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The Florence Statement on Triclosan and Triclocarban

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SUMMARY: The Florence Statement on Triclosan and Triclocarban documents a consensus of more than 200 scientists and medical professionals on the hazards of and lack of demonstrated benefit from common uses of triclosan and triclocarban. These chemicals may be used in thousands of personal care and consumer products as well as in building materials. Based on extensive peer-reviewed research, this statement concludes that triclosan and triclocarban are environmentally persistent endocrine disruptors that bioaccumulate in and are toxic to aquatic and other organisms. Evidence of other hazards to humans and ecosystems from triclosan and triclocarban is presented along with recommendations intended to prevent future harm from triclosan, triclocarban, and antimicrobial substances with similar properties and effects. Because antimicrobials can have unintended adverse health and environmental impacts, they should only be used when they provide an evidence-based health benefit. Greater transparency is needed in product formulations, and before an antimicrobial is incorporated into a product, the long-term health and ecological impacts should be evaluated. https://doi.org/10.1289/EHP1788

Introduction

In September 2016, the U.S. Food and Drug Administration (FDA) banned nineteen antimicrobial ingredients, including triclosan and triclocarban, in over-the-counter consumer antiseptic wash products based on insufficient evidence demonstrating their safety for long-term daily use and that they reduce the spread of illness and infection. Many of those 19 chemicals have been in widespread use for decades, and many are still allowed in a number of other over-the-counter personal care products as well as in consumer and building products. The FDA first indicated in a 1974 Tentative Final Monograph that there was insufficient evidence to show that triclosan was effective and safe for long-term use (Halden 2014). The FDA’s decades-long path to issuing a final rule, and the narrow scope of the September 2016 Final Rule (FDA 2016), indicate that existing regulatory practices are not sufficient to protect human and ecosystem health from adverse impacts of antimicrobial chemicals. Scientists from both academia and nonprofit organizations coauthored The Florence Statement in 2016 to share current scientific research on two widely used antimicrobial chemicals and to motivate broader consideration of the long-term impacts of antimicrobial use (see Appendix I). The Statement was introduced at DIOXIN 2016, the 36th International Symposium on Halogenated Persistent Organic Pollutants in Florence, Italy, and has been signed by more than 200 international scientists and medical professionals (see Appendix II).

The Florence Statement on Triclosan and Triclocarban

As scientists, medical doctors, and public health professionals, we are concerned about the continued widespread use of the chlorinated antimicrobials triclosan and triclocarban for the following reasons:

1. Triclosan and triclocarban are used as antimicrobials, a class of chemicals present in >2,000 products including soaps, toothpastes, detergents, clothing, toys, carpets, plastics, and paints. In personal care products like hand soap, there is no evidence that use of triclosan or triclocarban improves consumer or patient health or prevents disease.
2. Triclosan and triclocarban used in consumer products end up in the environment and have been detected in a wide variety of matrices worldwide.
3. Triclosan and triclocarban persist in the environment and are a source of toxic and carcinogenic compounds including dioxins, chloroform, and chlorinated anilines.
4. Triclosan, triclocarban, and their transformation products and byproducts bioaccumulate in aquatic plants and animals, and triclosan partitions into human blood and breast milk.
5. Triclosan and triclocarban have detrimental effects on aquatic organisms.
6. Humans are exposed to triclosan and triclocarban through direct contact with personal care products and from other sources including food, drinking water, and dust. Triclosan...
has been detected in the urine of a majority of humans tested.  
7. Triclosan and triclocarban are endocrine disruptors and are associated with reproductive and developmental impacts in animal and in vitro studies. Potential implications for human reproduction and development are of concern and merit further study.  
8. Human epidemiology and animal studies suggest triclosan exposure can increase sensitivity to allergens.  
9. Overuse of triclosan may contribute to antibiotic/antimicrobial resistance and may modify the microbiome.  
10. A number of authorities, including the FDA, have restricted the use of triclosan and triclocarban in certain types of soaps. These and other antimicrobial chemicals are generally not restricted from use in other products.

We therefore call on the international community to limit the production and use of triclosan and triclocarban and to question the use of other antimicrobials. We urge scientists, governments, chemical and product manufacturers, purchasing organizations, retailers, and consumers to take the actions recommended below.

Recommendations

1. Avoid the use of triclosan, triclocarban, and other antimicrobial chemicals except where they provide an evidence-based health benefit (e.g., physician-prescribed toothpaste for treating gum disease) and there is adequate evidence demonstrating they are safe.
2. Where antimicrobials are necessary, use safer alternatives that are not persistent and pose no risk to humans or ecosystems.
3. Label all products containing triclosan, triclocarban, and other antimicrobials, even in cases where no health claims are made.
4. Evaluate the safety of antimicrobials and their transformation products throughout the entire product life cycle, including manufacture, long-term use, disposal, and environmental release.

Appendix I: Supporting Information

1. Triclosan and triclocarban are used as antimicrobials, a class of chemicals present in >2,000 products including soaps, toothpastes, detergents, clothing, toys, carpets, plastics, and paints (Halden 2014; Smith 2013). In personal care products like hand soap, there is no evidence that use of triclosan and triclocarban improves consumer or patient health or prevents disease (Centers for Disease Control and Prevention (CDC) 2003; FDA 2016).

Triclosan and triclocarban are not well regulated and may be found in >2,000 consumer and building products (Halden 2014). In 1998, the worldwide annual production of triclosan was approximately 1,500 tons, with a majority produced in Europe (350 tons) and the United States (450 tons) (Dhillon et al. 2015). In 2006, an estimated 450 tons of triclosan was used within the European Union (EU) [Scientific Committee on Consumer Safety (SCCS) 2010]. In 2007, an estimated 85% of the total volume of triclosan in the EU was used in personal care and cosmetic products (SCCS 2010). Triclocarban has been primarily used in bar soaps at concentrations ranging from approximately 0.5% to 2% by weight (Halden 2014; Ye et al. 2016).

Epidemiological studies indicate that the use of triclosan and triclocarban by the general population has no significant health benefits for reducing common respiratory and gastrointestinal infections (Aiello et al. 2007, 2008). A 2003 report by the U.S. Centers for Disease Control and Prevention Healthcare Infection Control Practices Advisory Committee concluded, “No evidence is available to suggest that use of [antimicrobial-impregnated articles and consumer items bearing antimicrobial labeling] will make consumers and patients healthier or prevent disease” (CDC 2003).

According to the FDA, which is responsible for regulation of foods, drugs, cosmetics, medical devices, and similar products, there is no evidence that antibacterial soaps are more effective than nonantibacterial soap and water (FDA 2016). This is likely because the contact time during typical hand washing (an average of 6s) is too short to deliver measurable benefits (Borchgrevink et al. 2013) and because the antibacterial ingredient is highly diluted during the washing process.

2. Triclosan and triclocarban used in consumer products end up in the environment (Heidler and Halden 2009) and have been detected in a wide variety of matrices worldwide (Halden and Paull 2005; Singer et al. 2002). Triclosan and triclocarban are commonly used in products intended for washing [e.g., an estimated 96% of triclosan is used in products that are intentionally disposed of down the drain, such as soaps and detergents (Reiss et al. 2002)]. These substances are also used in products that may be frequently washed (e.g., textiles, food contact materials, plastic surfaces). A large amount of triclosan and triclocarban is therefore discharged directly to conventional wastewater treatment plants (Bester 2005; Halden and Paull 2005). During wastewater treatment, these chemicals partition preferentially into sewage sludge (Bester 2003, 2005; Heidler et al. 2006).

An analysis of U.S. sewage sludge found triclosan and triclocarban at high levels, on average in the tens of milligrams per kilogram dry weight (Halden 2014; U.S. Environmental Protection Agency (EPA) 2009). In the United States, ~15% of sewage sludge is incinerated, 30% is deposited in landfills, and 55% is deposited on land where the antimicrobial compounds and their transformation products may enter adjacent surface waters (Beecher et al. 2007; Buth et al. 2011). Through land application of biosolids, antimicrobials can also end up in livestock feed and in crops destined for human consumption (Aryal and Reinhold 2011; Prosser et al. 2014). Persisting fractions of triclosan and triclocarban that do not partition into the sludge are discharged to surface waters via effluent, where they can reach levels of thousands of nanograms per liter (Bester 2005; Buth et al. 2011; Coogan et al. 2007; McAvoy et al. 2002; Singer et al. 2002).

Triclosan and triclocarban have been detected in the environment throughout the world. Triclosan has been detected in both raw and finished drinking water (Loraine and Pettigrove 2006), in ocean water (Xie et al. 2008), and in fresh water (Kolpin et al. 2002). A nationwide survey detected triclosan in ~60% of U.S. streams (Kolpin et al. 2002). Triclocarban is expected to be similarly prevalent (Halden and Paull 2005). In surface waters, even when discharged at nanograms per liter concentrations, triclosan and triclocarban can concentrate and accumulate in sediments (Anger et al. 2013; Buth et al. 2010; Cantwell et al. 2010; Higgins et al. 2009; Kerrigan et al. 2015; Miller et al. 2008; Venkatesan et al. 2012).

3. Triclosan and triclocarban persist in the environment (Miller et al. 2008) and are a source of toxic and carcinogenic compounds including dioxins, chloroform, and chlorinated anilines (Buth et al. 2010; Ding et al. 2013; Fiss et al. 2007).

Triclosan and triclocarban are persistent in the environment. Both compounds are predicted to have half-lives on the order of 60d in water, 120d in soil, and 540d in sediment (Halden and Paull 2005).
Sediment cores indicate long-term preservation of triclosan and triclocarban dating to approximately 1964 (when triclosan was patented) (Anger et al. 2013; Bedoux et al. 2012; Cantwell et al. 2010; Kerrigan et al. 2015; Miller et al. 2008; Singer et al. 2002). In biosolids-amended soils, triclocarban and triclosan can persist for extended periods of time while exhibiting very slow or no measurable degradation (Langdon et al. 2012; Walters et al. 2010). Triclosan may also be transformed to methyl triclosan or to other products (Davis et al. 2015; Langdon et al. 2012; Walters et al. 2010). Methyl triclosan may be more persistent than triclosan (Balmer et al. 2004; Coogan et al. 2007), and it has been consistently detected in surface waters and sediments (Bester 2005; Sacks and Lohmann 2011).

Triclosan is a “pre-dioxin” and is associated with formation of polychlorinated dioxins and furans (PCDDs/Fs) throughout its life cycle. Triclosan contains detectable contaminant levels of polychlorinated dioxins and furans, including toxic and carcinogenic 2,3,7,8-substituted PCDD/Fs, which are formed in amounts that vary with the quality of production technology (Menoutis and Parisi 2002; United Nations Environment Programme (UNEP) 2013; Zheng et al. 2008; International Agency for Research on Cancer (IARC) 2012). The high persistence, bioaccumulation, and toxicity of these dioxins and furans in the environment is well-established (Sinkkonen and Paasivirta 2000; Van den Berg et al. 2006). Furthermore, triclosan undergoes conversion to 2,8-dibeno- dichloro-p-dioxin (2,8-DCDD) in water when exposed to natural sunlight (Aranami and Readman 2007; Latch et al. 2003) and during heating and combustion (Kanetoshi et al. 1987; 1988). In a recent study using an artificial skin model, topically applied triclosan transformed into 2,8-DCDD under ultraviolet irradiation (Alvarez-Rivera et al. 2016). Chlorinated triclosan derivatives (formed during chlorine disinfection of wastewater and drinking water) transform into tri- and tetra-chlorinated dibeno-p-dioxins in sunlight-exposed surface waters (Buth et al. 2009, 2010) and upon heating and combustion (Kanetoshi et al. 1987; Kanetoshi et al. 1988). Calculations suggest that incineration of sewage sludge containing triclosan and chlorinated triclosan derivatives contributes significantly to total dioxin emissions in the United States (Doudrick et al. 2010).

In water disinfection processes, triclosan can react with free chlorine to produce chloroform (Rule et al. 2005), a probable human carcinogen (U.S. EPA 2001) that is also recognized by the State of California as a developmental toxicant [State of California Environmental Protection Agency (CalEPA) 2017]. In a study testing household dishwashing soaps, lotions, and body washes in chlorinated water under simulated normal household use conditions, all of the products containing triclosan produced either chloroform or other chlorinated byproducts (Fiss et al. 2007). The results suggest that under some conditions, the use of triclosan in such products could potentially increase chloroform exposure to nearly double the background levels in tap water.

Triclocarban degrades via aerobic biodegradation and photolysis into 4-chloroaniline and 3,4-dichloroaniline (Ding et al. 2013; Miller et al. 2010). 4-Chloroaniline is recognized by the State of California as known to cause cancer (CalEPA 2017).

4. **Triclosan, triclocarban, and their transformation products and byproducts bioaccumulate in aquatic plants** (Coogan et al. 2007) and animals (Coogan and La Point 2008; Fair et al. 2009), and triclosan partitions into human blood and breast milk (Almyr et al. 2006).

Triclosan and triclocarban are highly hydrophobic and bioaccumulate in organisms living in aquatic systems exposed to effluent from wastewater treatment plants. Triclosan has been detected in wild bottlenose dolphins at levels similar to those in humans (Fair et al. 2009), and it has also been detected at high levels in fish (Adolfsson-Erici et al. 2002; Valters et al. 2005). These levels are potentially high enough to cause harm (Meador et al. 2016). Triclosan was recently detected in the eggs of skimmers, seabirds that serve as sensitive indicators of coastal health and of contaminant threats to fish-eating birds and animals (Millow et al. 2015). Methyl triclosan, an even more lipophilic and stable bacterial transformation product of triclosan, has been detected in fish at levels considerably higher than in the surrounding water (Balmer et al. 2004; Leiker et al. 2009). The bioaccumulation and slow conversion of methyl triclosan in lower-level consumers such as catfish could transfer environmental triclosan to higher-level consumers in the food chain, including humans (James et al. 2012). Triclocarban bioaccumulates in freshwater worms (Higgins et al. 2009) and fish (Schebb et al. 2011a). Triclosan, methyl triclosan, and triclocarban all bioaccumulate rapidly in algae and snails exposed to wastewater treatment effluent with calculated bioaccumulation factors in the thousands (Coogan et al. 2007; Coogan and La Point 2008).

In biosolids-amended soil ecosystems, triclosan, methyl triclosan, and triclocarban bioaccumulate in earthworms (Higgins et al. 2011; Kinney et al. 2008; Macherius et al. 2014), the basis of many terrestrial food webs. Phytoaccumulation of triclosan and triclocarban has been observed in certain vegetable crops grown in biosolids-amended soils. Calculations suggest that potential human exposure from contaminated vegetable consumption is less than exposure from personal care product use but greater than exposure from consumption of drinking water (Aryal and Reinhold 2011; Mathews et al. 2014).

Upon human exposure and uptake, triclosan and triclocarban are metabolized and excreted by the body within 36–72h (Sandberg-Englund et al. 2006; Schebb et al. 2011b, 2012). One study calculated a terminal plasma half-life of 21h for triclocarban (Sandberg-Englund et al. 2006). Blood-borne triclosan and triclocarban can cross the placenta, and triclosan and its metabolites have been detected in umbilical cord blood at birth (Almyr et al. 2006; Pycke et al. 2014; Shekhar et al. 2017), raising concerns about prenatal exposure to the developing fetus. Triclosan, triclocarban, and their metabolites have also been detected in human milk samples (Adolfsson-Erici et al. 2002; Almyr et al. 2006; Dayan 2007; Toms et al. 2011). For example, in one population sample (n = 151), triclosan levels were detected in >93% of milk samples over a wide range of concentrations (Toms et al. 2011). The ability of triclosan to partition into human milk raises concerns about impacts from exposure on nursing infants.

5. **Triclosan and triclocarban have detrimental effects on aquatic organisms** (Chalew and Halden 2009; Tamura et al. 2013).

The continuous exposure of aquatic organisms to triclosan and triclocarban, coupled with their bioaccumulation potential, have led to detectable levels of triclosan and triclocarban throughout aquatic food chains in species such as algae, crustaceans, fish, and marine mammals (Adolfsson-Erici et al. 2002; Chalew and Halden 2009; Fair et al. 2009; Meador et al. 2016). Highly sensitive indicator organisms, such as algae and crustaceans, experience potentially harmful exposures to triclosan and triclocarban in surface waters receiving raw and treated sewage (Chalew and Halden 2009). Benthic organisms such as worms, crabs, and shellfish can be exposed to triclosan and triclocarban via particulate matter and sediments (Miller et al. 2008).

In laboratory studies of algae, crustaceans, and fish, both triclosan and triclocarban have been shown to exhibit acute and subchronic toxicity at concentrations found in the environment (Tamura et al. 2013; Xu et al. 2015). Triclosan exposure inhibits...
algal growth (Orvos et al. 2002), which can alter aquatic ecosystem dynamics. Triclosan is acutely toxic to aquatic microbacteria at microgram per liter (µg/L) concentrations (Franz et al. 2008; Ishibashi et al. 2004; Ricart et al. 2010; von der Ohe et al. 2012), with acute toxicity values ranging from 1.4 µg/L to 3,000 µg/L (von der Ohe et al. 2012).

Triclosan affects reproduction and development in some fish (Dann and Hontela 2011) and may interfere with the action of thyroid hormones in amphibians at environmentally relevant concentrations (Veldhoen et al. 2006). Triclosan and triclocarban can also affect reproduction in snails at environmentally relevant concentrations (Geiß et al. 2016; Giudice and Young 2010).

6. Humans are exposed to triclosan and triclocarban through direct contact with personal care products (Quekkenberg et al. 2010; Schebb et al. 2011b) and from other sources including food, drinking water, and dust (Aryal and Reinhold 2011). Triclosan has been detected in the urine of a majority of humans tested (Calafat et al. 2008).

Human exposure to triclosan occurs primarily from the topical application and use of personal care products such as lotions, soaps, toothpastes, and mouthwashes (Bhargava and Leonard 1996; Moss et al. 2000; Quekkenberg et al. 2010). Minor routes of exposure could include contaminated food and drinking water (Aryal and Reinhold 2011; Holling et al. 2012; Li et al. 2010; Loraine and Pettigrove 2006; Macherius et al. 2012; Wu et al. 2010, 2013) and indoor dust (Fan et al. 2010; Geens et al. 2009).

A large U.S. national survey found triclosan in the urine of the majority of people tested (Calafat et al. 2008). Other studies have measured triclosan in the urine of pregnant women (Meeker et al. 2013; Mortensen et al. 2014; Pycke et al. 2014), children (Wolff et al. 2007), and a large sampling of people in Denmark (Frederiksen et al. 2014). Triclosan has been detected in breast milk (Dayan 2007; Toms et al. 2011; Allmyr et al. 2006), serum and plasma (Allmyr et al. 2006, 2008; Sandboorgh-Englund et al. 2006), cord blood (Pycke et al. 2014), amniotic fluid (Philippat et al. 2013; Shekhar et al. 2017), and fingernails and toenails (Yin et al. 2016).

Dermal exposure from personal care products is believed to be the main route of human exposure to triclocarban (Ye et al. 2011). A human study showed a small but significant amount of triclocarban was absorbed during showering for 15 min with triclocarban-containing antibacterial soap (Schebb et al. 2011b). In addition, minor routes of triclocarban exposure may include contaminated food (Aryal and Reinhold 2011; Macherius et al. 2012; Wu et al. 2010, 2013). In a recent study of 209 adults living in China, triclocarban was detected in the urine and in the nails of 99% and 100% of study participants, respectively (Yin et al. 2016). Triclocarban was detected in 86% of urine samples and in 23% of cord blood samples from 181 pregnant U.S. women between 2007 and 2009 (Pycke et al. 2014). In a 2012 study of 158 U.S. adults with no known exposure to triclocarban, the compound was detected in 35% of urine samples (Zhou et al. 2012). In a smaller 2011 study, triclocarban was detected in 50% of serum samples and in 28% of urine samples from U.S. adults (Ye et al. 2011).

Monitoring and explorative studies of other potential sources of triclosan and triclocarban exposure are warranted (Ginsberg and Balk 2016).

7. Triclosan and triclocarban are endocrine disruptors and are associated with reproductive and developmental impacts in animal and in vitro studies (Chen et al. 2008; Johnson et al. 2016; Wang and Tian 2015). Potential implications for human reproduction and development are of concern and merit further study.

Triclosan and triclocarban have been shown to interfere with estrogen and androgen systems in mammalian models (Chen et al. 2008; Duleba et al. 2011; Kumar et al. 2009; Stoker et al. 2010) and in vitro (Ahn et al. 2008; Gee et al. 2008; Henry and Fair 2013; Huang et al. 2014). In vitro screening assays suggest that triclosan can interact with the estrogen receptor (ER) in certain cell types at relatively low (nanomolar) concentrations (Ahn et al. 2008). In vitro studies have shown a weak estrogenic effect of triclosan and triclocarban in the ER reporter gene assay (Huang et al. 2014) and in MCF7-BOS breast cancer cells (Henry and Fair 2013). Triclosan has also shown estrogenic and androgenic activity in vitro in breast cancer cells at environmentally relevant concentrations (Gee et al. 2008). However, in vivo studies suggest that the estrogenic effects of triclosan may not be a result of direct binding with the estrogen receptor. Triclosan has been shown to enhance the estrogenic activity of synthetic estrogenic compounds (Louis et al. 2013) and to increase estradiol (Pollock et al. 2016) and bisphenol A (Pollock et al. 2014) uptake in certain tissues in adult mice. In male roaches, exposure to triclosan and to other anti-androgenic chemicals enhanced the feminizing effect of the estrogen 17α-ethinylestradiol on reproductive duct development (Lange et al. 2015). These studies suggest that the estrogenic effect of triclosan in vivo may be due to inhibition of estrogen metabolism. An in vitro study with sheep placental tissue also showed that triclosan is a potent inhibitor of estrogen sulfotransferase (James et al. 2010).

In rodent studies, triclosan exposure has been associated with reduced testosterone, luteinizing hormone, follicle stimulating hormone, and sperm production (Kumar et al. 2009), as well as with implantation failure (Crawford and DeCatanzaro 2012) and spontaneous abortion (Wang et al. 2015). The varying results of in vivo studies to date may result from the use of different rodent strains and experimental procedures (Wang and Tian 2015).

The possible effects of triclosan and triclocarban on human endocrine and reproductive systems have not been sufficiently studied. There is emerging evidence of associations between triclosan exposure and reduced semen quality (Zhu et al. 2016) and reduced inhibin B and luteinizing hormones in men (Den Hond et al. 2015) and with longer time-to-pregnancy in a large retrospective study of pregnant women (Velez et al. 2015).

Triclosan can disrupt the thyroid hormone system in animal models (Fang et al. 2015; Paul et al. 2010; Stoker et al. 2010; Zorrilla et al. 2009). A meta-analysis of rodent data found significant and dose-dependent reductions in serum thyroxine after early postnatal administration of triclosan (Johnson et al. 2016). Perinatal triclosan exposure can reduce blood levels of maternal, fetal, and neonatal thyroxine levels in rodents (Axelstad et al. 2013; Paul et al. 2013). Potential effects of prenatal exposure on thyroxine levels should be carefully considered because even small reductions in thyroxine in pregnant women can have adverse effects on the neurodevelopment of children (Ghassabian et al. 2014; Henrichs et al. 2013; Miller et al. 2009; Wise et al. 2012; Woodruff et al. 2008).

Few human studies have examined the potential impacts of prenatal triclosan and triclocarban exposure on fetal growth and development. However, there is suggestive evidence that prenatal triclosan exposure is associated with reduced fetal growth late in pregnancy (Philippat et al. 2014) and with smaller head circumference at birth in boys (Lassen et al. 2016; Philippat et al. 2014) and that prenatal triclocarban exposure is associated with decreased gestational age at birth (Geer et al. 2017).

8. Human epidemiology (Spanier et al. 2014) and animal studies (Anderson et al. 2013) suggest triclosan exposure can increase sensitivity to allergens.
Large cross-sectional analyses of U.S. National Health and Nutrition Examination Survey (NHANES) participants have found positive associations between urinary triclosan concentrations in children and aeroallergen sensitization (Savage et al. 2012; Spanier et al. 2014), atopic asthma (Spanier et al. 2014), diagnosis of allergic rhinitis or other allergies in those ≤18 y old (Clayton et al. 2011), and food sensitization (Savage et al. 2012). Similarly, a large cross-sectional analysis of Norwegian children found an association between urinary triclosan concentrations and allergic sensitization and rhinitis (Bertelsen et al. 2013). Among both child and adult NHANES participants with asthma, urinary triclosan concentration was associated with increased risk of asthma exacerbation in the previous year (Savage et al. 2014).

Animal studies support these findings and suggest that although triclosan may not be an allergen itself, it may act as an adjuvant and enhance allergic responses to a known allergen (Anderson et al. 2013). In mouse models, dermal exposure to triclosan at concentrations similar to those used in consumer products enhanced the hypersensitivity response to the egg-white allergen ovalbumin (Anderson et al. 2013), promoted sensitization and anaphylaxis to peanut (Tobar et al. 2016), promoted sensitization to the milk allergen alpha-lactalbumin (Tobar et al. 2016), and induced stimulation of the immune system (Anderson et al. 2016). Demonstrating a potential mechanism for this immune alteration, dermal triclosan exposure changed gene expression and cytokine levels promoting a food sensitization phenotype in mice and in a human skin model (Marshall et al. 2015).

9. Overuse of triclosan may contribute to antibiotic/antimicrobial resistance (Giuliano and Rybak 2015) and may modify the microbiome (Hu et al. 2016).

Concerns about triclosan-induced cross-resistance to antibiotics used in human medicine were voiced as early as 2001, although the extent to which triclosan and triclocarban contribute to antibiotic resistance is not yet clear (Halden 2014; Hartmann et al. 2016; Yazdankhah et al. 2006). One large randomized controlled trial that examined bacterial flora isolated from hands showed decreased susceptibility over time to triclosan in the studied community (Aiello et al. 2004). There is evidence that bacteria that develop resistance to triclosan can also exhibit lowered susceptibilities to other antimicrobial agents (Braoukda and Hilton 2004). Triclosan in stream sediments has been shown to trigger increases in triclosan resistance and changes in benthic bacterial community composition (Drury et al. 2013). The clinical significance of these observations is unclear, but a legitimate concern remains: antimicrobials may exacerbate the problem of bacterial resistance to antibiotics (Carey and McNamara 2015; Hartmann et al. 2016; Pycke et al. 2010).

Recently, several animal studies have suggested that exposure to triclosan modifies the microbiome, including in the gut and intranasally (Gaulke et al. 2016; Hu et al. 2016; Syed et al. 2014). However, longer-term human studies are needed to identify the impact of triclosan and other antimicrobial substances on the human microbiome both on the skin and in the gut.

10. A number of authorities, including the U.S. Food and Drug Administration, have restricted the use of triclosan and triclocarban in certain types of soaps [European Commission (EC) 2016; FDA 2016]. These and other antimicrobial chemicals are generally not restricted from use in other products.

Several jurisdictions have recognized the risks from triclosan and triclocarban and have taken steps to reduce their use. Following an evaluation of triclosan by the Biocidal Products Committee of the European Chemicals Agency (ECHA), the European Commission (EC) decided in 2016 that triclosan is not approved for use in human hygiene biocidal products (ECHA 2015; EC 2016). Beginning in February 2017, triclosan will no longer be available in such products in the EU. Triclosan has also been banned from use in consumer sanitizing and cleansing products by the state of Minnesota, effective January 2017 (State of Minnesota 2016). In September 2016, the FDA issued a final rule, effective in 2017, that over-the-counter consumer antiseptic wash products containing the antibacterial active ingredients triclosan and triclocarban, or any of seventeen other antimicrobial ingredients, can no longer be marketed because they "are not generally recognized as safe and effective" (FDA 2016). In the United States, the FDA regulates the use of antimicrobials in personal care products and medical devices, whereas the U.S. EPA regulates the pesticidal uses of antimicrobials in other products (Johnson et al. 2016). Triclosan is being phased out of certain products by Procter & Gamble, Johnson & Johnson, and other manufacturers. The use of triclosan and triclocarban may continue in household, building, and other products not covered under existing restrictions.

Despite regulatory restrictions on triclosan, triclocarban, and certain other antimicrobials, the overall market for antimicrobial products has been predicted to grow (Halden 2014; Smith 2013). It is not yet clear what impact the 2016 EC decision, the FDA Final Rule, and other authoritative actions may have on market growth. Alternative antimicrobial substances may be used in place of triclosan and triclocarban in personal care, consumer, and building products. These replacement substances may have little to no publicly available safety information.

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