ICMAD

Independent Cosmetic Manufacturers And Distributors

Members Helping Members

COVID-19

ICMAD Members Helping Members Webinar Series:

Hand Sanitizers: Temporary Guidance Documents vs OTC Monograph – Legal, Regulatory and Formulation Considerations

May 28, 2020

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COVID-19 Hand Sanitizer Guidance

- https://www.fda.gov/media/136289/download
- https://www.fda.gov/media/136118/download
- 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.

Covid 19 Hand Sanitizer Guidance

- The Agency is issuing this guidance to communicate its policy for the temporary 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 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.[2] When the public health emergency ends the manufacturing permitted by this Guidance will end

Covid 19 Hand Sanitizer Guidance

Because of the public health emergency posed by COVID-19, FDA does not intend to take action against firms that prepare alcohol-based hand sanitizers for consumer use and for use as health care personnel hand rubs. Provided there is compliance with the guidance requirements on formula ingredients to manufacture and distribute these products.

Covid 19 Hand Sanitizer Guidance

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 the FDA and do not need to wait for a further communication from FDA before they begin

Covid 19 Hand Sanitizer Guidance

Firms will need to have a way to accept adverse event reports for any products they manufacture, and submit 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).

Covid 19 Hand Sanitizer Guidance

This policy does not extend to other types of products, such as: products (1) that use different active ingredients; (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 including specific pathogen disease claims.

Covid 19 Hand Sanitizer Guidance

Note the guidance documents do not provide for product forms other than liquids- the OTC Antibac Monograph does provide other dosage forms gels, foams and sprays.

Use of ingredients to improve taste or small should not be used as they increase the risk of accidental ingestion and may affect potency and quality of the product

Covid 19 Hand Sanitizer Guidance

Decreases Bacteria on the skin
the Famous 99% kill comes from the 3 log reduction based on testing with the actives
Disease cure claims and virus kill claims have been the subject of numerous warning letters
these types of claims will render your product
an illegal new drug subject to enforcement by the FDA and by the FTC

Covid 19 Hand Sanitizer Guidance

Other Considerations
Product Liability
Facility Insurance
OSHA Compliance
Transportation/ Storage Conditions

Thank you,

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Hand Sanitizers

Presented by
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Consumer Product Testing Company, Inc.

Objectives

- Testing under the temporary guidance
  - WHO formula
  - Compounding pharmacies and FDA registered manufacturers
    - cGMP
- Monograph Testing requirements
  - In-vitro
  - In-vivo

Temporary Guidance WHO

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

Immediately in Effect Guidance for Industry

FDA is issuing this guidance for immediate implementation in accordance with 21 CFR 10.115(g)(2). 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 listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this document, contact FDA's human drug compounding team (CDER) at COVID-19-Hand-Sanitizers@fda.hhs.gov.

March 2020

Updated April 15, 2020

Compounding

Temporary Guidance WHO

- The hand sanitizer is compounded according to the following formula consistent with World Health Organization (WHO) recommendations:[17] 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.[18, 19]
- b. Glycerin (glycerol) (1.45% v/v).[20]
- c. Hydrogen peroxide (0.125% v/v).[21]
- d. Sterile distilled water or boiled cold water.

- **The compounder 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.**

Temporary Guidance WHO

- The compounder pays particular attention to ensure the ethanol or isopropyl alcohol active ingredient is correct and the correct amount of the active ingredient is used.

- The hand sanitizer is prepared under conditions routinely used by the compounder to compound similar nonsterile drugs.[22]

- The hand sanitizer product is produced as an aqueous solution and not as a gel, foam, or aerosol spray.[23] The compounder packages the finished hand sanitizer product in packaging appropriate for liquid drug products that will seal sufficiently to prevent evaporation of the alcohol or IPA.[24] Manual pump sprays that seal sufficiently to prevent evaporation are consistent with this policy.
- The hand sanitizer is labeled consistent with the attached labeling in Appendix A (Labeling for Ethyl Alcohol Formulation Consumer Use), Appendix B (Labeling for Isopropyl Alcohol Formulation Consumer Use), Appendix C (Labeling for Ethyl Alcohol Formulation Health Care Personnel Hand Rub Use), or Appendix D (Labeling for Isopropyl Alcohol Formulation Health Care Personnel Hand Rub Use).[25,26]
- This policy does not extend to other types of products, such as products: (1) that use different active ingredients; (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., pathogen-specific disease claims); (4) that are surgical hand rubs, patient preoperative skin preparations; or (5) whose advertising or promotion is false or misleading in any particular

Temporary Guidance WHO

- To use this guidance
- Use the exact
  - Formula
  - Labeling

Temporary Guidance

Policy for Temporary Compounding of Certain Alcohol-Based Hand Sanitizer Products During the Public Health Emergency Immediately in Effect Guidance for Industry FDA is issuing this guidance for immediate implementation in accordance with 21 CFR

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March 2020 Updated April 15, 2020 Compounding

Temporary Guidance

- Because of the public health emergency posed by COVID-19, FDA does not intend to take action against compounders[6] that prepare alcohol-based hand sanitizers for consumer use and for use as health care personnel hand rubs[7] for the duration of the public health emergency declared by the Secretary of HHS on January 31, 2020
- Prosecutorial discretion

Temporary Guidance

Reduced cGMP requirements

- Use of appropriate ingredients
  - Formula 40A or 40B with or without the tert-butyl alcohol
  - Formula 3C (isopropyl alcohol)
- Release Testing
  - Concentration of API

Temporary Guidance

- Labeling as per guidance
  - Should be able to make the kill 99.9% of germs claim
- No
  - COVID-19 claims
  - Corona virus claims
  - Viricidal claims

Monograph Testing

DEPARTMENT OF HEALTH AND

HUMAN SERVICES

Food and Drug Administration

21 CFR Part 310

[Docket No. FDA–2016–N–0124 (formerly

part of Docket No. FDA–1975–N–0012)]

RIN 0910–AH97

Safety and Effectiveness of Consumer

Antiseptic Rubs; Topical Antimicrobial

Drug Products for Over-the-Counter

Human Use

AGENCY: Food and Drug Administration,

HHS.

ACTION: Final rule; finding of

ineligibility for inclusion in final

monograph.

SUMMARY: The Food and

Monograph Testing

- FDA has not yet accepted (approved) any Active Pharmaceutical Ingredient (API) for inclusion in the OTC Drug Monograph for Consumer Antiseptic Rubs since suitable information has not yet been submitted which FDA feels will allow them to conclude any as being Generally Regarded as Safe (GRAS) and Generally Regarded as Effective (GRAE).
- Of the 31 possible active ingredients which had previously been used or proposed for use in OTC consumer antiseptic rubs, FDA has now ruled 28 ineligible for inclusion in the Monograph. Products containing any of these 28 active ingredients may no longer be placed into interstate commerce starting April 12, 2020.
- FDA is deferring action on the 3 remaining API's (Ethanol, IPA and Benzalkonium Chloride) for use in consumer antiseptic rubs saying they are the only API's that are eligible candidates for inclusion in the Monograph but that they have still not been officially accepted since their GRAS/GRAE status has yet to be fully demonstrated
  - Alcohol 60 to 95 percent
  - Isopropyl alcohol 70 to 91.3 percent
  - Benzalkonium chloride (BAC)

Monograph Testing

- Minimum Bactericidal Concentration (MBC) or Minimum Inhibitory Concentration (MIC)
- Organisms
  - 25 Clinical Isolates
  - 25 ATCC Reference Strains
- Time Kill Study Specifics:
  - Protocol to be prepared with study specifics
  - 31 organisms
  - Contact Times: Initial count plus 15 and 30 seconds contact time for each test organism based on use pattern of the final product as indicated by the client.
  - Sample preparation to be determined during protocol development for each sample.
  - 3 replicates for each test organism

	Test Organism	ATCC Number	*Contact Time
1	*Haemophilus influenzae*	33391	15 and 30 sec
2	*Bacteroides fragilis*	25285	15 and 30 sec
3	*Enterobacter species*	13047	15 and 30 sec
4	*Burkholderia cepacia*	25416	15 and 30 sec
5	*Burkholderia cepacia*	25608	15 and 30 sec
6	*Escherichia coli*	11775	15 and 30 sec
7	*Escherichia coli*	25922	15 and 30 sec
8	*Klebsiella pneumoniae*	13883	15 and 30 sec
9	*Klebsiella pneumoniae*	27736	15 and 30 sec
10	*Pseudomonas aeruginosa*	15442	15 and 30 sec
11	*Pseudomonas aeruginosa*	27853	15 and 30 sec
12	*Serratia marcescens*	8100	15 and 30 sec
13	*Serratia marcescens*	14756	15 and 30 sec
14	*Campylobacter jejuni*	33291	15 and 30 sec
15	*Campylobacter jejuni*	49943	15 and 30 sec
16	*Salmonella enterica serovar enteritidis*	13076	15 and 30 sec
17	*Salmonella enterica serovar typhimurium*	14028	15 and 30 sec
18	*Shigella sonnei*	9290	15 and 30 sec
19	*Shigella sonnei*	25931	15 and 30 sec
20	*Enterococcus faecalis*	19433	15 and 30 sec
21	*Enterococcus faecalis*	29212	15 and 30 sec
22	*Staphylococcus aureus*	6538	15 and 30 sec
23	*Staphylococcus aureus*	29213	15 and 30 sec
24	*Methicillin-resistant Staphylococcus aureus*	33591	15 and 30 sec
25	*Methicillin-resistant Staphylococcus aureus*	33592	15 and 30 sec
26	*Streptococcus pyogenes*	14289	15 and 30 sec
27	*Streptococcus pyogenes*	19615	15 and 30 sec
28	*Listeria monocytogenes*	7644	15 and 30 sec
29	*Listeria monocytogenes*	19115	15 and 30 sec
30	*Streptococcus pneumonia*	6303	15 and 30 sec
31	*Streptococcus pneumonia*	49619	15 and 30 sec

Monograph Testing

- Active ingredient Testing
  - In Vitro testing
  - Either
    - Minimum Bactericidal Concentration (MBC) or
    - Minimum Inhibitory Concentration (MIC)
  - Time-Kill testing using the bacteria specified in the 2016 Proposed Rule
- No decision has been made regarding final formulation testing

Monograph Testing

Clinical Efficacy Testing

- Two well controlled bacteria log reductions studies
  - Modified handwash studies
    - Three arm study
      - Minimum of 100 subjects per treatment arm
        - Treatment product
        - Negative control
          - Test product's vehicle or saline
        - FDA Positive control
          - Marketed product
  - The test product should be noninferior to an FDA-approved antiseptic control
    - 0.5 margin
  - Superior to the negative control
    - The average treatment effect (ATE)
    - Difference of the effect of two treatments
    - Correcting for baseline count.

Monograph Testing

- Complete cGMP Compliance
  - Ingredient testing
  - Process validation
  - Stability testing
    - Accelerated
      - Batch at least 20% of the proposed manufacturing batch size
    - Controlled room temperature
      - First 3 production lots
      - One commitment lot a year
    - Release testing

Monograph Testing

- Safety Testing
  - MUsT for the three API's
    - Looking for absorption
    - Based on MUsT data
      - Animal testing
  - No recommendations for final formula testing
- My safety testing recommendations
  - HRIPT
    - Volatilize for alcohol products
    - Neat for BAC products

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QUESTIONS? COMMENTS? CONCERNS?

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Webinar recording and slide presentation will be available on the COVID-19 page of ICMAD.org