Contains Nonbinding Recommendations

Temporary Policy for Preparation of Certain 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 guidance is being implemented without prior public comment because the Food and Drug Administration (FDA or the Agency) has determined that prior public participation for this guidance is not feasible or appropriate (see section 701(h)(1)(C) 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 webpage 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/covid-19-related-guidance-documents-industry-fda-staff-and-other-stakeholders, and the FDA Webpage titled "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 an additional 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 Preparation of Certain Alcohol-Based Hand Sanitizer Products During the Public Health Emergency (COVID-19) Guidance for Industry[1]

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.

This document updates the guidance of the same title issued in August 2020 (previous versions June, April, and March 2020). FDA is issuing this guidance in response to a number of queries from entities that are not currently licensed or registered drug manufacturers that would like to prepare alcohol-based hand sanitizers, either for public distribution or for their own internal use. The Agency is issuing this guidance to communicate its policy for the temporary preparation of certain alcohol-based[2] hand sanitizer products by firms that register their establishment with FDA as an over-the-counter (OTC) drug manufacturer, re-packager, or re-labeler[3] to prepare alcohol-based hand sanitizers under the circumstances described in this guidance ("firms") for the duration of the public health emergency declared by the Secretary of Health and Human Services (HHS) on January 31, 2020,[4] including any renewals made by the HHS Secretary in accordance with section 319(a)(2) of the Public Health Service

[1] This guidance has been prepared by the Center for Drug Evaluation and Research at the Food and Drug Administration. FDA has issued a separate guidance for industry entitled Policy for Temporary Compounding of Certain Alcohol-Based Hand Sanitizer Products During the Public Health Emergency (March 2020, updated March 27, 2020, April 15, 2020, June 1, 2020, August 7, 2020 and February 10, 2021), that describes the Agency's policy for the temporary compounding of certain alcohol-based hand sanitizer products by pharmacists in state or territory-licensed pharmacies or federal facilities and registered outsourcing facilities. 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.

[2] Alcohol-based hand sanitizer for purposes of this guidance can be prepared using alcohol or isopropyl alcohol (IPA) consistent with FDA policies outlined in this guidance. *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 (FCC). The USP and FCC documents, known as "monographs," establish test methods and acceptance criteria for identity and purity. The USP and FCC definitions of *alcohol* do not include IPA. Unless otherwise specified, and consistent with the USP and FCC monographs, references in this guidance to "alcohol" refer to ethanol.

[3] This includes pharmacies that repackage or relabel finished hand sanitizer products prepared consistent with FDA policies outlined 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.

Act (PHS Act) (42 U.S.C. 247d(a)(2)). 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. FDA is continually assessing the needs and circumstances related to this temporary policy, and as relevant needs and circumstances evolve, FDA intends to update, modify, or withdraw this policy as appropriate.

Given this public health emergency, and as discussed in the Notice in the *Federal Register* of March 25, 2020 (85 FR 16949), titled "Process for Making Available Guidance Documents Related to Coronavirus Disease 2019," *available at* https://www.govinfo.gov/content/pkg/FR-2020-03-25/pdf/2020-06222.pdf, this guidance is being implemented without prior public comment because the 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.

The contents of this document do not have the force and effect of law and are not meant to bind the public in any way, unless specifically incorporated into a contract. This document is intended only to provide clarity to the public regarding existing requirements under the law. FDA guidance documents, including this guidance, should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in FDA 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. The virus has been named "SARS-CoV-2" and the disease it causes has been named "Coronavirus Disease 2019" (COVID-19). On January 31, 2020, HHS issued a declaration of a public health emergency related to COVID-19 and mobilized the Operating Divisions of HHS.[5] In addition, on March 13, 2020, there was a Presidential declaration of a national emergency in response to COVID-19.[6]

Hand hygiene is an important part of the response to COVID-19. Washing hands often with soap and water for at least 20 seconds is essential, especially after going to the bathroom; before eating; and after coughing, sneezing, or blowing one's nose. If soap and water are not readily available, the Centers for Disease Control and Prevention (CDC) recommends consumers use an alcohol-based hand sanitizer that contains at least 60 percent alcohol (also referred to as ethanol or ethyl alcohol).[7,8]

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[5] Secretary of Health and Human Services, Determination that a Public Health Emergency Exists (originally issued Jan. 31, 2020, and subsequently renewed), *available at* https://www.phe.gov/emergency/news/healthactions/phe/Pages/default.aspx.

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

[7] See https://www.cdc.gov/handwashing/hand-sanitizer-use.html.

[8] Isopropyl alcohol and ethyl alcohol are two of the active ingredients currently being evaluated by FDA as part of the OTC Drug Review of hand sanitizers, separate from the current public health emergency, for use in reducing bacteria on the skin that potentially can cause disease or decreasing presence of bacteria on the skin. See "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

III. DISCUSSION

We understand that some consumers and health care personnel 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.

In response to the demand for alcohol-based sanitizers, certain entities that are not currently regulated by FDA as drug manufacturers have requested guidance on the preparation and distribution of 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 firms[9] that prepare alcohol-based hand sanitizers for consumer use and for use as health care personnel hand rubs[10] 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. The hand sanitizer is manufactured using only the following ingredients in the preparation of the product
    a. *Select one of two options:*
        (i) Alcohol (ethanol) that is not less than 94.9% ethanol by volume[11]; **OR**

Human Use; Tentative Final Monograph for Health-Care Antiseptic Drug Products," Proposed Rule, 59 FR 31402 (June 17, 1994) (1994 TFM). The temporary policies outlined in this guidance cover only alcohol-based (ethanol and isopropyl alcohol) hand sanitizer produced during the public health emergency and do not cover the use of other active or inactive ingredients not otherwise mentioned in this guidance for use in hand sanitizer, including benzethonium chloride or benzalkonium chloride.

[9] Specifically, FDA does not intend to take action against firms, for the duration of the public health emergency declared by the Secretary of HHS on January 31, 2020, including any renewals made by the Secretary in accordance with section 319(a)(2) of the PHS Act (42 U.S.C. 247d(a)(2)), for violations of sections 501(a)(2)(B), 502(f)(1), 505, or 582 of the FD&C Act (21 U.S.C. 351(a)(2)(B), 352(f)(1), 355, and 360eee-1), provided circumstances described in this guidance are present. These circumstances include (but are not limited to) preparation of hand sanitizer products using only the ingredients and formulas set forth in this guidance. FDA plans to continue to sample hand sanitizer products at the border and in distribution in the U.S. for quality issues, including potential contamination and impurity levels.

[10] Rubs are sometime referred to as "leave-on products," and are not rinsed off after use. Rub products include alcohol-based hand sanitizers for use by consumers and for use by health care professionals in hospitals or other health care settings. The health care antiseptic products include health care personnel hand rubs, surgical hand rubs, and patient antiseptic skin preparations. In the health care setting, this policy only applies to alcohol-based hand sanitizer for use as health care personnel hand rubs and does not apply to surgical hand rubs and patient antiseptic skin preparations. See "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).

[11] This is consistent with the USP and FCC grade requirements for purity. Lower ethanol content alcohol falls within this policy so long as it is labeled accordingly, and the finished hand sanitizer meets the ethanol concentration of 80%. (Also see below regarding the formula for finished hand sanitizer products.)

(ii) United States Pharmacopeia (USP grade) Isopropyl Alcohol (IPA)[12,13]

b. Glycerin (glycerol) USP or Food Chemical Codex (FCC) (also known as "food grade")
c. Hydrogen peroxide[14]
d. Sterile water (e.g., by boiling, distillation, or other process that results in water that meets the specifications for Purified Water USP). Water should be used as quickly as possible after it is rendered sterile or purified.

Additional Considerations for Ingredients in Preparation of the Product:

Alcohol (ethanol) [15] that is produced using fermentation and distillation processes typically used for consumable goods, and that is made in a facility used for producing consumable goods, may be considered for use in hand sanitizer, provided the alcohol meets the interim impurity levels in Attachment 1, Table 1.[16]

Alcohol derived from synthetic processes may be considered for use in hand sanitizer only if it meets USP or FCC[17] grade.

Alcohol produced in facilities normally producing fuel or technical grade alcohol (ethanol) may be considered for use in hand sanitizer provided the following circumstances are present:

(i) the alcohol is produced using fermentation and distillation processes typically used for consumable goods, and no other additives or other chemicals have been added to the ethanol;
(ii) the alcohol meets USP or FCC[18] grade requirements or the conditions in Attachment 1; and,
(iii) the alcohol has been screened for any other potentially harmful impurities not specified in the USP or FCC requirements but potentially present based on the specific manufacturing environment.[19]

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[12] Isopropyl alcohol used as the active ingredient should be USP grade. If a firm wishes to use other grades of isopropyl alcohol as an active ingredient, provide analytical data for the isopropyl alcohol tested against all of the elements of the USP monograph, including listed impurities, to COVID-19-Hand-Sanitizers@fda.hhs.gov and include "ISOPROPYL ALCOHOL DATA" in the subject line, for FDA's assessment regarding the use of this ingredient under this policy.
[13] USP has made available to the public materials related to hand sanitizer ingredients, including monographs and test methods at https://www.usp.org/sites/default/files/usp/document/health-quality-safety/usp-hand-sanitizer-ingredients.pdf.
[14] Hydrogen Peroxide Concentrate USP, Hydrogen Peroxide Topical Solution USP, or technical grade hydrogen peroxide. The hand sanitizer formula should be adjusted based on the actual concentration of hydrogen peroxide used.
[15] The discussion concerning alcohol (ethanol) in this guidance is limited to ethanol used as an active pharmaceutical ingredient (API) for hand sanitizer manufactured as part of the temporary policies outlined in this guidance. FDA's intent to not take action with regard to alcohol meeting the circumstances described in this guidance does not reflect the risk-benefit calculus that FDA would find acceptable outside of this public health emergency and temporary policies.
[16] Ethanol made using wet milling, fermentation, and distillation processes used for consumable goods (like alcoholic beverages made by distilleries) generally does not contain impurities above the limits listed in Attachment 1. However, all ethanol made for use in hand sanitizer should meet the limits in Attachment 1, if tested.
[17] FCC grade alcohol should be tested for impurities using the methods recommended in USP and confirmed to meet the limits in Attachment 1, Table 1.
[18] See footnote 17.
[19] Special caution should be taken to ensure any other chemicals on site are not introduced into the ethanol either intentionally or via cross-contamination.

Ingredients that are described as only meeting American Chemical Society (ACS) grade standards should generally not be used in hand sanitizers.[20]

Additional Considerations for Testing Stemming from Recent Methanol Substitution or Contamination in Hand Sanitizers

Recent FDA sampling and test results demonstrating methanol substitution for ethanol in hand sanitizer products have raised serious safety concerns. Substantial methanol exposure can result in nausea, vomiting, headache, blurred vision, permanent blindness, seizures, coma, permanent damage to the nervous system or death. Although all persons using these products on their hands are at risk, adolescents and adults who drink these products as an alcohol (ethanol) substitute and young children who accidentally ingest these products are most at risk for methanol poisoning. Accordingly, methanol cannot safely be used as an ingredient, or as a denaturant, in hand sanitizer. FDA is continuing to investigate methanol substitution and/or contamination to help safeguard consumers from hand sanitizers that may cause harm.

Use of alcohol (ethanol) or IPA procured from another source, rather than manufactured in-house by the firm, is consistent with this policy if the hand sanitizer manufacturer tests, or has tested, each lot of the active ingredient (either ethanol or IPA) for methanol content prior to use, regardless of the process used by the outside source in manufacturing the alcohol. For both alcohol (ethanol) and IPA, FDA recommends the test methods described in the USP monograph for alcohol (ethanol).[21] Given the risks to consumers (including death) associated with methanol substitution, FDA strongly recommends the test for methanol be conducted in a laboratory that has been previously inspected by FDA and found in compliance with Current Good Manufacturing Practice (CGMP).[22] As part of the Agency's evaluations of laboratory data, FDA may consider whether the laboratory has been previously inspected by FDA and found to be in compliance with CGMP.

Any alcohol (ethanol) or IPA that contains more than 630 ppm methanol is not consistent with this temporary policy and may be considered evidence of substitution and/or contamination. Hand sanitizers containing methanol-contaminated alcohol (ethanol) or IPA are subject to

[20] 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 and glycerin 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. If a firm wishes to use an ingredient that is described only as ACS grade, the firm should submit relevant information on the ingredient's concentration and impurity profile to COVID-19-Hand-Sanitizers@fda.hhs.gov with "*name of ingredient* DATA" in the subject line for FDA's assessment regarding the use of the ingredient under this policy.

[21] See footnote 13. See also FDA guidance for industry *Policy for Testing of Alcohol (Ethanol) and Isopropyl Alcohol for Methanol, Including During the Public Health Emergency (COVID-19).*

[22] FDA's public database on inspection classifications provides the final classification of the most recent inspection and can be found at https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/inspection-classification-database.

adulteration charges under the FD&C Act.[23] Such alcohol (ethanol) or IPA material should be destroyed, and the manufacturer should contact FDA regarding the material and its source.[24]

2. The alcohol (ethanol) is denatured either by the alcohol producer or at the point of production of the finished hand sanitizer product.[25] Alcohol and Tobacco Tax and Trade Bureau regulations in 27 CFR part 20 and 21, respectively, describe requirements pertaining to, and provide a number of formulas for, denaturing alcohol. These formulas for use in hand sanitizers under FDA's temporary policies include:[26]

    a. Formula No. 40A or No. 40B with or without the tert-butyl alcohol[27]
    b. Formula No. 3C (isopropyl alcohol[28])

    The alcohol also may be denatured with a formula using 3% triethyl citrate (w/w).[29]

Denaturing is critical because there have been reports of adverse events, including deaths, from ingestion of hand sanitizer. Most reports are from unintentional ingestion by young children.[30] The alcohol should be denatured at either (1) the point of production by the alcohol production firm or (2) the point of manufacture or compounding of the hand sanitizer. Attachment 2 provides more information on the formulas used to denature alcohol before it is used in alcohol-based hand sanitizers. Attachment 2 reproduces Appendix C from FDA guidance for industry *Temporary Policy for Manufacture of Alcohol for Incorporation into Alcohol-Based Hand Sanitizer Products During the Public Health Emergency (COVID-19).*

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[23] See, e.g., Sections 501(a)(2)(A), 501(a)(2)(B) and 501(d) of the FD&C Act (21 U.S.C. 351(a)(2)(A), 351(a)(2)(B) and 351(d)).

[24] Contact FDA at COVID-19-Hand-Sanitizers@fda.hhs.gov with "METHANOL" in the subject line. For more information see https://www.fda.gov/drugs/drug-safety-and-availability/fda-updates-hand-sanitzers-methanol.

[25] See FDA guidance for industry *Temporary Policy for Manufacture of Alcohol for Incorporation Into Alcohol-Based Hand Sanitizer Products During the Public Health Emergency (COVID-19).*

[26] FDA is continuing to evaluate other potential formulas for denaturing. Firms that wish to use different denaturants (bitterants) should contact FDA at COVID-19-Hand-Sanitizers@fda.hhs.gov with "DENATURANTS REQUEST" in the subject line.

[27] While Alcohol and Tobacco Tax and Trade Bureau (TTB) Formula Nos. 40A and No. 40B set forth in 27 CFR 21.75 and 21.76 require the use of tert-butyl alcohol, modified versions of these formulas that do not contain tert-butyl alcohol are consistent with this policy and are authorized by TTB through June 30, 2021 for use in manufacturing hand sanitizer products and denatured alcohol for use in hand sanitizer without first obtaining formula approval from TTB. See https://www.ttb.gov/public-guidance/ttb-pg-2020-1b.

[28] Using technical grade isopropyl alcohol that meets the requirements of 27 CFR 21.113 as a denaturant in the preparation of the finished hand sanitizer product is consistent with this policy.

[29] We note that the use of the triethyl citrate (TEC) denaturant formula in the preparation of alcohol-based hand sanitizer is consistent with this policy and is authorized by TTB through June 30, 2021 for use in manufacturing hand sanitizer products and denatured alcohol for use in hand sanitizer without first obtaining formula approval from TTB. See https://www.ttb.gov/public-guidance/ttb-pg-2020-1b.

[30] 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 percent compared to March 2019. The majority of these calls were for unintentional exposures in children 5 years of age and younger.

3. The finished hand sanitizer product is manufactured according to the following formula consistent with World Health Organization (WHO) recommendations:[31]
    a. Alcohol (ethanol) (formulated to 80%, volume/volume (v/v)) in an aqueous solution; **or** Isopropyl Alcohol (formulated to 75%, v/v) in an aqueous solution. [32, 33]
    b. Glycerin (glycerol) (1.45% v/v)
    c. Hydrogen peroxide (0.125% v/v).[34]
    d. Sterile distilled water or boiled cold water.[35]

4. **The firm 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.**

5. The firm pays particular attention to ensure the ethanol or isopropyl alcohol active ingredient is correct and the correct amount of the active ingredient is used. If using ethanol or IPA from another source, the firm has tested the active ingredient to ensure that the methanol content does not exceed 630 ppm. A simple record should be used to document key steps and controls to ensure each batch matches the formula developed for the drug product.

6. The hand sanitizer is prepared under sanitary conditions and equipment utilized is well maintained and fit for this purpose.[36]

7. The firm uses the most accurate method of analysis available at the site for verification of alcohol content in samples of the finished drug product before each batch is released for distribution. Methods can include gas chromatography (GC), alcoholmeter, hydrometer, or other chemical analysis of at least equivalent accuracy. The sample tested can be performed on in-process material before filling into the final containers to be distributed.

8. The hand sanitizer product is produced as an aqueous solution and not as a gel, foam, or aerosol spray.[37] The firm packages the finished hand sanitizer product in packaging appropriate for

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[31] WHO's recommendations, titled "Guide to Local Production: WHO-recommended Handrub Formulations," are available at https://www.who.int/gpsc/5may/Guide_to_Local_Production.pdf.

[32] These percentages are consistent with WHO's recommended formulation specifications of 80% alcohol and 75% isopropyl alcohol. In addition, they are consistent with the range of percentages for final products in the1994 TFM (see also FDA guidance for industry *Temporary Policy for Manufacture of Alcohol for Incorporation Into Alcohol-Based Hand Sanitizer Products During the Public Health Emergency (COVID-19)*).

[33] One benefit of FDA's policy relying on use of this particular aspect of the WHO formula is that minor errors in production are still likely to result in a finished hand sanitizer product that exceeds the CDC recommendations of at least 60% ethanol or 70% IPA (isopropanol) content (see FDA's 1994 TFM and the CDC Statement for Healthcare Personnel on Hand Hygiene during the Response to the International Emergence of COVID-19).

[34] Formulate 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 level of 80% for ethyl alcohol or 75% for isopropyl alcohol.

[35] Water that is boiled should be cold when used to prepare the finished hand sanitizer product.

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

[37] This policy does not apply to hand sanitizer gel or foam products because different or additional ingredients may impact the quality and potency of the product. This policy does not apply to aerosol sprays because aerosol sprays with propellent added to the formulation can result in altered potency of the finished hand sanitizer. Aerosol sprays with propellent outside of the formulation (bag on valve) may have safety and potency concerns due to the increased flammability risks of ethanol in

liquid drug products that will seal sufficiently to prevent evaporation of the alcohol or IPA.[38] Manual pump sprays that seal sufficiently to prevent evaporation are consistent with this policy.

9. The hand sanitizer is labeled consistent with the attached labeling in Appendix A (Labeling for Ethanol Formulation Consumer Use), Appendix B (Labeling for Isopropyl Alcohol Formulation Consumer Use), Appendix C (Labeling for Ethanol Formulation Health Care Personnel Hand Rub Use), or Appendix D (Labeling for Isopropyl Alcohol Formulation Health Care Personnel Hand Rub Use).[39,40]

10. 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).[41] Upon completion of registration and listing, firms receive automatic confirmation from the FDA and do not need to wait for a further communication from FDA before the firm can begin to 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.

11. Firms have a mechanism to accept adverse event reports for any products they manufacture under this enforcement policy, and submit such adverse event reports to FDA (for more information, please see FDA's guidance on adverse event reporting requirements, https://www.fda.gov/media/77193/download).[42] This guidance on adverse event reporting advises that "for reporting purposes, an ICSR [individual case safety report] should describe the known product attributes (e.g., dosage form, strength, color, SKU, NDC, lot number)." To facilitate reporting of adverse events and investigation of root causes, the immediate package also includes a lot/control number.

This policy does not extend to other types of products, such as products: (1) that use active ingredients other than ethanol or isopropyl alcohol; (2) whose potency falls above or below the formulation described above; (3) that are marketed with claims that do not conform to the "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) (e.g., persistence claims, pathogen-specific disease claims); (4) that are marketed with superiority claims; (5) that are surgical

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an aerosol, risk of overspraying, variability of delivery of the product, rapid evaporation of alcohol, and inhalational toxicities.

[38] We note that hand sanitizer offered for transportation or transported in commerce may be subject to the applicable requirements of the U.S. Department of Transportation's Hazardous Materials Regulations (49 CFR Parts 171-180). These regulations include classification, packaging, marking, labeling and other requirements relevant to transportation. More information is available on the U.S. Department of Transportation's Pipeline and Hazardous Materials Safety Administration website at: https://www.phmsa.dot.gov/standards-rulemaking/hazmat/hazardous-materials-regulations.

[39] The label should include the name and contact information of the manufacturer.

[40] See footnote 38.

[41] Every person required to register with the FDA must, at the time of initial registration, list all drugs manufactured, prepared, propagated, compounded, or processed for commercial distribution. See Section 510(j)(1) of the FD&C Act (21 U.S.C. 360(j)(1)); see also 21 CFR 207.17 and 207.41. Firms that are required to register their foreign establishment with FDA must list all known importers in the United States in their registration in accordance with Section 510(i)(1)(A) of the FD&C Act. See also 21 CFR 207.25(h)(2).

[42] See Section 760 of the FD&C Act (21 U.S.C. 379aa).

hand rubs or patient antiseptic skin preparations; (6) whose labeling is false or misleading in any particular; or (7) that are alcohol-based hand sanitizer for which FDA has identified a safety concern, including those that are subject to an FDA import alert due to safety concerns. (See the following website for a list of all FDA import alerts https://www.accessdata.fda.gov/cms_ia/ialist.html)

FDA encourages consumers and health care professionals to report adverse events experienced with the use of hand sanitizers 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

Except as described in this guidance, hand sanitizers imported into the United States must comply with all applicable requirements under the FD&C Act and the pertinent regulations found in Title 21 of the Code of Federal Regulations (21 CFR). For general information on human drug imports, please see https://www.fda.gov/drugs/guidance-compliance-regulatory-information/human-drug-imports.

Attachment 1

Use of Fuel or Technical Grade Alcohol (Ethanol)[43]

Quality standards and specifications for alcohol used in pharmaceuticals (including hand sanitizers) are set by the USP and enforced by FDA pursuant to section 501(b) of the FD&C Act. Alcohol (ethanol) used in pharmaceuticals that does not meet the USP monograph is considered adulterated under section 501(b) of the FD&C Act. The April 15, 2020 update to this guidance on fuel or technical grade ethanol reflected FDA's experience in which data submitted by fuel ethanol manufacturers producing ethanol via fermentation and distillation indicated that at least some fuel ethanol products included harmful chemicals, including gasoline and benzene, which is a known human carcinogen (cancer-causing agent). These impurities would not be expected from a typical fermentation and distillation process but may be present due to the manufacturing environment (e.g., equipment, containers). In addition, FDA has received data that indicate that certain fuel ethanol products contain excessive levels of acetaldehyde, which appears to be a genotoxic carcinogen when in direct contact with tissues.[44]

Consumer and health care personnel safety is a top priority for FDA, and an important part of FDA's mission is to protect the public from harm, including as we seek to increase supply of hand sanitizer. We are aware that some consumers and health care personnel are currently experiencing difficulties accessing alcohol-based hand sanitizers, and that the CDC recommends consumers use hand sanitizer containing at least 60% alcohol when soap and water are unavailable.[45] Therefore, FDA is working with industry to ensure that harmful levels of impurities are not present in ethanol used in hand sanitizer. Upon further review of the data, we are temporarily providing flexibility with respect to certain impurities at the levels established in Table 1 and Table 2 below. Based on our review of available data, we have determined these interim impurity levels can be tolerated for a relatively short period of time, given the emphasis on hand hygiene during the COVID-19 public health emergency and to avoid exacerbating access issues for alcohol-based hand sanitizer.

Accordingly, during this public health emergency, FDA does not intend to take action against firms that manufacture fuel or technical grade ethanol for hand sanitizer that does not meet the USP or FCC requirements or firms that use such ethanol to prepare hand sanitizer on an interim basis, provided all other circumstances in the guidance are present, including the interim limitations on the impurity levels listed below. FDA is continually assessing the needs and circumstances related to these temporary policies, including the use of fuel and technical grade ethanol in hand sanitizer, and as relevant needs and circumstances evolve, FDA intends to update, modify, or withdraw these policies as appropriate.

Accordingly, we are clarifying that fuel or technical grade ethanol that does not meet USP or FCC requirements may be considered for use in hand sanitizer under this temporary policy only if the following circumstances are present:

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[43] Ethanol that contains carcinogens or other harmful impurities at unacceptable levels poses a safety risk to consumers and health care personnel using hand sanitizers. Ethanol that contains harmful levels of impurities and hand sanitizer products containing such ethanol would be considered adulterated under the FD&C Act; products are adulterated if they are prepared, packed, or held under insanitary conditions whereby it may have been rendered injurious to health (see section 501(a)(2)(A)).

[44] The toxicology for acetaldehyde differs when ingested as part of an alcoholic beverage (versus applied to the skin as with hand sanitizer), in part due to the liver's metabolism of acetaldehyde.

[45] See https://www.cdc.gov/handwashing/hand-sanitizer-use.html.

- Fuel or technical grade ethanol does not contain gasoline or any of its components (e.g., n-heptane).

- Impurities meet the interim limits listed in Table 1 below and no other potentially harmful impurities are present other than those addressed in Table 1. If a firm wishes to use or supply a fuel or technical grade ethanol that does not meet USP or FCC requirements, the firm should test the ethanol (or have a third party laboratory conduct testing) to identify 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. These impurities and their interim limits in ethanol for use in hand sanitizer under this policy are provided in Table 1 below. These interim limits take into account the expected clinical usage and administration of hand sanitizers described under this temporary policy. We recommend using test methods described in USP.

Table 1

Impurity	Interim Limit under this policy
Methanol	NMT 630 ppm
Benzene	NMT 2 ppm
Acetaldehyde	NMT 50 ppm*
Acetal (1,1-diethoxyethane)	NMT 50 ppm
Sum of all other impurities	NMT 300 ppm

* Acetaldehyde appears to be genotoxic, and potentially carcinogenic, when in direct contact with tissues. Given the large number of applications of this product expected by consumers and health care personnel during the public health emergency, exposure to hand sanitizer with high levels of acetaldehyde poses a significant safety concern. We are aware that some consumers and health care personnel are currently experiencing difficulties accessing alcohol-based hand sanitizers and that the CDC recommends consumers use hand sanitizer containing at least 60% alcohol when soap and water are unavailable.[46] CDC recommends consumers use hand sanitizer containing at least 60% ethanol when soap and water are unavailable. Therefore, FDA is temporarily willing to consider ethanol containing acetaldehyde above that permitted by USP at an interim level no higher than 50 ppm, for use in hand sanitizer under this temporary policy. An interim upper limit of 50 ppm is based on available toxicity data for acetaldehyde considering the expected clinical usage and administration of hand sanitizers under this policy. FDA is continually assessing the needs and circumstances related to the COVID-19 temporary policies, including the use of ethanol containing acetaldehyde at an interim level no higher than 50 ppm, and as relevant needs and circumstances evolve, FDA intends to update, modify, or withdraw these policies as appropriate.

- In cases where fuel or technical grade ethanol that does not meet the interim limits in Table 1 because the sum of all other impurities exceeds the interim limit of 300 ppm, all individual impurities are identified and meet the interim limits in Table 2 below.

[46] See https://www.cdc.gov/handwashing/hand-sanitizer-use.html.

The interim impurity limits provided in Table 2 are generally based on ICH Q3C *Guideline on Impurities: Guideline for Residual Solvents*, considering the expected clinical usage and administration that has been defined for hand sanitizers under this policy.

Table 2

Impurity	Interim Limit under this policy
Acetone	NMT 4400 ppm
n-propanol (1-propanol)	NMT 1000 ppm
Ethyl acetate	NMT 2200 ppm
Sec-butanol (2-butanol)	NMT 6200 ppm
Iso-butanol (2-Methyl-1-propanol)	NMT 21700 ppm
n-butanol (1-butanol)	NMT 1000 ppm
iso-amyl alcohol (3-Methyl-1-butanol)	NMT 4100 ppm
Amyl alcohol	NMT 4100 ppm

- For any impurity identified not listed in Table 1 or Table 2, the firm submits data with the level for each individual impurity with information regarding the safety of each impurity, if available, for FDA's assessment regarding whether the ethanol is suitable for use under this policy.[47]

[47] Submissions should be sent 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.

Attachment 2

From FDA guidance for industry *Temporary Policy for Manufacture of Alcohol for Incorporation Into Alcohol-Based Hand Sanitizer Products During the Public Health Emergency (COVID-19)*: Appendix C. Formulas That May Be Used To Denature Alcohol Before It Is Used in Alcohol-Based Hand Sanitizers (Antiseptic Hand Rubs)

Preferred Formulas

1. **27 CFR 21.76 Formula No. 40-B**

   To every 100 gallons of alcohol add:
   One-sixteenth avoirdupois ounce of denatonium benzoate,[48] 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,[49] N.F.[50]

Alternative Formulas

2. **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[51]

3. **27 CFR 21.37 Formula No. 3-C**

   To every 100 gallons of alcohol add:
   Five gallons of isopropyl alcohol[52]

4. **Formula using 3% triethyl citrate (w/w)**[53]

   To every 100 gallons of alcohol add:
   9239.5 g (20.4 pounds) triethyl citrate (USP or FCC grade)

[48] Denatonium benzoate can be added as either a solid or in liquid form, provided the added amount is calculated on a dry basis.
[49] See footnote 48.
[50] See footnote 27.
[51] See footnote 27.
[52] See footnote 28.
[53] See footnote 29.

Appendix A. Labeling for Ethanol 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 at 1-800-222-1222.

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 at 1-800-222-1222.

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 Ethanol Formulation Health Care Personnel Hand Rub 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 at 1-800-222-1222.

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 Hand Rub 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 at 1-800-222-1222.

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