Triclosan

White Paper prepared by The Alliance for the Prudent Use of Antibiotics (APUA)

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Antimicrobial agents (substances that kill or inhibit the growth of microorganisms such as bacteria, fungi, or protozoans) are common ingredients in many everyday household, personal care and consumer products. There are growing concerns about the emergence of these chemicals in the environment and their potential negative effects on human and animal health. Triclosan is a synthetic, broad-spectrum antimicrobial agent that in recent years has exploded onto the consumer market in a wide variety of antibacterial soaps, deodorants, toothpastes, cosmetics, fabrics, plastics, and other products.
There is a current debate on the safety, effectiveness and regulation of use of triclosan. We have reviewed the state of knowledge regarding triclosan, and it is the purpose of this white paper to consider the following aspects that pertain to this issue: (i) the mode of action of triclosan; (ii) current usage of triclosan; (iii) the potential impact of triclosan on human and animal health; (iv) the possible association between triclosan usage and antibiotic resistance; (v) the potential impact of triclosan on the environment; (vi) current regulatory scrutiny of triclosan; and (vii) potential alternatives and next steps.

1. Introduction

Triclosan possesses mostly antibacterial properties (kills or slows down the growth of bacteria), but also some antifungal and antiviral properties. Triclosan is most often used to kill bacteria on the skin and other surfaces, although it sometimes is used to preserve the product against deterioration due to microbes. Its use began in the US in the 1970s in soaps, and its uses have risen dramatically in the past few years. Triclosan, as well as other antibacterial agents and their degradation by-products, are now found throughout the environment, including surface waters, soil, fish tissue, and human breast milk (1). Furthermore, the American Medical Association (AMA) has concerns about the use of these chemicals and has:

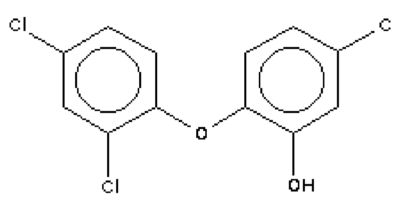
- encouraged the U.S. Food and Drug Administration to study the issue,
- stated that they will monitor the progress of the current FDA evaluation of the safety and
- effectiveness of antimicrobials for consumer use,
- encouraged continued research on the use of common antimicrobials as ingredients in
- consumer products and their impact on health, the environment and the major public health problem of antimicrobial resistance.

In 2009, the American Public Health Association (APHA) proposed that it would endorse the banning of triclosan for household and non-medical uses. At the time of writing, this proposal has not yet been taken any further.

Despite current and pressing efforts to review and regulate the appropriate use of triclosan, a scientific debate continues regarding its potential negative impact on human health, the environment and potential link to resistance to antibiotics.

2. What is Triclosan and How Does It Work?

Triclosan is a phenylether, or chlorinated bisphenol, with a broad-spectrum antimicrobial action which is classified as a Class III drug by the FDA (Class III drugs are compounds with high solubility and low permeability) (2).



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Triclosan (2,4,4′-trichloro-2′-hydroxy-diphenyl ether)

It is manufactured by Ciba Specialty Chemical Products under their trade names Irgasan® and Irgacare®. Triclosan (generic) is also produced by a number of other manufacturers outside of the U.S. located in Switzerland, the Netherlands, China, India, South Korea and elsewhere (3). Triclosan usually comes in the solid form of white powder. It has a faint aromatic, phenolic scent as it is a chlorinated aromatic compound. Triclosan can come in either ether or phenol form though the phenol forms are more popularly used as they have antibacterial properties. In addition, under the trade name of Microban®, triclosan is used as a built-in antimicrobial for product protection.

As a result of the potential for the formation of ultra-trace unwanted by-products which can affect the safety and efficacy of triclosan, the United States Pharmacopeia (USP) has issued a monograph for the specific testing of bulk triclosan. In addition to setting product specification standards and procedures to assay the purity and physical identity of triclosan, it also defines the limits and methods of testing for these unwanted ultra-trace by-products, which may be present (3).

2.1. Target organisms

Triclosan has a broad range of activity that encompasses many, but not all, types of Gram-positive and Gram-negative non-sporulating bacteria, some fungi (4), *Plasmodium falciparum* and *Toxoplasma gondii* (5). It is bacteriostatic (it stops the growth of microorganisms) at low concentrations, but higher concentrations are bactericidal (it kills microorganisms). The most sensitive organisms to triclosan are staphylococci, some streptococci, some mycobacteria, *Escherichia coli* and *Proteus* spp. (against which triclosan is effective at concentrations that range from 0.01 mg/L to 0.1 mg/L). Methicillin-resistant *Staphylococcus aureus* (MRSA) strains are also sensitive to triclosan (6, 7) and may or may not have an increased resistance to triclosan (it is sensitive to concentrations of triclosan in the range of of 0.1–2 mg/L). Showering or bathing with 2% triclosan has been shown to be an effective regimen for the decolonization of patients whose skin is carrying MRSA (8). Enterococci are much less susceptible than staphylococci (9) and *Pseudomonas aeruginosa* is highly resistant (9).

The microorganism *Clostridium difficile* presents a particularly hard to combat situation in hospitals. The noninfectious form, called a spore, can survive in hospitals, nursing homes, extended-care facilities, and newborns' nurseries. The spores cannot cause infection, but when they are ingested, they transform into the active virulent form. In severe cases, *C. difficile* can cause critical illness and death in elderly or immune-compromised patients (10). Studies have found spores on hospital items such as over-bed tables, side curtains, lab coats, scrubs, plants and cut flowers, computer keyboards (especially computers on wheels), bedpans, furniture, toilet seats, linens, telephones, stethoscopes, jewelry, diaper pails, and under fingernails; even physician's neck ties can be contaminated with *C. difficile.* (10)

Some researchers, like Dr. Dale Gerding, associate chief of staff research and development coordinator at Edward Hines Jr. VA Hospital, in Hines, Illinois, have proposed that, similar to anthrax spores, *C. difficile* spores have an “exosporium” — sticky chains of protein-containing substances — that confers a particular adherence, or stickiness, and they stick on hands. Dr. Gerding and colleagues assessed several commercially available hand washes for *C. difficile* spore removal, and concluded that care should be taken in assessing *C. difficile* spore claims from hand-hygiene manufacturers, which might not be supported by scientific evidence. In their analysis, the only agent that achieved a reduction in *C.difficile* spores was the heavy-duty printer's ink hand cleaner. Thus, there is a clear need for an effective way to combat the stickiness of *C.difficile* (10).

Table 1. Germs that are destroyed by triclosan
Staphylococci
Streptococci

Methicillin-resistant Staphylococcus aureus (MRSA)
Enterococci: *Escherichia coli* , *Klebsiella pneumonia*, *Klebsiella* spp, *Enterobacter* spp
Proteus spp
Acinetobacter spp
Mycobacteria
Proteus mirabilis

Table 2. Germs that are NOT destroyed by triclosan
Pseudomonas aeruginosa
Clostridium difficile

2.2. Mechanism of Action

Triclosan works by blocking the active site of the enoyl-acyl carrier protein reductase enzyme (ENR), which is an essential enzyme in fatty acid synthesis in bacteria (11). By blocking the active site, triclosan inhibits the enzyme, and therefore prevents the bacteria from synthesizing fatty acid, which is necessary for building cell membranes and for reproducing. Since humans do not have this ENR enzyme, triclosan has long been thought to be fairly harmless to them. Triclosan is a very potent inhibitor, and only a small amount is needed for powerful antibacterial action.

2.3. Uses of Triclosan

Triclosan has been used since 1972, and is now found in the following products:

- soaps
- hand-washes
- dish-washing products
- laundry detergents and softeners
- plastics (e.g., toys, cutting boards, kitchen utensils)
- toothpaste and mouth washes
- deodorants and antiperspirants
- cosmetics and shaving creams
- acne treatment products
- hair conditioners
- bedding
- trash bags
- apparel like socks and undershirts
- hot tubs, plastic lawn furniture
- impregnated sponges
- surgical scrubs
- implantable medical devices
- pesticides

Triclosan is used in hundreds of common commercial products. At this time, in the United States, manufacturers of products containing triclosan must say so somewhere on the label. So if triclosan is of concern, one must look for claims of a product being 'anti-bacterial', and then check the label for triclosan. Triclosan is used as a built-in antimicrobial product protection, under the trade name of Microban®, in antimicrobial solutions for consumer, industrial and medical products around the world. The Microban® technology is engineered into a breadth of materials including: polymers, textiles, coatings, ceramics, paper and adhesives. Microban® controls microbial growth and odors within the impregnated surface but does not offer the user any significant protection from infectious microbes on the exterior surfaces of those items. This could potentially create a false sense of security, and cause the user to relax other efforts to keep surfaces clean.

Table 3. List of products containing triclosan (12)
SOAPS: Dial® Liquid Soap; Softsoap® Antibacterial Liquid Hand Soap; Tea Tree Therapy™ Liquid Soap; Provon® Soap; Clearasil® Daily Face Wash; Dermatologica ® Skin Purifying Wipes; Clean & Clear Oil Free Foaming Facial Cleanser; DermaKleen™ Antibacterial Lotion Soap; Naturade Aloe Vera 80® Antibacterial Soap; CVS Antibacterial Soap, pHisoderm Antibacterial Skin Cleanser, Dawn® Complete Antibacterial Dish Liquid, Ajax® Antibacterial Dish Liquid.
DENTAL CARE: Colgate Total®; Breeze™ Triclosan Mouthwash; Reach® Antibacterial Toothbrush; Janina Diamond Whitening Toothpaste
COSMETICS: Supre® Café Bronzer™; TotalSkinCare Makeup Kit; Garden Botanika® Powder Foundation; Mavala Lip Base; Jason Natural Cosmetics; Blemish Cover Stick; Movate® Skin Litening Cream HQ; Paul Mitchell Detangler Comb, Revlon ColorStay LipSHINE Lipcolor Plus Gloss, Dazzle
DEODORANT: Old Spice High Endurance Stick Deodorant, Right Guard Sport Deodorant Queen Helene® Tea Trea Oil Deodorant and Aloe Deodorant; Nature De France Le Stick Natural Stick Deodorant; DeCleor Deodorant Stick; Epoch® Deodorant with Citrisomes; X Air Maximum Strength Deodorant
OTHER PERSONAL CARE PRODUCTS: Gillette® Complete Skin Care MultiGel Aerosol Shave Gel; Murad Acne Complex® Kit, ®; Diabet-x™ Cream; T.Taio™ sponges and wipes, Aveeno Therapeutic Shave Gel.
FIRST AID: SyDERMA® Skin Protectant plus First Aid Antiseptic; Solarcaine® First Aid Medicated Spray;Nexcare™ First Aid, Skin Crack Care; First Aid/Burn Cream; HealWell® Night Splint; Splint 11-1X1: Universal Cervical Collar with Microban
KITCHENWARE: Farberware® Microban Steakknife Set and Cutting Boards; Franklin Machine Products FMP Ice Cream Scoop SZ 20 Microban; Hobart Semi-Automatic Slicer; Chix® Food Service Wipes with Microban; Compact Web Foot® Wet Mop Heads
COMPUTER EQUIPMENT: Fellowes Cordless Microban Keyboard and Microban Mouse Pad
CLOTHES: Teva® Sandals; Merrell Shoes; Sabatier Chef's Apron; Dickies Socks; Biofresh® socks
CHILDRENS TOYS: Playskool®: Stack 'n Scoop Whale, Rockin' Radio, Hourglass, Sounds Around Driver, Roll 'n Rattle Ball, Animal Sounds Phone, Busy Beads Pal, Pop 'n Spin Top, Lights 'n Surprise Laptop
OTHER: Bionare® Cool Mist Humidifier; Microban® All Weather Reinforced Hose; Thomasville® Furniture; Deciguard AB Ear Plugs; Bauer® 5000 Helmet; Aquatic Whirlpools; Miller Paint Interior Paint; QVC® Collapsible 40-Can Cooler; Holmes Foot Buddy™ Foot Warmer, Blue Mountain Wall Coverings, California Paints®, EHC AMRail Escalator Handrails, Dupont™ Air Filters, Durelle™ Carpet Cushions, Advanta One Laminate Floors, San Luis Blankets, J Cloth® towels, JERMEX mops

2.4. Effectiveness considerations

A variety of methods are available for evaluation of the antimicrobial activity of antiseptic and disinfectant agents. An important but often overlooked variable in this type of studies is adequate neutralization of the chemical compund. Neutralization is essential to stop the antimicrobial activity and misleading interpretation of results. Triclosan is difficult to neutralize, therefore incomplete neutralization may overestimate the efficacy of triclosan-containing products (13).

While all antimicrobial hand soaps have demonstrated acceptable levels of effectiveness in accordance with the Topical Antiseptic Drug Monograph as measured by the Healthcare Personnel Handwash test (14), all are hampered to some degree by the interaction of the active ingredient with the surfactants (or cleaning agents) used. The triclosan molecules get encaged by the cleaning surfactant molecules, which help to keep the active triclosan from settling out in the solution. During lathering, a small percentage of the active ingredient is delivered to the skin, but the rest is simply washed down the drain, trapped in these cage-like structures. To address this problem an approach termed "activated triclosan" has been applied to triclosan-containing soaps to boost their performance. The activated triclosan uses a combination of different surfactants --sodium xylenesulfonate and dipropylene glycol-- to keep the triclosan in solution and prevent its settling out in the soap (14).

3. Health Impacts

Data from the 2003–2004 National Health and Nutrition Examination Survey showed triclosan in 75% of urine samples analyzed (15). Triclosan also has been found in rivers and streams and in sewage sludge applied to agriculture (16). Studies have yielded conflicting findings regarding links between triclosan and adverse health effects in humans and animals.

Acute Toxicity. In classical toxicological terms, triclosan is relatively non-toxic to humans and other mammals. However, there have been reports (17) of contact dermatitis, or skin irritation, from exposure to triclosan. There is also evidence (18) that triclosan may cause photoallergic contact dermatitis (PACD), which occurs when the part of the skin exposed to triclosan is also exposed to sunlight. PACD can cause an eczematous rash, usually on the face, neck, the back of the hands, and on the sun-exposed areas of the arms. Manufacturers of a number of triclosan-containing toothpaste and soap products claim that the active ingredient continues to work for as long as 12 hours after use. Thus, consumers are exposed to triclosan for much longer than the 20 seconds it takes to wash their hands or brush their teeth.

Chronic Health Effects. A Swedish study (1) found high levels triclosan in three out of five human milk samples, indicating that triclosan does in fact get absorbed into the body, often in high quantities. Additionally, triclosan is lipophilic, so it can bioaccumulate in fatty tissues. Triclosan has not clearly been found to have carcinogenic, mutagenic, or teratogenic effects.

Concerns over triclosan interfering with the body's thyroid hormone metabolism led to a study that found that triclosan had a marked hypothermic effect, lowering the body temperature, and overall causing a "nonspecific depressant effect on the central nervous system" of mice (19). Another study associated exposure to low levels (0.03 microg/L) of triclosan with disrupted thyroid hormone–associated gene expression in tadpoles, which encouraged them to prematurely change into frogs (20), while another linked triclosan exposure with reduced sperm production in male rats (21). The hypothesis proposed is that triclosan blocks the metabolism of thyroid hormone, because it chemically mimics thyroid hormone, and binds to the hormone receptor sites, blocking them, so that endogenous hormones cannot be used. Although the chemical structure of triclosan closely resembles certain estrogens, a study on a Japanese species of fish did not demonstrate estrogenic effects. However, it did find that triclosan is weakly androgenic, causing changes in fin length and sex ratios (22). A more recent paper in *Environment International* (23) shows that triclosan can hinder estrogen sulfotransferase in sheep placenta, an enzyme which helps metabolize the hormone and transport it to the developing fetus. The suspicion is that triclosan would be dangerous in pregnancy if enough of it gets through to the placenta to affect the enzyme.

Although information in humans from chronic usage of personal care products is not available, triclosan has been extensively studied in laboratory animals. When evaluated in chronic oncogenicity studies in mice, rats, and hamsters, treatment-related tumors were found only in the liver of male and female mice (24). Application of the Human Relevance Framework suggested that these tumors arose by way of a mode of action not considered to be relevant to humans (24).

Another area of debate involves the hypothesis that triclosan enhances the production of chloroform. A study published in 2007 illustrated that, under some circumstances, triclosan triggered the production of chloroform in amounts up to 40% higher than background levels in chlorine-treated tap water (25). But another study published the same year showed no formation of detectable chloroform levels over a range of expected tooth-brushing durations among subjects using toothpaste with triclosan and normal chlorinated tap water (26). The U.S. EPA classifies chloroform as a probable human carcinogen. As a result, triclosan was the target of a UK cancer alert, even though the study (26) showed that the amount of chloroform generated was less than is normally present in treated, chlorinated water and required brushing your teeth or washing your hands for times on the order of two hours or more.

Dioxin Link. There has been a number of concerns about triclosan and its link to dioxins. Dioxins can be highly carcinogenic and can cause health problems as severe as weakening of the immune system, decreased fertility, altered sex hormones, miscarriage, birth defects, and cancer. It needs to be clarified that "dioxin" is not one compound, but a family of compounds of widely ranging toxicity. Of the 210 dioxin family compounds, only 17 are considered to be of public health concern (27). Two dioxins, 2,8-dichlorodibenzo-*p*-dioxin (2,8-DCDD) and 2,4-dichlorophenol (2,4-DCP), are produced following photochemical degradation of triclosan, when chemical by-products are exposed to UV radiation after the reaction of triclosan with chlorine water (25). These dioxins could be formed in river water after exposure to sunlight of chlorinated triclosan, or even in treatment of triclosan-tainted water at water treatment

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plants. Despite these concerns, it was concluded in a study by University of Minnesota researchers that dioxin compounds formed from triclosan are not of public health concern because of the low concentrations of reactive oxygen species in natural waters and the low efficiency of the direct photolysis of triclosan (28).

4. Antibiotic Resistance

Scientists worldwide are concerned that the overuse and misuse of antibiotics and antimicrobials may lead to increased resistance among bacteria to these agents. Based on a review of published studies triclosan may, or may not, encourage the development of antibiotic resistance in pathogenic bacteria.

4.1. Bacterial resistance to triclosan

In the laboratory, triclosan-resistant bacteria can be produced fairly readily by serial passage in increasing triclosan concentrations or by isolation of resistant colonies within growth inhibition zones around a paper disc containing triclosan (29). In *E. coli* resistance may be due to overproduction of the enzyme enoyl reductase, or to changes in cellular permeability (29). While most resistant bacteria grow more slowly than sensitive bacteria, *E. coli* strains that are resistant to triclosan actually have increased growth rates. Constant exposure to triclosan will cause these resistant strains to tolerate it better, become increasingly hardy, and ever more resistant. In *P. aeruginosa*, which is intrinsically resistant to triclosan, resistance could be due to a non-susceptible enoyl reductase (both triclosan-susceptible and -non-susceptible enzymes have been found (30), an outer membrane permeability barrier or a pumping of the drug from the cell interior to its exterior. The latter has been stated to be the major reason for triclosan non-susceptibility (31-33). MRSA strains may or may not show decreased sensitivity to triclosan (34). Fan and colleagues (35) found that all *S. aureus* strains with decreased sensitivity overproduced the enzyme FabI by three- to five-fold, and the most resistant strains had mutations in FabI.

4.2. Possible association between triclosan and antibiotic resistance

A number of recent studies have raised serious concerns that triclosan and other similar products may promote the emergence of bacteria resistant to antibiotics. One concern is that bacteria will become resistant to antibacterial products like triclosan, rendering the products useless to those who actually need them, such as people with compromised immune systems. Scientists also worry that because triclosan's mode of action and target site in the bacteria is similar to antibiotics, bacteria that become resistant to triclosan will also become resistant to antibiotics. Triclosan does not actually cause a mutation in the bacteria, but by killing the normal bacteria, it creates an environment where mutated bacteria that are resistant to triclosan are more likely to survive and reproduce. An article coauthored by Dr. Stuart Levy in 1998 (36) warned that triclosan's overuse could cause the development of cross-resistance to antibiotics, and thereby result in the emergence of strains of bacteria resistant to both triclosan and antibiotics. In 2003, the Scottish *Sunday Herald* reported that some UK supermarkets and other retailers were considering phasing out products containing triclosan mostly due to the belief that it contributes to antibiotic resistance. It has since been shown that the laboratory method used by Dr. Levy does not translate into predicting bacterial resistance to biocides like triclosan in the environment. At least seven peer-reviewed and published studies have been conducted demonstrating that triclosan is not significantly associated with bacterial resistance over the short term, including one study coauthored by Dr. Levy (37-43).

Susceptibility of MRSA strains to triclosan has changed little over a 10 year period (8), and there does not seem to be any association between triclosan response in MRSA and other strains of *S. aureus* and antibiotic susceptibility or resistance (7).

It has been emphasized that laboratory studies have a useful role to play in evaluating mechanisms of action of and resistance to biocides, including triclosan, but that these should, wherever possible, be related to the clinical and other uses of these agents (44, 29). Do biocides therefore select for antibiotic resistance? Certainly, there are some similarities in the manner in which bacteria resist the action of antibiotics and biocides (45). Several authors have purported to show a relationship between the use of triclosan (and other biocides) and antibiotic resistance (46-48). Others have cast doubt on this proposal (49, 50) while emphasizing that, like all biocides, triclosan should be used only when appropriate.

Some recent surveys on the use of triclosan and other biocides add weight to these doubts. In a survey (51) conducted over a 10 year period, it was found that there was no relationship between triclosan usage and antibiotic resistance in MRSA and *P. aeruginosa*. Another survey (52) showed that there were no significant differences in overall titers of bacteria or frequencies of antibiotic resistance in a snap-shot analysis of homes that did or did not use surface antibacterial agents. A comprehensive survey by Cole *et al*. (53) found no relationship between the use of triclosan and other biocides and antibiotic resistance in homes where biocidal products were or were not being used.

What about the incorporation of triclosan into oral products? Will the use of triclosan in dental hygiene products result in the development of triclosan-resistant bacteria with reduced susceptibility to important antibiotics? An Expert Panel review concluded in 2000 that there was no evidence of resistant, opportunistic or pathogenic microorganisms developing subsequent to the introduction of triclosan (54). The short-term use of triclosan had no major impact on normal oral microflora or on the susceptibility of streptococci to antibiotics. Chronic exposure to triclosan did not demonstrate significant decreases in antibiotic susceptibility in dental bacteria (55). In general terms, the use of antimicrobial agents in dental care products in order to reduce plaque is considered to be justified (56).

While triclosan resistance in laboratory experiments may be associated with changes in antibiotic susceptibility, comprehensive environmental surveys have not yet clearly demonstrated any association between triclosan usage and antibiotic resistance. Triclosan has several important uses, and the future aim must be to retain these applications while eliminating the unnecessary ones.

Bacterial resistance to disinfectants in general is most certainly not a new phenomenon, and there are known examples of reduced susceptibility being described over a century ago (57). Triclosan, of course, is of more recent vintage. Consequently, it is necessary to continue to monitor whether reduced susceptibility to it and to antibiotics occurs. Although it is sometimes stated that resistance to triclosan and other biocides is increasing (58) this conclusion is generally based upon minimum inhibitory concentrations in lab settings rather than bactericidal estimations.

Since resistance often builds in a step-wise fashion, it is prudent to conserve use and continue surveillance of susceptibility to both antibiotics and to biocides like triclosan.

5. Triclosan in the Environment

Triclosan, as well as other antibacterial agents and their degradation byproducts, are now found throughout the environment, including surface waters, soil, fish tissue, and human breast milk (1). Swiss researchers found three out of five samples of human breast milk contained measurable concentrations of triclosan (at concentrations up to 30 µg/kg lipid weight). Over 95% of the uses of triclosan are in consumer products that are disposed of in residential drains. In a U.S. Geological Survey study of 95 different organic wastewater contaminants in U.S. streams, triclosan was one of the most frequently detected compounds, and in some of the highest concentrations. A study of triclosan in bodies of water in Switzerland also found high concentrations of the chemical in several lakes and rivers (12).

In a 1999-2000 study by the U.S. Geological Survey, triclosan was found in 57 percent of the 139 U.S. waterways that were thought to be susceptible to agriculture or urban activities (59). Triclosan has been found in both surface water and wastewater. Surface water sources may include wastewater treatment plant effluent, urban stormwater, rural stormwater, and agricultural runoff. When domestic wastewater is treated before discharge to surface waters, there is evidence that up to 95 percent of triclosan is removed via the wastewater treatment plant process (60). This removal efficiency is dependent on treatment plant operations. Swiss researchers observed a 94 percent removal rate of triclosan at wastewater treatment operations that employed mechanical clarification, biological treatment or nitrification, flocculation and filtration. The researchers estimated that 79 percent of the triclosan was removed via biological degradation while 15 percent adsorbed to the sludge. The remaining 6 percent in the effluent resulted in a concentration of 42 ng/Liter (61).

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The transport of triclosan to wastewater treatment plants occurs when people: wash hands with antibacterial soap, hand wash dishes with antibacterial soap, clean with antibacterial products, use antibacterial products in a dishwasher, bathe or shower with antibacterial soap or shampoo, brush teeth with toothpaste containing antibacterial products, wash clothes with antibacterial products, wash antibacterial cutting boards, etc. Unlike wastewater, most runoff that enters storm drains is untreated and directly flows into creeks, rivers and ultimately to the ocean. Triclosan may be transported into the stormwater system through commercial or residential washing of equipment outdoors with antibacterial soaps.

While our current understanding of triclosan's environmental effects is limited, there is evidence that triclosan can be toxic to aquatic organisms (62-64). The presence of triclosan may influence both the structure and the function of algal communities in stream ecosystems receiving treated wastewater effluent (65). These changes could result in shifts in both the nutrient processing capacity and the natural food web structure of these streams. According to a literature review by the Danish Environmental Protection Agency, triclosan bioaccumulates in fish (66) and the concentrations found in fish are thousands of times higher than what is found in the water. Furthermore, at least one transformation product of triclosan -methyl triclosan- is stable in the environment, making it also available for bioaccumulation. Once methylated, the lipophilicity of triclosan increases, meaning that it will be more likely to accumulate in fatty tissue and is not likely to photodegrade. In a Swiss study, the lipid-based concentrations of methyl triclosan detected in fish were considerably higher than the concentrations in lake water, suggesting significant bioaccumulation of the compound. For aquatic organisms, the potential uptake mechanisms of lipophilic contaminants are direct uptake from water through exposed surfaces, mainly gills, and uptake through the consumption of food (67).

6. Regulation of Triclosan Use

At the present time, triclosan is coming under close scrutiny. In March 2010, the European Union banned triclosan from any products that may come into contact with food, and in August 2009 the Canadian Medical Association asked the Canadian government to ban triclosan use in household products under concerns of creating bacterial resistance and producing dangerous side products. In the U.S., Federal agencies are reviewing triclosan's safety but haven't called for altered usage yet.

In the U.S. if an antimicrobial product is intended for use on the human body, it falls under the jurisdiction of the Food and Drug Administration (FDA). The FDA categorizes triclosan based on use and product claims. If a product makes a health related claim, such as "kills germs" (soap, first aid creams, etc.), FDA registers it as a drug. If it makes no claim at all or if its claims are cosmetic, such as "fights odors" or "improves skin" (deodorant, makeup, shaving cream), it is registered as a cosmetic. All uses not applied to the human body (bathroom and kitchen cleaners, hospital disinfectants), that make pesticidal claims, such as "kills bacteria and mildew" are regulated by the Environmental Protection Agency (EPA) as a pesticide. The FDA regulates drugs similar to the way that the EPA regulates pesticides, using a risk-benefit analysis based on data gathered from animal studies and human clinical trials. The manufacturer must prove that: the drug is safe and effective in its proposed use(s), and that the benefits of the drug outweigh the risks; the drug's proposed labeling is appropriate; and the manufacturing methods used are able to maintain the drug's quality, identity, strength, and purity. On the other hand, the FDA is only able to regulate cosmetics after products are released on the marketplace. Neither cosmetic products nor cosmetic ingredients are reviewed or approved by the FDA before they are sold to the public. The FDA cannot require companies to do safety testing of their cosmetic products before marketing. However, if the safety of a cosmetic product has not been substantiated, the product's label must read: "WARNING: The safety of this product has not been determined." FDA does not require, but maintains a voluntary data collection program. If cosmetic products are found to present a hazard, recalls are also voluntary.

On December 8 2010, the EPA published in the Federal Register a petition filed by 82 public health and environmental groups, led by Beyond Pesticides and Food and Water Watch, to ban triclosan for non-medical use (71). The Federal Register notice (72) invited the public to comment until February 7, 2011 on the need to ban triclosan under numerous federal statutes. The petition identifies pervasive and widespread use of triclosan and a failure of the EPA to address the impacts posed by triclosan's degradation products on human health and the environment, to conduct separate assessment for triclosan residues in contaminated drinking water and food, and to evaluate concerns related to antibacterial resistance and endocrine disruption. The petition cites violations of numerous environmental statutes, including laws on pesticide registration, the Clean Water Act, Safe Drinking Water Act, and Endangered Species Act. It also documents that triclosan is no more effective than regular soap and water in removing germs and therefore creates an unnecessary hazardous exposure for people and the environment.

On April 2010 the FDA announced it is conducting a scientific and regulatory review of triclosan in FDA-regulated products, with publication of results expected in spring 2011 (73). The agency also is collaborating with the EPA specifically to study the potential endocrine-disrupting effects of the compound (74). The FDA indicated that it currently has no evidence that triclosan is hazardous to humans and does not recommend consumers avoid it. However, the agency said there is no evidence that soap with triclosan is superior to soap without the ingredient. The FDA agreed to look into the safety of triclosan at the request of Congressman Edward Markey, D-Mass. According to the congressman's letter, his office contacted more than a dozen companies that make soaps, cutlery and other consumer goods, asking them to voluntarily remove triclosan from their products. The majority of companies said they would not change their products until the FDA issues its review. However, several companies are already phasing the chemical out, including Colgate-Palmolive, which plans to reformulate its dishwashing formula. Reckitt Benckiser, maker of Lysol spray along with several soap products, said it plans to reformulate its triclosan-containing products by 2011. Acme United Corp. and Victorinox both said they have already removed triclosan from their knives as a result of recent regulations passed in Europe.

In 2008, the EPA completed a Re-registration Eligibility Decision (RED) document for triclosan. This RED document described the conclusions of EPA's comprehensive review of the potential risks to human health and the environment resulting from the registered pesticidal uses of triclosan. In conducting the review for the RED, the EPA considered all available data on triclosan, including data on endocrine effects, developmental and reproductive toxicity, chronic toxicity, and carcinogenicity (74). The 2008 EPA assessment also relied in part on 2003–2004 biomonitoring data available from the National Health and Nutrition Examination Survey (NHANES) which reported measurements of urinary concentrations of triclosan in the U.S. population. Therefore, the 2008 EPA assessment was inclusive of all triclosan-related exposures (i.e., EPA and FDA regulated uses). The 2008 RED also considered new research data on the thyroid effects of triclosan in laboratory animals made available through the EPA's Office of Research and Development (ORD). Since the 2008 assessment, additional data on effects of triclosan on estrogen have also been made available from ORD. The ORD studies on the thyroid and estrogen effects led the EPA to determine that additional research on the potential health consequences of endocrine effects of triclosan is warranted. This research is underway and will help characterize the human relevance and potential risk of the results observed from initial laboratory animal studies. The Agency will pay close attention to the ongoing research and will amend the regulatory decision if the science supports such a change. Also, the Agency has previously indicated that because of the amount of research being planned and currently in progress, it will undertake another comprehensive review of triclosan beginning in 2013.

In 1997, the EPA acted to prevent the manufacturer of Playskool toys, Hasbro, Inc. (which sells toys made with Microban® plastic containing triclosan), from making false claims about protecting children from microbial infections. Hasbro could no longer claim that toys treated with triclosan protect children from infectious diseases caused by bacteria because it did not prove efficacy to EPA. Labels and advertisements for the toys suggested that the treatment protects children from health risks, when in fact it protects only the plastic in the toy. The company is prevented from making such claims due to a lack of reliable data to support them. Under the agreement, Hasbro had to publish large advertisements in certain newspapers and magazines about misrepresentation of the public health claim.

The current reality pertaining to regulation of triclosan in the U.S. is that we are in a conundrum, where there are data that show that triclosan is safe, and data that show its potential harmful effects. The challenge for the FDA and the EPA will be to figure out where these apparent conflicting data intersect.

7. Do We Have Alternatives to Triclosan?

When used in hospitals and other health care settings, or for persons with weakened immune systems, triclosan represents an important health care and sanitary tool. But outside of these settings, the American Medical Association has not endorsed the necessity or efficacy of triclosan and other antibacterial agents in personal care products, household products and commercial consumer products. According to the Centers for Disease Control and Prevention (CDC), vigorous hand washing in warm water with plain soap for at least 10 seconds is sufficient to fight germs in most cases, even for healthcare workers (75). For extra assurance, use of an alcohol- or peroxide-based hand sanitizer product is a good option.

Regarding the use of cutting boards, the following quote from the Mayo Clinic web site indicates that cutting boards impregnated with triclosan are ineffectual: *"There's no evidence that cutting boards containing triclosan, an antibacterial agent, prevent the spread of food-borne infections. These boards also may give a false sense of security and cause you to relax other efforts to keep the board clean. In addition, triclosan-treated boards don't kill germs. Antibacterial compounds only slow reproduction of microorganisms. Germs will die, but slowly enough to still contaminate other food or hands that come into contact with the board"* (76). For alternatives to triclosan-containing cutting boards, the Center for Food Safety and Applied Nutrition recommends that households use a two cutting board system. Use one board for cutting foods that will be cooked (e.g., raw meats, poultry, fish, vegetables) and one for ready-to-eat foods (e.g., breads, fresh fruits).

In a recent interview (77) Dr. Stuart B. Levy (President and Founder of The Alliance for the Prudent Use of Antibiotics, Director of the Center for Adaptation Genetics and Drug Resistance and Professor of Medicine at the Tufts University School of Medicine) indicated "… alcohol-based disinfectants are the way to go if you don't have an area to go wash hands with soap and water [...] I'm big on antibacterial products that don't leave a residue … that is those that contain alcohol, peroxide, or bleach. Let's say you bring in your meat and it's got salmonella, and you've been washing it on the counter. You may take peroxide or alcohol to clean it. That gets rid of both good and bad [bacteria]. The surface is now available for good and bad, and generally if you haven't brought more meat in, it's the good in the environment that take over. If you use a product with triclosan what's left on the counter, or in the sink, is a small and increasing amount of residue of that chemical. Now, bacteria come and sit down. Only the resistant ones can live on that environment. So you kind of help them to take over the world".

APUA published and distributed information to consumers regarding the use of antibacterials in household products and has made some recommendations as to alternatives to triclosan (78). These are guidelines on keeping clean without triclosan:

- Wash hands frequently and thoroughly. Regular soaps lower the surface tension of water, and thus wash away unwanted bacteria.
- Lather hands for at least 10 to 15 seconds and then rinse off in warm water.
- Dry hands with a clean towel to help brush off any germs that did not get washed down the drain.
- Complement with alcohol-containing hand sanitizers.
- Wash surfaces that come in contact with food with a detergent and water, or with bleach.
- Wash children's hands and toys regularly to prevent infection.
- When selecting products such as hand soap, toothpaste, and deodorants, it is recommended to read the label. If the product states "antibacterial" one should locate the active ingredients list to see if the product contains triclosan or other antibacterial agents. Consumers may opt to purchase products that either are not labeled "antibacterial" or contain alcohol or hydrogen peroxide as the antibacterial agent. In addition, non-organic antibiotics and organic biocides are effective alternatives to triclosan.

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8. Conclusions and Next Steps

There are growing concerns about the emergence and spread of triclosan residues in the environment, and its potential negative impact on human and animal health. However, the scientific debate continues regarding the safety and efficacy of its application in personal care and household products. Triclosan has several important medical uses, and the future aim must be to retain these applications while eliminating the more frivolous and unnecessary ones. It would be wise to restrict the use of triclosan to areas where it has been shown to be effective and most needed.

Below are the suggested next steps:

1. Follow the upcoming decisions by the FDA and the EPA in 2011, after their review of safety and efficacy data is concluded.

2. Support scientific and public health research on the cumulative effects and chronic use of triclosan.

3. Continue to follow scientific literature for additional information regarding heath impacts and environmental fate of triclosan and its by-products.

4. Adopt a precautionary principle attitude towards the use of triclosan (78). Coordinate with appropriate agencies and groups to develop a public factsheet as well as concise messages that resonate with the public and specific audiences. Possible messages include:
    - Antibacterial product residues are found in the environment
    - The use of antibacterial products may provide a false sense of security and lead to inadequate hand-washing practices
    - Effective alternatives include washing hands with soap and water and using alcohol or peroxide based hand gel sanitizing agents for extra assurance
    - Minimize use of antibacterial-containing cleaning products and personal care products; for surfaces, bleach-containing products are an alternative
    - Avoid antibacterial cutting boards

5. Review opportunities to include messages from water quality outreach efforts to specific audiences. Such audiences might include:
    - Primary purchasing agents in households and commercial institutions
    - Purchasing departments of public institutions
    - Health care and veterinary professionals
    - Parents and teachers
    - Manufacturers and distributors

6. Consider developing State and Federal legislation to limit the use of triclosan in consumer products.

7. Support advocacy initiatives that through the gathering of new knowledge and offering of solutions promote the prudent use of triclosan (78).

8. Support initiatives to gather relevant agencies and public health stake holders to engage in face-to-face conversations on the implementation of appropriate use of triclosan (78).

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