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Dockets Management Branch  
Food and Drug Administration (HFA-305)  
5630 Fishers Lane, Room 1061  
Rockville, Maryland 20852

Re: Reopening of the Administrative Record for Topical Antimicrobial Drug Products for Over-the-Counter Human Use; healthcare antiseptic drug products. 68 Federal Register 32003 (May 29,2003).  
**[Docket 75N-183H]**

Dear Sir:

I am submitting the comments listed below in response to the Food and Drug Administration's (FDA's) reopening of the administrative record dealing with the 1994 tentative final monograph (TFM) dealing with healthcare antiseptic drug products, published in the Federal Register, Vol. 59, pages 31402-31452 on June 17, 1994. These comments are based on a literature review conducted by the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force in preparation for writing the recently published evidence-based CDC Guideline for Hand Hygiene in Healthcare Settings.(1) **[See attached Guideline, which is being submitted for inclusion in Docket 75N-183H]** Co-authors of the Guideline reviewed over 700 published articles dealing with various aspects of handwashing, hand antisepsis, and topical antiseptic agents used for hand hygiene in hospitals, long-term care facilities and other medical care settings. Based on my role as a co-author of the Guideline and more than 20 years of experience in Infection Control and Hospital Epidemiology, I am concerned that adopting the TFM, as it currently exists, as the Final Monograph will adversely affect the availability of alcohol-based hand rubs, which have been recommended in the CDC Guideline for routine hand hygiene by healthcare workers.(1) Implementation of the CDC Guideline, including promoting the use of alcohol-based hand rubs, has been recommended by the Joint Commission on Accreditation of Healthcare Organizations.(JCAHO Sentinal Event Alert #28, issued on January 22, 2003) Therefore, it is crucial that such products, including those currently on the market, remain available for use in healthcare settings.

Alcohol preparations have been used in various healthcare settings for hand hygiene for many years. For example, alcohol-based hand rubs have been widely used for hand hygiene in hospitals for 10 to 20 years in some countries in

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northern Europe.(2;3) The 1994 TFM classified alcohol 60 percent to 95 percent as a Category I (safe and effective) active ingredient for use in antiseptic handwash or healthcare personnel handwash preparations [see TFM, page 31435]. In the 1994 TFM, the FDA proposed that antiseptic handwash or healthcare personnel hand wash products achieve (1) a 2-log reduction of the indicator organism on each hand within five minutes after the first wash, and (2) a three-log reduction in the indicator organism on each hand within five minutes after the tenth wash, when tested in a modified "glove-juice" test [see TFM, page 31432]. The rationale for requiring a 3-log reduction in counts of the indicator organism after a tenth wash is not clear, for several reasons.

- Alcohols are not considered to have any "persistent" or "cumulative" activity on the skin, and as a result, preparations containing alcohol as the only active ingredient would not be expected to be more effective after the tenth wash than after the first wash.
- Furthermore, since these products are used many times during the course of the day for decontaminating hands before and after patient contact, there is no reason that they should be required to be more effective at the end of the work day than at the beginning of a work shift. Patients cared for near the end of a work shift are no more or less likely to serve as reservoirs for transmission of potential pathogens than patients cared for at the beginning of a work shift.
- The extensive literature review conducted by the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force failed to reveal any evidence that a 3-log reduction in bacterial counts on the hands of healthcare workers is needed to reduce transmission of healthcare-associated pathogens.
- Numerous studies have observed handwashing adherence rates averaging only 40% (1), and as a result, after many patient care encounters, NO log reduction in bacterial counts occurs because no handwashing is performed. When handwashing is performed using soap and water, healthcare workers often wash their hands for 10 to 15 seconds or less,(1) which seldom if ever yields a 3-log reduction in bacterial counts on the hands.(4;5) Promoting increased use of alcohol-based hand gels that achieve a 2-log reduction in counts will result in less hand contamination than traditional soap and water handwashing practices.

Preparations on the market that achieve a 2-log reduction in counts after the first wash, but that may not achieve a 3-log reduction in counts after the tenth wash have been shown to improve hand hygiene adherence rates among healthcare workers in the United States.(6;7) For example, hospital-wide installation of such an alcohol-based hand gel product in late February 2001, combined with an ongoing educational and motivational program, has led to a significant increase in hand hygiene adherence rates at a 500-bed community teaching hospital in New Haven, CT (Figure 1).(7) The increased adherence was attributable in large part to an increase in the proportion of hand hygiene episodes performed by using the alcohol-based hand gel (Figure 2). Also, we documented that the increase in hand hygiene compliance was accompanied by

a significant increase in the number of liters of alcohol-based hand gel used/1000 patient-days (Figure 3). Importantly, the prevalence of all *Staphylococcus aureus* isolates resistant to methicillin (MRSA), which had increased steadily from 1995 through late 2000 at our hospital, subsequently leveled off in 2001, and subsequently decreased by 5% following promotion of the alcohol-based hand gel. While the 5% decrease in MRSA prevalence at our hospital is modest, it is important to note that MRSA prevalence rates in hospitals participating in the CDC's National Nosocomial Infections Surveillance (NNIS) system continued to increase in 2001 and 2002, and has shown no signs of decreasing (Scott Fridkin, CDC, personal communication). Our findings suggest that the increasing use of the alcohol-based hand gel contributed to the decreasing prevalence of MRSA in our facility, despite the fact that the alcohol-based hand gel product does not have "residual" or "cumulative" activity. Other investigators have also shown decreased infection rates after promoting the use of similar alcohol-based hand gels.(8)

Because the TFM methods and performance criteria for antiseptic handwash or healthcare personnel handwash products require a "persistent" or "cumulative" effect that alcohols do not possess, it would appear that only alcohol-based hand rub products containing an additional antiseptic agent will meet the TFM performance criteria. Given the increasing concern over the possible emergence of antiseptic-resistant bacteria, it seems unwise to require that all alcohol-based hand rubs contain an additional antiseptic in order to demonstrate a "persistent" or "cumulative" effect. There is considerable concern that some antiseptics such as triclosan may promote emergence of bacteria with resistance mechanisms similar to those responsible for antibiotic resistance.(9;10) Other antiseptics such as chlorhexidine gluconate have an increased propensity to cause irritant contact dermatitis when used frequently.

In addition, when finalizing the Final Monograph on Healthcare Antiseptic Drug Products, the FDA should review evidence from the United States and from Europe to determine the possible benefits of allowing products to contain other alcohols as active agents, such as n-propanol, which has been used in alcohol-based hand rub products in Europe for many years.(4) Also, there is considerable evidence that products that contain two active alcohol agents, both present in concentrations ranging from 30% to 45%, are effective and safe.(5;11-13)

Given the well-documented transmission of rotavirus, respiratory syncytial virus, norovirus, and SARS-associated coronavirus in healthcare facilities, and the possible widespread vaccination of healthcare workers with smallpox vaccine, the FDA should adopt standardized test methods for establishing the antiviral activity of antiseptic preparations used for hand hygiene in healthcare facilities, so that healthcare institutions can select products shown to be effective against these important viral pathogens.

In summary, if adopting the 1994 TFM as the Final Monograph on Healthcare Antiseptic Drug Products will result in removal of many currently available alcohol-based hand rub products from the market, efforts on the part of the CDC, the Society for Healthcare Epidemiology of America, the Association of Professionals in Infection Control and Epidemiology, the Infectious Disease Society of America, and the Joint Commission on Accreditation of Healthcare Organizations to improve patient safety by improving hand hygiene adherence rates and decreasing healthcare-associated infections may be jeopardized. Accordingly, I encourage the FDA to eliminate from the Final Monograph the requirement that alcohol-based hand rubs intended for routine use by healthcare personnel have “persistent” or “cumulative” activity.

Broadening the types (and concentrations) of alcohols that can be used as active agents in such products, and establishing the antiviral activity of hand hygiene antiseptic preparations will provide healthcare institutions with a greater variety of products to meet their needs.

Sincerely,



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