Cleaning After Manufacturing: The Forgotton Step of Scale Up

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ABSTRACT

Many cosmetic and personal care companies are expanding their businesses to include the manufacturing of products with drug claims (e.g., antibacterial soaps, sunscreens). There is growing scrutiny by the FDA on drug-manufacturers to prove that their cleaning validation programs are compliant (i.e., that they prevent cross-contamination and inadvertent microbial load in subsequent products). However, even before addressing cleaning validation, an evaluation of a company's entire cleaning system is needed. This includes evaluating cleaning equipment capabilities, types of soils, test methods, cleaning chemistry and the impact of cross-contamination on subsequent products. The selection of proper cleaning agents is vital, since some soils can be cleaned with water alone or with a commodity cleaner (e.g., NaOH, KOH), while other "difficult-to-clean" soils warrant additional cleaning mechanisms through the use of materials such as surfactants and chelants. This presentation will focus on some of the chemistries used for cleaning mixing tanks and vessels and will provide examples.

INTRODUCTION

In 1993, the FDA issued a guidance document to reinforce cGMP compliance requirements directed towards cleaning validation.[1] These requirements are aimed primarily at the pharmaceutical industry; however, as the cosmetic and personal care industries continue to expand into new markets, many are becoming manufacturers of both drug and non-drug products. This ongoing product expansion has required some to review and update their cleaning strategies and procedures.

The scale-up process, during which the entire manufacturing environment should be taken into account, is a strategic point where cleaning procedures can be addressed. The cleaning equipment used varies throughout the industry, including "clean-in-place" systems, agitated immersion, and manual methods. Some companies have equipment dedicated for the manufacturing of products that are classified as drugs, while others have equipment that are used for manufacturing both drug and non-drug products. Some employ grouping strategies, where similar products are made in one manufacturing vessel, and cleaned using one procedure when possible. When evaluating an entire facility, some even extend the same quality approach to all of their cleaning procedures, whether a drug product is manufactured in that tank or not. The underlying purpose is to eliminate residue that can carry over to and contaminate the next (drug) product.

Fundamental to cleaning performance are the actual cleaning chemistries employed. Some companies use commodity cleaners (e.g., hydroxides, acids, alcohols) to address their needs. Others may need more "complex" chemistries due to the types of soils they are trying to clean. For example, "formulated cleaning products" often contain surfactants, chelating agents, dispersants, suspending agents, hydrolyzing agents or other materials to assist in cleaning the targeted difficult-to-remove soils from product contact surfaces.

The most common materials used in formulated cleaning products are surfactants. These "surface-active" components provide wetting and assist in solubilizing and/or emulsifying soils. The choice of surfactants used in a cleaning system is dependent on the intended cleaning use. Such requirements as cleaning time, use-temperature, concentration, foaming properties and rinsability will help in deciding which surfactant systems are best for a specific application.

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[1] FDA. "Guide to Inspection of Cleaning Processes." Division of Field Investigations, Office of Regional Operations, Office of Regulatory Affairs, July 1993.

Often cleaners will employ acids or bases as sources for hydrolysis, which help break down complex chemical structures into more water-soluble entities. Chelating agents aid in limiting the effects of water hardness, and can assist in the actual cleaning action, due to their sequestering and anti-redeposition characteristics. Other chemistries used in formulated cleaners include solvents, enzymes, builders, and corrosion inhibitors. All of these ingredients assist in cleaning the surface, protecting the substrate (surfaces), and rinsing the soil and cleaning product away. Formulated cleaning products offer the advantage of providing a broad-spectrum cleaning approach for many different product types.

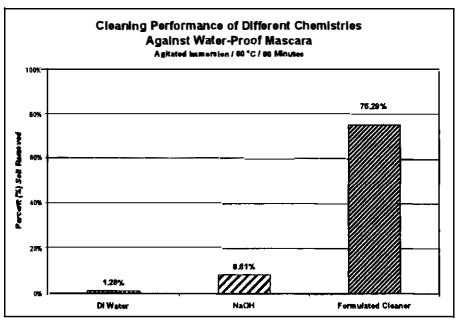
Methods

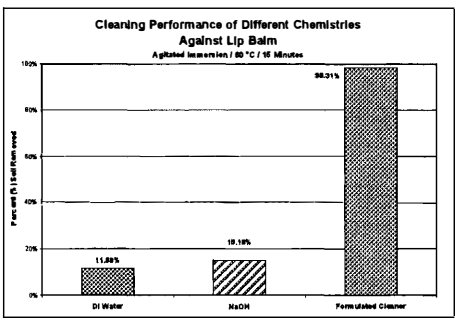
Two commercially available cosmetic products, waterproof mascara and lip balm, were tested separately in side-by-side cleaning studies. Each product (soil) was applied to a series of 316-grade stainless steel coupons, 7.6 x 2.5 cm in size, covering approximately 11 cm^2 of each coupon. The amount of soil varied with each product. The soiled coupon was allowed to dry for 48 hours at ambient laboratory conditions. The coupons were weighed before and after each product was applied, and after the cleaning process. The percentage of soil removed is calculated by the weight difference before and after cleaning.

Three cleaning solutions were evaluated: deionized water, sodium hydroxide solution and a formulated cleaner solution (which contains, among other ingredients, surfactant, chelating agents, and hydroxide). The formulated cleaner was diluted in deionized water to 5% wt/wt. The sodium hydroxide was diluted to match the alkalinity in the formulated cleaner.

Results and Discussion

The study depicted that the formulated cleaner had the best cleaning performance against these two cosmetic soils. The sodium hydroxide solution did outperform deionized water, showing that, for these soils, alkaline hydrolysis does provide some cleaning action. However, the cleaning is greatly improved when surfactants and chelating agents are added to the system. Most likely, the surfactant and chelating agent systems work in unison to lift, emulsify and suspend the soils during the cleaning process.





Conclusions

Cleaning performance is dependent upon the type of soil and the overall cleaning process used in a given manufacturing facility. Although water or commodity cleaners may clean certain soils, formulated cleaning chemistries with multiple modes of action are often needed to achieve the best cleaning results.