THE ANTIMICROBIAL PROPERTIES OF COPPER ALLOYS AND THEIR POTENTIAL APPLICATIONS

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ABSTRACT

Recent laboratory studies show that several bacteria, known to be human pathogens, die when they come in contact with copper and copper alloy surfaces. The amount of live bacteria drops by several orders of magnitude, to zero, on copper alloys in a few hours. In contrast, no reduction is seen in the concentration of live organisms on stainless steel during the six-hour test period. Aluminum painted and coated surfaces and plastics would show behavior similar to stainless steel and show no effect. Coatings and other surfaces claiming to be antimicrobial showed little to no effect. These results suggest the selection of copper alloys for surfaces exposed to human touch can materially assist in reducing the transmission of infectious organisms. In order to make antimicrobial claims in the United States, the approval of the US Environmental Protection Agency (EPA) is required. The EPA-required efficacy testing is described and the test results are summarized. It is anticipated, that once regulatory approval is obtained, that this will facilitate the introduction of antimicrobial copper alloys in hospitals, nursing homes and other healthcare facilities, as well as schools, and public buildings. Some of the application and barriers, to entry into the healthcare markets are mentioned.

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INTRODUCTION

Man has exploited the antimicrobial attributes of copper, even before the nineteenth century, when Louis Pasteur developed his *Germ Theory of Disease*, in which infections are attributed to microbes invading the human body. The Hippocrates Collection, to which the father of medicine contributed, recommends the use of copper for leg ulcers related to varicose veins. The ancient Aztecs used copper oxide and malachite, a copper carbonate compound, for treating skin conditions. In a recent laboratory study [1], pure cultures of a fecal indicator bacterium, *Escherichia coli*, were stored in a brass vessel of unidentified composition and an earthenware experimental control vessel for 6, 24 and 48 hours and then cultured. Results indicated that bacterial counts were reduced at 6 hours in the brass vessel versus the earthenware control. No bacteria were found in the brass vessel after 24 hours. As part of the same study, coliform bacterial counts were determined on brass and earthenware vessels in a village in Punjab, India, following overnight 12- to 15-hour storage. The initial counts at the source ranged from 1417 to 1773. A reduction in counts was seen in the brass vessel, down to a range of 53 to 131 although the counts remained high in the earthenware vessel, at 1270 to 1677. In an earlier study [2], carried out in a hospital, brass doorknobs showed sparse growth of bacteria, while stainless steel doorknobs were found to be heavily contaminated.

The inhibitory effects of the surfaces of a range of commercial wrought copper-base alloys, on bacteria, with stainless steel as an experimental control, are discussed. The tested organisms include *E. coli* O157:H7 and *Listeria monocytogenes*, which are food-borne pathogens associated with several large-scale food recalls, and methicillin-resistant *Staphylococcus aureus* (MRSA), a serious hospital-acquired, or nosocomial, infection.

According to the March 28, 2001 issue of the New York Times, 76 million illnesses associated with contaminated food were reported annually in the United States, which resulted in 325,000 hospitalizations and 5000 deaths. Although most *E. coli* strains are harmless to humans, the U.S. Dept. of Agriculture (USDA) estimates that the cost to society associated with infectious strains of *E. coli* is $5 billion annually. The recall of *E. coli* O157:H7 contaminated spinach, during the fall of 2006 in the US, indicates that this bacterium continues to be a concern. The Centers for Disease Control (CDC) reported in 1999 that *L. monocytogenes* accounts for the highest hospitalization rate (90%) and the second highest fatality rate (20%) of all food-borne human pathogens. On average, there are 2,500 cases *of L. monocytogenes* are reported each year, resulting in 500 fatalities. According to a July 2004 report by the Infectious Disease Society of America, two million people are infected each year while in the hospital, and 70% of those infections are resistant to at least one drug. This resulted in 90,000 deaths and a cost to society of $5 billion annually. The Committee to Reduce Infection Deaths, www.hospitalinfection.org, indicates that the annual healthcare cost of hospital infections is estimated to be $28 to $30 billion, which is much higher that previously thought.

RESULTS

Alloys

The nominal chemical compositions of the tested alloys, are listed in Table I, in accord with the UNS five-digit alloy numbering system, except for Y90. The alloys are often identified by their three digit designation for brevity. The alloys range from coppers to brasses and bronzes, copper-nickels and copper-nickel-zinc alloys. The latter are commonly referred to as nickel silvers because of their silver color. The experimental control is type UNS S304 stainless steel, a material widely used in food processing and healthcare applications, which does not exhibited antimicrobial efficacy.

Table 1 – Nominal alloy composition (weight%)

UNS Number	Cu	Zn	Sn	Ni	Al	Mn	Fe	Cr	P	Si
Copper										
C10200	99.95									
C11000	99.90									
C19700	99						0.7		0.3	
Brass										
C22000	90	10								
C24000	80	20								
C26000	70	30								
Y90*	78	12		3		7				
Bronze										
C51000	95		5						0.2	
C61500	90			2	8					
C63800	95				3					2
C65500	97									3
Cu-Ni										
C70600	90			10						
C71000	80			20						
Cu-Ni-Zn										
C75200	65		17	18						
C77000	55		27	18						
Stainless Steel										
S30400	0			8			74	18		

*no UNS number

E. coli O157:H7

The antimicrobial effect of copper alloys was initially investigated utilizing *E. coli* O157:H7. Details of the sample preparation, culturing of bacteria and the experimental procedures were presented previously [3-7]. The experiments were conducted at 20°C, room temperature, and in some cases at 4°C. The latter corresponds to the temperature at which food is refrigerated. A semi-log plot of time in minutes versus live bacteria count for C110, an alloy which essentially contains 100% copper, is shown in Figure 1. At 20°C, the bacterial count decreases by about one order of magnitude (one-log) over 75 minutes and then falls off rapidly and reaches zero at 90 minutes. The zero point, which corresponds to a nine-log drop in total, indicates that the bacteria are no longer viable and are dead. A similar pattern is seen at 4°C, but the times are longer, indicating that the time to kill the bacteria increases as temperature decreases. A rapid falloff to zero occurs between 180 minutes and 270 minutes at 4°C. Figure 1 represents data from a total of 71 test coupons. The tests were repeated four to six times at 20°C and three to four times at 4°C. A similar number of repeat tests were conducted to establish the data shown in the other figures.

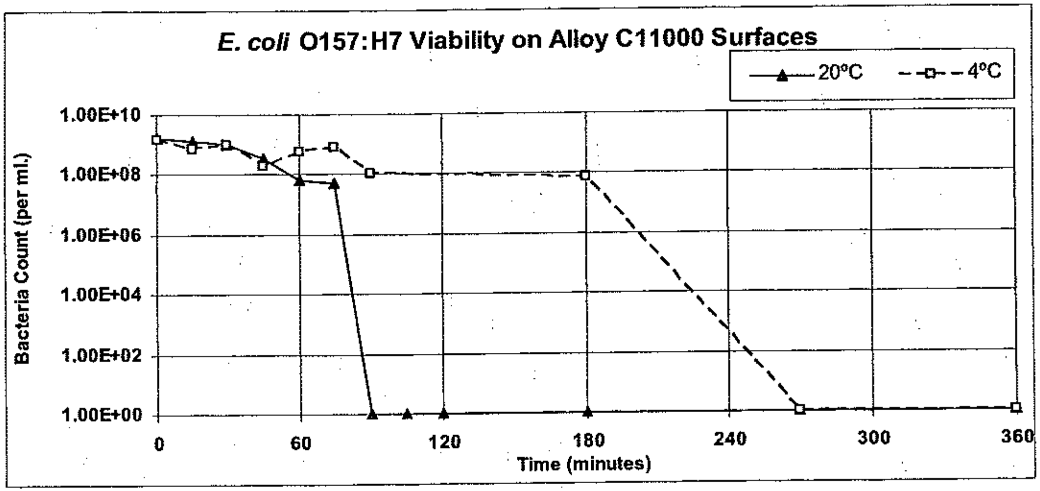

Figure 1 - Amount of live E. coli O157:H7 surviving on UNS alloy C1100 surfaces at 20°C and 4°C

The antimicrobial response, at 20°C, of three additional copper alloys, Y90-a manganese brass which is the alloy on the surface of the Sacagawea one-dollar US coin, UNS alloy C615-an aluminum bronze, and C752-a copper nickel zinc alloy, is compared to C110, as well as S304 stainless steel, which serves as an experimental control. As can be seen in Figure 2, all three of the copper alloys, Y90, C615, and C752, displayed similar but a somewhat delayed response relative to C110. For all three alloys, the bacteria count decreases by about one order of magnitude (one-log) between 90 and 120 minutes, compared to the 75 minutes seen in C110. The bacterial counts on these three alloys then fall off rapidly and reach zero at 105 to 180 minutes, compared to 90 minutes on C110. The zero point, which corresponds to a nine-log drop, indicates that the bacteria are no longer viable and are dead. The bacteria count on the stainless steel control, S304, remained constant for the first 90 minutes of the test, falls by one-log during the next 90 minutes and then remained constant for the next 90 minutes. The slight drop in live bacteria remaining on S304 is attributed to evaporation rather that any antimicrobial efficacy.

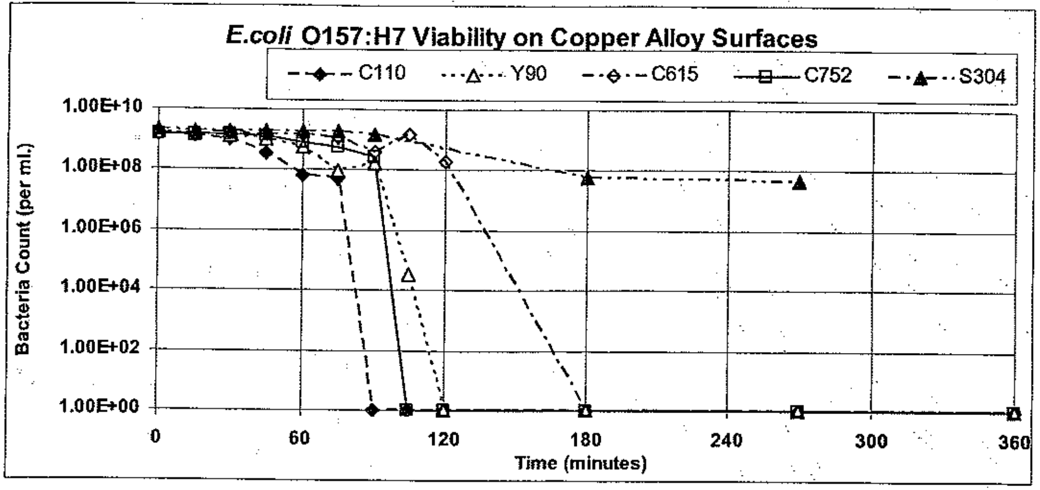

Figure 2 - Amount of live E. coli O157:H7 surviving at 20°C on copper alloy Y90 and UNS alloys C11000, C61500, C75200 and S30400 stainless steel

Listeria monocytogenes

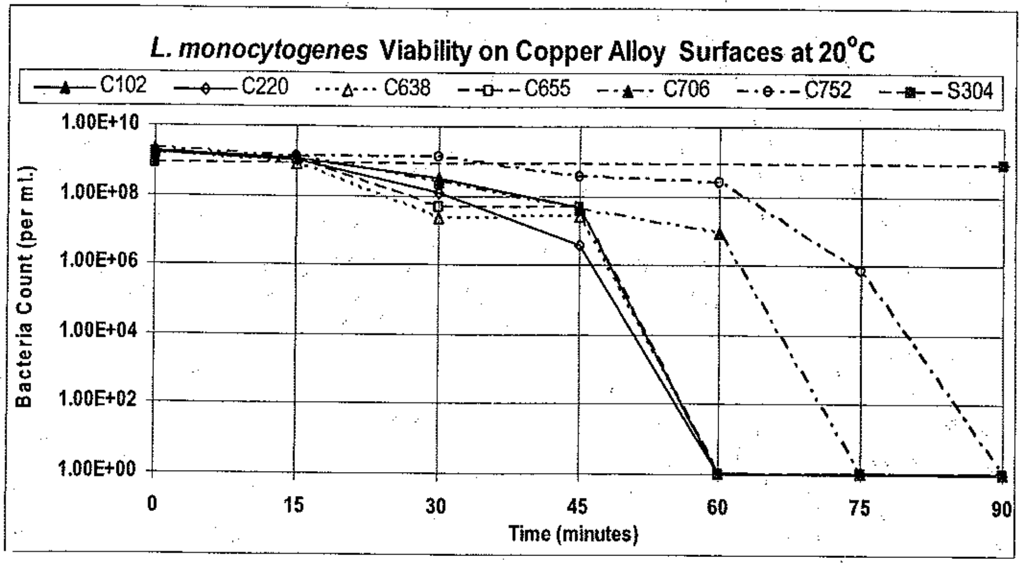

Figure 3 - The viability of *Listeria monocytogenes* on the surfaces of UNS alloys C10200, C22000, C63800, C70600, C75200 and S30400 at 20°C

The viability of *L. monocytogenes* was measured on the surfaces of seven alloys [8]. The results at 20°C are presented in Figure 3. Bacterial counts were taken on C102-an alloy containing essentially contains 100% copper, C220-a brass, C638-an aluminum bronze, C655-a silicon bronze, C706-a copper nickel alloy, and C752-a copper nickel zinc alloy, and the experimental control, S304 stainless steel. Four alloys, C102, C220, C638 and C655, which all contain 90% or a greater amount of copper, follow the same pattern. The bacterial counts drop slowly, by about two logs over the first 45 minutes and then fall rapidly over the next 15 minutes and reach zero at 60 minutes. A total reduction of nine-logs is seen in bacterial counts. Alloy C706 follows a similar but somewhat delayed pattern. The bacterial count drops slowly over the first 60 minutes, by about a half log, and then falls rapidly over the next 30 minutes and reaches zero at 90 minutes. In marked contrast, the stainless steel exhibits no change in its bacteria count during the 90 minute test.

Methicillin-Resistant *Staphylococcus aureus*

The viability of Methicillin-Resistant *Staphylococcus aureus* (MRSA) was measured on the surfaces of four alloys [9]. The results at 20°C are presented in Figure 4. The bacterial counts were taken on C197-an alloy containing 99% copper, C240-a brass, C770-a copper nickel zinc alloy, and S304, the experimental control. On C19700, a rapid seven-log falloff to zero is seen within 75 minutes, while on C220 a uniform seven-log drop to zero occurs in 270 minutes. In C770, a three-log drop is observed after 270 minutes. That three-log drop indicates only ten thousand out of ten million bacteria survived, which corresponds to a 99.9% reduction in live bacteria.

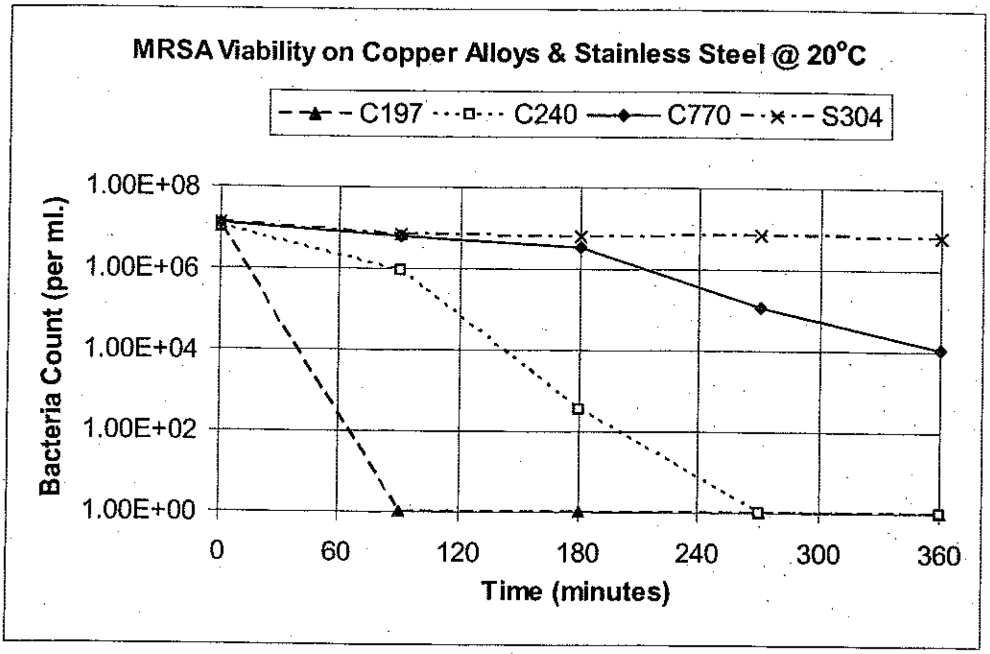

Figure 4 - The viability of methicillin-resistant *Staphylococcus aureus* (MRSA) on the surfaces of UNS alloys C19700, C24000, C77099 and S30400 at 20°C

The bacterial count of methicillin-resistant *Staphylococcus aureus* (MRSA) was measured at 20°C on the surfaces of a silver ion-containing coating applied to S304 stainless, a triclosan-containing polyethylene, C110 and uncoated type S304 stainless steel, the experimental control. The silver ion-containing zeolite coating is being promoted as an antimicrobial product in a variety of consumer, medical and industrial applications. Triclosan, a chlorinated hydrocarbon, is being marketed as an antimicrobial ingredient in soaps, as well as consumer products. As shown in Figure 5, only C110 exhibits an antimicrobial response, a seven-log drop in 75 minutes. The silver-containing coating and triclosan-containing polyethylene are quite similar to S304 and thus show no observable antimicrobial response. As will be discussed, both are registered with the EPA under a treated article exemption, and can not legally make public health claims.

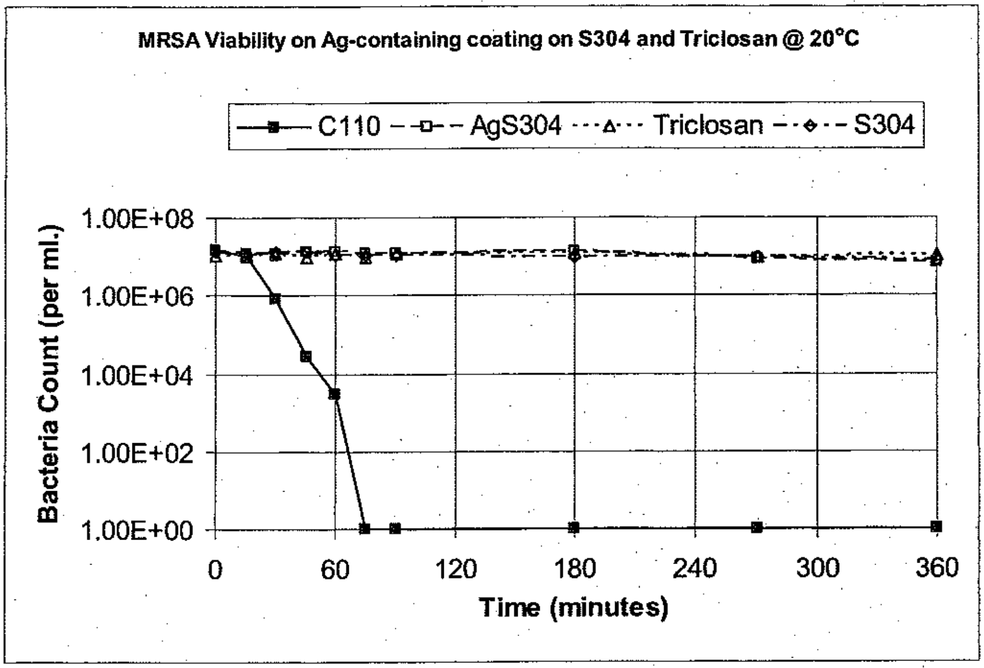

Figure 5 - The viability of methicillin-resistant *Staphylococcus aureus* (MRSA) at 20°C on the surfaces of a sliver-containing coating on UNS alloy S30400, Triclosan-containing polyethylene, UNS alloys C11000 and S30400 stainless steel

Testing Required for Regulatory Approval

In order to be legally permitted to make antimicrobial claims in the United States, products must be approved and registered by the US Environmental Protection Agency (EPA). Antimicrobial claims fall under the Federal Insecticide Fungicide and Rodenticide Act (FIFRA). The EPA only requires efficacy testing when the registrant wishes to make public health claims when marketing the product. Some products, such as the previously mentioned silver-containing coating, are registered under special provision. This provision is the "treated article of exemption", which indicates that the ingredient is protecting the article itself. For example, the addition of a fungicide to paint preventing mildew. The fungicide is protecting the paint and not public health. Thus products registered under the "treated article exemption" can not legally make public health claims. At present only sanitizing gases and liquids can make public health claims under FIFRA. The Copper Development Association has conducted the required EPA approved efficacy tests and is pursuing the registration under FIFRA, which will allow copper alloys that are registered to be legally be marketed as antimicrobial materials with public health claims. When registration is granted, copper alloys will be the first materials that will be permitted to make public health claims.

The tests were conducted in accord with EPA Good Laboratory Practices (GLP). Adherence to GLP testing insures integrity and accuracy of the data requires for registering products for public health use under FIFRA, and facilitates EPA audits of the test data. GLP tests were conducted on three separately manufactured lots of five copper alloys, which range in copper contents from 65% to 100%. Each of the five alloys is representative of a major family of alloys. The five alloys are: C110-a high copper, C510-a bronze, C706-a copper nickel, C260-a brass, and C752-a copper nickel zinc. In addition, S304 served as the experimental control. In the GLP tests, the number of survivors of the following five bacteria was determined after each test: *Staphylococcus aureus, Enterobacter aerogenes, Escherichia coli* O157:H7, *Pseudomonas aeruginosa* and methicillin-resistant *Staphylococcus aureus* (MRSA). The three EPA approved GLP test protocols are:

1. Efficacy as a Sanitizer-which measures bacterial count after two hours
2. Residual Self-Sanitizing Activity-which measures bacterial count before and after six wet and dry wear cycles in which bacteria are counted over 24 hours in a standard wear apparatus, which is shown as a schematic in Figure 6
3. Continuous Reduction of Bacterial Contaminants-which measures bacteria after inoculating an alloy surface eight times in a 24-hour period without intermediate cleaning and wiping

In many of the Continuous Reduction tests, there were no survivors. An exception to this observation is shown in Figure 7. During the first five inoculations, the bacterial count drops from approximately 700,000 to zero. A few survivors, less that 100, are seen after the sixth, seventh and eight inoculations. However, this is still greater than a 99.9% reduction.

The results of the 180 GLP tests, involving three test protocols, two to three lots of five different alloys, and five bacteria, are summarized in Table 2. In both the Efficacy as a Sanitizer test and Residual Self-Sanitizing test (wear test), a reduction in live bacteria >99.9% is seen in all sixty tests when compared to S304. In the Continuous Reduction of Bacterial Contaminants test, a reduction of >99.9% is found in fifty-four out of the sixty tests, again when compared to S304. In the remaining six tests, reductions ranged from 99.3% to 99.9%. In five of the tests, the reduction, on S. aureus, was 99.3% on one lot of C260, 99.7% on two lots of C260, and 99.6% on two lots of C752. In the sixth test, on MRSA on C706, the reduction was 99.9%. In summary, a reduction of >99.9 was seen on 174 out of 180 tests. The reduction seen in the remaining six tests ranged from 99.3% to 99.9%. These results indicate that the antimicrobial response of copper alloys is strong, enduring and reproducible and should help control human pathogens.

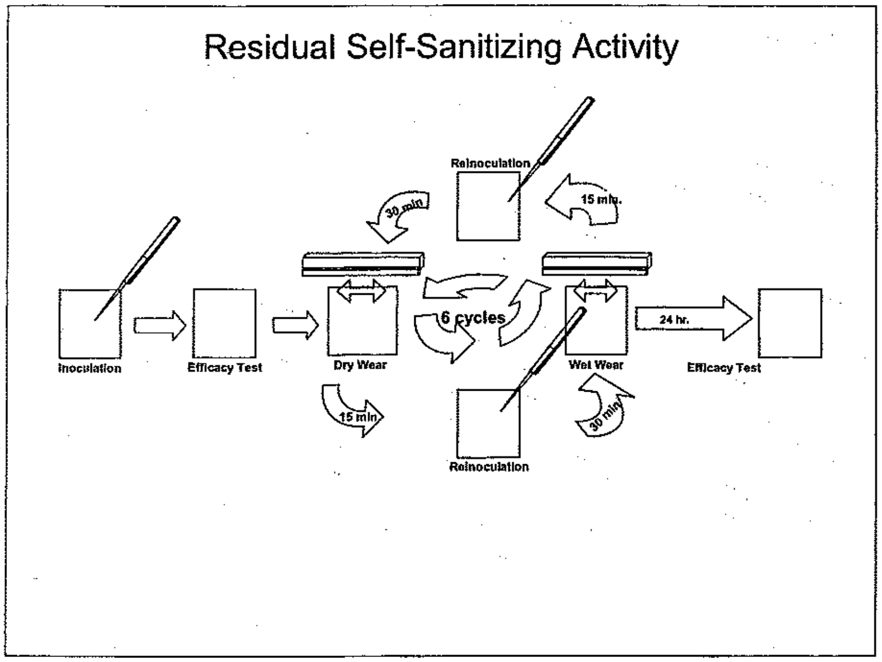

Figure 6 - Residual self sanitizing test, in which copper alloys were subjected to six alternate wet and dry cycles during a 24 hour period in a standard wear test apparatus

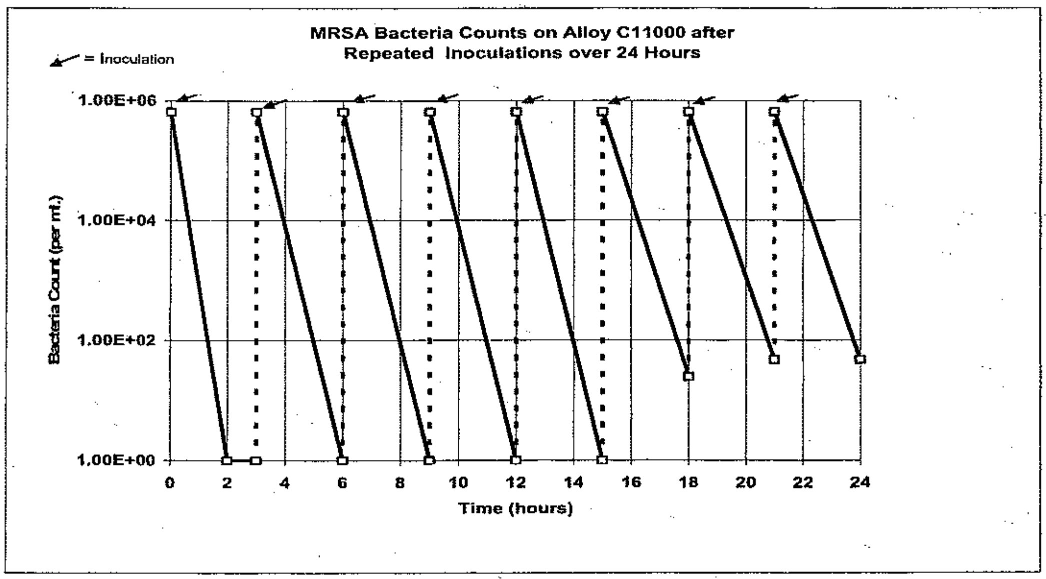

Figure 7 - Continuous reduction test results of methicillin-resistant *Staphylococcus aureus* (MRSA) on UNS alloy C11000

Table 2 - Summary of antimicrobial efficacy good laboratory practices (GLP) test results

		S. aureus*			E. aerogenes*			MRSA**		P. aeruginosa**		*E.coli* O157:H7**	
Efficacy as a Sanitizer	C110	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9
	C510	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9
	C706	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9
	C260	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9
	C752	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9
Residual Self-Sanitizing	C110	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9
	C510	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9
	C706	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9
	C260	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9
	C752	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9
Continuous Reduction	C110	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9
	C510	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9
	C706	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	99.9	>99.9	>99.9	>99.9	>99.9
	C260	99.3	99.7	99.7	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9
	C752	>99.9	99.6	99.6	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9	>99.9

* Testing of three independently manufacturer lots of each alloy required for *S. aureus* and *E. aerogenes*

** Testing of two independently manufacturer lots of each alloy required for Methicillin-Resistant *S. aureus* (MRSA), P. aeruginosa and E. coli O157:H7

CONCLUSION

The surfaces that humans touch in hospitals is the initial target market [10-11]. Subsequent markets include schools, public buildings, exercise facilities, shopping malls, mass transit systems, airports, and cruse ships. Applications within hospitals include door hardware, sink faucets handles, IV drip poles, bed footboards and rails, tray tables, nurse's work tables, furniture pulls and any other touched surface within the healthcare setting. The attainment of EPA approval is only the first of several barriers to entry into the hospital market. The applications with the highest likelihood of success must be identified, and the entire supply chain engaged. Copper alloy components must be fabricated, and made readily available. The insight into the decision making process in hospitals has to better be understood. It is also be necessary to gain acceptance in hospital settings and with the general public. The net result will be not only increases in copper alloy consumption, but also should help save lives. Success will be attained when it is generally understood and appreciated that copper alloys should be utilized in those applications where their unique intrinsic antimicrobial properties will benefit human health.

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