Triclosan Review

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BIS Prospectus Topic Review

Is the antimicrobial agent Triclosan safe following report of adverse effects to both humans and the environment?

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Table of Contents

Introduction

Summary

1. Background
   1.1 Regulatory History of Triclosan
   1.2 Antimicrobial U.S. Environmental Protection Agency (EPA) and U.S. Food and Drug Administration (FDA) classification

2. Chemical Description
   2.1 Chemical Structure
   2.2 Triclosan Nomenclature
   2.3 Chemical Properties
   2.4 Mode of Action
   2.5 Consumer Application
   2.6 Consumer Products

3. Human Health Concern
   3.1 Bodily Mean Concentration
   3.2 Breast Milk Contamination
   3.3 Hormonal Disruption
   3.4 Consumer Exposure
   3.5 Cosmetics

4. Environmental Concern
   4.1 Sewage Sludge/Biosludge
   4.2 Soil Environment
   4.3 Pharmaceutical and Personal Care Products
   4.4 Aquatic Environment
   4.5 Dioxins
   4.6 Hormone Disruption
   4.7 Antimicrobial Resistance

5. Compound assessment
   • FDA and EPA concern

Conclusion

References
Introduction
Triclosan, an antimicrobial ingredient, which is commonly found in several household and personal care products, has raised concern to its negative potential to environmental, human and animal health. Increased media coverage to the antimicrobials safety, effectiveness and regulation status has warranted much needed research to gain a firm understanding of its true benefit and necessity in consumer products. A review of data available was performed in providing a summary of regulatory, environmental and human issues that supports consumer advocacy arguments to the antimicrobial ingredients adverse potential.

In addition, this paper takes into account the 3 areas of emphases for my Bachelor of Integrated Studies, which is Health Administrative Services, English and Chemistry. The topic discusses an antibacterial chemical ingredient that raises public health concern to its adverse effect potential, and communicating this information with this research paper ties the three emphases together.

Summary
Concerns to ban the antimicrobial agent Triclosan from consumer products has gained momentum after reports cite risks associated with everyday use to human health and the environment. (Triclosan, Butler 2011) Triclosan was initially introduced in the United States as a pesticide agent in 1969 (FDA RED 2010) and later adopted into the healthcare setting as a surgical scrub for its similar properties to antibiotics as they both kill or inhibit growth of microorganisms. (Bhargava 1996) This antimicrobial agent was soon added to commercial goods and mass marketed to the public for everyday use. Triclosan’s infiltration of the market place is now found in many products such as clothing, kitchenware, furniture, toys, soaps, natural health, and drug products. A 2000 market study, by Eli Perencevich, M.D., determined over 75% of liquid soaps and 30% of bar soaps on the market contained one form of antibacterial agent, and of those approximately half contains Triclosan.

After years of common use it is being discovered that Triclosan has potential harmful effects to human health. These concerns are raised through unnecessary consumer exposure to the antibacterial products that has potential for endocrine disruption (thyroid and sex hormones), skin irritation and increased rates of allergies. (Crofton 2007, Zorrilla 2009, Rook 1998, Perencevich 2001) The Center of Disease Control and Prevention states washing hands with ordinary soap and warm water is an effective way to prevent infections and a way to avoid unnecessary use of antibacterial soaps. (Aiello 2007)

Environmental concern is increasing to the adverse effects Triclosan has on the environment. Over 95% of antibacterial consumer products are disposed into residential drains and noted as one of the most frequently detected contaminates found in our waterways. (Reiss 2007) Reports of Triclosan levels found downstream following wastewater treatment is becoming more evident and its detrimental effects on the aquatic ecosystem are becoming apparent. (Dann 2011) Potential carcinogenic Dioxins are also discovered in our waterway as a result of photo degradation of Triclosan.
Approximately 90% of human exposure to dioxins is through the food supply (fish, shellfish, meat and dairy). (WHO 2010, Med News 2004) Researchers have also raised concerns of emerging Triclosan resistance and antibiotic cross-resistance due to unnecessary everyday exposure to these antibacterials. While the United States Food and Drug Administration (FDA) holds to their statement of FDA is engaged in an ongoing scientific and regulatory review of this ingredient. FDA does not have sufficient safety evidence to recommend changing consumer use of products that contain Triclosan at this time. (US FDA 2012, Levy 2001, Ayoola 2013)

1. Background

1.1 Regulatory History of Triclosan

Triclosan received initial U.S. registration with the U.S. Environmental Protection Agency (U.S. EPA) as a pesticide in 1969 and later was solely introduced in the health care industry in 1972 as an antibacterial surgical scrub.

The FDA issued its first notice, in 1972, regarding the need for additional toxicological data for Triclosan, when at that time ruled the compound to be a Category III product based on current available data. A Category III product is defined by the FDA as having insufficient data available to permit at finalized classification. In addition, Congress that same year passed a law requiring the FDA to set guidelines for antibacterial type agents. (FDA Cat)

In response to congress, the FDA delivered their first proposal in 1974 to establish an Over-the-Counter (OTC) Drug Monograph Process for regulation of over-the-counter Topical Antiseptic Products that categorizes them as: antimicrobial soaps, healthcare personnel hand wash, patient preoperative skin preparation, skin antiseptic, skin wound cleaner, skin wound protectant and surgical hand scrub. The Monograph Process is a three step process designed to include a list of: acceptable ingredients, doses and formulations in determining the safety and effectiveness of the product. Unlike new drug applications; premarketing approval and clinical studies are not necessary, product labeling requirements are identical for like compounds, and the Final Monograph is open to all manufactures to market due to no sales exclusivity. (FDA Cat)

The FDA published in 1978 the first Tentative Final Monograph (TFM) for OTC Topical Antimicrobial Drug Products which is a precursor to the Final Monograph. The proposed TFM includes input recommendation from various OTC advisory review panels and public comment to the FDA’s proposed regulation. Based on current data available at that time, Triclosan holds as a Category III product, which is the FDA’s designation for ingredients declared to have insufficient evidence available to determine whether it is safe and effective.
The FDA amends the Tentative Final Monograph in 1991 for OTC first aid antiseptic ingredients, and the distinction between antimicrobial soaps as drugs and cosmetics was clarified. The TFM was again amended in 1994 and was the most current working version in which the notice expanded clarification to healthcare antiseptic drug products. The revision applies to all antibacterial hand soaps thus defining product dosage and removes them from evaluation as drug product category. In addition, hand wash need frequency was addressed and concluded products containing Triclosan as an antiseptic is not of concern based on supported documented data, that again left the Tentative Final Monograph unfinalized and Triclosan remains a Category III product due to insufficient data available regarding dermal carcinogenicity potential from dermal application.

The FDA approved Triclosan in 1997 for use in Colgate Total toothpaste products citing the manufactures supporting submission documentation did show benefit and effectiveness in preventing gingivitis.

The FDA issued a proposed rule in December 2013 that requires manufacturers to provide substantial data demonstrating the safety and effectiveness of antibacterial soaps, and indicated they have partnered with other federal agencies to additionally review effects on animal and environmental health. To date the monograph is not finalized and remains as a Tentative Final Monograph for Triclosan with the exception for dentifrices in preventing gingivitis. A final comment by the agency reports they are “engaged in an ongoing scientific and regulatory review of this ingredient. FDA does not have sufficient safety evidence to recommend changing consumer use of products that contain Triclosan at this time.” (US FDA 2012)

1.2 Antimicrobial U.S. Environmental Protection Agency (EPA) and U.S. Food and Drug Administration (FDA) classification

The EPA and FDA share dual roles in regulating antimicrobial products in the U.S. Both agencies categorize Triclosan and other antimicrobial products based on use and product claim.

- FDA regulated antimicrobial products are products intended for human use and categorized with a health related claim. For instance, if the product states a health related claim, such as “kills germs” the product is registered as a drug. If the product makes no claim or claims cosmetic, such as “fights odors” the product is registered as a cosmetic. (FDA 2007)

- EPA regulated antimicrobial products are compounds designed to disinfect, sanitize, reduce, mitigate growth of microbiological organisms, protect inanimate objects, surfaces and water. Basically all product uses when not applied to the human body and states a pesticide action, such as “kills bacteria” are registered with the EPA as a pesticide. (EPA 2010)
2. Chemical Description (Triclosan)

2.1 Chemical structure: Chemical formula is C12H7Cl3O2.

![Chemical Structure Diagram]

2.2 Triclosan Nomenclature:
- IUPAC name 2,4,4-trichloro-2-hydroxydiphenyl ether
- Triclocarban in plastics and clothing Triclosan and Microban.
- Triclosan and Biofresh in acrylic fibers.

2.3 Chemical Properties

Triclosan is an organic chlorinated aromatic compound that has functional groups to ethers and phenols. The raw material characteristics are: White to off-white crystalline powder with a mild aromatic odor, has low volatility, melting point is 54-57.3°C, soluble in alkaline and many organic solvents. (O'Neil 2001)

2.4 Mode of Action

**Bacteria cell membrane** provides a barrier that selectively allows oxygen, nutrients and waste to permeate in and out of the cell for its survival. Antimicrobial biocides are designed to disrupt various components of the cell to effectively reach the specified target site(s). Getting through the plasma membrane to deliver a chemical agent efficiently to alter internal cytoplasm or outer membrane structure is a major step that enables biocides to perform their desired bacteriostatic or bactericidal mode of action. Biocides have three methods in which to inhibit or kill the bacteria cell: interact with outer cellular components, interact with cytoplasmic membrane or interact with inner cytoplasmic constituents. Determining the organism type prior to biocide treatment is critical to determining the most effective biocide to control or destroy the pest. (Maillard 2002, Biomed 2008)
Triclosan acts as a biocide by effecting cytoplasmic and membrane targets. Lower concentration of Triclosan has shown to be bacteriostatic by inhibiting fatty acid synthesis that halting cell membrane growth and reproduction that inevitably inhibits or kills the cell.

Triclosan mode of action disrupts type II Fatty Acid Synthesis (FAS) by inhibiting the enoyl-acyl carrier protein reductase enzyme (ENR) pathway, which is responsible for synthesizing fatty acid chain growth in maintenance of bacteria cell membrane construction and cell reproduction. This action begins with Triclosan interfering with the gene (FabI) that regulates FAS by binding to the cells active site which then increases affinity for Nicotinamide Adenine Dinucleotide (NAD) that ultimately forms a stable ternary complex of ENR-NAD-Triclosan. Molecular complex formation now halts fatty acid synthesis thus ending the elongation process for cell survival. (RJ Heath 1999, RJ Heath 1998, MJ Stewart 1999, Y-M Zhang 2006)

2.5 Consumer Application

Triclosan is used as a biocide, fungicide and preservative in many consumer cleaning, medical device, house ware and cosmetic products. Currently there are 20 antimicrobial registrations with the U.S. EPA for Triclosan, and 4056 patents issued by the U.S. Patent and Trademark Office between 1976 and November 2013. (www.epa.gov, www.uspto.gov) The number of antimicrobial products has continually increased ever since the soap industry began adding the ingredient to their product line that coincide their antibacterial soap campaign. The New York Times commented that “makers of antimicrobial and antibacterial hand soaps, which represent about half of the $750 million market for liquid hand soaps in the United States, according to the market research firm Kline & Company.” (NYT 2011)

Consumer Antibacterial Products are now widely accepted in the marketplace. These disinfectants are found in soaps, body washes, laundry detergents, shampoos, toothpastes, dish soaps, plastics and textiles. The purchasing trend is controversial among federal regulators, members of the American Cleaning Institute, and consumer advocate groups for discontinuing manufacturing practice of including Triclosan as the active ingredient in common household product. (CDER 2005, FDA Nomination Profile 2008, Maillard 2005)

Conflicting reports to the effectiveness of Triclosan go either way regarding its effectiveness in killing bacteria. The FDA holds to their decision that “there currently is no evidence that over-the-counter antibacterial soap products are any more effective at preventing illness than washing with plain soap and water.” (FDA 2013) A peer data review study identified 13 studies that examined the effectiveness of Triclosan in reducing “incidences of infectious illnesses in the community setting” and “bacterial counts on the skin.” (Aiello 2007) The review shown: 4 community based studies determined the effectiveness of consumer soap containing Triclosan or Triclocarbon vs. plain soaps in reducing the number of incidences of infections had no significant reduction in illness symptoms. The 9 other studies reporting on bacterial
count reduction shown 5 of the 9 did have significant reduction in bacterial counts over plain soap, but also noted 4 of those studies used soap with higher Triclosan concentrations, 2 studies utilized multiple hand wash episodes and incidences extended washing for 30 seconds. (FDA 2013, Greenfield 2011)

2.6 Consumer products sold in the U.S. marketplace.

A non-profit organization Beyond Pesticides (formerly National Coalition Against the Misuse of Pesticides) includes this information and disclaimer on their website supporting their national campaign to protecting public health and the environment from errant misuse.

Soap: Dial® Liquid handsap and bodywash; Tea Tree Therapy™ Liquid Soap; Clearasil® Daily Face Wash; Dermalogica® Skin Purifying Wipes; DermaKleen™ Antibacterial Lotion Soap; CVS Antibacterial Soap, Ajax Antibacterial Dishsoap, Ultra Concentrated Dawn Antibacterial Dishsoap, Kimcare Antibacterial Clear Soap, Bath and Body Works Antibacterial Hand Soaps, Gels and Foaming Sanitizers.
Dental Care: Colgate Total®; Breeze™ Daily Mouthwash; Reach® Antibacterial Toothbrush
Deodorant: Arm and Hammer® Essentials Natural Deodorant; Queen Helene® Tea Tre Oil Deodorant and Aloe Deodorant; DeCleen Deodorant Stick; Epoch® Deodorant with Citrisomes.
First Aid: SyDERMA® Skin Protectant plus First Aid Antiseptic; Healwell Plantar Fasciitis Night Splint; Solarcaine® First Aid Medicated Spray; Nexcare™ First Aid, Skin Crack Care; Universal Cervical Collar with Microban.
Kitchenware: Farberware® Microban 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.
Other Personal Care Products: Murad Acne Complex® Kit, ®; Diabet-x™ Cream; Scunci Microban Comb, Sportslick Pocket Slick.
Clothes: Biofresh® socks, undergarments, tops and bottoms.
Office and School Products: Ticonderoga® Pencils with Microban Protection, Avery® Touchguard View Binders, C-line® products, Clauss® cutting instruments, Costco® products, Sharp® printing calculators. Westcott® scissors
Other: Bionare® Cool Mist Humidifier; Deciguard AB® Antimicrobial Ear Plugs; Bauer® Re-Akt hockey helmet and 7500 hockey helmet; Miller Paint Acro Pure Interior Paint; Holmes Foot Buddy™ HMH120U Antimicrobial Foot Buddy Foot Warmer, Blue Mountain Wall Coverings, California Paints®, Davis Paint® Perfection, Hirschfield’s Paint®, O’Leary Paint®, EHC AMRail Escalator Handrails, Dupont™ Air Filters, Winix Dehumidifiers, J Cloth® towels, select
Quickie cleaning products, Kimberly Clark® WYPALL X80 Towels, Canopy®
kitchen towels, ALUF Plastics®, BioEars earplugs, Petmate® LeBistro feeders
and waterers, Infantino cart covers and baby carriers, Oreck XL®, Bissell Healthy
Home Vacuum™, NuTone® Central Vacuum systems, Rival® Seal-A-Meal®
Vacuum Food Sealer, CleenFreek SportsHygiene Yoga Mat, Resilite Sports
Products, Rubbermaid® Coolers, Stufits sports gear, Venture Products® fitness
mats, Custom Building Products, DAP®Kwik Seal Plus®, Laticrete, Nisa
Biquichamp® mortar grout and sealant, ProAdvanced Products.

DISCLAIMER: Due to public pressure, many major manufacturers have quietly begun
reformulating their products without Triclosan. Product formulations may change without
notice. Listed is a small sampling of products formulated with, or used to be formulated
with Triclosan and is not to be considered a comprehensive list. Remember to always
refer to product labels to determine whether Triclosan is contained in your product.
Some retail outlets may still carry older formulations. Look out for labels that state:
"antimicrobial protection." Some antibacterial soap may use Triclosan's cousin,
Triocarban, in place of Triclosan.
(Beyond Pesticide)

3. Human Health Concern

Regulators and soap industry advocates consider Triclosan at lower concentration to be
relatively non-toxic to humans, safety data has reported mild dermatological cases of
contact skin irritation and photo allergic dermatitis in lower therapeutic doses, but data
to chronic health effects having direct causal relation between the antimicrobial and
humans is lacking. Public pressure not only in the U.S., but worldwide, is requesting
additional oversight of Triclosan products has led to increased media exposure
identifying possible long term side effects of the ingredient to humans, wildlife and
environmental exposure. (FDA, Dial 2009, CIBA 2009)

3.1 Bodily Mean Concentration

CDC information regarding Human Exposure to Environmental Chemicals reports the
average Triclosan urinary mean-level value has increased 24% and gives a mean
creatinine increase of 28% from 2003 thru 2004 survey data. (Calafat 2008, CDC 2013)

Greenpeace International and the World Wildlife Fund-United Kingdom conducted a
blood sample study showing hazardous chemicals can be passed from mother to child.
Results shown detectable levels of Triclosan were present in approximately half of 42
maternal blood serum and 27 cord blood serum samples collected. (Greenpeace 2005)

3.2 Breast Milk Contamination

High levels of Triclosan in human breast milk became apparent in a 2002 Swedish
study that reported 3 out of 5 randomly selected samples of human milk did test
positive. This exposure was attributed to consumer product use that has the
antibacterial as an active ingredient, but researchers could not confirm exposure due to lack of supporting information. (Adolfsson-Erici 2002)

As a follow up to the 2002 Swedish report researchers determined the primary source of human exposure could not be determined because prior evidence regarding the antibacterial transfer to human milk was not substantial. This gave rise to another study that focused on nursing mother’s exposure through personal care products. Data did show Triclosan plasma and milk concentrations were reported higher for 9 of the 36 woman tested with plasma having much higher concentration than milk, and the 9 higher concentration samples did correlate with mothers whom used personal care products containing the bactericide (toothpaste, deodorant or soap) versus mothers that did not. The study concluded personal care products are not the only source for antibacterial systemic exposure, and demonstrated infant exposure concentration from breast milk is less when compared to their mother. (Allmyr 2006)

3.3 Hormonal Disruption

Studies have shown Triclosan to be an endocrine disrupting chemical in both wildlife and humans. Animal studies have shown Triclosan inhibits estradiol and estrogen sulfonation during pregnancy. This potential raises concern due to possible false influences on placental supply of estrogen levels that can adversely affect fetal growth, development and puberty development. (James 2010, Goodsell 2006, Delbes 2006)

Triclosan hormonal effects stem from the additional chemical categorization as a xenoestrogen, also known as endocrine disruptor that can falsely imitate the body’s natural hormone levels. Research suggests xenoestrogen mimics endogenous hormones estrogen and androgen which in-turn influences thyroid hormone synthesis and metabolism leading to modification of hormone receptor site availability that’s otherwise reserved for natural endogenous hormones. (Sonnenschein 1998, LaValle 2012)

A major concern to endocrine disruptor interaction is the effects during critical developmental periods for human life cycle. The exposure assumption exists that effected abnormal hormone levels in mature adults are most likely to reverse once exposure is discontinued, but disruption during developmental periods for an at risk population have irreversible change. (Colborn 1993)

3.4 Consumer Exposure

Consumer exposure to Triclosan is primarily through use of personal care products that contain the antibacterial as an active ingredient where dermal and oral exposure is likely to occur. Evidence to human exposure and related effects are slowly presenting itself as additional research is coming forward following increased media scrutiny. Results from a study by the National Health and Nutrition Examination Survey for the U.S. reported participant urine samples had detectable levels of Triclosan in 74.6% of the 2517 samples analyzed. (Calafat 2008, FDA Nomination Profile 2008)
Exposure testing data for humans and various animal species show Triclosan is rapidly absorbed and distributed to fatty tissue. Dermal penetration for humans is approximately 6% of the dose. Oral mouthwash ingestion data suggests the ingredient reaches maximum plasma concentration within 1-3 hours and has a plasma half-life of approximately 21 hours. Both routes of exposure show most absorbed Triclosan is eliminated within the first 24 hours and plasma baseline levels typically return within 8 days following initial oral exposure. (Calafat 2008, Moss 2000, Queckenberg 2009, Sandborgh-Englund 2006) Supporting information from a 2008 toxicological evaluation for Triclosan reported that human volunteer following dermal exposure to the ingredient was: “not a sensitizer or irritant; skin irritation of triclosan did not exceed the irritations of the soap solution, and concluding that oral use of triclosan was safe.” (FDA Nomination Profile 2008) An additional dermal route administration study in 2009 did report four incidences of mild adverse events citing: skin irritation on chest and facial post shaving, and viral symptoms of running nose and common cold. Concluding Triclosan is safe for use in dermatological preparations. (Queckenberg 2009)

3.5 Cosmetics

Antimicrobials are often added to cosmetics and personal care products to inhibit microorganism growth, used as a product preservative and to prevent unwanted odor. Cosmetic requirements for the sales of cosmetics and drugs commonly fall within the U.S. Food and Drug Administration role based on the manufacturer's intended consumer use for the product. The FDA defines cosmetics as “articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body...for cleansing, beautifying, promoting attractiveness, or altering the appearance.” While drugs are defined as “articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease” and “articles (other than food) intended to affect the structure or any function of the body of man or other animals.” (FD&C Act 201) But in rare occasions a product does meet the definition of both cosmetics and drugs.

The Food Drug and Cosmetic Act maintains cosmetic product and its associated ingredients do not require FDA approval before they are sold on the U.S. market, nor do they have authority requiring companies to test their cosmetics before sales. The FDA does utilize the Voluntary Cosmetic Registration Program for only consumer cosmetic products. The program is not considered a cosmetic approval process by the agency but merely a surveillance tool to review registered ingredient information of cosmetic products on the market. Although this system is not perfect it does place responsibility on the cosmetic companies to ensure their products and ingredients are safe, properly labeled and in full compliance with the good manufacturing standards and federal regulations. (FD&C Act, sec 201, FDA Cosmetics)

Research has shown Triclosan is readily absorbed through the skin and non-toxic to humans at low concentrations. A project studying the dermal sensitizing potential of
Triclosan on subjects with chronic eczema resulted in the ingredient being well tolerated and deemed low sensitizing potential. (Schena 2008)

Another study reporting on absorption levels of hormone-altering cosmetic chemicals in teens reported “the antibacterial agent Triclosan was more widespread than would be suggested by CDC data.” (EWG 2008) Study data exhibited that all subjects had measurable levels of triclosan in the teenagers while the CDC tested at 78% for U.S. population. (EWG 2008) Both studies exhibited similar absorption data to the 2008 Nomination Profile Triclosan Toxicological Evaluation by the National Toxicology Program prepared by the U.S. FDA and Department of Health and Human Services. (FDA Nomination Profile 2008, Calafat A.M. 2008, Moss T. 2000)

4. Environmental Concern

The use of Triclosan containing products are raising concern for its environmental impact potential due to detectable levels in surface water, ground water and drinking water. Almost all Triclosan containing consumer products are disposed in residential drains leaving it to accumulate in waste water treatment plants for removal. Incomplete removal of the ingredient has been documented with downstream detectable levels following waste water treatment and identified in farmland soils resulting from post treatment bio-solid fertilization. (APUA 2011, CDC 2013)

Data from a 1999-2000 U.S. Geological Survey to measure concentrations of 95 Organic Wastewater Contaminants (OWC) in water resources show in 139 U.S. streams across 30 states has Triclosan as one of the most frequently detected compounds measured. Commentary from the survey states “measured concentrations were generally low with few compounds exceeding drinking water guidelines,” but only 14 of the 95 OWCs have drinking water guidelines established for U.S. regulation. (Kolpin 2002)

4.1 Sewage Sludge/Biosolids

Biosolids are nutrient rich organic material resulting from the treatment of domestic sewage in a treatment facility. When treated and processed, these residuals can be recycled and applied as fertilizer to improve and maintain productive soils and stimulate plant growth. (EPA, Sewage Sludge)

Soil contamination from antibacterial products can be attributed to the spreading of processed sewage sludge for soil amendment use over farm and public lands. Approximately 50% of the sewage sludge produced through wastewater treatment is applied to agricultural farmland for fertilization and 45% is used as landfill cover. (Apedaile 2001, EPA 2003) Currently Triclosan and Triclocarbon levels are not regulated in processed sewage sludge prior to their release. Surveillance data from a national sewage sludge survey report in which national standards for use and/or disposal over: land application, landfilling or surface disposal, and incineration, listed Triclocarbon as 1 of 145 analytes in which they are monitoring. The EPA “identified 15
chemicals for which it will conduct a more refined risk assessment and risk characterization process.” (EPA Sewage Sludge) Unfortunately Triclosan or Triclocarbon was not one of those chemicals identified for assessment. The agency did report they plan to prioritize regulatory measures based on public comment in an effort to maximize public health and environmental protection but no specifics to Triclocarbon or Triclosan was mentioned. (EPA 2003)

4.2 Soil Environment

Persistence of Triclosan and Triclocarbon in soil land application has led to bioaccumulation and eventual movement into surface waters has acute and chronic potential of affecting both terrestrial and aquatic organisms through bio-solid waste. (Cha 2009, McClellan 2010)

A bioaccumulation study looking at pharmaceuticals and other Anthropogenic Waste Indicators (AWI) in earthworms obtained soil and worm samples from 3 U.S. Midwest farming sites that previously received bio-solid waste for soil amendment. This study shown detectable AWI levels that demonstrate soil contaminants can be transferred to terrestrial species. Although earthworms are of a lower tropic state they do offer possible use as biological indicators to soil quality. This study did show 28 AWIs were detected in earthworm samples that were below detectable limits for the soil samples in which the worms were harvested. This observation demonstrates that subtle AWI contaminants do bio-accumulate within earthworm tissue when compared to host soil environments and possibly pass the contaminant up the food chain. (Kinney 2008)

4.3 Pharmaceutical and Personal Care Products

Incomplete removal of Pharmaceuticals and Personal Care Products (PPCP) from waste water treatment facilities is one source of surface water contamination. Often unused over-the-counter and prescription drugs are disposed down household drains, or excreted as metabolites, are a domestic contaminant source. (McClellan 2010)

Complete removal of biosolid PPCP contaminants is rarely achieved following waste water treatment. The U.S. removal rate for Triclosan/Triclocarbon in 2002 was reported to be 95-96% efficient, and other countries such as Canada, Germany, Switzerland and the United Kingdom, all reported similar removal percentages. Removal efficiencies for all countries can be attributed to dual treatment plant operation by way of a secondary treatment process with activated bio-solid sludge. (Singer 2002, Bester 2005)

4.4 Aquatic Environment

Increased residual levels of Triclosan and Triclocarbon are reported highest in aquatic sediment biota and municipal bio-solids with Triclocarbon being the higher of the two identified. Stream ecosystem balance is a reflection of the condition, abundance and diversity of its residing sediment biota, and algae systems. Both sediment biota and algae systems are influenced by stream environmental changes and minor disruptions
to this ecosystem can modify community structure and function not only to itself but the entire aquatic ecosystem and species that feed off the system including humans. (Cha 2009)

A 2009 study of aquatic and terrestrial biota presents toxicity threshold values for non-target organisms from known environmental concentration of both TCC and TCS cited “algae and crustacea groups are most sensitive to biocide exposures, fish and crustacea tend to be sensitive to Triclocarbon, whereas algae and microbes are easily inhibited by Triclosan.” Historical data for aquatic and terrestrial biota species to long-term biocide exposure is largely unknown due to minimal data even though usage and environmental release has been active since commercial introduction in 1972. Triclosan’s persistence in soil environments is often reported on the effects of the agent but realignment should also include downstream causal effects to non-target organisms. The study went on to note multiple generations exposure has taken place at concentrations that are “expected to trigger acute and chronic effects or possibly adaptation” and “studies examining these potential outcomes are lacking.” (Chalew 2009)

4.5 Dioxins

Dioxins are pollutants byproduct of industrial processes either chemically or by combustion where chlorine is involved. Other dioxin source contaminants are generated through volcanic and forest fires, incomplete burning of hospital and solid waste, and the burning of wood, coal and other fuels. Three main families exist for dioxins that number in the hundreds, and these families are grouped according to their chemical structures and biological characteristics. Not all dioxin compounds are toxic but do range in toxic severity which is rated by their properties to absorption, distribution metabolism and elimination in the body. Environmental dioxin pollutant levels have been found in water, air, soil and sediment. (Buth 2010, WHO 2010)

Residual Triclosan levels following wastewater chlorination treatment is shown to transform into Dioxins and Chlorinated Triclosan Derivatives (CTD). When CTDs are discharged in to natural surface waterways they can photo-degrade in sunlight and gives rise to dioxin type compounds.

Human exposure to dioxins is a concern regarding their harmful toxic potential similar to other dioxin families. Dioxins are known to be toxic, disrupt hormones, can cause reproductive and developmental problems, disrupt the immune system, and are cancerous. (WHO 2010)

Approximately 95% of human dioxin exposure will come from the consumption of our food supply. Dietary intake of fats from animal products, fish, shellfish and dairy products are the main source for the public. Because dioxins are chemically stable and readily absorbed in fatty tissue they easily bio-accumulate within the body given their half-life is approximate 7 to 11 years. (MDH 2006, WHO 2010)
Short term human exposure may result in skin lesions, altered liver function and darkening of the skin (Chloracne). Animal studies have shown cancerous effects when chronic exposure exists, and long term dioxin exposure can weaken the immune system, also interfere with developing nervous system and alter hormone function endocrine and reproductive systems. (WHO 2010, Vanden Berg 2006) Research from the University of Minnesota shown dioxin exposure from two separate lake core sediment samples have steadily increased since the 1960s while other dioxin contaminants have decreased. Researchers suspect this trend is most likely due to waste product disposal method improvements over the years. (Buth 2010)

4.6 Hormone Disruption

Animal studies have shown Triclosan and its metabolites inhibit male and female estradiol and estrogen sulfonation during pregnancy. These observations have significant concern to human and wildlife health because abnormal hormone levels in adults are most likely to reverse once exposure is discontinued but disruption during developmental periods like organogenesis my result in irreversible effects. (James 2010, Sonnenschein 1998, LaValle 2012, Goodsell 2006, Colborn 1993) Triclosan has potential to interfere with endocrine hormone pathways by disrupting thyroid, estrogen and androgen binding by mimicking, blocking or changing the binding action to cellular hormone receptor sites, and has the ability to enhance endocrine disruptors (xenoestrogen) to falsely stimulate thyroid signaling within the body. The body at the cellular level receives continual communication among cell activities that communicate and initiate action of other group of cells in maintenance of body system homeostasis. This is particularly important when body hormonal regulation is influenced by synthetic chemicals that possibly contribute to metabolism, growth and development disruption. Research suggests false hormonal signals during critical developmental time periods in one’s lifetime can have immediate or lasting adverse effects that may not become apparent until adulthood. (Colborn 1993)

Researchers at the University of California-Davis shown Triclosan can alter muscle contraction signaling activity at intracellular receptor sites for Excitation-Contraction Coupling (ECC) in both cardiac and skeletal muscle tissue. Laboratory study data indicates bi-directional signal disruption between two protein receptors interferes with calcium ions flow within intracellular receptor channels is the contributor in preventing muscle tissue contraction. Uncoupling potential with excitation-contraction shows “impaired grip strength and hemodynamics, and mobility in a model fish species,” where researcher commented as unexpected based on prior extensive toxicological testing for Triclosan. Adverse effects of ECC disruption could be indicative of cardiac dysregulation outcomes and even more problematic for susceptible groups with underlying cardiac conditions to stress induced arrhythmias. The study cited test controls were produced with Triclosan blood plasma levels consistent with reported levels found in humans and may demonstrate unrecognized risk factors for humans and wildlife. (Cherednichenko 2012, Scoote 2002)
Evidence show a weak androgenic effect in laboratory settings when Japanese Medaka fish in early life stages and reproduction were exposed to Triclosan levels did produce significant plasma concentrations of vitellogenin in test fish. Vitellogenin is a precursor to egg yolk proteins that are essential for embryonic development in oviparous organisms. Vitellogenin is a gene mainly produced by females during oogenesis and is silent in males. Researcher’s identified use for vitellogenin as a plasma biomarker in male fish when determining estrogenic contamination in aquatic environments. Based on study results it was suggested Triclosan is highly toxic for early life stages of medaka fish and considered a “weak estrogenic compound” due to its ability to induce vitellogenin in male fish. (Ishibashi 2004, Matozzo 2008)

A study to determine Triclosan’s effects with sheep placental Estrogen Sulfotransferase (EST) shown inhibition of estradiol and estrone sulfonation in placental estrogen supply to the fetus could significantly reduce and possibly affects fetal growth and development while in the womb. Other polychlorobiphenyls known as potent EST inhibitors with molecular structural similarities to Triclosan was the basis and established a foundation to compare human and animal estrogen sulfotransferase activity. Placental enzyme, estrogen sulfotransferase, facilitates the movement of nearly all estrogen concentration to fetal blood supply which is crucial for essential nutrients and oxygen. Through perpetual in-utero communication between placenta and fetus estrogen levels are maintained, but if the line of communication is disrupted and estrogen levels are inhibited key fetal bodily system may not develop, oxygen supply may be hindered, premature labor could induce or miscarriage. Prior research has confirmed estrogen sulfotransferase influence to specific protein expression has been observed in humans and other species when studying estrogens physiological role to pregnancy. (Albrecht 1999, Gamage 2006, James 2010, Zhang 1999)

4.7 Antimicrobial Resistance

Triclosans use in low concentration does effectively inhibit or kill many microorganisms, but scientists believe overuse and misuse even at low dosage can lead to bacterial resistance and possible cross-resistance to antibiotics. Resistance to biocides and antibiotics is a natural occurrence but one having influence over the other is of concern. Microorganisms such as bacteria, viruses, and fungi continually evolve to ensure survival to potentially harmful stimuli through genetic mutation or acquiring resistance from other bacterium. (Maillard 2002, Sheldon 2005)

Microorganisms are equipped with intrinsic properties that naturally provide resistance to foreign agents where interaction with external cellular components, cytoplasmic membrane, and cytoplasmic constituents limit what goes in and out of the cell. Triclosan and other antimicrobial agents effectiveness does vary between different microorganism specie types where intracellular composition and cell membrane structure provide varying resistance to biocide type penetration. Therefore biocides are often developed to target and disrupt the outer cellular components and cytoplasmic membrane allowing the agent inner access to intracellular targets.
A natural mode to biocide non-susceptibility can occur as a result of efflux pumps. It is common for a single organism to have multiple efflux pumps which are transport proteins imbedded in bacteria’s inner cell membrane that transport potentially harmful compounds out of the cell. Compounds affected can be specific to a particular cell or range in action for dissimilar compounds such as cellular waste, antibiotics and biocides. Bacteria strains gram negative and gram positive utilize efflux and are the topic of scientist because of their intrinsic resistant characteristics which can also be influenced by antibiotic and biocide interaction. (Webber 2003, Russell 2002)

Bacterium, Escherichia Coli, is an example that is naturally equipped with a multi-drug efflux pump mechanisms that has capacity to render itself non-susceptible to Triclosan. The bacterium limits antimicrobial effects by up-regulation of its efflux pump there by limiting toxin accumulation and reducing susceptibility to the agent. (Lambert 2002, McDonnell 1999, Meyer 2010, Russell 2002)

Microorganisms also acquire the ability to resist biocide compounds in which they were previously susceptible. Observances to this event have shown acquisition of resistant genetic material or genetic adaptation from another pathogenic strain has either raised the minimum inhibitory concentration or acquired resistance. Scientists believe biocides easily kill off normal, or more susceptible, bacteria types which allow and enable stronger microorganism strains to thrive and reproduce in the non-competitive environment. (Russell 2003)

Tolerant bacterial strains have been reported in laboratory settings where microorganism expose to biocides with varying concentration produced resistant colonies. Biofilms are one such mode in which bacteria are exposed environmentally to antimicrobial agents in varying conditions that can promote bacteria cell resistance by genetic adaptation. Commonly soap residue, or biofilm, insulates the antibacterial agent in a sub-lethal dose allowing bacteria to interact and mutate within the biofilms matrix that can lead to an evolved resistant strain by way of killing off the more susceptible strain and leaving the dominant species. (Anderson 1990, Weber 2007, Sauer 2007)

Scientist has demonstrated Triclosan can contribute to select biocide and antibiotic cross-resistant through promotion of bacteria target mutation that influences cell expression of their efflux pumps. Studies of Triclosan’s effect on Escherichia Coli, Pseudomonas Aeruginosa, and Staphylococcus Aureus all report a degree of gene encoding mutation that influences the up regulation of the efflux and multidrug efflux mechanisms within the cell. This is concerning because the mode of action and target site for both Triclosan and antibiotics are similar that could promote resistance. (Saheed 2012, McMurry 1998, Fan 2002, Chuanchuen 2001)

5. Compound assessment

FDA and EPA concern
The EPA’s granted Triclosan reregistration eligibility based on existing data in 2008, and the FDA holds to their current position that “triclosan is not currently known to be
hazardous to humans,” but both agencies agree the ingredient merits additional review and remains in continued use. (EPA RED, FDA consumer)

Conclusion

The ever growing argument to Triclosan’s widespread use and negative effects to the environment, wildlife and humans will continue to grow until soap manufactures and regulators come to an agreement regarding the antibacterial agent’s cumulative effects. These two groups also need to agree on how Triclosan’s, application methods can be shown as safe and effective among healthcare and household products.

Historically regulatory gaps existed from the time Congress instructed the FDA to set guidelines for antibacterial chemicals in 1972, to 1978 when their first Tentative Monograph for Triclosan was delivered of which could not be sufficiently reviewed because of insufficient information on the safety and effectiveness of current data. Four decades have passed and Triclosan still remains in tentative standings with the FDA. It seems our system is failing us while additional consumer products are developed and its by-product waste find their way into our homes and the environment. Since early media reporting of Triclosan’s adverse effects our global neighbors have set restrictions and even banned unnecessary use of the antibacterial ingredient. Some U.S. states, local communities and institutions have halted use in an effort to maintain safety to the public.

Alternatively Triclosan does retain medicinal value within the healthcare setting and it’s where the antibacterial agent made its initial debut for human application. Triclosan and other antimicrobial agents have significant roles in maintaining high disinfection standards and shown to be beneficial in controlling hospital associated infections when used appropriately. We all could benefit if similar ideology as hospitals disinfectant policies are subtly implemented to biocide type products for consumer use. The healthcare disinfectant policies are designed to control infection based on antimicrobial risk. Low microbial risk requires low level of disinfectant and so on. (Maillard 2005, Carling 2012, CDC 2008)

Eliminating unnecessary use within everyday consumer products is necessary based on current research information and its high potential to cumulative effects. Most of the data generated to Triclosan was derived in laboratory conditions and little environmental or clinical evidence has come forth confirming such claims. The fact Triclosan represents an environmental and public health risk does remain and most parties do agree based on research data to it cumulative adverse potential warrants action in setting regulatory standards, additional scientific research and public awareness.
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