzoate can be added as either a solid or in liquid form, provided the added amount is calculated on a dry basis.

²² See note 21.

²³ See note 15.