Copper Development Association Inc.
Copper Alliance

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Re: Submission of Information Concerning Inadequate Efficacy Data and Request to Reconsider Registration for "Antimicrobial Cupron Enhanced EOS Surface" (EPA Reg. No. 84542-7)

Dear EPA:

On behalf of the Copper Development Association ("CDA"), we hereby submit information and questions concerning the registration of "Antimicrobial Cupron Enhanced EOS Surface" ("Cupron/EOS Surface") (EPA Reg. No. 84542-7). In short, fundamental questions regarding the efficacy of the Cupron/EOS Surface, including the long-term durability and antibacterial performance of the product, must be addressed before the agency should allow the continued marketing and sale of this "public health" product intended to fight infection-causing bacteria in the healthcare environment and other settings. To do otherwise would pose a risk to the health of patients, users, and other consumers who rely on the "public health" antibacterial claims made for the product. While the issues discussed below remain unanswered, it would be arbitrary and capricious for the U.S. Environmental Protection Agency ("EPA") to conclude that the efficacy of the Cupron/EOS Surface has been demonstrated. Accordingly, under its FIFRA authority (7 U.S.C. §136a(g)(1)(B), §136d(b), §136d(c)(1)), EPA should reconsider and cancel or suspend the registration at this time pending resolution of these critical issues.

During the over four year registration process for Antimicrobial Copper Alloys (EPA Reg. Nos. 82012-1 through -6), which contain 60-99.9 percent copper, EPA developed new protocols to test the efficacy of these novel antimicrobial materials – solid metal surfaces with inherent antimicrobial properties (in comparison to more traditional antimicrobial sprays and similar treatments). While new to FIFRA, these metal alloys are the same brass, bronze, and numerous other copper-based alloys that have been manufactured to strict industrial specifications for many decades. Each alloy must meet the chemical specifications detailed in the

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ASTM Unified Numbering System ("UNS") for the durable life of the product. Because the copper and other metals that comprise the alloys are metallically bonded within a crystalline matrix, the chemistry of the alloy does not change over time. Accordingly, because the alloy chemistry does not change over time, the antimicrobial efficacy of Antimicrobial Copper Alloys is properly assessed by the two- and 24-hour testing. The long-term efficacy results were verified by testing a variety of older copper alloy products (such as doorknobs and pennies). In addition, real world efficacy has been confirmed through recently concluded clinical trials performed under the auspices of the U.S. Department of Defense.

Before registration was granted to Antimicrobial Copper Alloys, EPA required outreach to pose questions to experts in the infection control community, including the Association for Professionals in Infection Control and Epidemiology ("APIC"), the American Society for Healthcare Environmental Services ("ASHES"), Dr. William Rutala from the University of North Carolina-Chapel Hill, and others. The input received was critical in shaping the conditions and requirements of the registration and, significantly, in helping inform the agency of various efficacy questions to be asked of the product before registration should be granted. The issues raised included questions about the long-term efficacy of the product, the potential impact of various cleaning agents on the product, and the need for proper education and stewardship. APIC specifically raised critical points regarding the durability of the surface material and the need for clinical trial data. These points were addressed and resolved before the CDA registrations were issued.

Unfortunately, it does not appear that these same fundamental questions were asked of the Cupron/EOS Surface product. As a result, there remain critical unanswered questions about the long-term efficacy and durability of the product, as well as the product's suitability for the applications for which registration was granted. These issues are explained in detail below, with relevant questions highlighted.

(1) The Efficacy Test Protocols Were Not Designed to Assess the Performance of a Material That Changes Chemically Over Time

Unlike a sanitizing spray or similar antimicrobial treatment, which have an immediate but short-term sanitizing or disinfecting effect, an antimicrobial solid surface is intended to continually reduce bacterial load during the useful life of the product, which can be a decade or longer (such as a countertop in a hospital or home). Accordingly, to demonstrate

efficacy for solid metal materials, the three testing protocols are based on the presumption that the tested material will remain chemically and physically consistent during the useful life of the product. The consistency of copper alloys in this regard has been demonstrated for decades under the ASTM/UNS program, which guarantees the chemistry of the alloy. No such guarantee or demonstration has been made for the Cupron/EOS Surface. Accordingly, the antibacterial performance of the Cupron/EOS Surface over the two- and 24-hour testing protocols does not support efficacy over a longer period of time, and, therefore, does not support the efficacy of a product with an expected useful life of many years. Long-term efficacy of the product must be demonstrated through the development and use of new, more appropriate test protocols.

Question: How fast are the active copper ions depleted from the cuprous oxide on the surface?

Question: What is the long-term viability and efficacy of the cuprous oxide?

Question: What test protocol may be used to demonstrate long-term antimicrobial durability and efficacy of the product?

(2) Long-Term Efficacy and Durability of the Cupron/EOS Surface Has Not Been Demonstrated

The Cupron/EOS Surface consists of copper oxide particles (16 percent cuprous oxide by weight, or approximately 14 percent copper) that are impregnated into a polymeric substrate from which copper ions leach. The copper oxide particles, based on the densities of the active and inert ingredients, comprise approximately less than three percent of the volume and surface area of the product. Based on a long history of testing, CDA is aware that copper alloys containing roughly 50 percent or less copper do not demonstrate efficacy under the testing protocols.

Polymeric matrices, by their nature, degrade and do not have the inherent structural or mechanical stability of solid copper alloys. Degradation of the polymer may result from chemical or hydrogen peroxide cleaning systems, as well as from photo-degradation (*e.g.*, from ultraviolet cleaning systems) and/or heat. The long-term stability and durability of the polymeric counter tops has not been demonstrated.

Most importantly, the antimicrobial performance of the Cupron/EOS Surface is based on the leaching of copper ions from the material. These ions leach out of the surface and eventually will be depleted. While rapid copper ion release may account for efficacy in the short term (such as under the two- and 24-hour testing protocols), the leaching action suggests a finite limit to the active ingredient contained in the polymeric substrate. Further, common cleaning agents may deplete the active ingredient on the surface.

Upon depletion, due to the encapsulation of remaining copper oxide particles in the polymeric substrate, no active ingredient will be available to take the place of the depleted particles at the surface – unless a significant portion of the polymer is worn away (which, if so, raises questions about the durability of the surface). Accordingly, long-term efficacy of the product is questionable and has not been demonstrated.

Question: How, if at all, do the cuprous oxide particles embedded in the polymer matrix get to the surface, particularly after the surface particles are depleted of copper ions?

Question: Are the cuprous oxide ions active over the entire useful life of the product? How is this demonstrated, if at all?

The phenomenon is similar to (cuprous oxide-containing) anti-fouling paint, which must be reapplied periodically as the copper ions are released and the antimicrobial efficacy of the paint depleted. In contrast, copper alloys, containing 60-99.9% copper, do not deplete and there is a near-infinite supply of copper available throughout the alloy matrix.

(3) The Conditions of the Test Protocols Favor Surfaces That Leach the Active Ingredient

As observed in commercial silver-containing coatings (Michels *et al.*, *Letters in Applied Microbiology* 49 (2009) 191–195), the efficacy of surface materials impregnated with antimicrobial additives, is highly dependent on the presence of moisture. At high levels of humidity, these products demonstrate some level of efficacy, while little to no efficacy is seen at normal or low levels of humidity. The wet inoculation method utilized in the solid surface testing protocols likely enhances the efficacy performance of the Cupron/EOS Surface by promoting more rapid leaching of the copper ions from the polymeric substrate and distribution of those ions

across the surface. Under dry conditions, such as those involving the transfer of bacteria from contaminated hands, which are more likely to be experienced in hospital settings or the home, the copper ions would not be expected to be transported across the product surface as readily, resulting in reduced efficacy. [In contrast, the performance of copper alloys is not dependent on the transport of copper ions across the surface, as the high percentage of copper in the alloy results in direct bacterial contact with the copper.]

Question: How does the Cupron/EOS Surface, which is dependent on the spreading of copper ions across the surface, perform under dry inoculation test conditions?

Question: Will the copper ions be released in the typical dry environment?

Question: Under typical (dry) environmental conditions, how do the copper ions (which represent approximately three percent of the product surface area) impact the remaining 97 percent of the surface area that is comprised of inert ingredients?

(4) The Potential for Formation of Resistant Organisms Should Be Examined

As noted above, the relatively small amount of active ingredient – approximately less than three percent by volume and surface area – in the Cupron/EOS Surface means that large areas of the product may serve as havens for bacteria. While some bacteria would encounter the copper ions leached from the Cupron/EOS Surface – particularly, as discussed above, when the ions are spread across the surface during the wet inoculation method used in the testing protocols – many bacteria would be expected to be present in the approximately 97 percent of the surface that is non-copper. Organisms that reside on surfaces with lower concentrations of copper ions, or none at all, may receive a sub-lethal dose. Prolonged exposure to a sub-lethal dose of copper ions increases the potential for development of microbial resistance. Depletion of copper ions over time, as discussed above, is likely to exacerbate this potential risk.

Question: Has the issue of the potential formation of copper-resistant organisms been examined? How can the registrant guarantee that resistance will not develop given the potential for delivery of sub-lethal doses of copper

ions as the ions are depleted and/or bacteria reside on the non-copper polymer portion of the surface?

(5) How Is the Product Chemistry Guaranteed?

While Cupron/EOS indicate that the manufacturing process results in the uniform distribution of the active ingredient throughout the polymeric substrate, it is unclear how this guarantees a uniform concentration of copper ions at the surface level. How can consistent concentrations of cuprous oxide at the surface be guaranteed by the manufacturer, particularly across different manufacturing lots?

Moreover, downstream processing activities – such as buffing or polishing to achieve a semi-gloss finish, cutting, grinding, or forming into different shapes – would be expected to generate heat that could affect the polymeric substrate. This could cause the polymer to spread and coat the cuprous oxide, rendering it unavailable for contact with bacteria.

The EOS "fabrication manual" (available at a link at http://eos-surfaces.com/eos/commercial/) indicates that "the finish delivered to the fabricator is a 'factory finish,' and not a final finish. EOS Fabrication Manual at 102. The fabricator is required to use 'standard solid surface finishing steps' to create the desired finish." One option is a semi-gloss finish. CDA is concerned that the inherent heat associated with abrasion finishing techniques could alter the finish from the one that EPA evaluated in the tests submitted; and that there are no controls over how a surface finish (and hence efficacy) can be affected by an installer/fabricator. In fact, EOS expressly disclaims responsibility for the finish in its product warranty: "EOS™ Surfaces LLC does not warranty finishes, it is the responsibility of the fabricator to provide a proper finish to the consumer." EOS Fabrication Manual at 77. These issues and concerns do not exist with copper alloys.

Question: How does the registrant guarantee the batch-to-batch consistency of the Cupron/EOS Surface?

Question: How is chemistry certified? Under what universally-accepted standard?

Question: What assurance is there that the chemistry and performance of the Cupron/EOS Surface does not change throughout the manufacturing and fabrication processes? After downstream processing and finishing?

(6) There Is a Disconnect Between the Directions for Use and the Functioning of the Product

The Directions for Use state that the product must not be "coated" in any way. The purpose of this instruction is to prevent the formation of a barrier between the active ingredient and bacteria. Yet with the exception of a finite amount of cuprous oxide on the surface, the remaining active ingredient is encapsulated by the "non-porous" polymeric substrate and unavailable to replenish the cuprous oxide that will be depleted of copper ions over time (as discussed above). The EOS/Cupron website makes this point clear, stating that "[t]hese copper oxide-infused polymers are embedded into the material." (http://eos-surfaces.com/cupron/)

Question: How can the copper ions be available if the cuprous oxide is embedded in the polymeric substrate, particularly after the active ingredient is depleted at the surface?

(7) The Cleaning Instructions Are Contrary to the Required Claim Language

The product label includes mandated language, qualifying the basic antibacterial claims, that instructs users to "continue to follow all current infection control practices, including those practices related to cleaning and disinfection of environmental surfaces." Further, the Directions for Use state that "[c]leaning agents typically used for traditional touching surfaces are permissible; the appropriate cleaning agent depends on the type of soiling and the measure of sanitization required." However, the Cupron/EOS website states that "strong acidic cleaners" should not be used on the product. (http://eos-surfaces.com/eos/residential/product-care/) A number of common hospital cleaning agents, as well as those used in the home, are acidic, some of which are highly so (such as those containing acetic acid and citric acid).

Question/Issue: What effect will cleaners, acids, solvents, etc. have on the cuprous oxide? The Directions for Use must be amended to comport with the cleaning instructions that EOS/Cupron post on their website.

In addition, the EOS/Cupron website includes an article entitled "Self-cleaning countertop?" The article further states that the countertop "essentially cleans itself." These statements are in clear contradiction to the mandated label language noted above, and the fundamental stewardship concept that the product is a supplement to, not a substitute for, routine cleaning procedures.

(8) The Registration Should Be Specific to Countertops

If the Cupron/EOS Surface registration is to continue, it should only be approved for countertops. From the available information, it appears that only slab material used to make EOS Surface countertops was evaluated; there is no information regarding manufacture of the product into tubular and other forms. To make other forms entails different processing stages that can affect the chemistry of the final product. This is unlike copper alloys, which must meet ASTM/UNS specifications in any form in which the alloy is produced. In contrast, the polymeric base of the Cupron/EOS Surface can be altered through different processing stages. Accordingly, the performance of the material in slab/countertop form is not representative or a guarantee of performance in other forms (such as tubular railings, grab bars, hand rails, bed rails, cart handles, towel bars, exercise equipment, *etc.*). For this reason, the approved list of applications on the current label is overbroad and unsubstantiated.

In short, if allowed, the CuPron/EOS registration should be a ***product*** registration, and not a broad ***material*** registration, unless there is a universally (industry) agreed upon standard for certifying content, and unless the content can be assured not to change over the lifetime of the material. Unlike copper alloys that do not physically change by fabrication with the base metal, there is no evidence that all of the applications listed on the EOS registration are capable of being manufactured from the Cupron/EOS polymer matrix, nor that the processing requirements to manufacture these items would not alter the nature of the matrix and antimicrobial efficacy of the product.

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As the steward of Antimicrobial Copper that has worked diligently over the last several years to educate the public, and specifically the healthcare community, about the proper

use and role of antimicrobial copper products as part of an infection control program, CDA is concerned that the registration of a product, the Cupron/EOS Surface, with unproven long-term efficacy will undermine these stewardship efforts and cause substantial confusion. Fundamental unanswered questions exist regarding the efficacy of the product. These uncertainties pose risks to the health of consumers and users, particularly in the healthcare setting, who may rely on an ineffective product intended to help fight infection-causing bacteria. For these reasons, CDA requests that EPA cancel or suspend the registration pending resolution of the efficacy and other issues detailed above.

CDA appreciates and actively supports the efforts of EPA to promote a proper understanding of the role of antimicrobial products in addressing infection-causing bacteria. To do so effectively, the agency must ensure, as it has with Antimicrobial Copper Alloys, that fundamental questions of efficacy, chemistry, and durability are addressed for all solid surfaces that claim to be antibacterial. If you have any questions or would like further information, please contact CDA counsel, Joseph Green at 202.342.8849 or JGreen@KelleyDrye.com.

Respectfully submitted,

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