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

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INTRODUCTION
• The purpose of this presentation is to review and describe the importance of effective execution of design controls in the development and manufacturing environment associated with Valved Holding Chambers (VHCs).
• VHCs are widely prescribed for use with pressurized Metered Dose Inhalers (pMDIs).
• Focus is on device robustness as a critical quality attribute.

DESIGN CONTROLS APPLIED TO VHC DEVELOPMENT AND MANUFACTURING
• 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, in which the users’ needs are assessed and then translated into design inputs, also known as engineering requirements.
• These needs flow down through the development 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.

FDA ‘Waterfall’ Diagram for Medical Device Design Controls

User needs → Design input → Design process → Design output → Medical device → Validation → Review

IMPORTANCE OF ROBUSTNESS TESTING WITH VALVED HOLDING CHAMBERS
• 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,¹ the Canadian Standards Association has published a standard² that specifies appropriate tests for VHCs, to ensure they meet the end user requirements throughout their expected life.³
• Through the undertaking of a comprehensive risk analysis as part of the design control process, there are two requirements related to robustness that in our experience have the potential to affect the function of a VHC in a way that may impact safety and/or efficacy:
  1. Repeated cleaning in an automated dishwasher.
  2. The effect of impact forces in the event a user accidentally drops it.
• Laboratory tests for both requirements are described below to illustrate how a manufacturer can evaluate such potential risks as part of the design control process. Depending on the results from such tests, the device design may require modification prior to registration and use by patients.

Dishwasher Exposure Testing
• Life cycling of VHCs through a dishwasher, as they would be used in the home following the instructions for use.
• Dishwasher detergent is used (Finish* Powerball), the devices are placed on the top shelf of dishwasher (Amana® model ADE1600AWB1) and a normal cycle is selected.
• After each cycle, the VHCs are shaken to remove any excess water, followed by drip-drying in an air at room ambient conditions.
• Each wash cycle is then repeated 52 times, thereby mimicking a year of weekly cleaning.
• Devices are visually inspected at predetermined time points looking for aesthetic and physical deterioration.
• Previously reported observations of some marketed VHCs 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.

Dishwasher Exposure Testing Example outcome from repeated dishwashing test

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,³ 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.
• Device is examined for damage after each drop event.
• Test results have shown the potential for the flexible valve components, in some marketed VHCs, to become displaced following dropping. Such misalignment of critical components has the potential to negatively influence the delivery of medication to the patient.

Drop Testing Example of exhalation valve displaced following drop test

CONCLUSIONS
• An effective design control process is vital in order to ensure that robust medical devices, such as VHCs, are developed.
• The inclusion of carefully considered in vitro testing results reflecting patient/caregiver use and misuse scenarios should be a key component of the development process including post-marketing surveillance.
• The CSA for evaluation of VHC devices¹ has proven helpful for drop testing and could usefully be revised to address standardized dishwasher testing.
• Both the anticipated use scenarios demonstrated here have proven capable of damaging some VHCs to the point they pose a safety risk or do not perform as per 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.

²The Canadian Standards Association has published a standard that specifies appropriate tests for VHCs, to ensure they meet the end user requirements throughout their expected life.
³An effective design control process is vital in order to ensure that robust medical devices, such as VHCs, are developed.

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Respiratory Drug Delivery Europe
April 25 – 28, 2017
Nice, France

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