

# Consumer Antibacterial Soaps: Effective or Just Risky?

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**Background.** Much has been written recently about the potential hazards versus benefits of antibacterial (biocide)-containing soaps. The purpose of this systematic literature review was to assess the studies that have examined the efficacy of products containing triclosan, compared with that of plain soap, in the community setting, as well as to evaluate findings that address potential hazards of this use—namely, the emergence of antibiotic-resistant bacteria.

**Methods.** The PubMed database was searched for English-language articles, using relevant keyword combinations for articles published between 1980 and 2006. Twenty-seven studies were eventually identified as being relevant to the review.

**Results.** Soaps containing triclosan within the range of concentrations commonly used in the community setting (0.1%–0.45% wt/vol) were no more effective than plain soap at preventing infectious illness symptoms and reducing bacterial levels on the hands. Several laboratory studies demonstrated evidence of triclosan-adapted cross-resistance to antibiotics among different species of bacteria.

**Conclusions.** The lack of an additional health benefit associated with the use of triclosan-containing consumer soaps over regular soap, coupled with laboratory data demonstrating a potential risk of selecting for drug resistance, warrants further evaluation by governmental regulators regarding antibacterial product claims and advertising. Further studies of this issue are encouraged.

In October 2005, the Non-Prescription Drug Advisory Committee of the US Food and Drug Administration (FDA) was convened to discuss the potential benefits and risks associated with antiseptic products marketed for consumer use, such as soaps labeled as “antibacterial.” The conclusion of the FDA meeting resulted in a call for further research regarding the risks and benefits of specific consumer antiseptic products used in the community setting. Much of the debate regarding consumer antiseptic products has focused on the use of “antibacterial soaps” that contain the active ingredient triclosan. The majority of consumer liquid hand soaps labeled as “antibacterial” contain triclosan [1], and, although the FDA does not formally regulate the levels of triclosan used in consumer products, most of

the popular liquid hand soap brands contain between 0.1% and 0.45% weight/volume (wt/vol). A chemically related compound, triclocarban, is used in antibacterial bar soap formulations.

Triclosan is a phenoxyphenol antimicrobial that is marketed as an “antibacterial” ingredient in consumer hygiene products, but it also has some antiviral and antifungal activity [2]. It is bacteriostatic at low concentrations and bactericidal at high concentrations [3]. Triclosan has been shown to inhibit the growth of both gram-positive and gram-negative bacteria in situ, with varying effectiveness across bacterial species [2]. For example, triclosan is relatively ineffective at inhibiting the growth of gram-negative bacteria such as *Pseudomonas aeruginosa* and *Serratia marcescens* [2]. Although the bactericidal activity of triclosan involves some *non-specific* killing mechanisms, research findings suggest that the bacteriostatic action occurs by inhibiting a *specific* bacterial target, known as the “enoyl-acyl carrier protein reductase” [4–6]. Triclosan shares this bacterial biosynthetic fatty acid pathway target with the antibiotic isoniazid [5]. These findings have led researchers

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to explore whether triclosan may influence the emergence of resistance to antibiotics [7–9].

Similar to the methods used for testing clinical antibiotic resistance, a MIC method is used to assess reduced susceptibility to triclosan. Currently, there are no clinically meaningful MIC cutoff points for monitoring resistance to biocides, and, therefore, the term “reduced susceptibility” is commonly used when discussing bacterial tolerance to triclosan exposure. Similar to their resistance to antibiotics, bacteria may be intrinsically resistant to triclosan via mechanisms of impermeability, efflux pumps, biofilms, and enzyme inactivation. The decreased susceptibility of greatest concern regarding triclosan is acquired tolerance/resistance. The resistance mechanisms are similar to those producing antibiotic resistance and include mutations at the drug target site, chromosome-mediated drug efflux, and overexpression of the target protein. Acquired bacterial resistance mechanisms may lead to an increase in MICs to antibiotics as well as to triclosan [7, 9, 10].

Although several investigators have reviewed studies examining the mechanisms of antiseptic resistance [7, 9–16], there are few systematic reviews that have attempted to summarize the potential risks associated with triclosan in the context of the purported effectiveness of this antibacterial ingredient used in hygiene products in the community setting. The efficacy of soap containing triclosan generally refers to the additional level of effectiveness *beyond* the ability of plain soap to simply remove transient organisms via surfactants and the mechanical action of the wash procedure [17]. The level of effectiveness may be measured at the microbiological level or at the population level, as added protection against bacterial contamination or the occurrence of common infectious illnesses. Risks, on the other hand, include the potential for bacteria to become unsusceptible to triclosan, for the emergence of cross-resistance to antibiotics, and for the ingredients to become toxic to the environment and to humans.

Only in the past 5 years has the effectiveness of triclosan for preventing infectious illnesses in the community setting been assessed; the first studies of which we are aware were published in 2002 [18]. In this review, we identify and summarize the studies examining the efficacy of triclosan by reviewing research that has examined the effectiveness of these consumer antiseptic soaps at reducing the incidence of infectious illnesses in the community setting and bacterial counts on the skin. Second, we identify and summarize the literature that examines whether there is a potential risk associated with use of hygiene products containing triclosan in relation to emergence of microbes that are less susceptible to triclosan and/or resistant to clinically used antibiotics. Finally, we weigh the evidence regarding the risks and benefits and conclude with recommendations for further research and for examining the implications of the current data on regulation of consumer products containing triclosan.

## METHODS

The PubMed database was searched for English-language articles published during the period January 1980–July 2006, using keyword combinations for each search strategy. Keywords included “absence,” “absent\*,” “alcohol,” “antibacterial cleaning,” “antibacterial soap,” “antiseptic,” “behavior,” “child care,” “child day care,” “child morbidity,” “child\*,” “cold,” “community,” “day care,” “day care center,” “diarrhea\*,” “diarrhoea,” “education,” “hand,” “hand sanitizer,” “hand wash,” “hand wash\*,” “infection control,” “infectious disease,” “infectious illness,” “infectious\*,” “intervention,” “health intervention,” “hygiene,” “hygiene education,” “infants,” “infect\*,” “morbidity,” “preschool,” “prevent\*,” “respiratory,” “sanitation,” “soap,” “school,” “triclocarban,” “triclosan,” “wash\*,” and “water.” An asterisk (\*) denotes a truncated search method in which PubMed seeks the first 600 variations of terms with the same root (for example, “infect\*” would result in a search for “infect,” “infection,” “infectious,” etc.).

The search results were scanned for research articles and systematic reviews. In addition, the reference lists in retrieved review papers were searched for related articles. Articles that focused on triclosan in dentifrice were excluded, because the introduction of triclosan in dentifrice was relatively recent (1997), compared with its introduction in topical antiseptics (1960s) [3, 19].

Our review of the literature was limited to studies that allowed comparison of the effectiveness of triclosan-containing soap with that of plain soap. We also included studies that assessed the effectiveness of triclocarban soap, because this is a chemically similar compound found in most antibacterial bar soaps available to consumers. The study outcomes included reported or diagnosed gastrointestinal infection (such as shigellosis) or upper respiratory tract infection (such as pneumonia), general gastrointestinal and/or respiratory symptom(s) of infection (such as diarrhea or runny nose), gastrointestinal and/or respiratory infectious symptom–related absences (such as school absence for a “cold”), and/or skin infections. Microbiological end points were limited to studies that examined the effect of antibacterial soap containing triclosan on bacterial reductions on the hand, compared with plain soap. Studies conducted among volunteer participants that were not associated with the clinical setting were included if they were conducted in natural settings or in a controlled laboratory environment. Because this review focused on the use of hand products containing triclosan in the community setting, articles were excluded if the setting was a health care facility, such as a hospital or residential nursing home, or if the study subjects were health care workers. Lastly, studies in which triclosan was combined with other antiseptic ingredients, such as alcohol or iodine, were excluded, because it would not have been possible

to estimate the independent effects of triclosan compared with plain soap in these studies [20].

To review the literature associated with risks, articles were included if they (1) assessed mechanisms of cross-resistance, using serial culture adaptation methodologies and/or genetic manipulation of the bacterial molecular target site of triclosan; (2) assessed levels of susceptibility to triclosan among bacterial isolates obtained from humans in the community setting; or (3) examined the statistical association between in-use exposure to triclosan and reduced susceptibility to triclosan and/or antibiotic resistance among humans living in the community setting.

Using available data from the retrieved studies, we summarized the findings regarding the efficacy of triclosan for reducing infectious illness symptoms and bacterial growth on skin. Next, we summarized the studies examining in situ mechanisms of reduced susceptibility to triclosan and cross-resistance with antibiotics. In addition, we summarized the studies that examined the association between the use of triclosan and the emergence of antibiotic resistance among individuals living in the community setting. Lastly, the strengths and limitations of the studies were assessed by considering methods related to design and conduct, such as sample size and masking of treatment from study participants.

## RESULTS

The PubMed search identified 1793 citations. On the basis of our inclusion criteria, we identified a total of 27 studies that examined either the effectiveness of triclosan or the risks of antibiotic resistance associated with exposure to triclosan.

**Efficacy of triclosan.** We identified 4 community-based randomized intervention studies [18, 21–23] providing information on the effectiveness of consumer soaps containing triclosan or triclocarban compared with that of plain soap (table 1). Three of these studies were conducted in Pakistan, and 1 was conducted in an urban setting in the United States. The study sample sizes ranged from 162 to 600 household units, and all households were required to include a child  $\leq 4$  years of age. Interventions included household member use of consumer-available bar soap containing 1.2% triclocarban (wt/vol) or liquid hand soap containing 0.2% triclosan (wt/vol) over a 1-year period. The outcomes recorded infectious illness symptoms such as cough, fever, diarrhea, and skin infections. None of these studies included the collection of clinical samples for laboratory identification of the etiologic agent associated with illness symptoms. All 4 studies showed no significant reduction in illness symptoms among household members associated with the use of the biocide-containing soap versus plain soap.

We identified 9 studies that examined the effectiveness of soap containing triclosan versus plain soap in reducing bacterial levels on the hands (table 1) [24–32]. The majority of the

microbiological effectiveness studies ( $n = 8$ ) were conducted in a controlled laboratory setting [24, 26–32], and 1 was conducted under natural conditions in the household setting [25]. Study sample sizes ranged from 10 to 238 subjects, and study subjects were characterized as nonclinical volunteers. Slightly fewer than half (4/9) of the studies mentioned the use of randomization procedures, and only 22% reported masking of study treatments. Most of the studies examined the normal skin flora as the outcome, but 2 of the 9 studies used artificial contamination [24, 32] procedures, by inoculating the skin of volunteers with *S. marcescens*. Approximately half (5/9) of the microbiological studies compared soap with at least 1.0% triclosan (wt/vol) versus plain soap, whereas the others utilized a concentration of  $\leq 0.3\%$  triclosan (wt/vol) in the comparison. Five of the 9 studies reported a significant reduction in bacterial counts on hands in association with the use of triclosan-containing soap versus plain soap. All but 1 of these 5 studies utilized soap with a relatively high concentration of triclosan,  $\geq 1.0\%$  [29–31], and 2 of the 5 studies reported a significant reduction only after multiple hand washes [24, 31], over multiple hand-washing episodes [24, 31], or after washing for 30 s [24, 31]. Only 1 study assessing triclosan at a concentration of 0.3% wt/vol (a concentration closer to the 0.1%–0.45% wt/vol found in many consumer antibacterial soaps) reported a significant reduction in bacterial counts, and this reduction was observed only after 18 hand washes per day, for 30 s each, over 5 consecutive days [31].

**Risks associated with triclosan.** Our search identified 11 laboratory studies assessing the influence of triclosan exposure on the emergence of triclosan-tolerant species and cross-resistance to clinical antibiotics (table 2). A range of bacteria was examined, including gram-negative and gram-positive species; commonly studied species included *Escherichia coli*, *Staphylococcus aureus*, and *Salmonella enterica*. Seven of the 11 studies demonstrated cross-resistance to  $\geq 1$  antibiotic for at least 1 of the bacterial species examined (table 2). Commonly assessed antibiotics included isoniazid, ciprofloxacin, erythromycin, tetracycline, chloramphenicol, ampicillin, and methicillin. Three of 11 studies reported an increase in MICs to triclosan among bacterial species but did not demonstrate cross-resistance to clinically used antibiotics. One study examining *E. coli* reported no evidence of increased tolerance to triclosan or cross-resistance to antibiotics [39]. Given the variety of bacterial species and antibiotics tested across studies, it was not possible to assess whether a consistent pattern of cross-resistance for specific organism/antibiotic combinations existed.

We identified only 3 studies that examined the emergence of antibiotic resistance associated with use of triclosan in the community setting (table 3). The first study included a convenience sample of 60 households [43] divided into those that reported using  $\geq 1$  antibacterial hygiene products and those

**Table 1. Studies comparing the efficacy of antibacterial soap containing triclosan (Ts) with that of plain soap.**

Study type, reference	Sample size	Antibacterial soap study group, liquid/bar (concentration of Tc or Ts)	Nonmedicated plain soap control group, liquid/bar	Outcome(s)	Results (antibacterial soap vs. plain soap)
<b>Infectious illness studies<sup>a</sup></b>					
Luby et al. [21] <sup>b</sup>	600 households	Bar (1.2% Tc)	Bar	Multiple symptoms <sup>c</sup>	Not statistically significant: RR of symptoms—assessed independently—all ~1
Larson et al. [22]	240 households	Liquid (0.2% Ts)	Liquid	Multiple symptoms <sup>d</sup>	Not statistically significant: RR of 0.96 (95% CI, 0.82–1.12)
Luby et al. [23] <sup>b</sup>	600 households	Bar (1.2% Tc)	Bar	Diarrhea symptoms	Not statistically significant: mean incidence of diarrhea was 2.02 (antibacterial soap) vs. 1.91 (plain soap)
Luby et al. [18]	162 households	Bar (1.2% Tc)	Bar	Impetigo incidence	Not statistically significant: incidence density ratio <sup>e</sup> of 0.77 (95% CI, 0.48–1.24)
<b>Microbiological studies</b>					
Sickbert-Bennett et al. [24]	10 volunteers	Liquid (1.0% Ts)	Liquid	Reduction in mean log <sub>10</sub> <i>Serratia marcescens</i> colony-forming units after artificial contamination of hands	Not statistically significant: after 1 episode of hand hygiene, 1.90 (antibacterial soap) vs. 2.00 (plain soap) log <sub>10</sub> cfu reduction Statistically significant: after 10 episodes of hand hygiene, 2.49 (antibacterial soap) vs. 1.68 (plain soap) log <sub>10</sub> cfu ( $P < .0001$ ) reduction
Larson et al. [25]	238 primary care givers	Liquid (0.2% Ts)	Liquid	Mean log <sub>10</sub> bacterial colony-forming units on hands	Not statistically significant: after 1 episode of hand hygiene, 5.77 (antibacterial soap) vs. 5.62 (plain soap) log <sub>10</sub> cfu ( $P > .28$ ) Not statistically significant: after 1 year of use, 4.87 (antibacterial soap) vs. 4.93 (plain soap) log <sub>10</sub> cfu ( $P > .28$ )
Faoagali et al. [26]	33 nonclinical staff	Liquid (1.0% Ts)	Liquid	Mean difference in log <sub>10</sub> colony-forming units on hands	Not statistically significant: after an immediate episode of hand hygiene or after a second hand hygiene episode 3 h later, compared with baseline, mean difference, $-0.0564$ log <sub>10</sub> cfu ( $P > .05$ ) Not statistically significant: after 5 days of hand washing 3 times/day, 4.87 (antibacterial soap) vs. 4.93 (plain soap) log <sub>10</sub> cfu (all $P > .28$ )

Miller et al. [27]	20 workers in the food industry	Liquid (0.3% Ts)	Liquid	Percentage reduction in mean log <sub>10</sub> bacterial colony-forming units on hands	Not statistically significant: after 1 episode of hand hygiene, 48.2% (antibacterial soap) vs. 41.7% (plain soap) reduction
Namura et al. [28]	7 healthy adult men without eczema	Liquid (0.3% Ts)	Liquid	Percentage reduction in mean log <sub>10</sub> bacterial colony-forming units on hands	Not statistically significant: after washing for 3 min, 32.86% (antibacterial soap) vs. 44.93% (plain soap) reduction
Leyden et al. [29]	20 students and employees of a university	Liquid (1.0% Ts)	Liquid	Percentage change in mean log <sub>10</sub> bacterial colony-forming units on hands	Statistically significant: after 30-s hand wash, 48.3% (antibacterial soap) vs. 21.9% (plain soap) reduction ( $P < .001$ ) Statistically significant: after 3-min hand wash, 70.1% (antibacterial soap) vs. 31.9% (plain soap) reduction ( $P < .05$ )
Bendig [30]	20 volunteer laboratory staff with no recent contact with antimicrobial products	Liquid (2.0% Ts)	Bar	Mean log <sub>10</sub> reduction in bacterial colony-forming units on hands	Statistically significant: after 5 sequential washes spaced 20 min apart, 0.79 (antibacterial soap) vs. 0.16 (plain soap) log <sub>10</sub> cfu reduction ( $P < .001$ )
Larson et al. [31]	40 nonmedical volunteers	Liquid (0.3% Ts)	Liquid	Mean log <sub>10</sub> bacterial colony-forming units on hands	Not statistically significant: after 1 day of use at 6 hand washes/day, 6.17 (antibacterial soap) vs. 5.71 (plain soap) log <sub>10</sub> cfu ( $P > .05$ ) Not statistically significant: after 1 day of use at 18 hand washes/day, 6.11 (antibacterial soap) vs. 5.75 (plain soap) log <sub>10</sub> cfu ( $P > .05$ ) Not statistically significant: after 5 days of use at 6 hand washes/day, 5.42 (antibacterial soap) vs. 5.25 (plain soap) log <sub>10</sub> cfu ( $P > .05$ ) Statistically significant: after 5 days of use at 18 hand washes/day, 4.56 (antibacterial soap) vs. 5.45 (plain soap) log <sub>10</sub> cfu ( $P < .05$ )
Bartzokas et al. [17]	12 volunteers	Liquid (1.5% Ts)	Liquid	Reduction in mean log <sub>10</sub> <i>S. marcescens</i> colony-forming units after artificial contamination of hands	Statistically significant: significant reductions were observed after 1 (2.91 log <sub>10</sub> cfu), 4 (3.22 log <sub>10</sub> cfu), 7 (3.50 log <sub>10</sub> cfu), and 10 (3.78 log <sub>10</sub> cfu) episodes of hand hygiene with antibacterial soap, compared with 1 episode with plain soap (2.72 log <sub>10</sub> cfu) (all $P < .01$ )

**NOTE.** RR, relative risk; Tc, triclocarban.

<sup>a</sup> All infectious illness studies followed participants for 1 year.

<sup>b</sup> These studies did not provide a statistical comparison of the antibacterial treatment arm versus the plain soap treatment arm, so we computed statistical comparisons using the data available from the study. It was not possible to control for clustering effects in these calculations.

<sup>c</sup> Infectious illness symptoms such as diarrhea, cough, congestion, pneumonia, and impetigo.

<sup>d</sup> Infectious illness symptoms such as diarrhea, cough, sore throat, fever, and vomiting.

<sup>e</sup> Models adjusted for covariates.

**Table 2. Triclosan (Ts) adaptation and antibiotic cross-resistance studies.**

Reference	Types of bacterial species	Exposure parameters	Results
Ledder et al. [33] <sup>a</sup>	Coagulase-negative <i>Staphylococcus</i> species, <i>Enterobacter asburiae</i> , <i>Escherichia coli</i> , <i>Klebsiella</i> species, <i>Salmonella enterica</i> (serotypes Enteritidis, Typhimurium, and Infantis), <i>Stenotrophomonas maltophilia</i>	Ts/antibiotics <sup>b</sup>	Ts MIC was increased among <i>E. coli</i> , <i>Klebsiella</i> species, and <i>S. maltophilia</i> only; among bacteria with high MICs to Ts, there was no increase in MICs to 4 antibiotics after exposure to Ts
Sanchez et al. [34]	<i>S. maltophilia</i>	Ts/antibiotics <sup>b</sup>	Ts-adapted mutants showed reduced susceptibility to tetracycline and chloramphenicol but not to tobramycin, compared with the wild-type strain; these strains overexpressed the multidrug-resistance pump SmeDEF
Braoudaki and Hilton [35] <sup>a</sup>	<i>S. enterica</i> (serotypes Enteritidis, Typhimurium, and Virchow)	Ts/antibiotics <sup>b</sup>	<i>S. enterica</i> serotype Virchow became more tolerant to Ts and erythromycin after gradual exposure to higher concentrations of these agents (up to 1024 µg/mL) over 6 days; adaptive resistance to Ts and erythromycin was stable for at least 30 days of passage in Ts/antibiotic-free medium
Braoudaki and Hilton [36] <sup>a</sup>	<i>E. coli</i> O111:H24, <i>E. coli</i> O157:H7, <i>E. coli</i> O55, <i>E. coli</i> K-12	Ts/antibiotics <sup>b</sup>	Four sublethal exposures of <i>E. coli</i> O157:H7 led to an increase in MICs to Ts of 0.25 µg/mL to 1024 µg/mL; Ts-adapted <i>E. coli</i> O157:H7 demonstrated cross-resistance to a number of antibiotics, including amoxicillin, chloramphenicol, ciprofloxacin, tetracycline, and trimethoprim; <i>E. coli</i> K-12 and <i>E. coli</i> O55 adapted to Ts showed reduced susceptibility to chloramphenicol and trimethoprim, respectively; other strains did not demonstrate cross-resistance
Braoudaki and Hilton [37]	<i>E. coli</i> O157:H7, <i>E. coli</i> K-12, <i>S. enterica</i> (serotypes Enteritidis, Typhimurium, and Virchow)	Ts/antibiotics <sup>b</sup>	An increase in MICs to Ts and cross-resistance with erythromycin and ciprofloxacin was demonstrated for <i>E. coli</i> O157:H7; adaptation of <i>E. coli</i> O157:H7 to erythromycin also led to an increase in MICs; <i>S. enterica</i> serotype Virchow demonstrated reduced susceptibility to Ts and cross-resistance with erythromycin after serial passage
Randall et al. [38]	<i>S. enterica</i>	Ts/antibiotics <sup>b</sup>	Increase in the mean frequency of mutations that confer resistance to ampicillin
Walsh et al. [39]	<i>E. coli</i>	Tc <sup>c</sup>	No evidence of increased tolerance to Ts
Fraise [40]	MRSA	Ts <sup>d</sup>	Threefold increase in MICs to Ts
Chuanchuen et al. [41]	<i>Pseudomonas aeruginosa</i>	Ts/antibiotics <sup>b</sup>	A 94-fold increase in MICs to ciprofloxacin was observed among strains that showed high levels of tolerance to Ts
Suller and Russell [42]	Methicillin-susceptible <i>S. aureus</i> , MRSA	Ts/antibiotics <sup>b</sup>	No consistent pattern between high Ts MICs and antibiotic-resistance profiles after exposure over 1 month; 2 of 3 MRSA strains that were resistant to mupirocin and several other antibiotics were also less susceptible to Ts; however, coresistance with mupirocin was not plasmid mediated
McMurry et al. [5]	<i>Mycobacterium smegmatis</i>	Ts/isoniazid <sup>e</sup>	A mutation originally selected for on isoniazid also mediated Ts resistance, and vice versa

**NOTE.** MRSA, methicillin-resistant *Staphylococcus aureus*; Tc, triclocarban.

<sup>a</sup> This study also looked at drain bacteria; this information is not presented here.

<sup>b</sup> Repeated exposure to sublethal Ts concentrations in nutrient broth and subsequent exposure to several antibiotics.

<sup>c</sup> Repeated exposure to sublethal Tc concentrations in nutrient broth.

<sup>d</sup> Repeated exposure to sublethal Ts concentrations in nutrient broth.

<sup>e</sup> Repeated exposure to sublethal Ts concentrations and subsequent exposure to isoniazid

**Table 3. Community-level studies of the relationship between exposure to triclosan in home hygiene products and antibiotic resistance.**

Reference	Sample size (location)	Isolate source	Organism(s)	Antibiotics, no.	Results
Cole et al. [43]	60 households; 8 bacterial isolates (US, UK)	Hands of 1–2 household members reporting use of antibacterial products vs. those reporting use of nonantibacterial products	<i>Staphylococcus aureus</i>	18	Comparable triclosan MICs among antibacterial vs. non-antibacterial user homes; <sup>a</sup> no patterns discerned with antibiotic susceptibilities
Aiello et al. [44]	240 individuals; 628 bacterial isolates (US)	Hands of primary caregivers in households using antibacterial vs. nonantibacterial products	<i>Acinetobacter</i> species, <i>Enterobacter</i> species, <i>S. aureus</i> , coagulase-negative staphylococcal species, <i>Klebsiella</i> species, <i>Pseudomonas</i> species	8	Not statistically significant: several staphylococcal species showed reduced susceptibility to triclosan
Aiello et al. [45]	240 individuals (US)	Hands of antibacterial vs. nonantibacterial user households	Carriage of $\geq 1$ antibiotic-resistant organism <sup>b</sup>	...	Not statistically significant

<sup>a</sup> This study did not assess statistical significance because the number of final isolates for analysis was limited. Other bacterial isolates obtained in this study were from environmental sources within the household and are not presented here. The authors reported that the results for the environmental isolates also showed no evidence of cross-resistance.

<sup>b</sup> The organisms were the same as those listed for Aiello et al. [44].

that reported no use of antibacterial hygiene products. Bacteria were isolated from the hands of household members and their home environments. There was no information on the concentration or prevalence of triclosan-containing products among the reported antibacterial-user households. Although the sample size was not sufficient to make statistical comparisons, the authors of the study still concluded that there was no association between use of antibacterial products and the presence of antibiotic-resistant species among household members and their environment.

The next 2 studies were derived from a randomized and masked intervention trial of 238 households allocated to using either 0.2% triclosan-containing liquid hand soap or plain soap [44, 45]. Bacterial samples were obtained from the hands of household members at baseline and after 1 year of using the assigned hand hygiene product. Neither of these studies demonstrated the emergence of antibiotic resistance associated with use, over a 1-year period, of the liquid hand soap containing 0.2% triclosan compared with plain soap. The authors did note that several species, such as *P. aeruginosa* and some coagulase-negative staphylococcal species, demonstrated unexpectedly high MICs to triclosan at both baseline and the end of the year [44].

## DISCUSSION

Triclosan has been used in personal hygiene products in the United States since the 1960s, and this chemical is now the most prevalent biocide ingredient in consumer liquid hand soaps [1]. Our study is, to our knowledge, the first systematic review of research assessing the risks and potential benefits associated with the use of soaps containing triclosan in the community setting. The available data do not support the effectiveness of triclosan for reducing infectious disease symptoms or bacterial counts on the hands when used at the concentrations commonly found in consumer antiseptic hand soaps. The effectiveness was similar to that of plain soap in the majority of studies, and a difference in the reduction of bacterial levels on the hands was generally observed only after longer hand washes with soap containing relatively high concentrations of triclosan (i.e.,  $\geq 1.0\%$  wt/vol). Regarding the risks associated with triclosan, we identified several studies that supported a relationship between exposure of bacteria to triclosan in the laboratory and increased MICs to clinically utilized antibiotics. In contrast, research conducted at the population level showed little evidence of cross-resistance with antibiotics associated with household use of hygiene products containing triclosan.

Hand hygiene is an important practice for reducing the transmission of infectious illnesses in both the clinical and community setting [46, 47]. Although there are numerous studies examining the efficacy of antimicrobial hand hygiene agents in

the clinical setting (reviewed in [46]), few have examined the efficacy of biocide-containing hand hygiene products frequently utilized in the community setting. The 4 available studies that examined the efficacy of biocide-containing soap compared with that of plain soap at reducing infectious illnesses showed no significant differences in any of the infectious illness symptoms that were assessed [18, 21–23]. All of these studies were large, randomized, 1-year intervention studies that included rigorous follow-up of study participants and illness outcomes. The study populations ranged in age, but all 4 studies required households to have at least 1 child residing in the home. The null findings were consistent across various study settings, ranging from urban upper Manhattan to squatter settlements in Pakistan. Even in areas with high rates of infectious illnesses, such as the urban squatter settlements in Karachi, there was little benefit associated with use of the soap containing triclocarban compared with plain soap.

None of these studies gathered clinical isolates for the identification of the biological agent associated with the illness symptoms, so it is not possible to assess whether the reported symptoms were associated with organisms other than bacteria, such as viruses. Triclosan is less effective against viral agents [2]; therefore, it is possible that this ingredient showed no impact on infectious illnesses in the household setting because a majority of the infectious etiologies may be associated with viral pathogens. Still, when examining impetigo, for which a viral etiology is unlikely, the results can be regarded more decisively and suggest that triclosan provides little benefit for reducing skin infections caused by bacteria in the community setting [18]. Symptoms such as coughing, sneezing, fever, and diarrhea are commonly observed for many of the significant infectious illnesses observed in the community setting and may be related to infection by viruses or bacteria [48]. Therefore, the available community-based intervention studies suggest that consumer products containing triclosan or triclocarban are not effective against the most common infectious illnesses affecting individuals in the community setting. For these reasons, the public health utility of this antibacterial ingredient for preventing common infectious illnesses, as a measure of added protection beyond that afforded by plain soap use, has not been shown. We were unable to identify any studies that examined the efficacy of soaps containing triclosan among other populations living in the community setting, such as elderly or immunocompromised individuals. Therefore, it is unknown whether soaps containing triclosan could provide protection to groups potentially at higher risk for infection.

Many of the available bacterial reduction studies we reviewed tested the efficacy of hand hygiene agents used for  $\geq 30$  s. Similar to our review, others have shown that an increased application time of various hand hygiene agents tends to result in greater efficacy [49]. It is unlikely that a  $\geq 30$ -s duration

reflects the normal hand-washing practices in the community setting. Even health care professionals generally wash their hands for a much shorter duration [46], and studies of hand washing in the community setting indicate suboptimal hand-washing practices [50].

Another factor that has been identified as an important parameter for enhancing the efficacy of antiseptic hand hygiene agents is the concentration of the ingredient [49]. In our review, the majority of studies that identified a significant reduction in bacterial levels on the hands utilized soap with a concentration of  $\geq 1.0\%$  triclosan. Other factors, such as experimental contamination versus normal flora, may also lead to findings of enhanced efficacy [49]. Likewise, we identified 2 studies that used artificial contamination [24, 32], and both reported significant reductions with the use of the soap containing triclosan, compared with plain soap. Study design issues, such as a lack of randomization to treatment arms and a lack of masking among study subjects, may also have affected the findings in some of these reports.

Collectively, the microbiological efficacy studies strongly suggest that concentrations of triclosan used in consumer liquid hand soaps do not provide a benefit over plain soap for reducing bacterial levels found on the hands. Although some of these studies were limited by study design flaws and variability in testing procedures, the results regarding the lack of efficacy were consistent among studies utilizing a concentration of triclosan found in most consumer liquid hand soaps.

Research regarding the risks associated with triclosan use has primarily been conducted under controlled laboratory conditions. This research has elucidated several molecular mechanisms by which sublethal exposure to triclosan may lead to the emergence of antibiotic-resistant bacteria among select species [10]. Some of the triclosan-adapted bacterial species, such as *E. coli* and *P. aeruginosa*, were able to grow in cultures with concentrations of triclosan of up to 1024  $\mu\text{g}/\text{mL}$ , which is close to the concentrations added to many consumer soaps (i.e., 1000  $\mu\text{g}/\text{mL} = 0.1\%$  triclosan [wt/vol]). These findings were relatively species specific, and much lower concentrations were required to inhibit other organisms, such as staphylococci. Most of the studies followed similar testing procedures for assessing triclosan MICs and antibiotic resistance. However, the bacterial species tested and the antibiotics assessed varied across studies. This limited our ability to classify species- and antibiotic-specific cross-resistance patterns.

There have been only a few studies that have attempted to assess the relationship between biocide-containing soap use and the emergence of antibiotic resistance in the community setting. Interestingly, the laboratory findings have not been corroborated among the intervention studies that were conducted in the community under in-use conditions. There are several factors that might explain the discrepancy. First, laboratory testing

may not be generalizable to the emergence of antibiotic resistance in the environment. Laboratory exposure conditions may not mirror exposures that occur in the environment under natural antiseptic use conditions. For example, it is possible that bacterial species are exposed to higher concentrations of triclosan under in-use conditions in household settings, compared with relatively low concentrations often used in laboratory studies. This may reduce the selective pressures for antibiotic-resistant bacteria under in-use conditions in the household. Second, selective pressures in the environment may weed out cross-resistant organisms. Organisms that are selected for resistance to both triclosan and antibiotics may be less fit for survival in the environment when they are carrying plasmids or must maintain costly genetic target mutations. Despite these caveats, there are many examples with antibiotics in which difficulty in obtaining resistant mutants in the laboratory did not predict the relative ease of their emergence in the clinical settings—for example, the fluoroquinolones.

Studies that have assessed whether there is an association between exposure to products containing triclosan and antibiotic resistance in the community setting may not be large or long enough to identify the emergence of antibiotic resistance. For example, the 2 studies by Aiello et al. [44, 45] suggest a trend toward resistance, but the studies were powered to detect only moderate to high changes in antibiotic resistance over a 1-year period. The study by Cole et al. [43] examined only *S. aureus* from the hands and had a relatively small number of isolates available for comparison. Moreover, this study did not randomize households to antiseptic product use or utilize masking of treatments, which could reduce the ability to detect a difference between user groups. The longest period of follow-up among these studies was 1 year [44, 45], which may not adequately reflect the time course for the development of resistance associated with use of products containing triclosan. Lastly, baseline levels of susceptibility to triclosan among bacterial species in the community setting are virtually unknown. Thus, it is difficult to show a change if the organisms have already achieved some level of resistance [44]. Most of the data on MICs to triclosan are from studies of clinical laboratory strains and culture type collections [2]. Consumer hygiene products containing triclosan have been used since the 1960s, and no formal surveillance mechanisms exist for assessing susceptibilities of bacteria to this agent in the community setting. Further research is clearly needed to assess whether the emergence of antibiotic resistance in the community setting is associated with the growing use of soaps containing triclosan.

Because our key aim in this review was to assess the efficacy of and risks associated with the use of soaps containing triclosan in the community setting, our literature search excluded studies conducted in the clinical setting and those with health care workers as study subjects. We did include 3 studies that did

not specifically state the source of volunteers included in their studies [20, 24, 28], because there was no indication that these subjects were derived from the clinical setting. Because of our focus on the community, we also excluded studies that assessed exposure to triclosan in the clinical setting and the emergence of antibiotic resistance. Two of the studies by Luby et al. [21, 23] did not present a statistical comparison of the antiseptic treatment arm and the plain soap treatment arm, so we computed statistical comparisons by use of the data available from the study. Therefore, it is possible that these 2 studies did not have adequate sample sizes to detect differences between treatment arms using biocide-containing versus plain soap. The differences, however, were very small and showed an even slightly higher level of infectious illness symptoms, for some of the outcomes, among the biocide-containing soap users compared with the plain soap users.

Because hand soaps are one of the most commonly available hygiene products containing triclosan, we limited our review to studies that provided the results of exposure to these products among isolates of bacteria from humans. Two of the studies included in our review isolated bacterial species from humans and the environment [33, 43]. For these studies, we reported only the results regarding the isolates from humans. Importantly, the results were similar regardless of isolate source [33, 43]. In addition, our search did not include studies that were published in languages other than English. PubMed was the only search database utilized; therefore, print sources such as conference abstracts were excluded.

## CONCLUSIONS

The results of our review call into question the marketing of soaps containing triclosan as a product providing efficacy *beyond* the use of plain soap in the community setting. Soaps containing triclosan at concentrations used in the community setting (0.2% or 0.3% wt/vol) were generally no more efficacious than plain soap at preventing infectious illness symptoms and reducing bacterial levels on the hands. Several studies demonstrated laboratory evidence of triclosan-adapted cross-resistance with antibiotics among multiple species of bacteria. There are still too few studies that have been conducted in the community setting to adequately assess whether the emergence of antibiotic resistance in that setting is associated with the use of consumer soaps containing triclosan. Longitudinal studies are needed to assess changes in levels of antibiotic resistance associated with use of soap containing triclosan over time, and large databases of isolates are required to examine within-species changes in antibiotic-resistance profiles. Still, current findings warrant actions by the FDA for evaluating consumer product advertising claims. Future research should be directed at addressing both the efficacy of and risks associated with the use of triclosan. For instance, data are needed to assess whether

products containing triclosan provide an added level of protection among high-risk groups, such as immunocompromised individuals living in the household setting.

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