Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling Guidance for Industry and Food and Drug Administration Staff

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Introduction/Purpose
This article focuses on the newly released FDA guidance, “Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling Guidance for Industry and Food and Drug Administration Staff”¹ and the effects it will have on the industry. The objective of this guidance is to provide more robust recommendations for reprocessing medical devices with the intent of reducing the risk of patient infection. The guidance focuses on the criticality of manufacturers developing reprocessing instructions which can be easily understood and followed by end users to ensure that reusable devices remain safe and effective for reuse after reprocessing.

Background
This FDA guidance document includes clarification and additional information not provided in the draft guidance released in 2011, including information applicable to validation of reprocessing methods and instructions. Inadequate processing of medical devices is a major concern in health care facilities.² Outlined in this guidance is the agency’s expectations for manufacturers to conduct scientifically sound testing to validate their reprocessing instructions prior to marketing.³ Special emphasis is given to the importance of proper cleaning to ensure that the device is adequately prepared for sterilization or disinfection steps. To that end, the FDA instructs manufacturers to pay specific attention to other important human factors, such as usability for end users wearing protective gear.

This guidance was finalized following highly publicized outbreaks of hospital-acquired infections, resulting in two deaths and infecting five more at UCLA Medical Center early this year (2015), attributed to multidrug-resistant bacterial infections from carbapenem-resistant Enterobacteriaceae (CRE), such as Klebsiella species and Escherichia coli.⁴ Although other outbreaks have been attributed to breaches of approved cleaning validation process, no breach in duodenoscope reprocessing was identified in the UCLA cases. The FDA issued a safety alert in response to these events indicating that “the complex design of duodenoscopes causes challenges for cleaning and high-level disinfection [such that] effective cleaning of all areas of the duodenoscope may not be possible.”⁵ Finalizing this medical device reprocessing guidance is one of the steps FDA has taken in order to reduce the risk of infection from reprocessed reusable devices.

In addition, FDA’s Gastroenterology-Urology Device Advisory Committee met on May 14th and 15th to discuss effective reprocessing of duodenoscopes to advise health care providers, researchers, manufacturers, etc., on how to implement more rigorous, but realistic, reprocessing instructions that will improve the safety of these procedures.⁶ This direction included the importance of improving the training and education of the individuals conducting the reprocessing procedures. The committee defined that duodenoscopes are medical devices regulated under 21 CFR 876.1500; therefore, manufacturers should submit 510(k) premarket notifications, which includes safety testing, biocompatibility, and reprocessing validation, to the FDA prior to marketing a new device or device.
Modification. Best practices and guidelines for reprocessing duodenoscopes and endoscopes to minimize the risk of patient infections was outlined by the committee, including the importance of defining appropriate patient selection criteria. The FDA committee meeting summary stated, “The panel discussed the role of pre-market human factors testing in reprocessing instructions and concluded human factors testing is important and therefore, should be a part of the pre-market assessment.”

Formulation of Reprocessing Instructions: Human Factors

The instructions need to consider the reprocessing environment and protective gear requirements in health care facilities as well as the risk to users from potential errors that could occur during processing/reprocessing of a device. The instructions should reflect each step of the actual reprocessing requirements from the end of the treatment procedure to the beginning of the next procedure. Additionally, the instructions should consider user educational levels and balance media types for the visual, auditory, and kinesthetic sensory input channels to meet the human factors needs of the end user population. The reprocessing instructions should be standardized across a product line to make them consistent and easier to follow for users. The instructions should also include a combination of text and images to aid in comprehension, and the language should be easily readable.

Validation of Human Factors

Human factors studies address risk mitigation and allow visibility to any modifications that need to be made before pre-market submission. “For devices that are subject to design controls under 21 CFR 820.30, you should validate your reprocessing instructions to ensure that users will be able to successfully understand and follow them.” Conducting human factors studies lowers the number of potential use or user errors, reduces the risks associated with the use of the device, lowers training costs for the end-users, and reduces costly device service and support.
The basic objective of a human factors study is for the users to demonstrate whether the instructions allow the device to be successfully cleaned when evaluated against pre-defined endpoints. The study sample size is determined by a biostatistician based on the study design, objectives, and endpoints. The endpoint for a device reprocessing human factors study can be defined simply, such as the number of times the instructions were properly followed or the proportion of devices that were successfully reprocessed, or it can be defined more intricately. The endpoint is defined from the risk assessment of the device to ensure the usability of the device and instructions.

There are various considerations when designing a human factors study, including study objectives, sample size, endpoints, participant eligibility criteria, study procedures, the testing environment, user protective gear, the device system/components which are to be cleaned, reprocessing materials, and the study assessments. These must all be clearly defined in the study protocol. The study design can be simple or complex, depending on the complexity and intended use of the device to be cleaned. Study participant eligibility criteria must be precisely defined and should exclude employees of the manufacturer and the study sponsor. It is important to define the testing environment as it should mimic the intended use scenario as much as possible. Participants should be selected from the targeted users of the device and should be instructed to wear the required protective gear, even in cases where testing does not involve use of the actual detergent or other cleaning materials. Researchers should interact in a consistent manner with all participants to avoid introducing bias. Observer(s) must be present, not to assist the participant, but to record activities taken in response to the instructions. The study protocol must clearly define whether the entire device system or just certain components or accessories are to be tested, and whether the reprocessing will simulate the reprocessing steps or actually reprocess the device. Lastly, study assessments and questionnaires need to be developed prior to study initiation and should be as objective as possible. All required study data, including participant demographic information, device use, results of each step and any difficulties, user errors, or device malfunctions, are recorded on these forms. The questionnaires should allow for feedback on the wording of the instructions and whether the instructions were found to be confusing, misleading, or incomplete. The observer’s and participant’s data should be documented and compiled in order to identify and understand the nature of any issues encountered. If, as a result of the study findings, changes are made to the instructions, they will need to be retested and validated.

“For usability studies, as in any clinical trial, the safety and welfare of the subjects must be protected; therefore informed consent and Institutional Review Board (IRB) approval are generally required. The FDA’s perspective is that all human subject research, even sociology and educational studies, require IRB approval.”

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FDA will review reprocessing instructions and documentation of reprocessing method validation in pre-market submissions to evaluate use-related risk analyses, human factors/usability information, and validation study data as part of the following types of pre-market submissions: 510(k) (for those devices identified in Appendix E of the guidance), PMA, HDE, de novo, or IDE. Validations should be completed prior to pre-market submission.

What does this mean for Industry?
More human factors studies will be initiated to ensure reprocessing instructions are clear and comprehensive. To date, human factors studies have been required for device usability testing of devices ranging from simple hand-held items to complex multipart devices, including auto-injectors, pen injectors, inhalation products and pre-filled syringes, infusion pumps, transdermal patches, etc. Primarily, these are used at the patient-user level. Human factors studies to validate reprocessing instructions will now be required for disinfectants used by hospital supply personnel. This introduces human studies to manufacturers whose products previously did not require any ‘clinical’ evaluation with IRB approvals, participant informed consent, and collection of both objective and subjective data. These human factors considerations will impact timelines and costs for which device manufacturers should account for during their device design and effect.

The FDA highlighted the importance of designing devices that are less challenging to reprocess. In recent years, device designs have become much more complex, and therefore, more difficult to reprocess effectively. “Manufacturers should consider using designs that facilitate cleaning, disinfection, and sterilization methods that are easily and effectively implemented by users”, in addition to being safe and effective. It is recommended that manufacturers have the perspective of the user in mind earlier in the process while designing the device and developing the user instructions. To ensure the entire process is integrated well, individuals involved in human factors efforts should be included in the device design and risk assessment. Risk assessments should analyze the formative study

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questions and objectives, including the extent of training required, whether used by experienced or naïve participants, possible usage errors, and challenges to understanding the instructions.

Conclusion
Human factors studies are an iterative process, critical in meeting FDA’s requirements and keeping clinicians and consumers safe and protected. Manufacturers should provide labeling that includes instructions for reprocessing and reusing devices and device accessories safely. All cleaning, disinfection, and sterilization procedures provided in the labeling should be validated. Finally, the labeling should provide sufficient instructions on how to prepare the device for the next patient use. Manufacturers should identify the materials and equipment that users will need to reprocess the devices. These materials and equipment should be readily available to users. Human factors is a fundamental component in risk management for device manufacturers and should now be implemented to validate device reprocessing instructions as FDA will expect summaries of these human factors studies in many pre-market submissions.
REFERENCES
“Everything we do must be in our clients’ best interests.”
Ted Gorski, NAMSA Founder

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