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Antimicrobial Plastics
Reducing Infections and Protecting Products

Abstract

This paper examines the development and application of antimicrobial plastic resins as a response to public, private and institutional demands for plastic products and product components that inhibit microbial growth. In the U.S. alone, 1.8 million hospital-associated infections lead to 99,000 deaths each year, killing more people annually than aids, breast cancer and automobile accidents combined. While medical research continues to target constantly-evolving microbes including so called "super bugs," advances in resin-compatible antimicrobial additive technology have drawn the plastics industry into the germ battle on several fronts. Plastic products with enduring antimicrobial properties include medical devices and equipment, food preparation surfaces, household appliances, automobile interior parts, computers, phones and other personal electronic devices, sports equipment, construction supplies and other contact surfaces. Typical antimicrobial resin formulations include silane, N-butyl-1, 2-benzisothiazolin-3-one, copper, zinc and silver. Incorporation of these proven antimicrobials into a variety of plastic resins is generally performed to achieve either biostabilization (preservation) of the plastic article or to impart active biocidal properties to the plastic article. While there may be some overlap in these two primary purposes, producers, compounders and product manufacturers must distinguish their antimicrobial intent carefully to ensure proper product classification under, and compliance with, the appropriate regulatory framework.

Background

Microbes have been around since our earth took her first breath. The oldest known fossilized microbes date back 3.5 billion years. So resilient are these tiny single-celled organisms (millions of them could fit in the eye of a needle) that scientists claim to have successfully "revived" a dormant bacteria estimated to be 250 million years old.[1] Microbes include bacteria, fungi, protista, viruses and archaea (which until recently were thought to be bacteria). Because of their high-profile and seemingly constant influence on human life and health, bacteria and viruses are perhaps the most well-known categories of microbes.

Most bacteria living in and on humans are harmless; some are actually beneficial such as those that reside in the intestinal tract and aid in digestion. The fermentation mechanism of certain microbes was harnessed by humans for creating such things as bread, wine, beer, yogurt and cheese long before those organisms were first observed via microscope in the 17th century. Prior to that time food spoilage had also been a mystery and was attributed to a widely held belief that life somehow arose from non-living things in a process dubbed "spontaneous generation." The work of several scientists, culminating with Pasteur in the 19th century, put to rest the spontaneous generation theory and gave rise to scientifically-supported germ theory as the reason for food spoilage, infection, etc.[2]

There are an estimated 10 trillion to 100 trillion cells in and on the average person, with microbes outnumbering "human cells" by 10 to 1. So great is the number of microbes - scientists

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estimate the number of bacteria alone at 5 nonillion or 5,000,000,000,000,000,000,000,000,000,000 – that the mass of all microbes combined would exceed that of all animals on earth. With as many as 10 million different species of bacteria, it's noteworthy that the same handful (e.g., E. coli, S. aureus or "staph") are able to grab human headlines year after year – and not in a good way.[3]

For a humorous yet nonetheless scientific glimpse into microbial life on humans, researchers conducted the Belly Button Biodiversity study in 2012. Swabbing the navels of some 500 volunteers, they discovered over 2,300 distinct microbes living in the average belly button.[4]

Microbes have also been employed to speed decomposition of waste matter. Researchers at North Carolina State University recently isolated one species of anaerobic bacteria they believe is responsible for production of methane gas in landfills.[5] So-called biodegradable plastics rely on microbes as well, and the task of digesting plastic can be specialized. One study showed that several strains of a pseudomonas bacteria have a particular appetite for polyethylene terephthalate (PET) plastic commonly used to produce drink bottles.[6] While the benefits of these "good" microorganisms make them a welcome addition to human life, it's a microbe's pathogenic role in human health that garners the most attention from scientists and researchers in all parts of the world. And rightly so. The Spanish Flu in 1918 is credited with killing over 20 million people.[7] Other bacterial and viral pandemics and epidemics such as the plague/black death of the 14th century remain etched in human history hundreds of years after they occurred. Ebola, HIV, Swine Flu, Avian Flu, cholera, tuberculosis, smallpox, gonorrhea, meningitis, ear infections and the common cold all result from the proliferation of bad microbes in or on the human body.

While advances in microscope technology beginning in the 17th century started bringing these pathogens to light, it would take several hundred more years of research before the scientific community would be able to combat microscopic health threats on a large scale.

Fighting microbes with microbes

During the second half of the 19th century microorganisms were discovered to be responsible for many of the infectious diseases that had been plaguing humanity for centuries. Scientists began to formulate treatments for these diseases based on destruction of these organisms. The first antimicrobial agent used to treat disease was Salvarsan, a remedy for syphilis created in 1910. This was followed by the class of drugs known as sulfonamides in 1935.[8] However, these drugs were synthetic compounds, with limitations in safety and efficacy. Penicillin, a natural compound produced by Penicillium mold, had the safety and efficacy that synthetic antimicrobial agents lacked. It was discovered in 1928 by Alexander Fleming and came into clinical use in the 1940s. Penicillin was used to save the lives of many wounded soldiers during World War II.[9] During the next twenty years, new classes of antimicrobial agents were developed one after another, many from natural sources such as soil bacteria. Some of these bacteria-fighting "antibiotics" included streptomycin, chloramphenicol, tetracycline, macrolide, and glycopeptide (e.g., vancomycin).[10]

As new and more powerful antibiotics were developed through the mid-20th century, it may have seemed for a time that eradication of most if not all bacteria-caused diseases was close at hand.

But pathogens don't survive hundreds of millions of years without the ability to adapt. Many bacteria have quickly evolved in response to antibiotics, developing resistance to even the most powerful drugs. One of the most well-known examples is Methicillin-Resistant Staphylococcus Aureus (MRSA). Most MRSA infections occur in people who have been in hospitals or other health care settings, such as nursing homes and dialysis centers.[11]

While MRSA has been among the most feared bacterial adaptations to antibiotic therapy, the CDC is now warning of an even more lethal threat. A strain of enterobacteriaceae has evolved with resistance to carbapenem, a so-called "last resort" antibiotic. The Carbapenem Resistant Enterobacteriaceae (CRE) bacteria kill half of patients who become infected. **"**In addition to spreading among patients, often on the hands of health care personnel, CRE bacteria can transfer their resistance to other bacteria within their family," according to the Centers for Disease Control. The CDC adds that this type of spread can create additional life-threatening infections for patients in hospitals and potentially for otherwise healthy people. Currently, almost all CRE infections occur in people receiving significant medical care in hospitals, long-term acute care facilities, or nursing homes. "CRE are nightmare bacteria. Our strongest antibiotics don't work and patients are left with potentially untreatable infections," said CDC Director Tom Frieden, M.D., M.P.H. "Doctors, hospital leaders, and public health, must work together now to implement CDC's 'detect and protect' strategy and stop these infections from spreading."[12]

MRSA, CRE and other so-called super bugs seem to thrive in hospital and long term care environments. Approximately 1.7 million healthcare-associated infections (HAIs) were estimated to have occured in 2002, with nearly 6 percent of these infections resulting in the death of the patient. These infections are not limited to the most vulnerable patients. While approximately 500,000 were in newborns, children, and adults in ICU settings, the other 1.2 million infections were in patients in non-ICU areas of the hospital.[13]

Although they may be the site of most super bug infections, the spread of pathogens is hardly limited to health care settings. A recent University of Arizona study demonstrated how illness spreads in an office environment when researchers took a group of 80 office workers and placed water droplets on the hands of all but one of them. One person received droplets containing artificial viruses that mimicked cold, flu and stomach bug. When researchers sampled commonly touched surfaces in the office, as well as the hands of all 80 volunteers, roughly half of the tested surfaces and participants were contaminated with at least one of the viruses. This translated to a 40-90 percent chance of infection with one of the three viruses by the end of one eight-hour work day.[14]

While health care settings are certainly the frontline for major infection battles, the Arizona study and others like it point to an opportunity to skirmish with pathogens at home and in the office as well. Although many pathogens are transferred from host to host via air and direct personal contact, the prevalence of microbes on common surfaces and the ease with which these microbes appear to be transferred from person to person on contact indicate a possible need to address microbial activity on a much broader scale.

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Antimicrobials in Plastics

Antimicrobials are added to plastics for two primary purposes – as an active biocide to kill germs and as a biostabilizer/preservative for the plastic. The main difference lies in the antimicrobial activity profile.[15] Plastics with active biocides are often formulated for use in implantable medical devices and items with known high infection potential such as catheters.[16] But with the spread of pathogens tied more closely to regular contact with contaminated surfaces on common items such as desks, tables, keyboards, towel dispensers and trays, biostabilized plastics are becoming more prominent not only in medical settings but in home, industrial and office applications as well**.**

Frost & Sullivan predict that by 2015 the global antibacterial plastic industrial applications market will reach 1.4 billion pounds.[17] Global antimicrobial coatings demand was worth $1.6 billion in 2012 and is estimated to reach $3.3 billion in 2018, expanding at a compound annual growth rate of over 12 percent from 2012 to 2018, according to a report from Transparency Market Research.[18] The U.S. is reportedly the global leader in antimicrobial coatings and dominates the demand for these products.

Why plastics?

The sheer ubiquity of plastics in modern society makes them a logical candidate for antimicrobial use. It would be difficult in a developed nation to go through an average day without contacting a plastic surface in your car, home, work or virtually any other public or private setting. To the extent that contact with plastic is practically unavoidable, efforts to minimize the spread of pathogens via that contact are clearly worthwhile.

Imparting antimicrobial properties to plastics also serves to protect the product against the ravages of microbial action. The ability of a microbe to degrade a plastic depends not just on the type of microbe but on the type of plastic. In some cases, microbes that might normally find a plastic inhospitable could readily colonize on the surface because of additives. For example, plasticizers, fillers and lubricants tend to make PVC susceptible to fungal attack, while some polyurethanes, particularly those that are ester-based (e.g., dioctyl phthalate and dioctyl acetate), are inherently vulnerable even before compounding/processing.[19]

The risk of microbial degradation is substantial in common household plastic items, particularly those that are prone to moist conditions. Building products are also prime targets for microbial degradation.

Microbes that degrade plastic (including Aureobasidium pullulans, Aspergillus paecilomyces, Penicillium, and Verticillium*)* are capable of utilizing one or more ingredients in the plastic as their sole carbon source, and, to a smaller extent, a source of nitrogen. The most common plastic ingredients that can be used as a carbon source are epoxidized oil (a plasticizer-stabilizer) and calcium-zinc stearate. A common source of nitrogen is stearamide. Utilization of these components by microbes can result in brittleness, discoloration, and loss of mass in the plastic "host."[20]

While some microbes are able to eat plastic by colonizing on the surface, others can insert fibrils into the material in order to access nutrients. In these cases, they can mechanically destabilize the

plastic and add another component to the degradation. Extensive microbial activity on plastics can result in a breakdown of critical physical/mechanical properties resulting in brittleness, dimensional changes, increase in gas permeability and loss of structural integrity. Other common adverse effects include staining, odor and changes in electrical properties such as resistance due to colonization on plastic wire insulation coatings.[21]

In addition to the obvious consumer goods impact, the degradation of plastic items via antimicrobial action has cultural significance as well. In *Microorganisms Attack Synthetic Polymers in Items Representing Our Cultural Heritage*, Francesca Cappitelli and Claudia Sorlini note that "As museums keep acquiring objects that reflect both everyday life and technological and historical events, the proportion of plastics in museums is increasing dramatically."[22] Additionally, the authors explain that synthetic polymers (e.g., adhesives, consolidants, protective coatings) are often employed to preserve many artifacts from further deterioration. Ironically, the polymers used for preservation are themselves prone to several forms of bio-deterioration including:

- biological coating masking surface properties
- increased leaching of additives and monomers that are used as nutrients
- production of metabolites (e.g., acids)
- enzymatic attack
- physical penetration and disruption
- water accumulation
- excretion of pigments[23]

Barbie dolls, toys and numerous other scientific and pop culture items found in museums are made from PVC which is highly susceptible to fungi that consume plasticizers found on the surface of the object. PVC products are also susceptible to a loss of plasticizers from bacteria such as Pseudomonas aeruginosa. Polyurethane materials suffer enzymatic degradation at the hands of fungi such as Chaetomium globosum and bacteria such as Bacillus subtilis, while nylons can suffer physical damage from wood-degrading fungi such as Bjerkandera adusta and bacteria such as Bacillus pallidus. Even space technology isn't immune from microbial attack on earth. At the National Air and Space Museum in Washington, DC, fungi belonging to the genera *Paecilomyces* and *Cladosporium* have been cultured from two synthetic polymers in Apollo-era space suits. [24]

Microbial action on plastic items increases the risk of damage not just to the item itself, but to any information the plastic item might contain or encase. "Plastics have allowed novel ways of recording information; audiotapes, computer diskettes, and compact discs are now commonly stored in archives and libraries," explain Cappitelli and Sorlini. "Also, photographic materials, binders, and supports can be made of plastics. Plastic audiovisual material, including compact discs, can be subject to biodeterioration. Initial fungal colonization of plastics in audiovisual materials generally means failure because of interruption of the signal." [25]

Regardless of the object/product or type of plastic, the onset of degradation by one type of microbial can yield smaller organic compounds that invite additional microbes to join and

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accelerate the rate and type of bio-deterioration and compromise multiple characteristics of the plastic and ultimately shortening the product life. In addition to microbes that can break down plastics and use certain components as food sources, secondary microbial colonies may form well after the initial colony has formed. These secondary colonies are not able to break down the plastic themselves, but are able to utilize the components after they have been broken down, which can accelerate the rate of deterioration.[26]

Resistance in numbers

Microbes have four basic needs for survival: moisture, suitable temperature, a food source and a suitable surface for growth and replication.[27] Because of their composition and exposure to moisture, many plastic products provide an ideal surface for the formation of complex microbial colonies called *biofilms*. A biofilm is "a complex aggregation of microorganisms growing on a solid substrate. Biofilms are characterized by structural heterogeneity, genetic diversity, complex community interactions, and an extracellular matrix of polymeric substances."[28]

Biofilms are common in nature, as bacteria commonly have mechanisms by which they can adhere to surfaces and to each other. Dental plaque is a common biofilm. Bionewsonline explains that in industrial environments, "biofilms can develop on the interiors of pipes and lead to clogs and corrosion. In medicine, biofilms spreading along implanted tubes or wires can lead to pernicious infections in patients."

> *Biofilms can also be harnessed for constructive purposes. For example, many sewage treatment plants include a treatment stage in which waste water passes over biofilms grown on filters, which extract and digest harmful organic compounds. Bacteria living in a biofilm can have significantly different properties from free-floating bacteria, as the dense and protected environment of the film allows them to cooperate and interact in various ways. One benefit of this environment is increased resistance to detergents and antibiotics, as the dense extracellular matrix and the outer layer of cells protect the interior of the community.* [29]

Biofilms are not only resistant to many antimicrobial agents and disinfectants, they can acquire enhanced resistance through the transfer of resistance plasmids. Such resistance could be especially acute in the health-care environment for patients with urinary catheters and collection bags. Many of the enteric organisms shown to colonize urinary catheters carry plasmids encoding resistance to multiple antimicrobial agents. Resistant organisms such as MRSA have also been shown to form biofilms. [30]

Even with increased awareness about the dangers of contaminated surfaces, and the widespread availability of antimicrobial agents (e.g., disinfectants) within the home and health care settings, pathogens continue to flourish. "Many disinfectants contain nonvolatile antimicrobial agents such as quaternary ammonium compounds (QACs) that can leave an antimicrobial residue on treated surfaces," according to Dorjnamjin, Ariunaa, and Shim in the *International Journal of Molecular Science*. "The potential of these agents to prevent bacterial colonization is limited because of their lack of persistence on surfaces after some environmental insult, such as water contact or rubbing. These moist environments and physically contacted surfaces are the most likely to be contaminated, to allow bacterial proliferation, and to act as a pathogenic reservoir."

The authors conclude that "For a given disinfectant technology to realize a significant residual antimicrobial benefit, it must persist under such conditions." [31]

Antimicrobial plastics – fighting on all fronts

Pharmaceutical approaches to pathogen control (e.g., antibiotics) have succeeded to some degree. But the ability of microbes to mutate and re-emerge even stronger is a clear indicator that drugs alone will not control the spread of pathogens. Topical measures such as disinfectants may help in the battle but are of little use against particularly stubborn free-floating pathogens and entrenched biofilms. However, the proliferation of plastic items in virtually all settings subject to human contact provides an opportunity to address all of these concerns by engaging microbes proactively on the surfaces where they colonize and are spread via contact. Using select antimicrobial formulations matched to appropriate resins, the plastics industry is producing a wide variety of antimicrobial polymers for use in medical, industrial, commercial, marine and home applications.

Among the most common antimicrobial agents incorporated into plastics are quaternary ammonia compounds (QACs), silanes and metals including silver and zinc. While a much broader scale of antimicrobial additives may be available, plastics manufacturers and compounders must be careful in their selections to ensure that any additives/masterbatches are resin-compatible and able to maintain their antimicrobial efficacy through every stage of the manufacturing process. To be effective, antimicrobial agents in general must have broad spectrum antimicrobial activity (equally effective against a wide variety of bacteria, fungi, and algae), pose little risk to the product or to the people applying the product, must easily fit current production systems, must be environmentally friendly, and must be compliant with all relevant biocidal regulations. [32]

Generally, antimicrobial additives can be classified as either leaching or non-leaching depending on their mechanism of action. Leaching antimicrobial agents are defined as agents that must come off the treated substrate in order to exert the antimicrobial properties. Any antimicrobial agent that must enter the cell to work is considered a leaching agent. Non-leaching agents are fixed to the treated surface (usually by covalent bonds) and subsequently do not need to leave this surface to provide antimicrobial action. As these agents are physically attached, there is generally no means for removal and therefore no means to diminish the overall strength.

Use of antimicrobial additives has been expanding rapidly into polyolefins, TPEs, nylons, and acrylics in consumer, industrial and healthcare applications. [33]

Mechanisms of action

Silane-based QACs or "Si-Quats" act as antimicrobials by disrupting the ionic charge of the cell wall in these single-celled organisms. The Si-Quat polymer consists of a long uncharged carbon chain interspersed with positively charged ammonium moieties. The charge differential of the treated surface interferes with the integrity of the cell wall or cellular membrane, resulting in the rupture of and death of the microorganism. These agents also prevent the formation of biofilms

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through the same mechanisms. In addition, the hydrophobic properties of the polymerized carbon chain interfere with the adhesion of microorganisms to the substrate surface. [34]

Zinc pyrithione (also known as Zinc Omadine® or Zinc 2-pyridinethiol-1-oxide) is used to preserve a wide variety of food/drinking water contact, and non-food contact articles, and is the active ingredient in many anti-dandruff shampoos. It kills microbes by interfering with the microbe's proton pump activity. Proton pumps are used by the cell to open pores in the cell wall, allowing the transport of nutrients into the cell and waste products out of the cell. Without this capability, the microbe is unable to grow or thrive and dies as a result. [35]

Zinc pyrithione is incorporated into various polymers and plastics as a liquid, powder, or aqueous dispersion during the manufacturing process of these materials, and during the manufacture of finished articles from these materials. Zinc pyrithione is added usually by metering pump if it is a liquid, and by open pouring if it is the powder form. It is added at a point where thorough mixing will take place. [36]

The antimicrobial mechanism of action for Isothiozolanones such as 10,10'-Oxybisphenoxarsine (OBPA) and 4,5-dichloro-2-n-octyl-4-isothiazoline-3-one (DCOIT) is enzyme inhibition. Enzymes regulating cellular respiration, energy production, and cellular growth are destroyed. Protein destruction, and the subsequent production of free radicals, is the actual cause of cell death. [37]

A silver lining?

Silver has long been employed as an antimicrobial, although its specific mechanism of action was unknown throughout centuries of usage. Hippocrates referenced the use of silver in wound care. At the beginning of the twentieth century surgeons used silver sutures to reduce the risk of infection and physicians used silver-containing eye drops to treat ophthalmic problems, various infections, and sometimes internally for diseases such as epilepsy**,** gonorrhea, and the common cold. During World War I, soldiers used silver leaf to treat infected wounds. With the development of modern antibiotics in the 1940s, the use of silver as an antimicrobial agent diminished.[38]

Silver and most silver compounds have an oligodynamic effect and are toxic for bacteria, algae, and fungi in vitro. The oligodynamic effect is typical for heavy metals such as silver, lead and mercury, but silver is considered the least toxic for humans. The antibacterial action of silver is enhanced by the presence of an electric field. Applying an electric current across silver electrodes enhances antibiotic action at the anode, likely due to the release of silver into the bacterial culture. The antibacterial action of electrodes coated with silver improves in the presence of an electric field. [39]

Silver has multiple mechanisms of action that lead to the death and destruction of microbial cells. Silver reacts with the cell wall of microbes to inhibit essential functions of the cell wall, including cellular respiration and nutrient uptake. Silver can also interfere with the structural integrity of the cell wall/cellular membrane, leading to proton leakage, cytoplasmic leakage, or complete rupture of the cell wall all resulting in cell death. Silver ions can also interfere with enzymatic functions within the cell. The enzymes affected are responsible for a wide range of

intracellular activities, such as the breakdown of nutrients, production of proteins, and DNA replication. These effects are secondary, however, as the effects on the cellular membrane are the primary mechanism of antimicrobial action.[40]

In 2012 researchers at Rice University were able to isolate silver ions from nanoparticles and demonstrate the mechanism of antimicrobial action. They discovered that the silver nanoparticles themselves were ineffective in killing microbes. It was only upon oxidation – when the nanoparticles released silver ions – that bacteria were effectively killed. The experiment in an anaerobic environment demonstrated that silver ions were 7,665 times more toxic to bacteria than the nanoparticles. "These findings suggest that the antibacterial application of silver nanoparticles could be enhanced and environmental impacts could be mitigated by modulating the ion release rate, for example, through responsive polymer coatings," researcher Zongming Xiu said.[41]

Antimicrobial regulation in the U.S.

According to the U.S. Environmental Protection Agency (EPA), approximately one billion dollars each year are spent on a variety of antimicrobial products, and more than 5000 antimicrobial products are currently registered with the EPA and sold in the marketplace. Nearly 60 percent of antimicrobial products are registered to control infectious microorganisms in hospitals and other health care environments. Because antimicrobials are considered pesticides, regulation of antimicrobial plastic additives in the U.S. is generally the domain of EPA under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA). If certain dental uses are claimed, or if the plastic or product containing the plastic is intended for use on or in humans or animals, it could be classified as a drug and regulated by the Food and Drug Administration (FDA).[42]

Though rare, there are some antimicrobial additives for which the proposed use makes them both a food additive and drug (e.g., a no-rinse hand sanitizer used by food handlers). In this case, the product may have to comply with the requirements of FIFRA applicable to both food additives and drug products. [43]

According to the EPA, antimicrobial pesticides have two major uses:

1. disinfect, sanitize, reduce, or mitigate growth or development of microbiological organisms;
2. protect inanimate objects, industrial processes or systems, surfaces, water, or other chemical substances from contamination, fouling, or deterioration caused by bacteria, viruses, fungi, protozoa, algae, or slime.

The EPA regulatory framework also considers antimicrobial articles/products as belonging to one of two categories – public health products and non-public health products. Public health products are intended to control microorganisms infectious to humans in any inanimate environment. Non-public health products are used to control growth of algae, odor-causing bacteria, bacteria which cause spoilage, deterioration or fouling of materials and microorganisms infectious only to animals. [44]

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Because antimicrobials can't discern whether their purpose is to preserve an article or protect human health, EPA provided a carve-out known as the Treated Articles Exemption. Under the TAE, articles (products) that employ broad spectrum antimicrobials as a biostabilizer/preservative can be exempt from EPA registration as long as no claims are made regarding the ability of the article to provide a human health benefit. To qualify for the exemption, treated articles must display appropriate clarifying statements. If an article claims to be effective in controlling specific microorganisms (e.g., E. coli, S. aureus, Salmonella) it must be registered as a pesticide because EPA considers this a public health claim that goes beyond the preservation of the treated article itself. In these cases EPA requires chemical data supporting the claims. Upon review, EPA could still determine that the product is exempt from registration as a pesticide and limit the manufacturer to claiming only that the product contains a pesticidal preservative to protect the product itself.

Any pesticide-treated product that is not registered by EPA must not make public health claims, such as *fights germs, provides antibacterial protection,* or *controls fungus*. EPA's policy is predicated on the fact that no scientific evidence exists that these products prevent the spread of germs and harmful microorganisms in humans.[45]

Penalties for making unsubstantiated claims can be severe. In 2010 the EPA levied the following penalties, among others:

- VF Outdoor (parent company of The North Face), $207,500 for unsubstantiated antimicrobial claims related to shoe products
- Califone International, $220,000 for unproven antimicrobial claims related to headphones
- Component Hardware Group and John S. Dull Associates, $98,000 for unsubstantiated antimicrobial claims related to certain plumbing and electrical products[46]

The EPA provides the following classification guidance for some of the more commonly used public health antimicrobial products:

- *Sterilizers (Sporicides):* Used to destroy or eliminate all forms of microbial life including fungi, viruses, and all forms of bacteria and their spores. Spores are considered to be the most difficult form of microorganism to destroy. Therefore, EPA considers the term Sporicide to be synonymous with "Sterilizer." Sterilization is critical to infection control and is widely used in hospitals on medical and surgical, instruments and equipment. Types of sterilizers include autoclaving, ovens, low temperature gas (ethylene oxide), and liquid chemical sterilants which are used for delicate instruments which cannot withstand high temperature and gases.
- *Disinfectants:* Used on hard inanimate surfaces and objects to destroy or irreversibly inactivate infectious fungi and bacteria but not necessarily their spores. Disinfectant products are divided into two major types: hospital and general use. Hospital type disinfectants are used on medical and dental instruments, floors, walls and bed linens. General disinfectants are used in households, swimming pools, and water purifiers.
- *Sanitizers:* Used to reduce, but not necessarily eliminate, microorganisms from the inanimate environment to levels considered safe as determined by public health codes or regulations. Sanitizers include food contact rinses for dishes, cooking utensils and food processing plants as well as non-food contact products such as carpet sanitizers, air sanitizers, laundry additives, and in-tank toilet bowl sanitizers.

- *Antiseptics and Germicides:* Used to prevent infection and decay by inhibiting the growth of microorganisms. Because these products are used in or on living humans or animals, they are considered drugs and are thus approved and regulated by the Food and Drug Administration (FDA).
-

- When EPA registers a disinfectant product for use in a hospital or other public health setting, the product effectiveness must be demonstrated against a target organism concentration that significantly exceeds concentrations typically found on surfaces in hospitals or other public health settings. For example, a product's effectiveness against Pseudomonas aeruginosa is demonstrated against a minimum concentration of a million microorganisms. This level is 1,000 to 10,000 times higher than the contamination level that is typically found on surfaces in healthcare facilities. This rigor in the Agency's registration requirements provides an added margin of effectiveness for real world use of disinfectant products. Nevertheless, EPA cautions that antimicrobial products alone are never relied on to control infectious processes in health care settings. [47]

Food contact surfaces and the EPA/FDA tug of war

The Food Quality Protection Act of 1996 (FQPA) amended FIFRA as well as the Federal Food, Drug and Cosmetic Act (FFDCA), changing the definitions of "food additive" and "pesticide chemical" to the extent that "These changes had a significant impact on the regulatory authority for many antimicrobial products that are used in food-contact applications," according to the U.S. Food and Drug Administration (FDA).[48]

The federal government sought to clarify the antimicrobial oversight confusion that arose under FQPA with the Antimicrobial Regulation Technical Corrections Act of 1998 (ARTCA), which amended the definition of a *"pesticide chemical"* and "corrected the unintended transfer of regulatory authority, from FDA to EPA, that resulted from the passage of FQPA, for certain food-contact antimicrobials," according to the FDA. "Specifically, ARTCA reestablished FDA's traditional regulatory authority for certain antimicrobials that are used in or on food-contact articles."

FDA currently regulates antimicrobial substances incorporated in, or applied to, food packaging materials regardless of whether the substance is intended to have an ongoing effect on any portion of the packaging. FDA does not regulate "antimicrobials that are incorporated in, or applied to, objects that have a semi-permanent or permanent food-contact surface, other than food packaging, to provide a sanitizing effect on such surface." [49]

Regardless of the regulatory framework under which an antimicrobial additive may fall, there are uniform testing standards to benchmark performance. These include:

- ISO 22196, *Measurement of antibacterial activity on plastics and other non-porous surfaces*
- AATCC Test Method 147-2004, ***Antibacterial Activity Assessment of Textile Materials: Parallel Streak Method***

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- JIS Z 2801 (Japan), ***Antimicrobial products – Test for antimicrobial activity and efficacy***
- QB/T 2591 (China), *Antimicrobial Plastics, Test for Antimicrobial Activity*
- ASTM E2149-10, 10 *Standard Test Method for Determining the Antimicrobial Activity of Immobilized Antimicrobial Agents Under Dynamic Contact Conditions*

Conclusion

While antibiotic and antiviral advancements have eradicated some diseases and limited the impact of many others, pathogens continue to plague societies around the world, with some developing resistance to even the most potent drug therapies. Research and development efforts continue as the pressure to find new and more powerful response options is unrelenting. Meanwhile, the contact-based spread of pathogens throughout medical, home, office and industrial environments presents a continuing risk to personal health as well as product performance and longevity.

Antimicrobial plastics bring proven broad spectrum germ-fighting capabilities to thousands of common use items and public area plastic surfaces. Antimicrobial additives and masterbatches also serve to protect plastic items and surfaces from microbial degradation thus maintaining their performance and prolonging their service life. Given the pervasiveness of plastics in developed nations and the ability of manufacturers and compounders to impart antimicrobial properties across a variety of formulations, plastic products and components could play a key role in keeping pathogens at bay in both medical and non-medical settings for years to come. U.S. manufacturers and compounders involved in the production of antimicrobial plastics need to understand the complex dual agency regulatory scheme in order to appropriately classify their formulations and products.

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