Advanced Materials & Processes® Web Exclusive
November 2008
DOI: 10.1361/amp1108copper

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This article was the basis for Antimicrobial Properties of Copper Alloy Surfaces, which appeared in the November 2008 issue of Advanced Materials & Processes. This is the original manuscript submitted by the authors. It contains much more information than was possible to include in the magazine.

Antimicrobial Properties of Copper Alloy Surfaces, with a Focus on Hospital-Acquired Infections

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ABSTRACT

Recent laboratory studies show that several bacteria, known to be human pathogens, die when they come in contact with dry copper and copper alloy surfaces at room temperature. The amount of live bacteria drops by several orders of magnitude, to zero, on copper alloys in one to two hours. In contrast, almost no reduction is seen in the concentration of live organisms on stainless steel after several hours and even days. Aluminum painted and coated surfaces and plastics would also exhibit behavior similar to stainless steel and show no effect. In addition, coatings and other surfaces claiming to be antimicrobial also showed little to no effect. These results suggest the selection of copper alloys for surfaces exposed to human touch can materially assist in reducing bacterial contamination, which should lead to a reduction in 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 regulatory approval 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 barriers to entry into the healthcare markets are mentioned.

INTRODUCTION

Copper as a metal and in alloys has many useful characteristics which account for its continuing wide use. These include high thermal and electrical conductivity, good corrosion resistance, and ease of formability. However, one attribute has been forgotten and overlooked in recent times, its antimicrobial property.

Man exploited the antimicrobial attributes of copper 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, 460 to 380 B.C., to which the father of medicine contributed, recommends the use of copper for leg ulcers related to varicose veins. Pliny, 23 to 79 A.D., used copper oxide with honey to treat intestinal worms. The Aztecs gargled with a mixture containing copper to treat sore throats. In a laboratory study (1), water inoculated with a fecal indicator bacterium, Escherichia coli, was stored in water vessels made of brass, a copper alloy, as well as in earthenware vessels. The vessels contained either distilled water or natural water from the Punjab region in rural India. No live bacteria were found in the brass vessels after 48 hours, while the water in the earthenware vessel remained contaminated. In an earlier study (2) carried out in a hospital, brass doorknobs showed sparse growth of pathogenic bacteria, while stainless steel doorknobs were heavily contaminated. Previously published results (3-11) show that several bacterial species die on copper alloy surfaces in a matter of minutes to hours, and that Influenza A virus particles become inactivated on copper surfaces (12).

This paper discusses tests that were conducted on a range of commercial copper alloys. The tested organisms include E. coli O157:H7, a food-borne pathogen 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 are reported annually in the United States, which results

in 325,000 hospitalizations and 5,000 deaths. Although most E. coli strains are harmless to humans, the US Dept. of Agriculture (USDA) estimates that the cost associated with infectious strains of E. coli is US $5 billion annually. In the fall of 2007, E. coli O157:H7 contamination resulted in the recall of 9.84 kilotonnes of hamburger meat. Although E. coli O157:H7 is commonly associated with processed meat, the recall of spinach during the fall of 2006 indicates that it is also a concern in packaged fresh vegetables. 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 these hospital-acquired or nosocomial infections are resistant to at least one drug. This results in 90,000 deaths and a cost of $5 billion annually. The New York Times (July 27, 2007) stated that the US Centers for Disease Control projects the number of deaths to be 99,000 in 2007 and officials estimated that the cost of treatment may approach 1% of the total national cost of healthcare, or $20 billion.

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 registrants wish to make public health claims. Some products, such as the commercially available silver ion-containing coatings, are registered under a special provision in FIFRA, the “treated article exemption.” This provision indicates that the antimicrobial ingredient only protects the article containing the ingredient. EPA grants the “treated article exemption” only for non-public health uses of a pesticide that is intended only to protect or preserve the treated article. One example of a “treated article exemption” is the addition of a fungicide to paint to prevent mildew. Thus, the fungicide is protecting the paint, and not public health. Therefore, products registered under the “treated article exemption” cannot legally make public health claims. At present, only antimicrobial gases and liquids, such as sterilizers, disinfectants and sanitizers, can make public health claims under FIFRA. The results presented represent a summary of the required EPA-approved efficacy tests. They were submitted along with the other required information, in pursuit of FIFRA registration. When registration is granted, antimicrobial copper alloys will be the first solid materials legally permitted to make public health claims.

MATERIALS AND METHODS

Table 1 – Nominal Alloy Composition (Weight %)

UNS Number	Cu	Zn	Sn	Ni	Al	Mn	Fe	Cr	P	Si
Copper										
C11000	99.90									
C19700	99						0.7		0.3	
Brass										
C22000	90	10								
C24000	80	20								
C26000	70	30								
Bronze										
C51000	95		5						0.2	
Cu-Ni										
C70600	90			10						
Cu-Ni-Zn										
C75200	65		17	18						
C77000	55		27	18						
Stainless Steel										
S30400	0			8			74	18		

The chemical compositions of the copper alloys tested are listed in Table 1. As can be seen, they range from coppers to brasses and bronzes, copper-nickels and copper-nickel-zinc alloys (nickel silvers). The other materials tested include polyethylene, a common kitchen cutting board material, and a silver ion-containing coating which is being marketed as antimicrobial. The experimental control

is type UNS S304 stainless steel, a material widely used in food processing and healthcare applications, which does not exhibit antimicrobial efficacy.

Standard microbiological techniques were used to culture, recover and count bacteria and are described elsewhere (3-6). Small square coupons of each alloy, either 1 cm or 2.54 cm on each side, were inoculated with a predetermined concentration of bacteria and exposed for the pre-selected time. The remaining live bacterium is then recovered, cultured and counted.

The tests were conducted in accord with EPA Good Laboratory Practices (GLP). Adherence to GLP testing insures integrity and accuracy of the data required for registering products for public health use under FIFRA, and facilitates EPA audits of the test data. GLP tests were conducted at ambient temperature and humidity on either two or 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). Three lots of each alloy were mandated for the S. aureus and E. aerogenes tests, and two lots were required for the Methicillin-Resistant S. aureus (MRSA), P. aeruginosa and E. coli O157:H7 tests. The three EPA approved GLP test protocols, listed below will be described later in this paper:

- Efficacy as a Sanitizer
- Residual Self-Sanitizing Activity
- Continuous Reduction of Bacterial Contaminants

RESULTS

E. coli O157:H7

A semi-log plot of time in minutes versus bacteria count on C110, a 99.90% copper alloy, is shown in Figure 1. At 20°C, the bacteria 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 9-log drop, indicates that the bacteria, E. coli O157:H7, are no longer viable and are dead. A similar pattern is seen at 4°C, but the times are longer, indicating that the rate of inactivation decreases as temperature decreases. A rapid falloff occurs between 180 minutes and 270 minutes at 4°C. A similar number of repeat tests and coupons were used to establish the plots shown in the other figures.

Three copper-free materials were also evaluated. These included stainless steel S304, which contains 74% iron, 18% chromium and 8% nickel and is widely used in food processing and healthcare applications, polyethylene, a common food cutting board material, and a stainless steel with a silver-containing coating. The latter is a commercial antimicrobial product. As can be seen in Figure 2, the bacteria count at 20°C is virtually unchanged on the uncoated stainless steel for the first 90 minutes and then falls by one log during the next 90 minutes. Although this S304 test happened to be stopped at 270 minutes, other test show that the bacteria count would remain the same through 360 minutes. The bacteria count on polyethylene was unchanged for the first 180 minutes, and decreased by one log over the next 180 minutes. When compared to uncoated stainless steel, both the polyethylene and the silver-containing coating on stainless steel, displays a similar but slightly less of a drop in bacteria count, as is also shown in Figure 2. In summary, all three materials show a similar response.

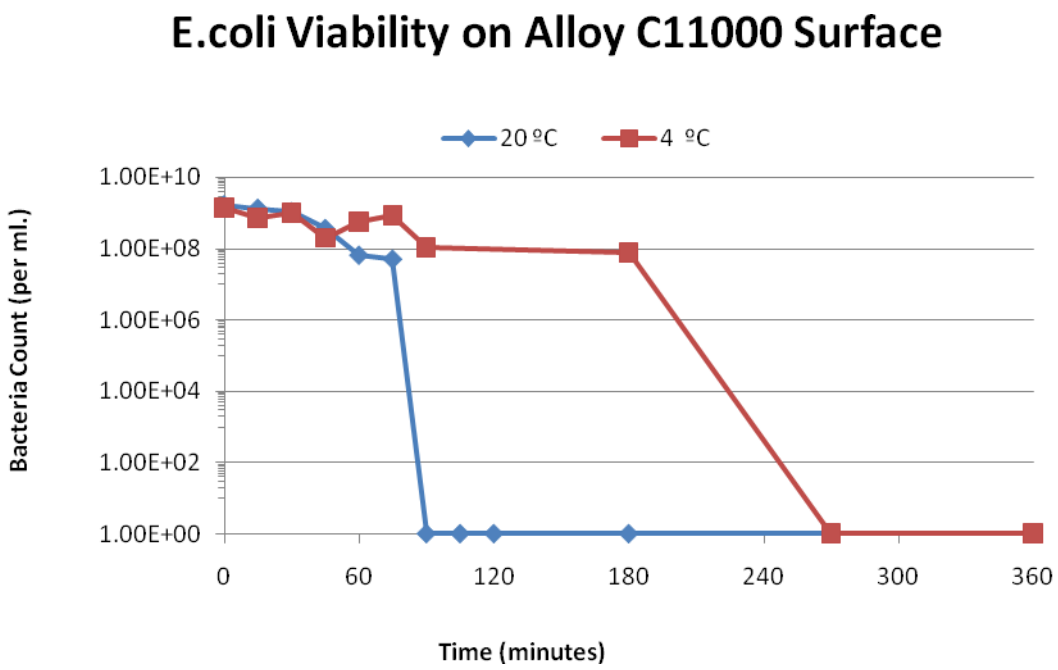

Figure 1. E. coli O157:H7 on Alloy UNS C110 Surfaces at 20°C and 4°C.

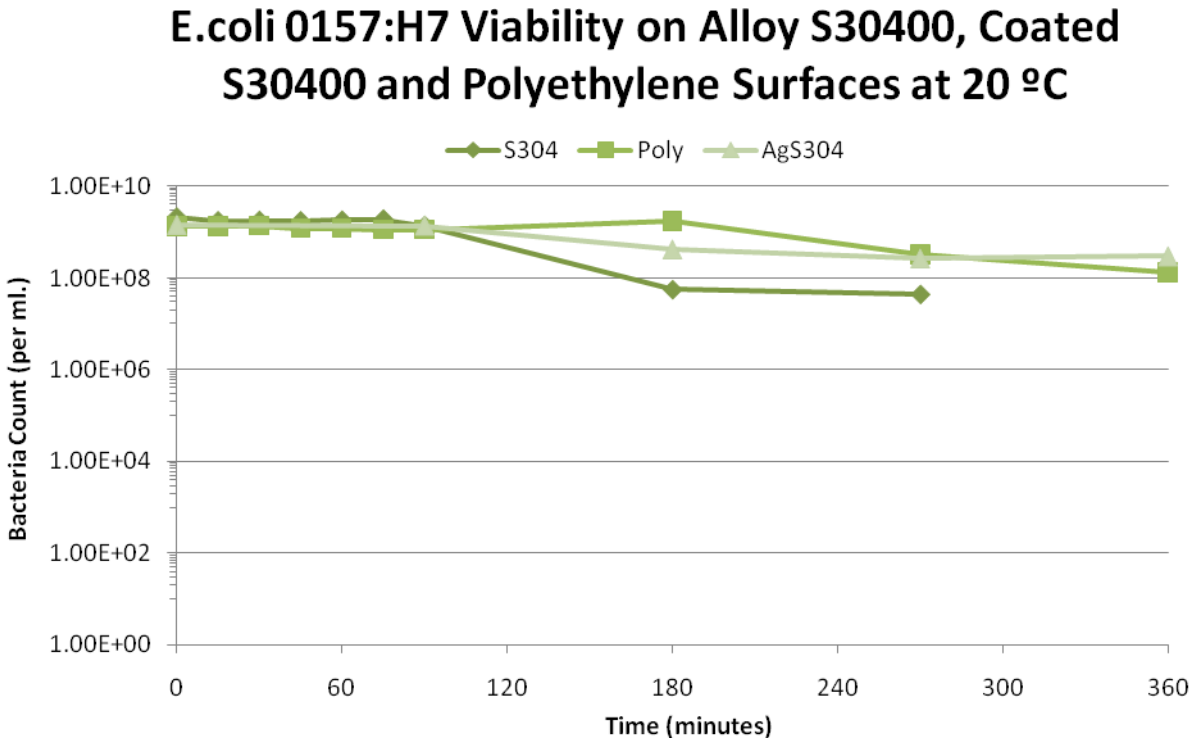

Figure 2: E. coli O157:H7 on the Surfaces of UNS S30400, Polyethylene, and a Silver-containing Coating on UNS S30400 at 20°C.

During a long-term 28-day test at 20°C, uncoated stainless steel, exhibited a 5-log drop over two days, as shown in Figure 3. The bacteria count then remained constant at around 4 logs, for the next 26 days. Although this is a reduction of the bacteria count to 4 logs on stainless steel, it is known that only 10 to 50 organisms are sufficient to cause an infection in humans. During a long-term 28-day test at 4°C, stainless steel exhibited a 4-log drop over 7 days. The bacteria count then decreased slowly by one log, over the next 21 days.

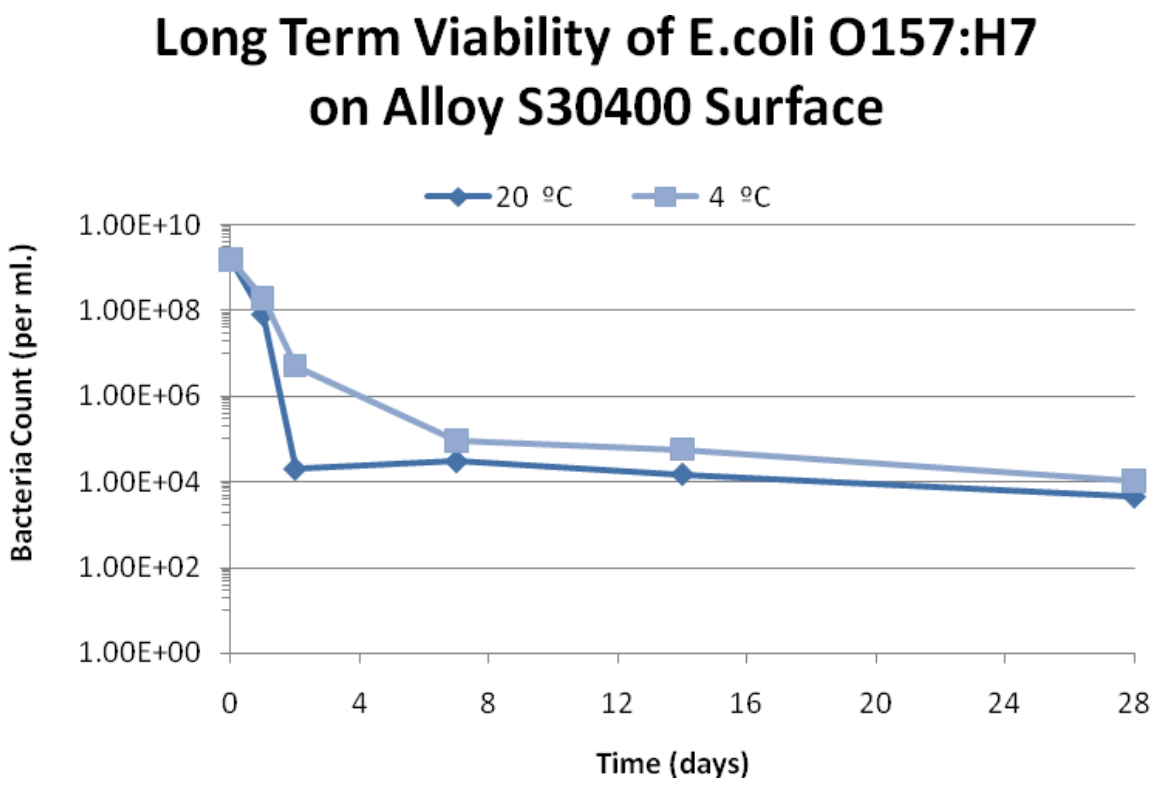

Figure 3. Long-term 28-day E. coli O157:H7 Viability on the Surfaces of Alloy UNS S30400 at 20°C and 4°C.

Tarnishing

The effect of tarnishing on the viability of three copper alloys was evaluated. Tests were run on three alloys which developed a brown tarnish film, which is probably cuprite (Cu2O), after a year of outdoor exposure in suburban New York City. E. coli O157:H7 counts were measured over only a 60-minute test period. The tarnish films were then removed with an abrasive cloth, and the alloys were retested in the bright condition, again, in a 60-minute test. The results for the three alloys, C197, an alloy containing 99% copper; C220, a brass containing 90% copper and 10% zinc; and C770, an alloy containing 55% copper, 27% zinc and 18% nickel, in both the tarnished and bright condition, are shown in Figure 4. Tarnished C197 exhibited a 5-log drop over 60 minutes, as shown in Figure 4. When the tarnish was removed from each test coupon and the 60-minute test rerun, the results were much less dramatic and only a one-half log drop was recorded. In C220, a similar but somewhat less of difference was seen. In the tarnished condition, C220 dropped by 3 logs in 60 minutes, but when tested in the bright condition, this fell to less than one-half log. In C770, no change in bacteria count was observed during the 60-minute test in either the tarnished or the bright condition. This was as expected, since no decrease in bacteria count was seen on C770 until 105 minutes in a previously reported 360-minute test of C770 (7).

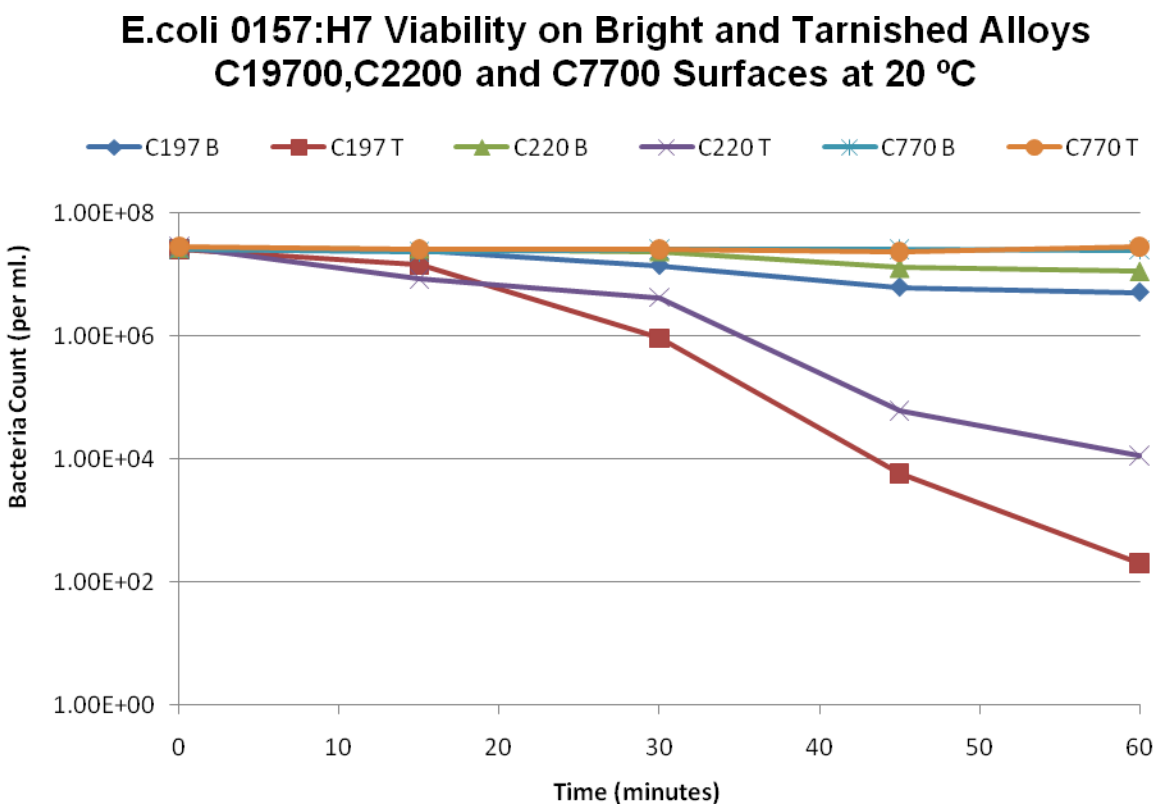

Figure 4: A Comparison of E. coli O157:H7 Viability on the Surfaces of Tarnished and Bright Alloys UNS C19700, C22000 and C77000 at 20°C.

MRSA

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 5. 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 C197, 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. However, the three-log drop indicates only ten thousand out of ten million bacteria survived, which corresponds to a 99.9% reduction in live bacteria.

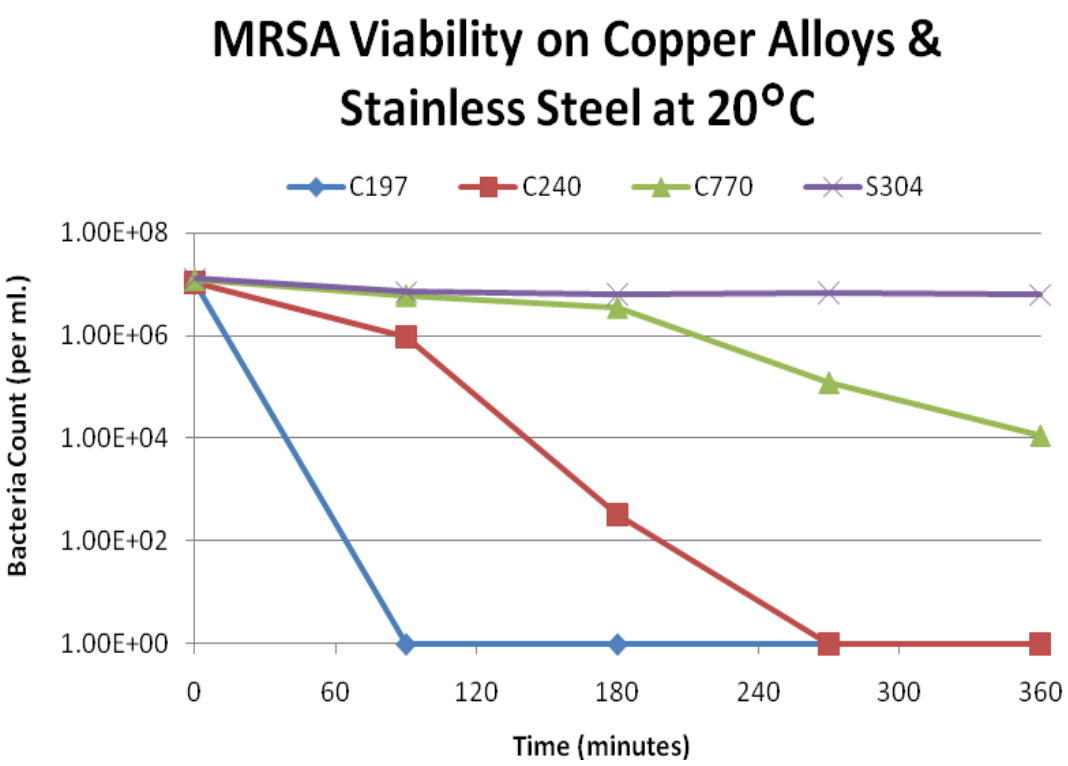

Figure 5. The Viability of Methicillin-Resistant Staphylococcus aureus (MRSA) on the Surfaces of UNS Alloys C197, C240, C770 and S304 at 20°C

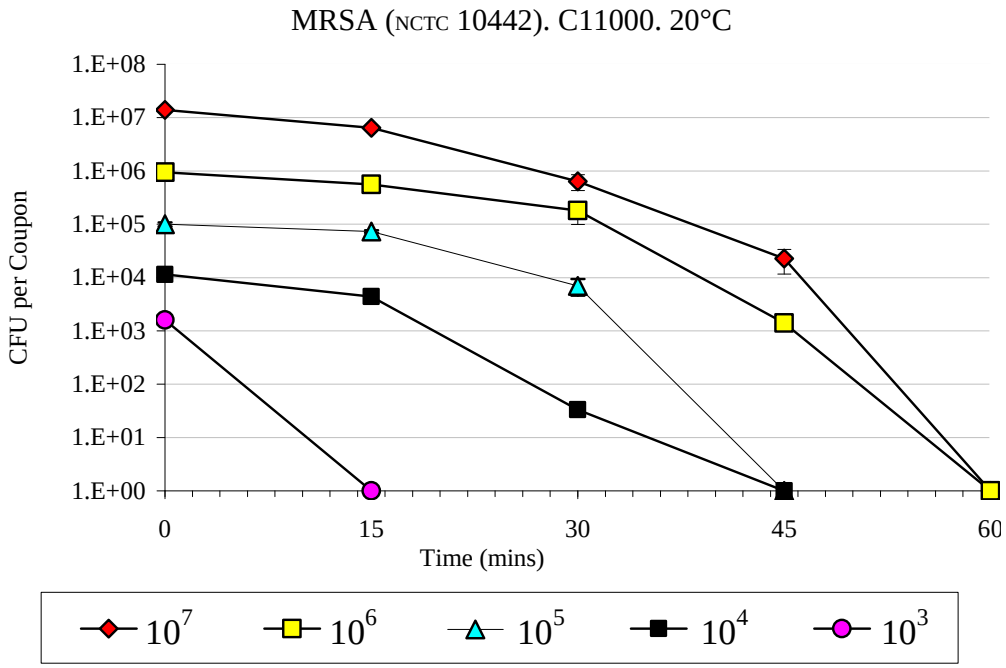

Figure 6. Effect Concentration of MRSA on Total Kill Time on C110

The effect of lowering the concentration of bacteria on the coupon to achieve a complete kill is shown in Figure 6. While it takes 60 minutes to achieve a six to seven log drop to zero survivors, it takes less time, 45 minutes to achieve a four to five log drop to zero survivors. It takes even less time, only 15 minutes to achieve a three log drop to reach zero. This is significant since contaminated surfaces typical contain bacterial concentrations of hundreds to thousands colony forming units (CFUs) per 100 square centimeters (6), while concentrations utilized in the tests shown in Figures 1 through 5 are orders of magnitude higher.

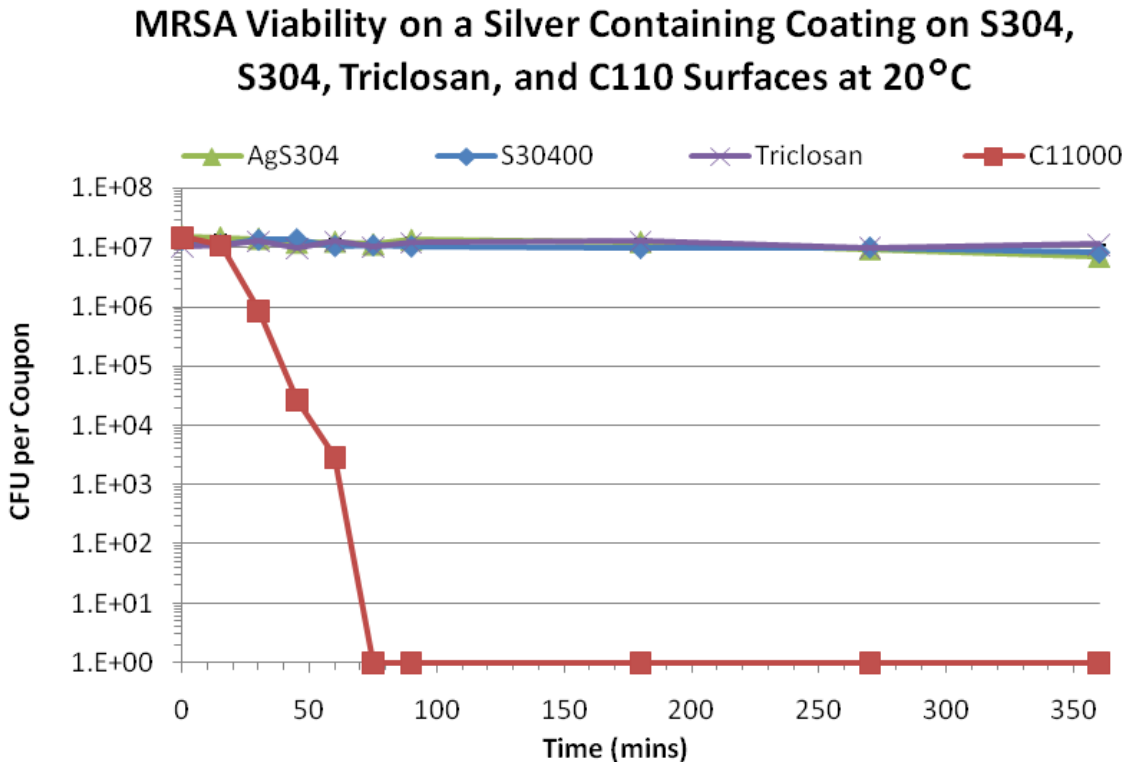

Figure 7. The Viability of MRSA at 20°C on the surfaces of a sliver-containing coating on UNS Alloy S30400, Triclosan-containing polyethylene, UNS Alloys C110 and S304 stainless steel

The bacterial count of 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 7, only C110 exhibits an antimicrobial response at ambient conditions, 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 cannot legally make public health claims.

Testing Required for Regulatory Approval

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 during which bacteria are added in a standard wear apparatus (shown as a schematic in Figure 8).

3. Continuous Reduction of Bacterial Contaminants-which measures bacteria after inoculating an alloy surface eight times in a 24-hour period without intermediate cleaning or wiping.

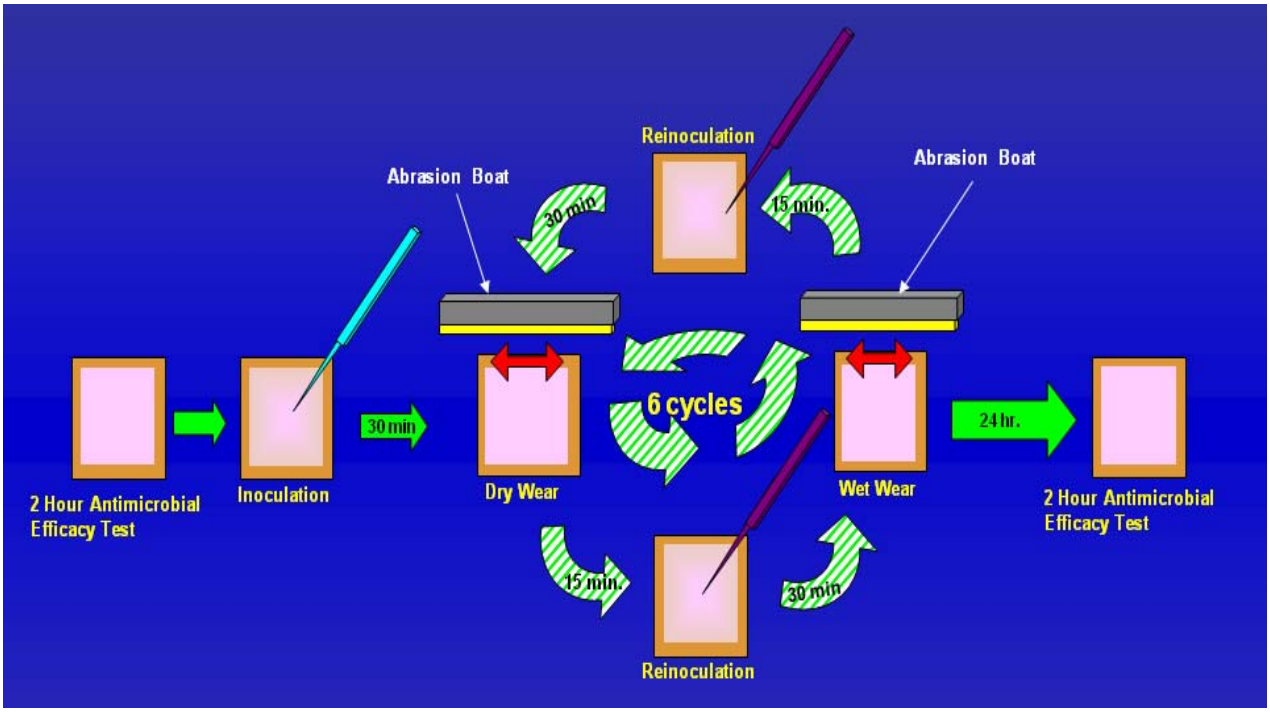

Figure 8. Residual Self-Sanitizing Test

In most of the Continuous Reduction tests, there were no survivors. An exception to this observation is shown in Figure 9. During the first five inoculations, the bacterial count drops from approximately 700,000 to zero. A few survivors 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

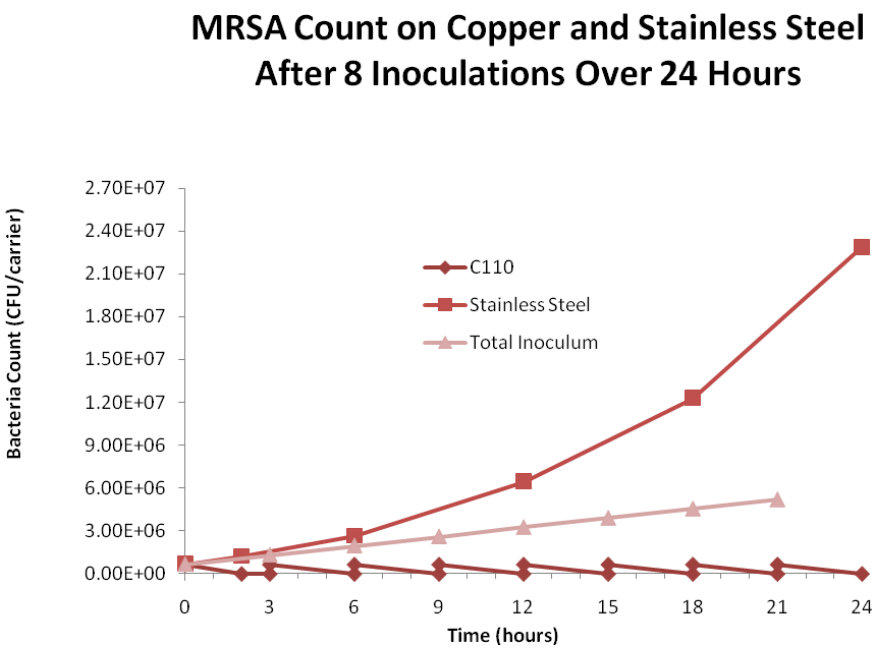

Figure 9. Continuous Reduction Test results for MRSA on Alloy C11000

Table 2. Summary of Efficacy Test Results Conducted for Regulatory Approval

Alloy	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

>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 >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.

DISCUSSION

Initially, copper alloys will be introduced into hospitals as surfaces and objects that humans frequently touch. Specific applications within hospitals include door hardware, sink faucet handles, IV drip stands, bed rails and footboards, over-the-patient tables, nurse's call buttons and work stations, furniture pulls, instrument knobs, arms of chairs and other routinely touched surfaces within the healthcare setting. Copper alloys should also be used in nursing homes, assisted living facilities, schools, public buildings, exercise facilities, shopping malls, mass transit systems, airports, the interiors of passenger aircrafts and cruise ships and even in the home.

The attainment of EPA approval is the first of several barriers to introducing copper alloys into hospitals. The applications with the highest likelihood of success are being identified, and the entire supply chain is being engaged. Clinical trials are underway. Copper alloy components are being fabricated and made readily available. Insight into the decision-making process in hospitals is gained and better understood. It is necessary to gain acceptance among hospital administrators, infection control practitioners, government healthcare officials and the general public, as well as architectural firms engaged in hospital construction. Widespread application of copper alloys should significantly decrease the number of viable bacteria found on human touch surfaces. The net result should be an increase in copper alloy utilization, a reduction in nosocomial infections and ultimately, the saving of lives. Success will be attained when it is generally understood and appreciated that copper alloys should be utilized in those applications where their unique and intrinsic antimicrobial properties will benefit human health.

ACKNOWLEDGEMENTS

Support was provided by both the International Copper Association Ltd. (ICA) and Copper Development Association Inc. (CDA).

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