

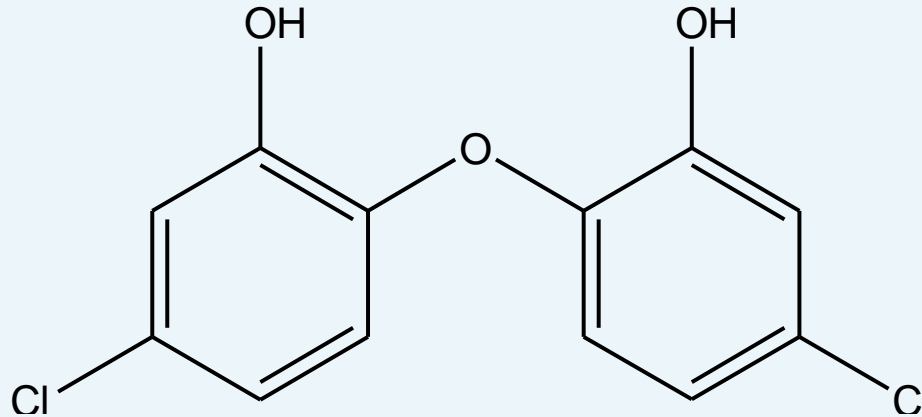
Triclosan

Potential effects on Health &
the Environment

Mr Jamie Page
The Cancer Prevention and Education Society

9th June 2011
Silver and Biocide conference, Vienna

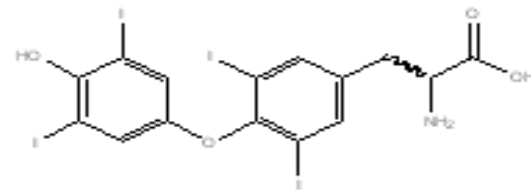
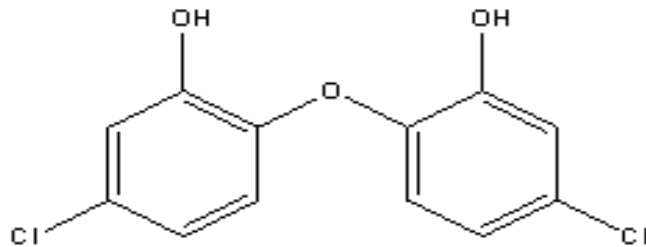
Molecular structure of triclosan



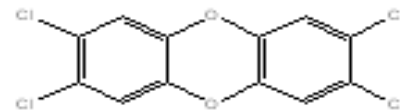
- Chlorinated biphenol ether
- Used as preservative and anti-septic
- Anti bacterial action is specific to bacteria – disables the enzyme ENR (humans do not have this)
- Fat soluble

Comparison with other molecules

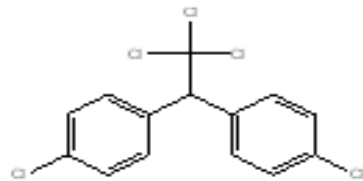
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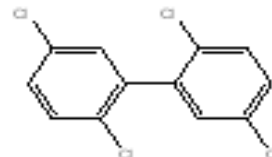
T4 thyroxine



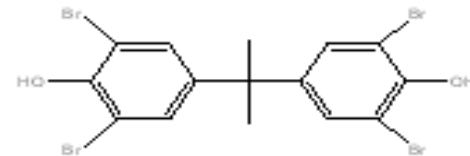
TCDD



DDT



PCBs



PBDEs

Where triclosan is used

- Personal care products-where it acts as preservative in cosmetics, soaps, toothpaste, sunscreens etc.



- Plastic products-due to its stability up to 200°C e.g. hairbrushes, chopping boards, children's toys, Trade name *Microban*. (name of US corporation)
- Textiles, sports clothing . Trade name *BioFresh*
- Used in *healthcare products* such as surgical scrubs, surgical drapes, sutures, urinary catheters.

Triclosan use in hospitals

- Surgical Handwashes: no Triclosan in UK
- *Derman plus (Triclosan)*, only used in Italy not UK
- Also used in hospitals in:
 - coating on catheters e.g. Foley catheter
 - sutures are impregnated with Triclosan (US – not sure if in UK)
 - coating on acrylonitrile–butadiene–styrene (ABS) plastic for use in hospital furniture
 - Austria: Sutres, wound antiseptics
 - Finnish hospitals do not use triclosan for routine cleaning in hospitals

US consumer products containing Triclosan

List of Products Containing Triclosan

SOAP: 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; DeCleur 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; 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 AM-Rail Escalator Handrails, Dupont™ Air Filters, Durelle™ Carpet Cushions, Advanta One Laminate Floors, San Luis Blankets, J Cloth® towels, JERMEX mops

Source: Beyond Pesticides Fact sheet

Present in 75% of US liquid soaps

The Cancer Prevention & Education
Society

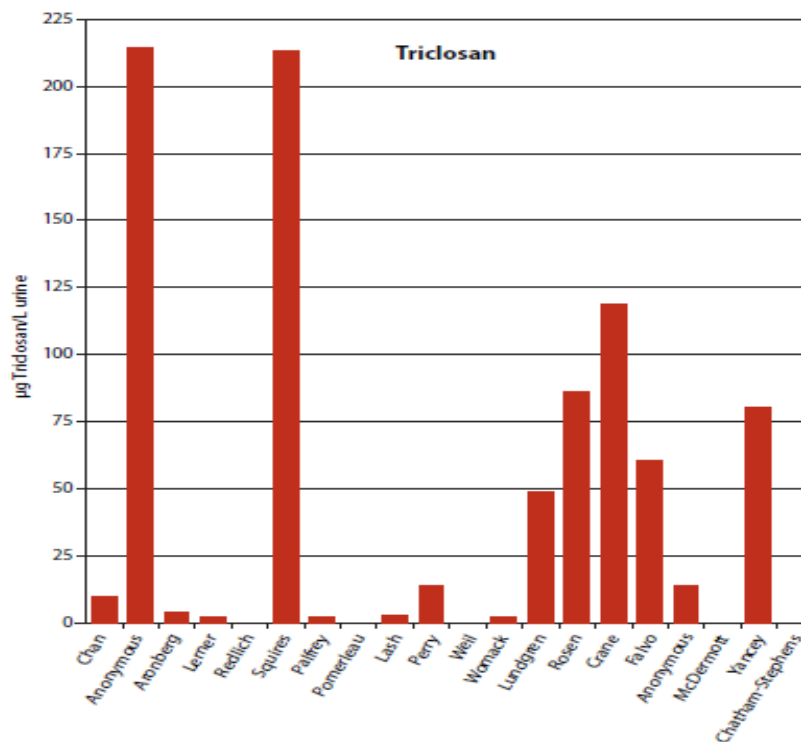
Pharmacology and metabolic fate

- Triclosan present in human blood plasma and breast milk.
- Plasma half life <1day
- Lipophilic: can bioaccumulate
- Enzymes in liver turns triclosan into conjugates-more readily soluble and excreted with urine.
- Main route of excretion in humans via urine. However, oral intake resulted in only 50% of intake excreted via urine-maybe other excretory routes, accumulation in tissues or undetected metabolites
- Triclosan found in 75% of urine samples analysed (NHANES 2003-2004)

Triclosan contamination in doctors & nurses

TRICLOSAN

Fifteen of our participants had triclosan in their bodies, which mirrors CDC's finding that 74.6% of 2003-2004 samples contained triclosan. Our project median of 31.5 $\mu\text{g/L}$ was roughly three times higher than CDC's 9.2, though our study maximum was below CDC's 95th percentile.



Source: Physicians for Social Responsibility (2009)

Toxicity & Endocrine effects

- 95% of triclosan products goes down residential drains
- EC Directive 67/548 classifies triclosan as ‘*very toxic to aquatic organisms*’
- Affinity for human pregnane x receptor, a nuclear receptor involved in the detoxification and clearance of toxic substances from the body

Endocrine effects:

- Inhibition of testicular androgen in rats at 10mg/kg/day
- Antagonistic activity to action of oestradiol and testosterone receptors (Ahn et al 2008, Chen et al 2007)
- It has oestrogenic and androgenic activity in vitro (Gee et al 2008)
- Metabolites of triclosan weakly oestrogenic (tested in fish), and also weakly androgenic in other assays.
- Suppression of thyroid hormones in male and female rats (Crofton 2007). Triclosan alters hepatic clearance of Thyroid hormones

Carcinogenicity / genotoxicity

- Many reviews state lack of evidence for carcinogenicity.
- However chronic oncogenicity tests in rodents found treatment related tumours in liver but not other organs.
- Triclosan cytotoxic to *in vitro* breast cancer cells (Darbre 2006)
- Currently being investigated by FDA

Health effects

- Thyroid disruption
- TCS (at a dose of 4.2 ng/ egg) was generally toxic to medaka fish embryos (2010)
- Triclosan is a potent inhibitor of estradiol and estrone sulfonation in sheep placenta: This high potency of Triclosan raises concern about its possible effects on the ability of the placenta to supply estrogen to the fetus, and in turn on fetal growth and development (2010)
- Triclosan showed a positive association with allergy/hayfever (EHP 2009)
- Contact allergy less than 1%; deodorants may be a different matter as left on the skin
- Triclosan has been shown to help alleviate the symptoms of atopic dermatitis. In a study of atopic dermatitis patients by Breneman and colleagues, daily washing with triclosan- or triclocarban-containing soaps resulted in significantly greater improvement in skin lesions than did washing with placebo soap. Overall, daily use of an antibacterial soap was well tolerated, provided clinical improvement, and reduced levels of skin microorganisms (2000)

Risk Assessment

- Margin of Safety (MOS) for men, women and children: 1,000, 730 and 630.
- Studies found exposures via dermal routes of cosmetics, etc.
- Germany's Federal Institute for Risk Assessment, BfR, raised concerns about the substance saying "consumers may already be at risk from the wide-spread use of triclosan in cosmetics". The body has recommended the substance be banned in Germany.



Bacterial resistance of triclosan

- Triclosan acts specifically upon bacteria- enters cell, blocks site of specific enzyme, stops production of fatty acids (essential to build cell wall) bacteria cannot reproduce
- Triclosan most effective bactericide to Gram + ve bacteria e.g. *staphylococcus* and less effective against Gram - ve bacteria e.g. *E coli* and *Salmonella*
- Bacteria evolve ways of growing in presence of antibacterial agents- resistant genes selected.
- Widespread use of triclosan, evidence that it does have ability to select for anti-bacterial resistance. i.e. resistance to other related or unrelated antibacterial agents. For example, a study has demonstrated multidrug resistance (MDR) conveyed by triclosan to *Pseudomonas aeruginosa* (Chuanchien et al. 2004), which is a cause of death in many hospital-acquired infections due to its intrinsic resistance to many antibiotics
- **The 'widespread use of triclosan may represent a potential public health risk in regard to development of concomitant resistance to clinically important antimicrobials'**. *The Norwegian Scientific Committee for Food Safety 2006*

Triclosan resistance mechanisms

These include:

Target mutations, increased target expression, active efflux from the cell, and enzymatic inactivation/degradation.

These are the same types of mechanisms involved in antibiotic resistance and some of them account for the observed cross-resistance with antibiotics in laboratory isolates.

Therefore, there is a link between triclosan and antibiotics, and the widespread use of triclosan-containing antiseptics and disinfectants may indeed aid in development of microbial resistance, in particular cross-resistance to antibiotics

Published by Federation of European Microbiological Societies (2001)

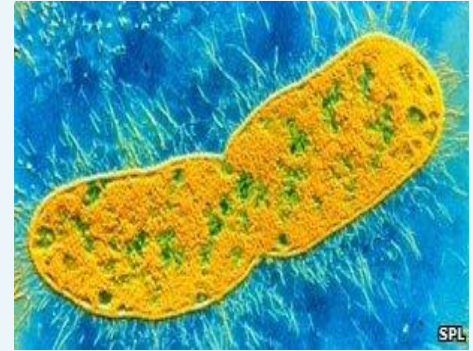
SCENIHR report: Assessment of the Antibiotic Resistance Effects of Biocides (2009)

Antibiotic use is still the major cause of antibiotic resistance in clinical practice. Since antibiotic resistance remains a major concern and decreases our ability to treat infections, appropriate infection control strategies is paramount and ***involves prevention through good hygiene which encompass the appropriate use of biocides.***

(Anon 1999, 2000).

“Europe 'losing' superbugs battle”

BBC News 6 April 2011



- Antibiotic-resistant infections have reached unprecedented levels and now outstrip our ability to fight them with existing drugs, European health experts are warning.
- Each year in the EU over 25,000 people die of bacterial infections that are able to outsmart even the newest antibiotics.
- The World Health Organization says the situation has reached a critical point.
- 37,000 NHS patients have died after catching either the MRSA or C-difficile hospital superbugs between 1997-2007 (The Observer, 28 September 2008)

Where Triclosan is found

Environment

- Sewage sludge
- Agricultural land (from use of sewage sludge on land)
- Waste water
- Rivers & lakes – high concentrations in Switzerland
- Aquatic sediments
- Marine sediments
- Household dust
- Fish

Humans

- Humans: measured in urine, breast milk and serum.
- Concentrations in milk and plasma highly raised in mothers using products containing Triclosan
- '*In utero* exposure should be regarded as an issue of concern' Karolinska 2009

Fate in environment of triclosan

- Biodegradation of triclosan occurs in sewage. However 6% Triclosan in receiving streams:
- One study found during waste water treatment most of triclosan adsorbed into sludge. Triclosan derived dioxins found in core samples from Mississippi river. (*Env. Sci Tech*2010)
- UV light from sunlight produces photoproducts dibenzofurans and dioxin congeners.
- Chlorinated tap water (from waste water treatment) may also transform triclosan into chloroform, chlorinated biphenols and dioxin congeners.
- Dioxin plume reported downstream of sewage plant
- Triclosan has been found in compost (San Francisco 2010)
- Dioxin may be formed during manufacture and incineration

Effect on aquatic organisms

Crustacea and algae have been identified as the most sensitive species, susceptible to adverse effects from biocide exposures in the parts-per-trillion range. *J Am Water Works Assoc.* 2009

Triclosan reported to kill algae important for photosynthesis (Spain 2010) Triclosan inhibits photosynthesis in diatom algae which are responsible for a large part of the photosynthetic activity on Earth (*Aquatic Toxicology* 2010)

Company actions on Triclosan

- Sarah Lee Corporation replaced Triclosan with Lactic Acid (Natural Human Skin Moisturizer, low Human Toxicity & Environmental Impact)
- Unilever has phased out Triclosan in Europe
- Ciba (part of BASF) who holds patents on Triclosan withdrew Triclosan from provisional list of additives for food contact materials (2009)



Country actions on Triclosan: EU



On March 19, 2010, the European Union (EU) acted 1 to prohibit (starting in 2011) the use of triclosan in products intended to come into contact with food, saying that Ciba/BASF, triclosan's manufacturer, believed that **“it does not consider the use of the substance in plastics intended to come into contact with food appropriate any more.”** This follows the EU's 2009 regulations to impose limits on the amount of triclosan contained in cosmetics.

Country actions on Triclosan: Denmark, Norway, Sweden and Finland



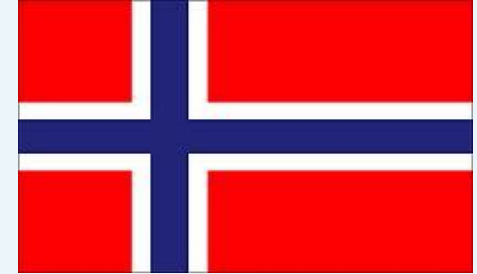
These countries have issued consumer advisories related to triclosan. Denmark found that use of triclosan fell by 54% between 2000-2004, following its warning. The five Swedish government agencies advised that consumer products containing anti-bacterial agents do not work better than products that do not contain them, and that these products can lead to adverse environmental and health effects. ***Consumers were therefore advised not to use such products unless special medical reasons exist.***

Triclosan Report (Karolinska Institute 2009)

“None of the exposed mothers were aware of their triclosan use. This indicates that the explicit labelling of triclosan toothpaste in Sweden, *which aims at helping the customer in making an informed choice*, is not effective.”

“In light of the frequently disputed claims of the beneficial effects from general use...is it wise to spread and use this chemical in the unrestricted manner we see today[?]”

Country actions on Triclosan: Norway



In October 2008, Norway's Pollution Control Authority recommended restrictions on "ten substances which are particularly harmful to health and environment," including triclosan.

The supporting documents state that ***"triclosan has no necessary function in most products. Regulation will reduce occurrences in the environment, as well as reduce the risk of damage to health...it is our assessment that the measure will not entail significant economic costs. On the basis of the documentation we have, we expect that the benefit will be greater than the costs."***

Country actions on Triclosan: Germany



In 2006 Germany's Federal Institute for Risk Assessment said that it believed *triclosan should not be included in consumer products and should be used only in hospitals and other medical establishments. It further advised consumers "to refrain from using biocide-containing cleaning agents and products in the home."* In 2009, this body reiterated its view, *stating it believes that "the use of triclosan should be reduced to the absolutely necessary minimum."*

Country actions on Triclosan: Canada



In 2009, Canada's Health Ministry acted to restrict human exposure to triclosan by requiring labeling provisions on some consumer products.

For example, for oral cosmetics, such as lipsticks, packaging labels must be included that states that "*the product is not to be used by children under the age of 12.*"

Country actions on Triclosan:USA



- Federal agencies are reviewing triclosan's safety but haven't called for altered usage.
- The American Medical Association: ***"It may be prudent to avoid the use of antimicrobial agents in consumer products"***



BEYOND PESTICIDES

Protecting Health and the Environment with Science, Policy and Action

March 28, 2011

From Yoga Mats to Toothpaste: Tell EPA to ban triclosan by April 8

Triclosan, found in many consumer products like yoga mats, cosmetics, kitchen utensils and toothpaste is now found in the bodies of 75% of the US population, is linked to hormone disruption, bacterial and antibiotic resistance, dioxin contamination, and contaminated fish and biosolids. Studies this past year show that triclosan can interfere with pregnancy hormones and possibly impact fetal development. This is critical since pregnant women have elevated levels of triclosan in their bodies. Triclosan is also an endocrine disruptor that interferes with the thyroid hormone. Triclosan contaminates our waters, food and accumulates in wildlife.

Join us by April 8th to tell EPA to protect public health and ban triclosan from consumer products. [Take Action](#).

Your voice is critical in generating public comments on a petition, published in the Federal Register, to ban the antibacterial chemical triclosan. This chemical, now found in the bodies of 75% of the U.S. population, is linked to endocrine disruption, bacterial and antibiotic resistance, dioxin contamination, and contaminated fish and biosolids.

Please send your own comments and notify your networks, listserves, faith organizations, etc. and post on your website, urging other people/organizations to comment.

Thank you!

Beyond Pesticides

Take Action!

Tell EPA to protect health and ban triclosan.

More...

Sign the Pledge! Go Triclosan-Free

Join the thousands of those that have taken a stand against triclosan. [Take the pledge](#) to be triclosan-free. Or get your employer, school, place of worship or favorite retailer to sign the pledge.

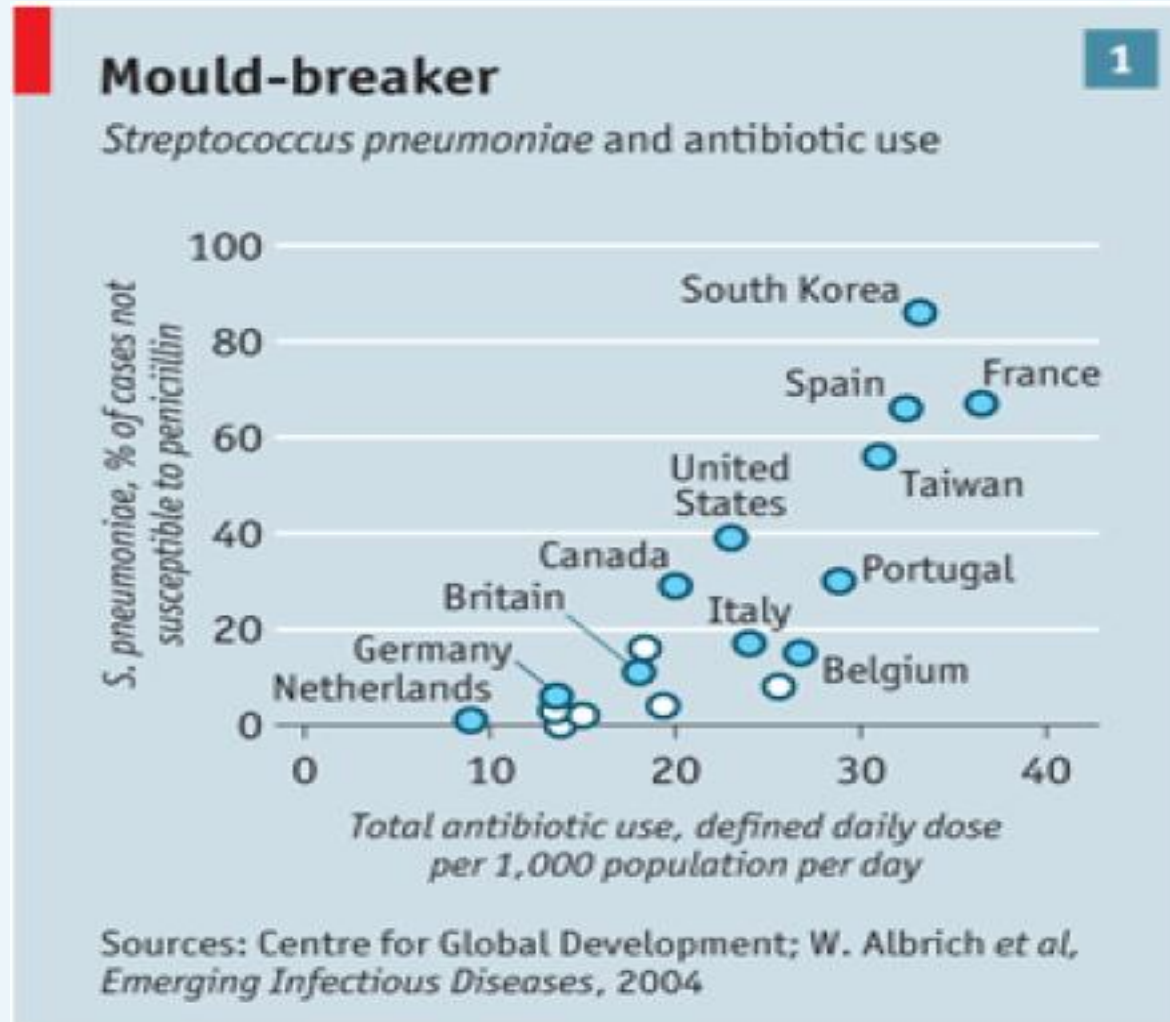
Do you really need toxic antibacterial products?

Ask your friends to [take this poll](#) and test their knowledge on antibacterials.

Want to stay in the loop?

[Let us know](#) you would like to receive Beyond Pesticides' weekly Daily News Headlines email update.

Country antibiotic use and resistance



Clearly, the time has come to depart from the 'wait and see' attitude when considering a link between triclosan and antibiotics, and actively engage in a policy of increasing public awareness concerning the possible consequences of triclosan overuse, and to teach and heed the lessons we hopefully learned from antibiotic overuse.

H.P. Schweizer, FEMS
Microbiology Letters (2001)
Federation of European
Microbiological Societies

Hospitals cannot be viewed in isolation!

Focus | The Landscape of Antibiotic Resistance

ANTIBIOTICS in the Environment

How Antibiotics Enter the Environment

HOMES
In one study, more than half of survey respondents reported flushing unused antibiotics down the toilet.

PHARMACEUTICAL FACTORIES
Current regulations address discharges of chemicals used to produce antibiotics but not antibiotics themselves that end up in plant effluent.

FARMS
Application of farm waste to lands can put antibiotics and resistant bacteria in soil and water.

HOSPITALS
Studies since the 1970s have shown hospital effluent to contain higher levels of antibiotic-resistant enteric bacteria than waste from other sources.

How Resistance Works

- 1 Efflux pumps are transport proteins that remove an antibiotic entirely or reduce its concentration below effective levels. They may be specific to one compound, or they may work on a range of dissimilar compounds.
- 2 Antibiotics can be inactivated by enzymes that (a) modify or (b) degrade them. These enzymes typically are specific to a particular antibiotic or class of antibiotics.
- 3 Molecular binding sites can be modified, for instance, through mutation of ribosomal RNA or other key elements.

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Summary

- Structural similarity with other molecules
- Huge use in consumer products
- Concerns about endocrine effects and toxicity (particularly aquatic)
- Bacterial resistance
- Should it be banned in all/ most consumer products?
- Role of hospitals in bringing in legislation