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# Persistent and Residual Antimicrobial Effects:

Are They Important  
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Antiseptics marketed as surgical scrub formulations must meet certain effectiveness requirements that relate to their immediate, persistent, and preferably, residual antimicrobial properties. Immediate antimicrobial properties are the antimicrobicidal effect on resident microorganisms immediately (within one minute) after the antiseptic has been applied. Generally, this is measured as reductions from the baseline microbial population present on the skin of the hands prior to product application. The persistent antimicrobial effect measures how long after its application an antiseptic is able to prevent microbial counts from exceeding the baseline population numbers. This is a severe challenge for surgical scrub/wash products, in that the hands are occluded inside surgeon's gloves following product application. Occlusion presents a favorable environment for microbial growth. Residual antimicrobial effects measure the product's cumulative antimicrobial effects when used repeatedly over a number of days; that is, some antimicrobials, when used over time, are adsorbed to the stratum corneum of the skin and, as a result, will prevent microbial re-colonization of the skin surfaces to baseline levels.

The Food and Drug Administration's (FDA) specific test requirements must be met in order to label the product as a surgical scrub. Although *in vitro* antimicrobial efficacy must be demonstrated in time-kill kinetic and minimum inhibitory concentration studies, the focus of this paper is *in vivo* simulated human clinical trials. The FDA surgical scrub evaluation is four weeks in duration. It begins with a two-week "wash out" period, during which subjects do not use any antimicrobial products so that the population numbers of their normal hand flora are stabilized. It is followed by a one-week baseline period, during which the normal number of microorganisms per hand is measured. All the subjects'

baseline measurement data are pooled to provide a baseline point-estimate value to which the post-product use values are compared. The next week (week four) is the test week, when the antiseptic is used eleven times over the course of five days, per label instructions. Table 1 provides the product application and sampling schema.

To meet FDA label claim requirements, the antiseptic must produce at least a one  $\log_{10}$  reduction from baseline population on test day one, at least a 2  $\log_{10}$  reduction from baseline population on test day two, and at least a 3  $\log_{10}$  reduction from baseline population on test day five. Further, the microbial populations of the gloved hands cannot exceed baseline population over the six-hour post-application period on any of the three evaluation days.

Figure 1 depicts a surgical scrub formulation that meets the FDA requirements, starting with a baseline population at a  $\log_{10}$  value of five, the minimum permitted by the FDA for testing of surgical scrub antiseptics. The figure illustrates plainly the immediate, persistent and residual antimicrobial effects of the product.

Figure 1.

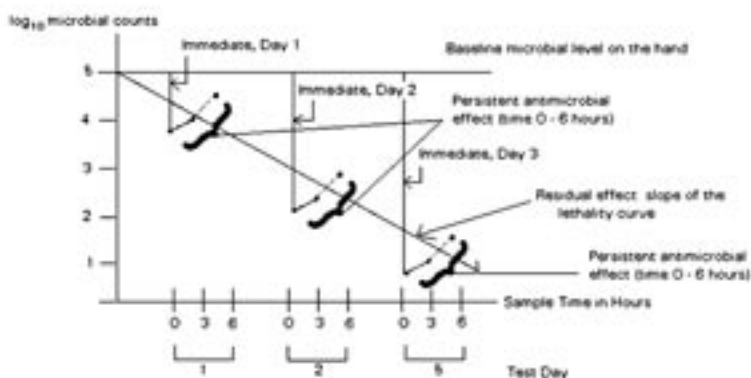
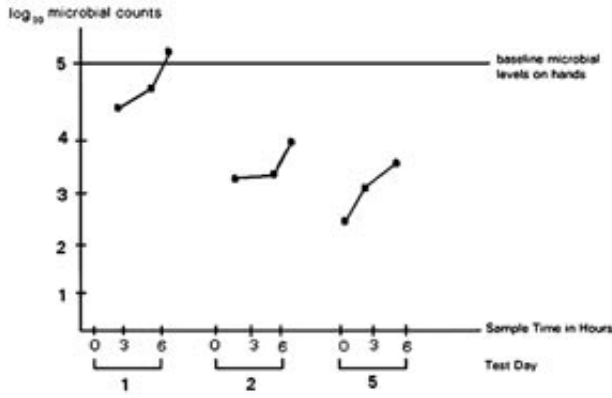


Table 1. Test Week Product Application and Sampling Schema

Day	1	2	3	4	5
	1 product application followed by sampling immediate, 3-hours and 6-hours post-product application	1 product application followed by sampling immediate, 3-hours and 6-hours post-product application	3 product applications, at least 1 hour apart	3 product applications, at least 1 hour apart	1 product application followed by sampling immediate, 3-hours and 6-hours post-product application
	no additional applications	2 additional surgical product applications, at least 1 hour apart	no samples	no samples	no additional applications
	1 total product application	3 total product applications	3 total product applications	3 total product applications	1 total product application

Figure 2 portrays the results from the testing of an antiseptic that did not meet the FDA's requirements for immediate antimicrobial reductions on any test day nor day one's persistent effectiveness criterion, because the microbial count at six hours exceeds the baseline counts.

**Figure 2.**



Whether an antiseptic meets the FDA requirements, to a large degree, depends on the active ingredient and its concentration, and on the overall product formulation. Table 2 presents the performance of common antimicrobial actives that is typically observed, when they are used as surgical scrub hand antiseptics.

**Table 2. Activities of Common Antimicrobial Chemicals**

Antiseptic	Antimicrobial Properties		
	Immediate	Persistent	Residual
70% Isopropyl Alcohol	High	None*	None
4% Chlorhexidine Gluconate (CHG)	High	High	High
Povidone Iodine	Moderate	Moderate	None
Alcohol and Povidine Iodine	High**	High	None
PCMX	Moderate	Moderate	None
Alcohol and Chlorhexidine Gluconate (CHG)	High	High	High

\*Even though a six hours, so technically, it can pass the FDA requirements.  
 \*\* Alcohol (6

Recall that persistent and residual antimicrobial effects can be achieved by merely "inhibiting" microbial growth of normal flora; a passive antimicrobial effect. So, for hands contaminated with microorganisms subsequent to product use, the FDA has no requirement that the treated hands demonstrate any antimicrobial effects. Yet, one of the main arguments for handwashing and scrubbing with an effective antiseptic is to provide not only persistent and/or residual activity that maintains microbial counts of normal flora below baseline levels, but also to provide "active" extended antiseptic effectiveness against contaminating microorganisms. But do any of the commonly used topical antimicrobials provide active properties that actually prevent growth of or kill microorganisms that contaminate the hands after they have been scrubbed? To answer this question, six types of antiseptic products were evaluated in this study.

**Methods and Materials**

A simple, visual test was designed to demonstrate active and residual properties of six antiseptic products, if they were present. The antimicrobial actives used in this test were:

- 4 percent Chlorhexidine gluconate (CHG)
- 15 percent Povidone Iodine (PVP-I) Cleansing Solution
- 3.3 percent Parachlorometaxlenol (PCMX) Emollient Cleansing Solution
- 61 percent Ethyl Alcohol
- 70 percent Isopropyl Alcohol
- 1 percent CHG in 61 percent Ethyl Alcohol

**Methods**

**Step 1.** The seven days prior to the commencement of the evaluation constituted the wash-out period.

**Step 2.** On test day one, subjects, with the assistance of a trained technician, placed their hands, palm-side down, firmly onto agar plates inoculated with *Staphylococcus aureus* (ATCC #6538). The hands remained pressed onto the plates for 60 seconds. This constituted the "no-treatment," or baseline measurement.

**Step 3.** Following the baseline hand-imprinting procedure, the subjects washed their hands with their assigned product and again pressed their hands onto inoculated agar plates, as described in Step 2. This constituted an immediate antimicrobial sampling, following which subjects applied their assigned antiseptic product two additional times before being allowed to leave the laboratory.

**Step 4.** On test days two through five, subjects returned to the laboratory to apply their assigned product to their hands three consecutive times on each day.

**Step 5.** Approximately one hour and six hours after the final product application on test day five, subjects again performed the hand-imprinting procedure, as described in Step 2.

**Step 6.** The hand-imprinted agar plates were incubated at 35 degrees ± 2 degrees C for 24 to 48 hours.

**Step 7.** The agar plates imprinted for baseline and post-product application on days one and five were photographed, following incubation. They provided the growth/no growth data to be evaluated visually.

**Results**

Photograph 1 shows a representative inoculated agar plate touched by an untreated hand. A hand imprint can be observed, but the *Staphylococcus aureus* within the imprint outline obvious was neither killed nor inhibited by the untreated hand.



Photograph 1: Baseline, non-treated sample

A hand imprint six hours after the application of the 4 percent CHG product on day five, as displayed in photograph 2, plainly provided a high degree of antimicrobial activity. That is, the antimicrobial was actually transferred to the plate, preventing microbial growth over the period of incubation. This effect was the result of both persistent and residual activity of the CHG.



Photograph 2:  
4 percent CHG, six-hour sample

The 1 percent tincture of CHG, at six hours post-application on day five, showed a high degree of antimicrobial effectiveness, although less than expected (Photograph 7). This result likely was due less to a lack of persistent and residual properties in the CHG, itself, but rather to some blocking by emollients contained in the product formulation.



Photograph 7:  
1 percent CHG and 61 percent ethyl alcohol, six-hour sample



Photograph 3:  
15 percent Povidone Iodine (PVP-I) cleansing solution, six-hour sample

A hand imprint six hours after the use of the 15 percent PVP-I product on day five produced essentially no "active" antimicrobial effects (photograph 3). In fact, bacterial proliferation within the hand print is indistinguishable from that for the hand imprinted for baseline (Photograph 1).

Essentially no active antimicrobial effects are noted for a hand treated with the 3.3 percent PCMX product at the six-hour post-product application sampling time on day five (Photograph 4).



Photograph 4:  
3.3 percent Parachlorometaxylenol (PCMX) emollient cleansing solution, six-hour sample

Neither of the alcohols, 61 percent ethyl and 70 percent isopropyl, produced any antimicrobial effect on the *Staphylococcus aureus* six hours after application on day five (Photographs 5 and 6). This was as expected, because once alcohols dry, they no longer have any antimicrobial properties.



Photograph 5:  
61 percent ethyl alcohol, six-hour sample



Photograph 6:  
70 percent isopropyl alcohol, six-hour sample

### Discussion

This evaluation clearly demonstrated visually that some antiseptics will remain antimicrobially active on the hands, able not only to keep microbial populations of normal flora below baseline levels, but also to kill or inhibit microorganisms contacted by the treated hands. Perhaps, then, it is reasonable to refer to two types of persistent and residual antimicrobial properties, as opposed to only "latently passive" activity that keeps microorganisms on the hands below baseline counts. The second type of persistent/residual antimicrobial effects, which this study has graphically illustrated, can be termed latently active. This is because these products not only provide "latent passive" protection, but they also show persistent activity against contaminative bacteria for an extended period after use. Such a property assuredly is of value in the medical arena.

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## Skin Antisepsis Basics

The recommendations from the CDC Guideline for Hand Hygiene in Healthcare Settings place great emphasis on the thorough decontamination of healthcare workers' hands. The guidelines, in part, recommend the performance of surgical hand antisepsis using either an antimicrobial soap or an alcohol-based hand rub with persistent activity before donning sterile gloves when performing surgical procedures. When performing surgical hand antisepsis using an antimicrobial soap, healthcare workers should scrub their hands and forearms for the length of time recommended by the manufacturer, usually two to six minutes. When using an alcohol-based surgical hand scrub product with persistent activity, healthcare workers should follow the manufacturer's instructions. Before applying the alcohol solution, pre-wash hands and forearms with a non-antimicrobial soap and dry hands and forearms completely. After application of the alcohol-based product as recommended, allow hands and forearms to dry thoroughly before donning sterile gloves. Healthcare workers should also solicit information from manufacturers regarding any effects that hand lotions, creams, or alcohol-based hand antiseptics may have on the persistent effects of antimicrobial soaps being used in the institution.

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