Validation of cleaning methods using MHRA criteria

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Focal points

• The work revalidates existing cleaning methodology bringing them in line with recent MHRA requirements
• The results demonstrate the robustness of the approach taken, validate the choice of the “worst case” drug product and justify the acceptance criteria
• The application of the revised validation method to the relevant products will provide further assurance that equipment are cleaned and products are made to higher standards

Introduction

The manufacturing unit at Colchester Hospital was inspected in January 2010 under the new risk-based MHRA inspection system. Although there were cleaning validations already in place, the concerns raised by the MHRA warranted the undertaking of this project to address them, and revalidate the cleaning methods.

Method

1. Worst Case Product
• 2% Salicylic Acid in Dermovate Ointment (0.05% Clobetasol Propionate in White Soft Paraffin)
• Clobetasol Propionate is a highly potent steroid which can present a significant hazard to patient safety
• White Soft Paraffin ointment is difficult to remove from contaminated surfaces

2. Acceptance Criteria
• Determined using a combination of the dose criterion, the 10ppm criterion, and the visually clean criterion (2,3)
• Residue limit of no more than 3.5µg of Clobetasol Propionate and no more than 100µg of Salicylic Acid per swabbed area

3. Sampling
• Simple and quick analytical method using TLC with UV light detection was developed
• Sensitivity and recovery of the analytical method were sufficient to give a limit of detection below the acceptance criteria
• Sampling method consisted of swabbing a defined area of selected cleaned equipment
• Swabs were extracted with dichloromethane
• Aliquots were applied to the TLC plate
• Following development any residue was confirmed by viewing the plate under UV light at a wavelength of 254nm

Results

• Negative control samples from cleaned equipment showed the absence of either Clobetasol propionate or Salicylic acid prior to spiking.
• Positive control samples from equipment contaminated with known amounts of marker product showed the presence of both Clobetasol propionate and Salicylic acid.
• Validation samples showed the absence of either Clobetasol propionate or Salicylic acid on cleaned equipment. These results were consistent in the triplicate application of the test.

Discussion/Conclusion

The results demonstrate that the cleaning method, when correctly applied, is satisfactory and capable of removing significant and detectable residues.

The validation approach and the MACO values employed in this work are simple, logical, achievable and verifiable. This approach can be applied to a variety of other settings.

References


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