DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2018–N–3458]

Food Handler Antiseptic Drug Products for Over-the-Counter Human Use; Request for Data and Information

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice; request for data and information.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the establishment of a docket to obtain data, information, and comments that will assist the Agency in assessing the safety and effectiveness of food handler antiseptic drug products (*i.e.,* antiseptic hand washes or rubs intended for use in food handling settings) for over-the-counter (OTC) human use. We are asking manufacturers of food handler antiseptics and other interested parties to submit safety and effectiveness data on OTC food handler antiseptics marketed for use by food handlers in commercial or regulated environments where growth, harvest, production, manufacturing, processing, packaging, transportation, storage, preparation, service, or consumption of food occurs. We also are inviting comments and requesting data on definitions, eligibility, current conditions of use of food handler antiseptics; safety and effectiveness criteria; as well as test methods to demonstrate the effectiveness of food handler antiseptics. In general, we are seeking input on current use conditions of antiseptics used in the food handler setting and recommended testing to establish the effectiveness of OTC food handler antiseptics. This information and data will inform FDA's ongoing review of OTC antiseptic drug products and will specifically inform our review of food handler antiseptic products.

DATES: Submit either electronic or written comments, data, or information by February 5, 2019.

ADDRESSES: You may submit data and comments as follows. For each comment, indicate the specific question to which you are responding. Please note that late, untimely filed comments will not be considered. Electronic comments must be submitted on or before February 5, 2019. The *https://www.regulations.gov* electronic filing system will accept comments until 11:59 p.m. Eastern Time at the end of February 5, 2019. Comments received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are postmarked or the delivery service acceptance receipt is on or before that date.

Electronic Submissions

Submit electronic comments in the following way:

- *Federal eRulemaking Portal: https://www.regulations.gov.* Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to *https://www.regulations.gov* will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on *https://www.regulations.gov*.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see ''Written/Paper Submissions'' and ''Instructions''). We note however, that the OTC drug monograph process is a public process; and, the Agency intends to consider only non-confidential material that is submitted to the docket in response to this request for information, or that is otherwise publicly available in evaluating if a relevant ingredient is generally recognized as safe and effective (GRAS/GRAE).

Written/Paper Submissions

Submit written/paper submissions as follows:

- *Mail/Hand Delivery/Courier (for written/paper submissions):* Dockets Management Staff (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in ''Instructions.''

Instructions: All submissions received must include the Docket No. FDA–2018–N–3458 for ''Food Handler Antiseptic Drug Products for Over-the-Counter Human Use; Request for Data and Information.'' Received comments, those filed in a timely manner (see **ADDRESSES**), will be placed in the docket and, except for those submitted as ''Confidential Submissions,'' publicly viewable at *https://www.regulations.gov* or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday.

- Confidential Submissions—To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states ''THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.'' The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on *https://www.regulations.gov.* Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as ''confidential.'' Any information marked as ''confidential'' will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: *https://www.gpo.gov/fdsys/pkg/FR-2015-09-18/pdf/2015-23389.pdf.*

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to *https://www.regulations.gov* and insert the docket number, found in brackets in the heading of this document, into the ''Search'' box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Pranvera Ikonomi, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Rm. 5418, Silver Spring, MD 20993–0002, 240–402–0272.

SUPPLEMENTARY INFORMATION:

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I. Introduction

We are seeking public input regarding the safety and effectiveness of food handler antiseptics to inform FDA's ongoing review of OTC antiseptic drug products and the Agency's review of the active ingredients used in these products in the food handler setting. The Agency seeks data and information about these topical antiseptics and how the active ingredients should be tested and evaluated for safety and effectiveness.

This Request for Information (RFI) covers only OTC food handler antiseptics that are intended for use by food handlers in commercial or regulated environments where growth, harvest, production, manufacturing, processing, packaging, transportation, storage, preparation, service, or consumption of food occurs. This RFI does not cover consumer antiseptic washes (78 FR 76444, December 17, 2013; 81 FR 61106, September 6, 2016); health care antiseptics (80 FR 25166, May 1, 2015; 82 FR 60474, December 20, 2017); consumer antiseptic rubs (81 FR 42912, June 30, 2016); or antiseptics identified as ''first aid antiseptics'' in the 1991 First Aid tentative final monograph (TFM) (56 FR 33644, July 22, 1991).

FDA has tentatively concluded that, based on FDA's current categorization of other antiseptic products and considering factors that may include specific microorganisms of concern in food handling environments as well as the safety of repeated-exposure use patterns, food handler antiseptics may differ from antiseptic products addressed in other rulemakings. There has been support from industry and interested parties for an OTC food handler antiseptic category, and some information and data have been submitted in support of establishing such a category. However, we believe more data and information are needed to assist the Agency in evaluating the safety and effectiveness criteria appropriate for food handler antiseptics.

II. Table of Abbreviations/Commonly Used Acronyms in This Document

Abbreviation/ acronym	What it means
ANPR	Advance Notice of Proposed Rule.
AOAC	Association of Official Analytical Chemists (now ''AOAC International'').
ASTM	American Society for Testing and Materials (now ''ASTM International'').
ATCC	American Type Culture Collection.
CDC	Centers for Disease Control and Prevention.
FDA	Food and Drug Administration.
FD&C Act	Food Drug and Cosmetic Act.
FR	Federal Register.
GRAS/GRAE	Generally recognized as safe and effective.
HACCP	Hazard analysis and critical control point.
HCCM	Health Care Continuum Model.
MIC	Minimum Inhibitory Concentration Testing.
OTC	Over-the-counter.
PCPC	Personal Care Products Council.
RFI	Request for information.
SDA	Soap and Detergent Association.
TFM	Tentative final monograph.
U.S.C.	United States Code.

III. Background

A. Background on Topical Antiseptics

This RFI is part of FDA's ongoing evaluation of the safety and effectiveness of OTC drug products marketed in the United States on or before May 11, 1972 (OTC Drug Review). The OTC topical antimicrobial rulemaking has had a broad scope, encompassing drug products that may contain the same active ingredients, but that are labeled and marketed for different intended uses. In 1974, the Agency published an advance notice of proposed rulemaking (ANPR) for topical antimicrobial products that encompassed products for both health care and consumer use. The 1974 ANPR covered seven different intended uses for these products: (1) Antimicrobial soap; (2) health care personnel hand wash; (3) patient preoperative skin preparation; (4) skin antiseptic; (5) skin wound cleanser; (6) skin wound protectant; and (7) surgical hand scrub (39 FR 33103 at 33140, September 13, 1974). FDA subsequently identified skin antiseptics, skin wound cleansers, and skin wound protectants as antiseptics used primarily by consumers for first aid use and referred to them collectively as ''first aid antiseptics.'' FDA published a separate TFM covering the first aid antiseptics in the 1991 First Aid TFM (56 FR 33644). The remaining categories of topical antimicrobials were addressed in the 1994 TFM for healthcare antiseptic drug products (59 FR 31402, June 17, 1994). The 1994 TFM covered: (1) Antiseptic hand wash (*i.e.,* consumer hand wash); (2) health care personnel hand wash; (3) patient preoperative skin preparation; and (4) surgical hand scrub (59 FR 31402 at 31442).

The 1994 TFM did not distinguish between consumer antiseptic washes and rubs and health care antiseptic washes and rubs. In the 2013 Consumer Wash Proposed Rule, we proposed that our evaluation of OTC antiseptic drug products be further subdivided into health care antiseptics and consumer antiseptics (78 FR 76444 at 76446). These categories are distinct based on the proposed use setting, target population, and the fact that each setting presents a different level of risk for infection. In the 2013 Consumer Wash Proposed Rule (78 FR 76444 at 76446–76447) and the 2016 Consumer Rub Proposed Rule (81 FR 42912 at 42915–42916), we proposed that our evaluation of OTC consumer antiseptic drug products be further subdivided into consumer washes (products that are rinsed off with water, including hand washes and body washes) and consumer rubs (products that are not rinsed off after use, including hand rubs and antibacterial wipes).

B. Regulatory History on Food Handler Antiseptics

In the 1994 TFM, FDA also identified a new category of antiseptics for use by the food industry, which historically had been marketed for use by food handlers in federally inspected meat and poultry processing plants, and other food handling establishments (59 FR 31402 at 31440). As stated in the 2016 Consumer Wash Final Rule (81 FR 61106 at 61109; September 6, 2016) and the 2017 Health Care Antiseptic Final Rule (82 FR 60474 at 60483, December 20, 2017), we classify the food handler antiseptics as separate and distinct from the other OTC topical antiseptics. Based on FDA's current categorization of other OTC antiseptic products and given the additional issues raised by the public health consequences of foodborne illness, differences in frequency and type of use, and contamination of the hands by dirt, grease and other oils, we believe that a separate evaluation of food handler antiseptics is warranted. Food handler antiseptics include antiseptic products labeled for use in commercial or other regulated settings where food is grown, harvested, manufactured, packed, held, transported, prepared, served, or

consumed. The intended use of these products (the reduction of microorganisms on the skin for the purpose of preventing disease caused by transfer of microorganism from hands to foods) makes them drugs under the provisions of the Federal, Food, Drug, and Cosmetic Act (FD&C Act), which defines a drug to include an article intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man (section 201(g)(1) of the FD&C Act; 21 U.S.C. 321(g)(1)).

FDA has determined that the safety and effectiveness of active ingredients intended for use in food handler antiseptic products needed to be demonstrated, and we proposed to include an evaluation of the safety and effectiveness of these active ingredients in the rulemaking for OTC topical antimicrobial drug products (59 FR 31402 at 31440). In the 1994 TFM, we requested relevant data and information to assist in characterizing this category of food handler antiseptics (59 FR 31402 at 31440), but we did not discuss what data would be necessary to support a GRAS/GRAE determination. In response to the 1994 TFM, we received public comments pertaining to food handler antiseptic hand washes (see section IV), including an industry proposal, the Health Care Continuum Model (HCCM), which refers to the effectiveness, effectiveness testing requirements, and labeling of antiseptic products discussed in the 1994 TFM, including the antiseptic hand wash products used by food handlers (Refs. 1 and 2). We also received comments in response to the 1994 TFM regarding antiviral testing for antiseptic products used by food handlers (59 FR 31402).

FDA also received comments pertaining to food handler antiseptics in response to the 2013 Consumer Antiseptic Wash proposed rule. One of these comments was submitted from the Personal Care Products Council (PCPC) and American Cleaning Institute in the form of a citizen petition (FDA–1975–N–0012–0493) (Ref. 3) requesting that FDA, among other things, define food handler antiseptic hand washes or rubs as antiseptic products for use in commercial establishments and other regulated settings, establish food handler antiseptic hand washes as a separate category, and consider food handler antiseptic products as professional use products similar to health care antiseptics.

IV. Proposed Effectiveness Models and Indications for Food Handler Antiseptics

In response to the 1994 TFM, FDA received comments pertaining to food handler antiseptic hand washes. The comments that addressed food handler antiseptic hand washes generally agreed that they should be evaluated in the review of antiseptic products. FDA also received comments and a citizen petition proposing an effectiveness model for antiseptic products in general, including food handler antiseptics, as well as a proposal on specific indications for food handler antiseptics (Refs. 1, 2, 33, and 14). We describe and respond to the proposed model and indications in sections IV.A. through IV.D.

A. Health Care Continuum Model

A comment from two trade associations proposed regulating food handler antiseptics as part of the HCCM (Ref. 1). This regulatory model included proposed labeling, final formulation testing requirements, and effectiveness testing criteria. The proposed testing included in vitro and in vivo testing that is modeled after FDA's previously proposed testing for OTC health care antiseptic drug products (Ref. 1). Table 1 summarizes the HCCM's proposed in vitro and in vivo testing and other effectiveness criteria for food handler antiseptics.

TABLE 1—SUMMARY OF INDUSTRY PROPOSED TESTING OF FOOD HANDLER ANTISEPTICS

[Health Care Continuum Model]

Proposed test method	Test organisms (American type culture collection strain number (ATCC))	Efficacy criteria
Establish in vitro spectrum of antimicrobial activity of active ingredient (Minimum inhibitory concentration testing (MIC)).	*Candida albicans.* (ATCC 10231).*	None Stated.
	Enterobacter cloacae. (ATCC 13047).	
	Entercoccus faecalis. (ATCC 19433).	
	Escherichia coli. (ATCC 25922).*	
	Klebsiella pneumoniae (ATCC 10031).	
	Listeria monocytogenes (ATCC 7644).*	
	Proteus mirabilis (ATCC 7002)..	
	Pseudomonas aeruginosa (ATCC 9027)..	
	Pseudomonas stutzeri (ATCC 17588)..	
	Salmonella choleraesuis (ATCC 10708).*	
	Salmonella enteritidis (ATCC 13076).*	
	Salmonella typhi (ATCC 6539).*	
	Salmonella typhimurium (ATCC 11311).*	
	Shigella dysenteraiae (ATCC 13313).	
	Shigella sonnei (ATCC 11060).*	
	Staphylococcus aureus (ATCC 6538).*	
	Streptococcus pyogenes (ATCC 19615).*	
Establish in vitro spectrum of antimicrobial activity of end-use formulation (MIC).	*Escherichia coli* (ATCC 25922).*	None Stated.
	Klebsiella pneumoniae. (ATCC 10031).	
	Listeria monocytogenes. (ATCC 7644).*	
	Pseudomonas stutzeri. (ATCC 17588).	
	Salmonella choleraesuis (ATCC 10708).*	
	Salmonella enteritidis (ATCC 13076).*	
	Salmonella typhi (ATCC 6539).*	
	Salmonella typhimurium (ATCC 11311).*	
	Shigella sonnei (ATCC 11060).*	
	Staphylococcus aureus (ATCC 6538).*	

TABLE 1—SUMMARY OF INDUSTRY PROPOSED TESTING OF FOOD HANDLER ANTISEPTICS—Continued

[Health Care Continuum Model]

Proposed test method	Test organisms (American type culture collection strain number (ATCC))	Efficacy criteria
Establish broad spectrum and fast acting claims for formulations (In vitro Time Kill Test).	*Escherichia coli* (ATCC 11229) ..... *Klebsiella pneumoniae* (ATCC 10031). *Listeria monocytogenes* (ATCC 7644).* *Salmonella typhi* (ATCC 6539).* *Staphylococcus aureus* (ATCC 6538)	1 minute: 1 $\log_{10}$ reduction 5 minutes: 2 $\log_{10}$ reduction Must meet criteria for 4 of 5 strains.
General Use Hand Wash Method (Formulation).	*Serratia marcescens* (ATCC 14756) or ..... *Escherichia coli* (ATCC 11229)	1st wash 1.5 $\log_{10}$ reduction. 5th wash: 2 $\log_{10}$ reduction.
American Society for Testing and Materials International (ASTM) Hand Rub Method (Formulation).	*Serratia marcescens* (ATCC 14756) or ..... *Escherichia coli* (ATCC 11229).	Rubs: 2 $\log_{10}$ reduction.

* Organisms included in the Hazard Analysis and Critical Control Point Principles and Application Guidelines (Ref. 4).

The HCCM proposal explained that the ATCC strains recommended for in vitro testing were chosen to represent a broad spectrum of bacteria that ''present a challenge to antisepsis'' and are the principal foodborne pathogens and contaminants. The model also proposed the use of clinical simulation studies to demonstrate the effectiveness of final formulations that rely on the reduction of the same surrogate organisms that historically have been used to demonstrate the effectiveness of health care personnel and antiseptic hand washes. More specifically, two protocols were proposed for clinical simulation studies: (1) A General Hand Wash Method for the demonstration of fast-acting and persistent activity of products used with water; and (2) an ASTM method for the evaluation of alcohol-based hand rub formulations to demonstrate the fast-acting antimicrobial activity of leave-on products. The proposal also provides log-reduction effectiveness criteria that are similar to the effectiveness criteria for health care personnel hand antiseptics proposed in the 1994 TFM (59 FR 31402 at 31444) (see table 1). The Soap and Detergent Association (SDA) stated that the proposed HCCM ''log reduction and acceptance criteria will demonstrate the appropriate effectiveness of products used in a food handling environment'' (Ref. 5). However, the HCCM did not define the appropriate level of effectiveness or include data to support corresponding effectiveness testing criteria.

The SDA also recommended the continued use of the Association of Official Analytical Chemists (AOAC International) chlorine equivalency test for in vitro effectiveness testing of food handler antiseptics (Ref. 6). The SDA suggested that an antiseptic activity equivalent to 50 parts per million of available chlorine be a strict requirement for food handler antiseptic products (Ref. 5).

B. FDA Comments on the Proposed Health Care Continuum Model

FDA identified several issues in the proposed HCCM. The use conditions of food handler antiseptics vary widely. Heavily soiled items are common in food preparation and food handling settings, and in general, antiseptic products are considered to be less effective in soiled hands (Ref. 7). Studies simulating moderate and heavily soiled hand conditions showed decreased efficacy of antiseptic products, suggesting that the organic load, *i.e.,* the amount of fat, grease, blood, and debris associated with food handling, affects the efficacy of antiseptic products (Ref. 8). The transfer of bacteria from contaminated food items and surfaces to hands may also be affected by the organic load contained in such items (Ref. 9). Use conditions vary in both organic and bacterial load, resulting in moderate to high levels of bacterial contamination. These differences are, in some cases, related to the setting in which a product is used. The differences may be related to other factors as well. The proposed HCCM does not take into consideration the wide-ranging use conditions of food handler antiseptics, and it raises the question of how to best address the broad spectrum of situational challenges stemming from these varied uses.

Contact time is another factor that is expected to impact an antiseptic's effectiveness. The Food Code, a model that represents FDA's advice for a uniform system of provisions that address the safety and protection of food offered at retail and in food service establishments, specifies that a food handler's hand cleaning regimen should last ''at least 20 seconds'' using a cleaning compound in a hand washing sink (Ref. 10). In the method for in vivo efficacy testing proposed in the HCCM, contact times vary from 30 seconds to 5 minutes. These timeframes do not reflect the hand cleaning procedures recommended in the Food Code. The contact times used in effectiveness testing should be appropriately related to reasonable real-life conditions of use, as reflected in product labeling. We are interested in comments on appropriate contact times for in vivo effectiveness testing.

The HCCM proposal also requires the demonstration of an antiseptic's effectiveness after multiple hand washes or rubs and proposes effectiveness criteria that range from 1.5 to 2 $\log_{10}$ reduction of the test organism. Given the manner in which food handler antiseptics are currently used (*i.e.,* short contact times with use of antiseptics, high bacterial loads, and expectations that these products be effective after a single use), the proposed in vivo effectiveness testing does not appear to reflect food handler antiseptic use situations and raises the question of what criteria best demonstrate the effectiveness of food handler antiseptics.

When evaluating food handler antiseptics, it is important to focus on the foodborne pathogens most often known to cause foodborne illness through contamination of food by food employee's hands (Ref. 11). The list of ''*Pathogens Transmitted by Food Contaminated by Infected Person Who Handle Food, and Modes of Transmission of Such Pathogens*'' is available on the Centers for Disease Control and Prevention (CDC) website (*https://www.cdc.gov/foodsafety/pdfs/pathogens-by-food-handlers-508c.pdf*). The in vitro testing proposed in the HCCM includes only bacterial species.

However, in 2014, the CDC reported that bacterial foodborne illness accounted for only 51 percent of food-borne disease outbreaks. Viruses were cited as the second most common cause of disease outbreaks (43 percent). Thus, over one-third of food-borne disease outbreaks included in the CDC report were not caused by bacteria (Ref. 12). Further, norovirus was reported as the most common cause of confirmed, single-etiology outbreaks, accounting for 284 outbreaks (43 percent); its transmission from contaminated hands to food items plays a major role in this foodborne illness. Parasites, including the protozoan species *Giardia lamblia, Cryptosporidium* species, and *Cyclospora cayentanensis,* accounted for a much smaller number of outbreaks, but should also be taken into consideration. These considerations raise questions concerning the antimicrobial spectrum of activity that food handler antiseptic active ingredients should demonstrate to be considered effective and the appropriate in vitro studies to assess such activity (see section IV.C and IV.D.).

In addition, in a 2005 meeting of FDA's Nonprescription Drugs Advisory Committee (Ref. 13) the committee observed that the existing test methods for topical antiseptics used in consumer and professional settings are based on the premise that bacterial reductions translate to a reduced potential for infection. Although bacterial reduction can be demonstrated using tests that simulate conditions of actual use, no corresponding clinical data demonstrate that bacterial reductions of the required magnitude produce a corresponding reduction in infection. For consumer antiseptic wash products, FDA has since recommended clinical outcome studies to demonstrate the products' clinical benefit and their superiority compared to plain soap and water (78 FR 76444, 81 FR 61106). This concern—whether the product's efficacy can be evaluated solely by in vitro tests—remains valid also for food handler antiseptics.

In light of the questions raised by FDA's review of the proposed HCCM, we have concluded that additional public input is needed before a proposed monograph for OTC food handler antiseptics can be developed. Therefore, FDA is seeking comments and requesting submission of data and information relevant to a number of questions related to OTC food handler antiseptics (see section V.)

C. Inclusion of Antiviral Indications in Food Handler Antiseptics

In response to the 1994 TFM, the Agency also received a citizen petition in 2003 from the SDA and Cosmetic Toiletry and Fragrance Association [1] (SDA/PCPC Petition) requesting that the proposed rule be amended to include antiviral indications for OTC consumer, food handler, and health care personnel antiseptics (Ref. 14). The SDA/PCPC Petition proposed labeling, final formulation testing requirements, and effectiveness criteria to demonstrate the antiviral activity of antiseptics (Ref. 15). Table 2 summarizes the SDA/PCPC Petition's proposed testing and other effectiveness criteria for food handler antiseptics.

TABLE 2—SUMMARY OF PETITIONER'S PROPOSED TESTING FOR DEMONSTRATION OF ANTIVIRAL EFFECTIVENESS OF FOOD HANDLER ANTISEPTICS

Proposed test method	Test organisms (ATCC strain No.)	Effectiveness criteria (reduction of viral load)
Establish antiviral activity of active ingredient (None).	Rotavirus Wa (ATCC VR–2018) ..... Rhinovirus Type 37 (ATCC VR–1147) or Rhinovirus Type 13 (ATCC VR–284).	None stated.
Establish antiviral activity of formulation. (ASTM E1838 [1]—fingerpad method). (ASTM E2011 [2]—entire-hand method).	Rotavirus Wa (ATCC VR–2018) ..... Rhinovirus Type 37 (ATCC VR–1147) or Rhinovirus Type 13 (ATCC VR–284).	2 $\log_{10}$. Contact time: Unspecified, should reflect use conditions

[1] ASTM E1838; ''Standard Test Method for Determining the Virus-Eliminating Effectiveness of Hygienic Handwash and Handrub Agents using Fingerpads of Adults.''

[2] ASTM E2011; ''Standard Test Method for Evaluation of Hygienic Handwash and Handrub Formulations for Virus-Eliminating Activity Using the Entire Hand.''

The SDA/PCPC Petition included studies and publications in which the antiviral activity of several active ingredients included in the 1994 TFM and their final formulations were assessed by both in vitro test methods and clinical simulation studies (*i.e.,* studies that simulate conditions of use to evaluate a product's efficacy in human subjects).

The SDA/PCPC Petition recommends testing against respiratory and enteric viral pathogens to determine the antiviral activity of the antiseptics: Rhinovirus Type 37 (ATCC VR–1147) or Rhinovirus Type 13 (ATCC VR–284) and Rotavirus Wa (ATCC VR–2018). The rationale for this recommendation is based on the premise that both viruses are important hand-transmitted pathogens, less susceptible to inactivation than enveloped viruses, and are known to survive for a significant period on skin and surfaces commonly contacted by hands. As such, they present an adequate challenge for testing the antiviral activity of antiseptic products.

Regarding the test methods for demonstration of virucidal effectiveness, the SDA/PCPC Petition proposed two specific methods: ASTM E1838 and ASTM E201. Both these methods present simulation models of viral contamination, and both measure the reduction of viral load on fingerpads (ASTM E1838) or on the entire hand (ASTM E201) after the application of the antiseptic test product. The SDA/PCPC Petition also proposed a 2 $\log_{10}$ reduction of the test virus or viruses as the criterion for antiviral effectiveness. Although several in vitro tests such as the carrier method (Ref. 16) and suspension tests (Ref. 17) are presented in the submission, there is no recommendation with regard to in vitro test methods for demonstration of

[1] In 2007, the CTFA changed its name to the Personal Care Products Council (PCPC).

virucidal activity of antiseptic products and/or their active ingredients.

Lastly, the SDA/PCPC Petition suggested a two-step approach for antibacterial and antiviral labeling: Providing that the antibacterial criteria as laid out in the rulemaking have been met, the antiviral labeling would be optional for products that in addition to antibacterial criteria, meet the antiviral criteria.

D. FDA Response to the Proposed Model for Antiviral Indications of the Antiseptic Products

FDA responded to the SDA/PCPC Petition on March 26, 2010, and denied the petition's request that FDA amend the 1994 TFM (Ref. 18). The submitted data were reviewed by FDA, and the following points were addressed:

In vitro data included in the SDA/PCPC Petition do not clearly demonstrate the effectiveness of the antiseptic active ingredients or product formulations against viruses. Primarily, the in vitro results obtained may not predict the antiseptic's effectiveness against viruses on human skin. An evaluation of effectiveness against viruses on human skin would need to be supported by adequate in vivo studies. In most of the studies, the test conditions and results vary considerably. Also, most studies lacked vehicle and neutralization controls; this undermines the validity of the data and makes it difficult to evaluate the contribution of the antiseptic product in the reduction of the viral concentration.

Clinical simulation studies included in the SDA/PCPC Petition were not adequately controlled to distinguish the antiviral effectiveness of the antiseptic and eliminate bias. These studies lacked proper controls and adequate statistical analyses. Most studies lacked either vehicle or placebo controls such as washing with plain soap and water. In the few studies in which a vehicle control was included, the advantage of the antiseptic product use was not demonstrated. Moreover, the use of plain soap and water was often found to be as or more effective than using the test antiseptic. Most studies also lacked proper documentation of neutralization and they were not randomized or blinded. Overall, the lack of adequate comparison controls rendered the submitted studies insufficient to demonstrate antiviral effectiveness.

The SDA/PCPC Petition proposed using an enteric pathogen, Rotavirus Wa Type 30, and a respiratory pathogen, Rhinovirus Type 37, for testing antiseptic viral activity. After reviewing submitted data and current publications, FDA determined that viruses vary significantly in their susceptibility to antiseptics and that this variability makes it difficult to extrapolate the effectiveness results obtained from the proposed viruses to a broader range of viruses (Ref. 19).

The SDA/PCPC Petition's proposed 2 $\log_{10}$ reduction of viral contamination as the criterion for determination of effectiveness is inadequate; viruses vary in their infectivity titers, and 2 $\log_{10}$ titer reduction achieved in the proposed viruses may be irrelevant to other viral pathogens. We currently have no data to evaluate the significance of 2 $\log_{10}$ reduction of test viruses and how such reduction would relate to a reduced risk of viral infections. In addition, the 2 $\log_{10}$ reduction of viral titers was achieved in alcohol-based products, but in studies where soap and water were used, the virus reduction was in the range of 1 $\log_{10}$. In conclusion, FDA determined that given these large variations, the clinical relevance of the proposed criterion for antiviral effectiveness was not supported by the data and may not be applicable to many viral pathogens. The surrogate measure of antiviral effectiveness would need to be validated and its significance should be supported by clinical data.

FDA found the test methods proposed in the SDA/PCPC Petition inadequate to support a general antiviral indication; the proposed ASTM methods do not account for data variability, nor do they provide guidance on adequate study size and data analysis. Moreover, the studies submitted in support of the proposed methods are insufficient to demonstrate comparable results between the two ASTM methods proposed due to the small study size.

In short, data reviewed by FDA are insufficient to support general antiviral labeling for antiseptic products including food handler antiseptics. Additional data that adequately demonstrate the antiviral effectiveness of antiseptic active ingredients and their product formulations are needed to properly address the antiviral activity of food handler antiseptics.

V. Data

Data to support the effectiveness of several antiseptic active ingredients were also submitted to the FDA–1975–N–0012–0494 docket by the PCPC in response to the Consumer Wash Proposed Rule (Ref. 20). Comments received from the PCPC asserted that the data provided demonstrated effectiveness based on the industry's proposed standard of effectiveness for food handler antiseptic products. However, because FDA currently has insufficient information to determine what constitutes an adequate demonstration of effectiveness of antiseptic active ingredients intended for use in the food handler setting, an evaluation of the submitted data would be premature.

VI. Questions for Public Input

Based on the history of food handler antiseptics and a review of our records and data received, we have determined that additional new data and information are needed to inform FDA on the safety and effectiveness of the active ingredients used in food handler antiseptics and drug products containing them. Thus, we are soliciting data and information that will help address the questions that follow.

A. Definition of Food Handler Antiseptics

As discussed in section III, we view food handler antiseptics as a category that includes antiseptic products used in regulated settings where food is grown, harvested, produced, manufactured, processed, packed, transported, prepared, served, or consumed.

In response to the questions that follow, FDA is seeking data and other information on defining food handler antiseptic products and any other information relevant to their definition.

- What are the categories of workers who might use the food handler antiseptic products?
- In what settings are food handler antiseptics used? What should be the boundaries (*e.g.,* growth, harvest, production, manufacturing, processing, packaging, transportation, storage, preparation, service, and consumption) of regulated use of food handler antiseptics? Are there any additional details and information to be considered related to scope-of-use settings of food handler antiseptics?
- What types of antiseptic products are used by food handlers and what terms are used in the food industry to describe such products (*e.g.,* wash, or leave-on products)?
- How frequently are food handler antiseptics used?

B. Active Ingredients for Food Handler Antiseptic Products

An OTC drug is eligible for the OTC Drug Review if its conditions of use existed in the OTC drug marketplace on or before May 11, 1972 (37 FR 9464), or if drug products with the same conditions of use have been marketed for a material time and extent such that they meet the requirements for eligibility under FDA's time and extent application regulation (§ 330.14 (21 CFR

330.14)). Conditions of use include, among others, active ingredient, dosage form and strength, route of administration, and specific OTC use or indication of the product (§ 330.14(a)).

To determine eligibility for the OTC Drug Review, FDA typically must have actual product labeling or a facsimile of labeling that documents the conditions of marketing of a product prior to May 1972 (21 CFR 330.10(a)(2)). FDA considers a drug that is ineligible for inclusion in the OTC monograph system to be a new drug that will require FDA approval under a new drug application (NDA) or an abbreviated new drug application (ANDA). Also, an active ingredient's ineligibility for evaluation under the OTC Drug Review for a specific indication does not affect its eligibility for evaluation for other indications under the OTC Drug Review.

FDA's recognition of the potential eligibility of food handler antiseptic products for evaluation under the OTC Drug Review is relatively new. We expect that many of the antiseptic active ingredients found in products currently used by food handlers may not have been on the U.S. market when the OTC Drug Review was first established, or that it may be difficult to establish eligibility based on use at that time. It may be possible, however, that some of the active ingredients currently used in these products have been in use in or outside of the United States for a material time and extent such that they meet the requirements for eligibility under FDA's time and extent application regulation (§ 330.14). We are, therefore, seeking information about food handler antiseptic active ingredients and the products in which they are found.

For the active ingredients used in food handler antiseptics, we ask for submission of the following information:

- What are the active ingredients currently used in food handler antiseptic products?
- How long and to what extent (*e.g.,* number of units or volume sold) have currently marketed active ingredients been in the marketplace inside and/or outside of the U.S. market?
- What active ingredients were in products on the market for food handler use prior to 1972, and what evidence of eligibility for evaluation for use in food handler antiseptic products under the OTC Drug Review is available for these active ingredients?
- What other information relevant to the eligibility of active ingredients for use in food handler antiseptic products is available?

C. Safety

In the consumer antiseptic wash and rubs, and in the health care antiseptics rulemakings for OTC topical antiseptic active ingredients, the following data are required to determine the safety of these active ingredients as part of the risk-to-benefit evaluation of the product's use (81 FR 61106 at 61117, 81 FR 42912, 80 FR 25166):

- Animal toxicology data
- Carcinogenicity
  - Dermal and Oral Exposure
- Absorption, Distribution, Metabolism & Excretion
  - Dermal and Oral Exposure
- Developmental & Reproductive Toxicology
- Hormonal Effects
- Human absorption data from a Maximal Usage Trial
- Development of Antimicrobial Resistance

To better assess the criteria for a determination of the safety of active ingredients used in food handler antiseptics, we welcome information to answer the following questions and any other issues related to evaluating the safety of these products:

- Should the data required to demonstrate the safety of active ingredients intended for use in food handler antiseptic products be the same as the safety criteria for active ingredients intended for use in consumer antiseptic and health care antiseptic products?
- If antiseptic hand rubs or leave-on products are used, the presence of residual antiseptic products on the hands of food handler professionals may result in indirect consumer exposure (*i.e.,* ingestion of residual antiseptic due to transfer of such residues from food handlers to food contact surfaces and/or food). Are additional studies required to address this concern?
- If additional studies are required to address indirect consumer exposure to antiseptic ingredients, what should they be?
- On a daily basis, how frequently do food handlers use food handler antiseptic products in the workplace? Are there any requirements related to the frequency of using food handler antiseptics in the workplaces where food is handled (*e.g.,* produce safety standards)?
- What data are available to support the long-term safety of the active ingredients of these products (*e.g.,* oral and dermal carcinogenicity studies)?
- How should the potential for antimicrobial resistance to these active ingredients be assessed?
- What data are available regarding antimicrobial resistance for these products, and how should the potential of food handler antiseptics' use with potential emergence of antimicrobial resistance be assessed?
- What other issues should be taken into consideration to support evaluation of the safety of food handler antiseptic products?

D. Effectiveness

New information on potential risks posed by the long-term use of certain antiseptic active ingredients prompted us to reconsider the data necessary to determine that active ingredients used in consumer or health care antiseptic products are generally recognized as safe and effective for their intended use. Based on new data as well as on input provided during the Nonprescription Drugs Advisory Committee meeting of March 2005, we have reevaluated the effectiveness data needed for consumer and health care antiseptic active ingredients (78 FR 76444, 81 FR 42912, 80 FR 25166).

For topical antiseptics used both in consumer and health care settings, the following studies in table 3 are required or proposed to be required to demonstrate effectiveness.

TABLE 3—EFFECTIVENESS DATA REQUIREMENTS FOR OTC CONSUMER AND HEALTH CARE ANTISEPTICS

Required tests	In vitro	In vivo
Consumer Antiseptic Washes	• Time-kill Assay *	• Clinical Outcome Studies ○ Evaluates the effect of antiseptic use in decreasing the incidence of infections.
Consumer Antiseptic Rubs	• Minimal Bactericidal Concentration *. • Time-kill Assay *.	• Clinical Simulation Studies ○ Measures the reduction of bacteria on skin due to antiseptic use.

TABLE 3—EFFECTIVENESS DATA REQUIREMENTS FOR OTC CONSUMER AND HEALTH CARE ANTISEPTICS—Continued

Required tests	In vitro	In vivo
Health Care Antiseptics	• Minimal Bactericidal Concentration **. • Time-kill Assay **.	• Clinical Simulation Studies ○ Measures reduction of bacteria on skin due to antiseptic use ○ Evaluates the persistence of bactericidal activity by measuring bacteria on skin 6 hours post product application for surgical hand scrub and patient preoperative skin preparation antiseptic products.

* Test organisms are representative of infections occurring in consumer settings.
** Test organisms are representative of infections occurring in health care settings.

To assess the effectiveness criteria for food handler antiseptic active ingredients, as well as the testing methods necessary to demonstrate effectiveness, we are interested in gathering information on the following questions related to in vivo testing:

- What studies should be used for a demonstration of efficacy in vivo?
- Should effectiveness be established through clinical outcome study (*e.g.,* show a statistically significant reduction in food-borne illness associated with the use of a food handler antiseptic in comparison to vehicle or washing with plain soap and water)?
- Do the data support use of a simulation model as a surrogate for effectiveness, such as bacterial log reduction on the hands of a food handler or on food following use of the product? What data can be used to link a simulation model to clinical outcomes related to food-borne illness (*i.e.,* model validation)?
- If the bacterial log reduction method for assessing effectiveness is used, what should be the required log reduction criteria for food handler antiseptics and what are the data that support such log reduction criteria?
- Are there any other criteria, such as reduction of transmission of microorganisms after use of food handler antiseptics that should be considered to determine the effectiveness of food-handler antiseptics?
- The Health Care Antiseptics Final Rule requires that for surgical hand scrub and patient preoperative skin preparation indications, the antiseptic activity of the product must be both immediate and persistent (82 FR 60474 at 60488). The effectiveness criteria for such products require that, in addition to the immediate antibacterial activity demonstrated by log reduction, bacterial growth is also suppressed for 6 hours after product use. Should food handler antiseptics' action be persistent?
- How are food handler antiseptics used in food handler settings? Are they used according to the manufacturer's directions of use or according to establishment-based standard operating procedures?
- Given the importance of a consistently effective product, should the dose of a food handler antiseptic vary with the product or should a standard dose be required?
- For the same reasons noted earlier, should the recommended length of time and/or frequency of use of the antiseptic product be consistent and standardized for all food handler antiseptics?

We would also like information as it relates to the following questions on in vitro testing:

- How should the products demonstrate effectiveness in vitro?
- What in vitro test methods should be used, *e.g.,* minimal bactericidal concentration and Time-kill Assay?
- What organisms should food handler antiseptics be required to demonstrate effectiveness against? Should viruses and other organisms (*e.g.,* protozoa) be tested as well as bacteria?
- Should the test methods address the effects of organic load (*i.e.,* high fat content, blood, or other materials) and dirt or soil on the effectiveness of food handler antiseptics?
- What other variables could impact the effectiveness of food handler antiseptics besides organic load, and how should the effect of such variables be taken into consideration during testing?
- How quickly must these products demonstrate effectiveness?
- At what specific time point(s) should effectiveness be measured?

VII. References

The following references marked with an asterisk (*) are on display at the Dockets Management Staff (see **ADDRESSES**) and are available for viewing by interested persons between 9 a.m. and 4 p.m., Monday through Friday; they also are available electronically at *https://www.regulations.gov.* References without asterisks are not on public display at *https://www.regulations.gov* because they have copyright restriction. Some may be available at the website address, if listed. References without asterisks are available for viewing only at the Dockets Management Staff. FDA has verified the website addresses as of the date this document publishes in the **Federal Register**, but websites are subject to change over time.

*1. Comment submitted in Docket No. FDA–1975–N–0012–0111, Volume 1 of 4, Part A. Available at *https://www.regulations.gov/document?D=FDA-1975-N-0012-0111.*

*2. Comment submitted in Docket No. FDA–1975–N–0012–0085. Available at *https://www.regulations.gov/document?D=FDA-1975-N-0012-0085.*

*3. Comment submitted in Docket No: FDA–1975–N–0012–0493. Available at *https://www.regulations.gov/document?D=FDA-1975-N-0012-0493.*

*4. FDA, ''HACCP Principles & Application Guidelines.'' Available at *https://www.fda.gov/Food/GuidanceRegulation/HACCP/ucm2006801.htm.* Accessed on May 15, 2018.

*5. Comment submitted in Docket No. FDA–1975–N–0012–0081. Available at *https://www.regulations.gov/document?D=FDA-1975-N-0012-0081.*

6. AOAC International ''AOAC 955.16–1955, Chlorine (available) in Disinfectants. Germicidal Equivalent Concentration.'' Available at *http://www.aoacofficialmethod.org/index.php?main_page=product_info&cPath=1&products_id=1578.* Accessed on May 15, 2018.

7. Boyce, J.M. and D. Pittet, ''Guideline for Hand Hygiene in Health-Care Settings; Recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force,'' *Morbidity and Mortality Weekly Report,* 51:1–45, 2002.

8. Edmonds, S.L., R.R. McCormack, S.S Zhou, et al., ''Hand Hygiene Regimens for the Reduction of Risk in Food Service Environments,'' *Journal of Food Protection,* 75(7):1303–1309, 2012.

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*10. FDA, Food Code 2017 2–301.12. Available at *https://www.fda.gov/downloads/Food/GuidanceRegulation/RetailFoodProtection/FoodCode/UCM595140.pdf.* Accessed on May 15, 2018.
*11. ''Diseases Transmitted through the Food Supply: Pathogens Transmitted by Food Contaminated by Infected Person Who Handle Food, and Modes of Transmission of Such Pathogens.'' Available at *https://www.cdc.gov/foodsafety/pdfs/pathogens-by-food-handlers-508c.pdf.*
*12. Gould, H., et al. ''Surveillance for Foodborne Disease Outbreaks-United States 1998–2008,'' *Morbidity and Mortality Weekly Report,* Surveillance Summaries 62 (2).
*13. Transcript of the October 20, 2005, Nonprescription Drugs Advisory Committee Meeting. Available at *http://wayback.archive-it.org/7993/20170404055923/https:/www.fda.gov/ohrms/dockets/ac/05/transcripts/2005-4184T1.pdf.* Accessed May 15, 2018
*14. Comment submitted in Docket No. FDA–1975–N–0012–0037. Available at *https://www.regulations.gov/searchResults?rpp=25&po=0&s=FDA-1975-N-0012-0037&fp=true&ns=true.* Accessed May 15, 2018.
*15. Comment submitted in Docket No. FDA–1975–N–0012–0038. Available at *https://www.regulations.gov/searchResults?rpp=25&po=0&s=FDA-1975-N-0012-0038&fp=true&ns=true.*
16. ASTM International, ''ASTM E2720, Standard Practice for Evaluation of Effectiveness of Decontamination Procedures for Air-Permeable Materials when Challenged with Biological Aerosols Containing Human Pathogenic Viruses.'' Available at *https://www.astm.org/search/fullsite-search.html?query=E2720&toplevel=products-and-services&sublevel=standards-and-publications.* Accessed on May 15, 2018.
17. ASTM International, ''ASTM E1052, Standard Test Method to Assess the Activity of Microbicides against Viruses in Suspension.'' Available at *https://www.astm.org/search/fullsite-search.html?query=e1052&resStart=0&resLength=10&toplevel=products-and-services&sublevel=standards-and-publications&.* Accessed on May 15, 2018.
*18. Petition Denial Response Letter from FDA to PCPC and SDA. No. FDA–1975–0012–0042. Available at *https://www.regulations.gov/document?D=FDA-1975-N-0012-0042.* Accessed on May 15, 2018.
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Dated: December 3, 2018.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2018–26561 Filed 12–6–18; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2015–N–2126]

Agency Information Collection Activities; Submission for Office of Management and Budget Review; Comment Request; Food and Drug Administration's Research and Evaluation Survey for the Public Education Campaign on Tobacco Among the Lesbian Gay Bisexual Transgender Community

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing that a proposed collection of information has been submitted to the Office of Management and Budget (OMB) for review and clearance under the Paperwork Reduction Act of 1995.

DATES: Fax written comments on the collection of information by January 7, 2019.

ADDRESSES: To ensure that comments on the information collection are received, OMB recommends that written comments be faxed to the Office of Information and Regulatory Affairs, OMB, Attn: FDA Desk Officer, Fax: 202–395–7285, or emailed to *oira_submission@omb.eop.gov.* All comments should be identified with the OMB control number 0910–0808. Also include the FDA docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: Amber Sanford, Office of Operations, Food and Drug Administration, Three White Flint North, 10A–12M, 11601 Landsdown St., North Bethesda, MD 20852, 301–796–8867, *PRAStaff@fda.hhs.gov.*

SUPPLEMENTARY INFORMATION: In compliance with 44 U.S.C. 3507, FDA has submitted the following proposed collection of information to OMB for review and clearance.

Food and Drug Administration's (FDA's) Research and Evaluation Survey for the Public Education Campaign on Tobacco (RESPECT) Among the LGBT Community

OMB Control Number 0910–0808—Extension

The 2009 Family Smoking Prevention and Tobacco Control Act (Tobacco Control Act) (Pub. L. 111–31) amended the Federal Food, Drug, and Cosmetic Act (FD&C Act) to grant FDA authority to regulate the manufacture, marketing, and distribution of tobacco products to protect public health and to reduce tobacco use by minors. Section 1003(d)(2)(D) of the FD&C Act (21 U.S.C. 393(d)(2)(D)) supports the development and implementation of FDA public education campaigns related to tobacco use. In May 2016, FDA began implementing a public education campaign to help prevent and reduce tobacco use among Lesbian, Gay, Bisexual, and Transgender (LGBT) young adults and thereby reduce the public health burden of tobacco. The campaign continues to be implemented in 12 U.S. cities and features events, television and radio and print advertisements, digital communications, including videos, social media, and other forms of media. For the purpose of this notice, these campaign elements will be referred to as ''advertisements'' or ''ads.''

In support of the provisions of the Tobacco Control Act that require FDA to protect the public health and to reduce tobacco use, FDA requests OMB approval to collect information needed to evaluate FDA's campaign to reduce tobacco use among LGBT young adults. Comprehensive evaluation of FDA's public education campaigns is needed to ensure campaign messages are effectively received, understood, and accepted by those for whom they are intended. Evaluation is an essential organizational practice in public health and a systematic way to account for and improve public health actions.

To evaluate the effectiveness of FDA's RESPECT at reducing tobacco use among LGBT young adults aged 18 to 24, FDA contracted with RTI International to conduct Web-based surveys with the target population in the 12 campaign cities and 12 comparison cities. The surveys include measures of tobacco-related knowledge, attitudes, beliefs, intentions, and use as well as measures of audience awareness of and exposure to campaign events and advertisements. The voluntary surveys also collect information on demographic variables, including sexual orientation, age, sex, race/ethnicity, education, and