Using Notebook Studies to Help Ensure a Successful Reusable Device Cleaning Validation

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Device manufacturers need to ensure their product will be sufficiently cleaned by healthcare professionals. This article will focus on the areas of the FDA's guidance document that are causing difficulties in cleaning validations, and will demonstrate how pre-validation laboratory work can help save time and money.

The FDA Draft Guidance for Industry and Staff, Processing/Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling, was released in May 2011. Even though this document is labeled draft, experience has shown that most reusable device cleaning validations are being evaluated on this document.

It is important to note that the cleaning validation being discussed is a challenge to the manufacturer's cleaning instructions document [typically referred to as Instructions for Use (IFU)]. The point of the validation is to prove that when the instructions are followed, as written, the device will be cleaned adequately to allow further processing, and ultimately be used safely on a patient.

The validation approach with this guidance focuses heavily on proving the removal of physical soil to prevent buildup from repeated reprocessing. In order to accomplish this, quantitative chemical-based test methods are used in place of traditional microbial-based assays, since the former are better suited to measuring residual soil. Also, the guidance recommends using a worst-case approach when planning the validation to reduce the effect of reprocessor variability in healthcare facilities.

Microtest Laboratories [1] routinely performs cleaning validations following the guidance for various instrument types and have identified several areas that can cause issues during the validation if they are not thoroughly addressed prior to initiating the protocol. Almost all of these issues can be eliminated with some up-front work. This preparatory work can best be performed by notebook studies prior to initiating GLP studies. The information obtained in these relatively quick studies often saves significant time later in the filing process.

One example is verifying the compatibility of the device materials and the test methods. On several occasions, the GLP studies were initiated only to find that the test soil was not compatible with the device, resulting in corrosion that stained the device surface or extracted a component that interfered with the residual assay.

The use of worst-case conditions throughout the validation protocol can have a major impact on its success. The worst-case conditions are selected to challenge those presented in the cleaning instructions. For example, if the IFU states to "brush for one minute and then rinse for 30 seconds with 40°C to 50°C tap water," the

validation protocol may use, as worst-case parameters, “brush for 30 seconds and then rinse for 15 seconds with 20°C to 25°C tap water.” If the validation protocol can meet its acceptance criteria with the worst-case conditions then it is assumed a healthcare facility following the steps given in the IFU would produce an acceptably clean device.

As mentioned previously, one of the biggest changes taking place is the switch from microbial-based assays to chemical-based assays. A big concern with the microbial-based assays is that acceptable results could be obtained by killing the bugs, but the medium they traveled on could still be present. The chemistry-based assays are chosen to be specific to a clinically relevant test soil, such as protein, hemoglobin, or carbohydrates. These assays, since they are specific, are able to detect lower residual levels remaining on the devices after cleaning.

Using the combination of worst-case conditions and more sensitive chemical-based assays may yield detectable levels of residuals (protein and hemoglobin), while in the past, microbial-based assays would have shown acceptable results. Testing the cleaning instructions for devices using a notebook study prior to initiating the GLP validation can save time and money from repeated testing. A common worst-case condition used is to allow the test soil to dry on the device prior to beginning the cleaning procedure. In several instances, devices were having difficulty getting cleaned, so notebook studies were used to determine a sufficient pre-cleaning soak time.

Determining what an acceptable residual level is has been another concern. The FDA guidance does not identify specific acceptable levels of the residuals, but only uses the term “predetermined cleaning endpoints” in several locations. Setting these predetermined cleaning endpoints requires knowledge of the assay’s detection limit, device surface area, and extract volume. Preliminary work in the lab to determine the most efficient method for extracting residual soil can be a great help in setting endpoint limits and to save time during execution of the protocol.

In many cases, the validation of a reusable device’s cleaning instructions is the last bit of information needed for the device’s submission package. In a rush, there is a tendency for device manufacturers to use general cleaning instructions that have worked for similar devices in the past. Manufacturers using this approach, assuming they will pass because they have previously, and who are now having their cleaning validations performed following the FDA’s 2011 draft guidance, may be surprised when they receive failing results.

The use of notebook studies prior to beginning the validation to eliminate as many unknowns as possible is recommended. The cost of a notebook study is roughly one-third the cost of a GLP study, and without the protocol/report generation and review process, can easily be performed in one quarter of the time. While adding a slight amount of time and money at the beginning of the validation project, the potential savings can be significant by ensuring the cleaning instructions can adequately clean the device and that the selected test methods can give the results needed to prove it.

Links:
[1] http://www.microtestlabs.com/