Designing for Medical Device (Valved Holding Chamber) Robustness – Best Practice Approaches

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KEYWORDS: valved holding chamber (VHC), design controls, robustness, in-use testing

INTRODUCTION

The implementation of design controls was historically initiated following recalls that were related to poor design for medical devices [1]. In the United States, the Food and Drug Administration (FDA) provides guidance to medical device manufacturers on how to structure and implement a formal design controls process [2, 3]. In practice, medical device manufacturers generally adopt an internationally recognized quality management system (QMS) such as that described by the International Standards Organization (ISO) [4], which is closely aligned with FDA regulatory practice. An effective design controls process can also improve the probability that the product is a commercial success, since it may also capture marketing/end user requirements not necessarily related to safety or efficacy. The various design control guidance documents state in general terms the procedures that should be followed. However, they provide little practical detail on how to go about developing a safe and effective medical device that is robust. The purpose of this article is to review and describe the importance of effective execution of design controls in a development/manufacturing environment associated with valved holding chamber (VHC) add-on devices that are widely prescribed for use with pressurized metered dose inhalers (pMDIs), citing two examples that focus on device robustness as a critical quality attribute.

DESIGN CONTROLS APPLIED TO VHC DEVELOPMENT AND MANUFACTURE

VHCs are devices that are used for medication delivery primarily by the patient who may have limited knowledge of their function, rather than by clinicians with expert knowledge of their correct use [5]. Furthermore, patients can range in age from neonate to geriatric adult with a consequent wide range in cognitive ability and manual dexterity. Caregivers generally assist
patients at the extremes of the age spectrum, or those with limited ability to use the devices for themselves. Developers must therefore be aware that users may have limited knowledge of these devices, and consider intended and unintended mode of use scenarios [6].

The underlying principle of a design control regimen is to ensure that the process used to develop a product is documented. It generally follows the “waterfall” concept developed by the FDA [3], in which the users’ needs are assessed and then translated into design inputs, also known as engineering requirements. These needs flow down through the design process resulting in outputs, such as drawings, parts, and prototype devices. These outputs are verified, in general by laboratory testing, throughout the development to ensure that the input requirements (the user’s needs) are met.

**IMPORTANCE OF ROBUSTNESS TESTING WITH VHCs**

The term robustness is often used by medical device developers when evaluating extremes of use and expected misuse. It implies that the device can tolerate its treatment by the user, without affecting its efficacy or posing a safety concern. In addition to the design control guidance [3], explicit standards can be applied to specific classes of devices. For example, in 2004, the Canadian Standards Association published a standard revised four years later [7] that specifies appropriate tests for VHCs, to ensure they meet the end user requirements throughout their expected life [8].

Through the undertaking of a comprehensive risk analysis as part of the design controls process, there are two requirements related to robustness that we have found in our experience of developing these products that clearly have the potential to affect function of a VHC as a hand-held device in a way that may affect safety and/or efficacy:

- The effect of impact forces in the event a user accidentally drops it;
- Repeated cleaning in an automated dishwasher.

Dropping can potentially cause cracks to appear in plastic walls and areas of stress, while fragments and inhalation and exhalation valves could become dislodged and rendered inhalable. Additionally, cleaning by dishwasher exposes the devices to elevated temperatures, harsh cleaning chemicals and high pressure water jets. Such a process has the potential to impact negatively both the appearance and physical integrity of the VHC.

Laboratory tests covering both dishwasher exposure and drop tests are described below to illustrate how a manufacturer needs to evaluate identified risks as an integral part of their design control process. If the results of such testing provide any indication of a change in physical form or function, then the device design should be improved to rectify the problem prior to it being registered for use by patients.

**DISHWASHER EXPOSURE TESTING**

The procedure developed in our laboratories involves life cycling of VHCs through a dishwasher, as they would be used in the home following the instructions for use. Thus, normal dishwasher detergent is used (in our case Finish® Powerball), the devices are placed on the top shelf of dishwasher (Amana model ADB1600AWB1) and a normal cycle is selected with high temperature wash and heated dry settings on. After each cycle, the VHCs are shaken to remove any excess water, followed by drip-drying in air at room ambient conditions. Each wash cycle is then repeated 52 times, thereby mimicking a year of weekly cleaning. The devices are visually inspected at predetermined time points looking for aesthetic and physical deterioration.

Previously reported observations [9] have indicated that stress cracks can develop during repeated dishwashing, resulting in fracturing of the plastic mouthpiece. This behavior may have a significant impact on safety and efficacy.
DROP TESTING

Drop testing is a simulation of a real-life scenario representing a worst-case fall from the level of the face to the ground. Following the CSA standard [7], a VHC is released from a 1.8 m height onto a concrete floor. The procedure in our laboratories, involves dropping the VHC six times – initially with the long axis of the device vertically oriented followed by repeating the procedure with the long axis horizontally positioned. The device is examined for damage after each drop event.

Drop testing according to this type of protocol using a range of marketed VHCs has shown the potential for the flexible valve components, in some designs, to become displaced following dropping.

Such misalignment of critical components has the potential to negatively influence the delivery of medication to the patient.

CONCLUSIONS

An effective design control process is vital in order to ensure that robust medical devices, such as VHCs, are developed. Although documentation of such a process is important for regulatory purposes, the inclusion of carefully considered in vitro testing results reflecting patient/caregiver use and misuse scenarios should be a key component of the entire development process including post-marketing surveillance. The Canadian standard for evaluation of VHC devices [7] has proven helpful for drop testing and could usefully be revised to address standardized dishwasher testing. Both these anticipate use scenarios have proven capable of damaging some VHCs to the point they pose a safety risk or do not perform their intended function, while other VHCs have shown no visible signs of deterioration. It is recommended that neither test should be weakened from that specified in this abstract in order to save time or cost during device development.
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