CLEANROOMS

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Choosing the Correct Swab for Cleaning Validation

Kathy Miscioscio, *The Texwipe Company*

During the manufacture of pharmaceutical and biotechnology products, care must be taken to ensure that these products are not contaminated either by the previous manufacturing run or by the cleaning process itself. The cleaning process can be validated by sampling various parts of the manufacturing equipment and analyzing the sampling material for contaminants.

Typically, swabs are used for sampling. Any product or cleaning residue can be eluted from the swab and analyzed using standard analytical techniques such as high performance liquid chromatography (HPLC) or gas chromatography. Recently, total organic carbon (TOC) has been gaining favor as the analytical method of choice because it is a sensitive technique that will measure all oxidizable carbon compounds, regardless of organic functional groups.

Three of the most important criteria for choosing a swab for cleaning validation include:

- **Minimal Background**— Background is the amount of contaminant on a swab measured by the analytical technique after testing has been performed according to the analytical protocol before sampling. Blank contribution from the swab must be minimal.

- **High Recovery Rate**— Recovery means the percentage of contaminant actually measured by the analytical technique when the swab is spiked with a known quantity of that species. Sixty-percent recovery rates are acceptable; however, higher recovery rates are desirable.

- **Low Particle Generation**—It is critical that the swabbing material leave the swabbed surface free from particles which would further contaminate the surface.

Jenkins et al. [1] recently screened a number of materials for their suitability as swabbing materials for TOC analysis. They tested the following materials: quartz wool, hydroentangled polyester, cotton, polyurethane foam, glass fiber with an acrylic binder, a nonwoven polyester/cellulose blend, a 100 percent continuous-filament, double-knit polyester, and polypropylene-cellulose-polypropylene composites. Four of these materials—the quartz wool, hydroentangled polyester, glass fiber with acrylic binder, and 100 percent continuous-filament, double-knit polyester—met the first criteria of minimal background. Of these, only the quartz wool and 100 percent continuous-filament, double-knit polyester demonstrated recovery rates of 60 percent or higher when spiked with samples of methscopolamine bromide, a water-soluble drug. Although background and recovery rates for the quartz wool were acceptable, its excessive particle generation eliminated quartz wool as a material for surface sampling for TOC analysis. The cleanroom-laundered, 100 percent polyester materials were the only materials tested that met all the requirements for TOC swabbing: minimal background, high recovery rates, and low particle generation.

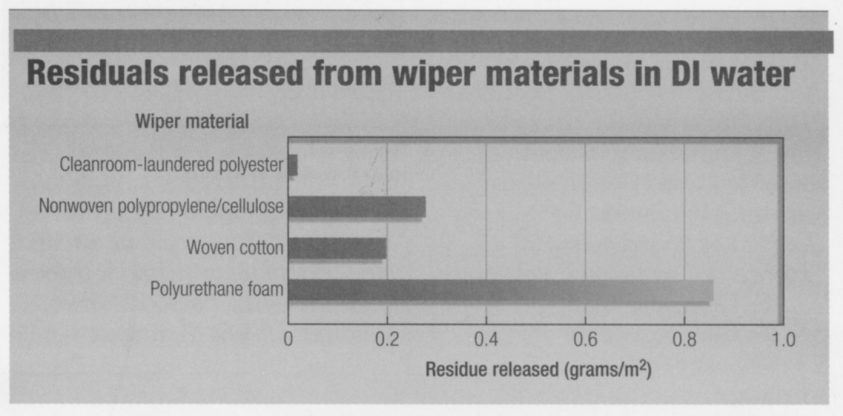

Figure 1. The ultra-low background levels of carbon reported by Jenkins et al., coupled with low extractable levels, provide a minimal background for the samples. The swabs also have demonstrated high analytical recovery rates when spiked with control samples used in validation studies. These features make cleanroom-laundered polyester swabs ideal for sampling surfaces for TOC analysis and for some other pharmaceutical cleaning validation methods.

Swabs made with cleanroom-laundered 100 percent polyester-knit heads feature low particle generation and extremely low nonvolatile residues. Figure 1 compares the levels of non-volatile residues of laundered polyester with other commonly used swab head materials. Each sample was boiled in deionized water for 10 minutes and the residuals weighed.

Reference

1. Jenkins, K.M., Vanderwielin, A.J., Armstrong, J.A., Leonard, L.M., Murphy, G.P., and Piros, N.A., "Application of Total Organic Carbon Analysis to Cleaning Validation," *PDA Journal of Pharmaceutical Science & Technology*, Vol. 50, No. 1, 1996, pp. 6–15.

Texwipe's Large Alpha Swab is used for pharmaceutical validation.

Kathy Miscioscio *has a BS degree in Chemistry and an MBA in Marketing. For the past three years, she has been a Market Manager for The Texwipe Company and is currently responsible for developing new cleanroom and sterile products for the pharmaceutical industry.*

Typical Cleaning Validation Problems and Solutions

Andrew Thorpe, *The Texwipe Coompany*

Q. A manufacturer of specialty proteins needed to perform sampling for routine testing of stainless steel machinery. Swabs were to be used to wipe inside surfaces, and any residue removed would be used to determine the possibility of cross-contamination between batches.

A. Methods for detecting bacteria and total organic carbon (TOC) require cleanroom-laundered and/or autoclavable swabs or wipers. A 100 percent laundered, double-knit polyester was suggested for high recovery rates when tested against other cleanroom and non-cleanroom wipers. These wipers absorb at least 400 milliliters of water per square meter and rinse out cleanly, allowing critical analysis of residues in liquids. Also, polyester can be steam-autoclaved, if necessary.

Q. A pharmaceutical company needed swabs to perform cleaning validation tests on machines used in manufacturing dental anesthetics. Only swabs with low residues would be appropriate.

A. Cleanroom-laundered polyester swabs were recommended because polyester fabric is resistant to most solvents. After immersion in boiling alcohol for 10 minutes, the residue released from a polyester swab with a head size of 0.25 in. × 0.66 in. is approximately 0.05 milligrams per swab. At room temperature, residues should be much lower, making the swab acceptable for validation testing.

Q. A manufacturer of high-purity drugs needed swabs for cleaning inside blending vessels. Residue picked up from the swabs would then be analyzed for contaminants using high performance liquid chromatography (HPLC). The customer was worried about glues used in the swabs that might be released in the testing apparatus.

A. The use of cleanroom swabs manufactured without adhesives was recommended. These types of swabs have heads that are heat-bonded to the shafts, so cleanroom quality will not be compromised. This allows HPLC analysis to proceed without background signals from the glue.

Q. A supplier of animal health drugs was conducting TOC testing on its manufacturing machinery. Its concern was that swabs would release particles and create background signals in the VOC detectors.

A. The number of particles released in some laundered polyester swabs is negligible, due to cleanroom washing and packaging. Residue levels of less than 0.4 milligrams per swab with head dimensions of 0.50 in. × 1.01 in. can be detected only after boiling the tips in alcohol for 10 minutes.

Andrew M. Thorpe *is The Texwipe Company's Senior Technical Representative. He has a seventeen-year background in the chemical, pharmaceutical and polymer industries, focusing primarily on research and development and technical support. As technical liaison in contamination control, he divides his expertise among the pharmaceutical, aerospace, chemical, semiconductor and optical industries.*