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Antimicrobial Fabrics – Issues and Opportunities in the Era of Antibiotic Resistance

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If your company designs, makes or markets antimicrobial fabrics, you know first hand the special benefits these products bring to consumers. You have put time and effort into learning about antimicrobials, and have probably learned a great deal about microorganisms and laboratory testing in the process. Undoubtedly you also have gained an appreciation for the commercial potential of these highly functional fabrics.

To design, make, or sell an antimicrobial fabric, a company must understand their technology, the regulatory implications of selling such a product, and the current, changing nature of microorganisms and infectious disease control. Understanding the technology helps to bring out the fabric's performance potential and limitations. Understanding the regulatory landscape highlights the restrictive bearing of governmental regulations on the ultimate marketing message for many antimicrobial fabrics. Understanding current trends in infectious disease helps manufacturers to make an important choice: Help to control the spread of infectious diseases through the legitimate, direct action of an antimicrobial fabric in "real-life" situations, or forego unsubstantiated health-related claims in order to aid in the general battle against environmentally-transmitted infections.

There are major differences between the way that antimicrobial fabrics and other antimicrobial products are regulated in the United States. Data requirements for various antimicrobial products reflect current opinion with respect to their importance as means to prevent the spread of infection: Sterilants, used to decontaminate critical medical instruments, are regulated by the United States Food and Drug Administration (FDA) and must meet extraordinary performance standards. Efficacy data, which is usually generated by third party laboratories, is carefully reviewed by the FDA. Disinfectants and sanitizers must meet similar requirements, but they are regulated by the United States Environmental Protection Agency (EPA) and are not expected to kill the hardiest pathogens. "Treated articles" (a term that includes most antimicrobial fabrics) are exempt from efficacy and safety review by EPA provided they meet certain conditions.[1] In EPA's words, "The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) requires the registration of any substance intended to prevent, destroy, repel, or mitigate pests [microorganisms]. However, the Code of Federal Regulations prescribes the conditions under which an exemption from registration is allowed for treated articles or substances designed to protect products from microbial attack."

Note: The FDA regulates antimicrobial fabrics, such as certain gauzes, which function as "medical devices." Such fabrics undergo a thorough review of safety and efficacy prior to sale, and lie outside of the scope of this article.

As a condition of the exemption from registration with EPA, manufacturers and sellers of antimicrobial fabrics are limited in terms of marketing claims and the fabric must be treated with an EPA-registered antimicrobial.

The following are examples of appropriate marketing language for non-medical antimicrobial fabrics given by EPA[2]

- Guards against degradation from microorganisms
- Treated to resist bacterial odors
- This product contains an antimicrobial agent to control odors

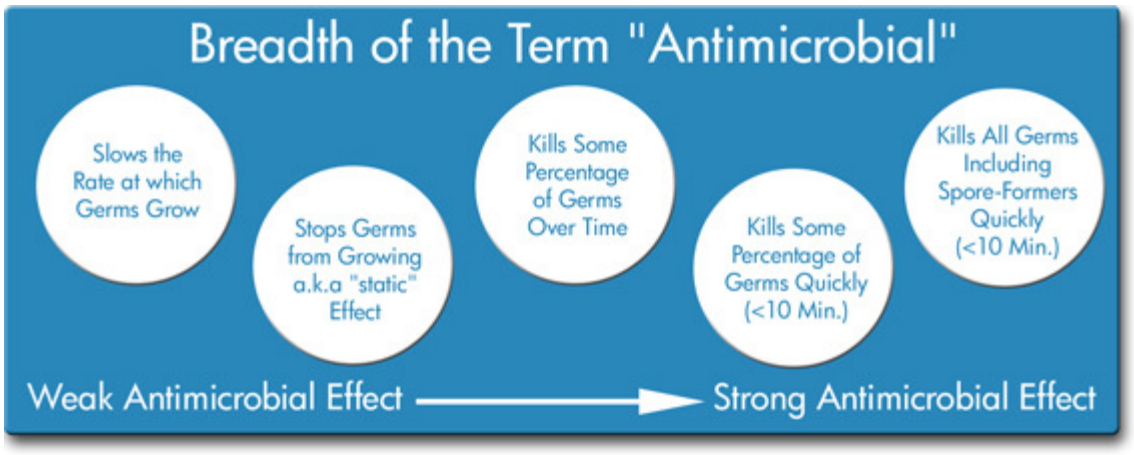
The following are examples of inappropriate (health-related) marketing language for non-medical antimicrobial fabrics:

- Antimicrobial
- Protects users from pathogenic microorganisms
- Helps prevent the spread of pathogenic microorganisms
- Kills pathogenic microorganisms

All of the claims allowed by EPA for antimicrobial fabrics highlight the function of the antimicrobial agent as protector of the textile, not the person. EPA also states "The preservative claim and qualifying statement on the product packaging (type, size color) must be given no greater prominence than other described product features."[2]

Although health-related claims for antimicrobial textiles are not permitted by EPA, they still impact public health and infectious disease transmission. Most antimicrobial fabrics are essentially unregulated with respect to efficacy, so it is crucial to understand the level of antimicrobial activity that *your* company's fabric brings to bear.

So just what is antimicrobial? Most define the term broadly, using it to describe anything that has a negative impact on microorganisms. The figure below highlights the span of this common term:



On the lowest end of the antimicrobial spectrum, a fabric might slow the rate of microbial growth, possibly for just one or a few species. Such activity would help to control odors and possibly impart some aesthetic protection, but would not impact the spread of microorganisms through the environment in any kind of meaningful way. Stronger antimicrobial fabrics kill a percentage of microorganisms over time. The strength of an antimicrobial is a product of its concentration and the time of contact, so the fabrics that kill microorganisms faster are usually the most potent. The vast majority of antimicrobial fabrics on the market today inhibit growth or kill some percentage of microorganisms over long periods of time, but only do so under certain circumstances. Thus, most antimicrobial fabrics perform at a level that would be considered useful for aesthetic protection but not for infection control. Few antimicrobial fabrics kill appreciable percentages of microorganisms quickly (defined here as under 10 minutes). Such antimicrobial activity is roughly equivalent to that that would be brought about by the use of a low-level disinfectant or sanitizer. The upper end of the antimicrobial spectrum is occupied primarily by toxic sterilant chemicals; no publicly known fabric technologies yet deliver such a benefit.

The only way to measure an antimicrobial fabric's degree of activity is through carefully performed, realistic microbiological testing. Microbiological tests used to characterize antimicrobial fabrics vary and are at the discretion of the companies undertaking them, since EPA does not review efficacy data (companies are required to keep data substantiating antimicrobial activity on file). In general, the methods commonly used to test antimicrobial fabrics are designed to detect low-level activity over long periods of time, in contrast to the methods used to test liquid chemical disinfectants and sterilizers, which look for high-level activity over short periods of time. Many of the commonly used antimicrobial fabric test methods do not have success criteria at all – interpretation of the test results is entirely up to the interested parties.

Four test methods are commonly used within the textile industry to measure the activity of antimicrobial fabrics. They are AATCC 100[3], AATCC 147[4], ASTM E2149[5], and JIS L 1902[6]. The table below highlights some aspects of each:

Table 1. Methods Commonly Used to Test Activity of Antimicrobial Fabrics

Method	Title	Summary	Strengths	Weaknesses	Realistic Model System?
AATCC 147	Antibacterial Activity Assessment of Textile Materials: Parallel Streak Method	Thin strips of test fabrics are laid onto petri dishes that have been inoculated with test microorganisms. Zones of growth inhibition are qualitatively analyzed after incubation.	Relatively inexpensive and quick. Fabrics must normally have considerable activity levels to demonstrate "zones of inhibition."	Non-quantitative method makes comparisons with other products or technologies difficult. The method cannot differentiate "kill" from growth inhibition.	Not realistic - The microbial inoculum generally only contacts the surface of the fabric, and the surface of the agar is wetter and more nutritive for a longer period of time than would be expected in real situations.
AATCC 100	Assessment of Antibacterial Finishes on Textile Materials	Test and control fabrics are effectively saturated, side-by-side, with a nutritive but dilute suspension of microorganisms. Microbial concentrations on the fabrics are enumerated at "time zero" and also after the contact period has elapsed. Differences between test and control fabrics are used as the basis for antimicrobial activity level (microbial reduction or growth inhibition) determinations.	Quantitative method that is well designed in terms of technicalities related to the testing of antimicrobial agents (includes antimicrobial agent neutralization controls, etc).	Only a single replicate of the test is normally performed. No clear standards are set for "pass" or "fail" by the method.	Very realistic with respect to prevention of microbial growth or kill of microorganisms in wet fabrics, and possibly even a conservative model. Unrealistic in that fabrics are kept wet (most antimicrobial agents work best in the presence of liquid) for the full contact period, which is often a full 24 hours. Thus, reductions of dried microbial inocula on fabrics in "real-life" may not be as dramatic as results might suggest.
ASTM E2149	Standard Test Method for Determining the Antimicrobial Activity of Immobilized Antimicrobial Agents Under Dynamic Contact Conditions	Test and control fabrics are placed individually into 50 mL of a non-nutritive suspension of test microorganisms and shaken vigorously for the contact period (usually 24 hours). Microbial concentrations in solution are determined at "time zero" and after the contact period. Microbial reductions are calculated.	Quantitative method.	Only a single replicate of the test is normally performed. No clear standards are set for "pass" or "fail" by the method.	Not realistic in any sense - fabrics are submerged in a great relative volume of liquid and shaken in a non-nutritive suspension for long periods of time. The method states that active ingredient should be "non-leaching" but does not include sufficiently sensitive methods for testing for leaching of the antimicrobial into the test solution.
JIS I 1902 (Quantiative Aspect)	Testing for Antibacterial Activity and Efficacy on Textile Products	3 replicates of test and control fabrics are inoculated, side-by-side, with a slightly nutritive and dilute suspension of microorganisms. Microbial concentrations on the fabrics are enumerated at "time zero" and also after the contact period has elapsed. Differences between test and control fabrics are used as the basis for antimicrobial activity level (microbial reduction or growth inhibition) determinations.	Quantitative method that is well designed in terms of technicalities related to the testing of antimicrobial agents (includes antimicrobial agent neutralization controls, etc). Three replicates are required.	The microbial inoculum used for this method is much less nutritive than that used for AATCC 100, making the method less conservative.	Fairly realistic with respect to kill of microorganisms in wet fabrics, but may not be representative of activity in dirty fabrics. Unrealistic in that fabrics are kept wet (most antimicrobial agents work best in the presence of liquid) for the full contact period, which is often a full 24 hours. Thus, reductions of dried microbial inocula on fabrics in "real-life" may not be as dramatic as results might suggest.

It is important to accurately communicate the capabilities of antimicrobial textiles to customers because many of them may decide to forego other pathogen control measures if they are given the impression that the fabric will provide protection from the spread of infectious microorganisms. Even many professionals do not understand how the degree of antimicrobial protection varies from one class of product to the next. For example, hospital staff may choose to

lengthen the laundering interval for bed sheets, expecting that an incorporated antimicrobial will confer protection against infectious microorganisms. If a fabric indeed provides such protection – great! If it does not, however, people may needlessly become exposed to pathogens living in or on the fabric.

As antimicrobials, treated textiles tie into the overall picture of infectious disease control and antibiotic resistance. Responsible manufacturers will recognize and respect the role their products play in the ever-changing ecology of infectious microorganisms.

> **Summary of the Antibiotic Resistance Issue:** No more than 100 years ago, if a person acquired a bacterial infection, the body had to clear the infection by itself or else the infection would eventually result in death. After penicillin and many other effective antibiotics were discovered, however, that changed. In the decades after penicillin was discovered in 1928, a number of powerful antibiotics were developed. They were used plentifully and often carelessly - prescribed needlessly for certain bacterial infections and even for viral infections where they have no effect. Farmers found that animals fed low levels of antibiotics grow faster and are less subject to disease, so thousands of tons of antibiotics were (and still are) added to animal feed. The problem: unlike disinfectants, antibiotics generally act against a single component of a bacterium. Thus, in environments where antibiotics are present, there is great selective pressure toward bacteria that can make the relatively minor mutations needed to render them resistant. Once a single bacterium has developed resistance to an antibiotic, it can be amplified across bacterial species by quick propagation and the tendency to share antibiotic resistance genes with other bacteria. In the last decade, resistance to antibiotics - even antibiotics once thought to be "last ditch" treatments has increased remarkably and is continually on the rise. Doctors are finding many once-treatable infections are now deadly (e.g. highly publicized Methicillin-resistant *Staphylococcus aureus* (MRSA) infections). Large pharmaceutical companies, once major sources of new antibiotics, have exhausted most "easy" targets for new antibiotics and have shifted their research and development focus to long-term, chronic diseases rather than antibiotic discovery to increase profits.

The first way that antimicrobial fabrics affect the phenomenon of antimicrobial resistance is quite positive – robust antimicrobial fabrics may actually prevent resistant bacteria from propagating or surviving in fabrics and causing infections. In the era of antibiotic resistance, prevention of infections is critical. Imagine an antimicrobial fabric powerful enough to kill hardy pathogens on the dry environmental fabric of a chair in a hospital waiting room - it would almost certainly reduce disease transmission rates!

The second way that antimicrobial fabrics are related to the overall picture of antibiotic resistance is through the potential to engender cross-resistance to antibiotics. Cross-resistance to antibiotics develops when a bacterium, responding to pressure from an antimicrobial agent (such as silver, Triclosan, or a quaternary ammonium), develops a mutation related to the antimicrobial that *also* increases resistance to a therapeutic antibiotic. Cross-resistance to antibiotics has not been demonstrated in "real-life" studies to date, but it appears to be fairly easy to bring about in laboratory settings.[7,8,9] Cross resistance is not thought to be a major cause of antibiotic resistance, but it is reasonable to think that the proliferation of antimicrobials could increase microbial resistance to antibiotics, not to mention the antimicrobials themselves. It is important to note that the specter of cross-resistance from antimicrobial fabrics may be amplified because fabrics are often in close contact with the skin as clothing or upholstery. Low levels of antimicrobial agents and long term interaction with the millions of bacteria that naturally live on the skin may enhance the chances for cross-resistance.

In light of the information above, one thing becomes clear: The stakes are high and becoming higher. Bacteria are acquiring resistance to antibiotics at an alarming rate and an ever-growing number of fabrics are being marketed and mis-marketed as means to control the spread of infectious disease.

With the potential for commercial gain from antimicrobial fabrics comes a special responsibility to communicate openly and accurately about the strengths and weaknesses of the technologies. Manufacturers may wish to engage regulatory agencies proactively, based on data they have generated, to expand allowable claims as they are supported by the science and scale back allowances for claims that are questionable. A push for greater enforcement of existing regulations will also help to ensure a more level playing field for all. In addition, antimicrobial fabric manufacturers and distributors may consider investing in public and governmental education about the benefits and drawbacks of antimicrobials in textile applications – the more the public and government know about antimicrobials, the more likely they will be to promulgate fair and appropriate regulations in the future.

Commercial opportunities abound for antimicrobial fabrics. There are obvious unfulfilled needs for odor control, prevention of degradation, and controlling the spread of infectious microorganisms. As a maker or marketer of antimicrobial textiles, your company is in a unique position to lead the industry ethically into the future, and more importantly, into the era of antibiotic resistance.

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