Assessment of Risk using PM140

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The current USP <800> Hazardous Drugs – Handling in Healthcare Settings was made compendially applicable through USP <795> and USP <797> guidelines, in November of 2023. This guideline details requirements for handling hazardous drugs through every part of the process from receiving to administration or to dispensing and shipping. In an effort to protect personnel and patients, the guideline calls for a series of environmental controls and procedures along with required personal protective equipment (PPE) for handing hazardous drugs across a wide range of settings, including compounding pharmacies, hospitals, veterinary offices, and other sites that handle hazardous drugs. Though protective measures are necessary, the burden of these regulations can be prohibitive, especially for small pharmacies or hospitals. In some instances, the guidelines permit healthcare facilities to perform an "assessment of risk", which may allow pharmacies to use alternative containment strategies for handling hazardous drugs, rather than meeting all the requirements set out in the guidelines. Question 13 of USP <800> FAQs specifies that the "reconstitution, mixing, and dilution of Table 2 HDs" may be considered under an assessment of risk. This could allow for some hazardous drugs commonly compounded into suspension form, such as tacrolimus, to be compounded using alternative containment strategies. This study aims to evaluate the appropriateness of the FagronLab™ PM140, a closed system planetary mixing device, for the dissolution of whole capsules into a suspension vehicle while preventing hazardous drug contamination.

Materials and Methods

In ideal circumstances, a NIOSH Table 2 drug would be used to validate the FagronLab™ PM140 mixing system for prevention of hazardous drug contamination during compounding. However, a review of available environmental wipe sampling kits from ChemoGLO revealed that testing for tacrolimus or similar active pharmaceutical ingredients (APIs) commercially available in dry powder capsule form were not currently available. An alternative drug candidate was needed that was available in dry powder capsule form and could be subject to the same procedure that would be used for a Table 2 drug such as tacrolimus. Cyclophosphamide was selected as a proxy as tests exist to measure this active ingredient with existing wipe kits and it exists in a dry powder capsule form. Though cyclophosphamide is a Table 1 drug, the intent of this study is not to justify the use of table 1 drugs outside of a negative pressure room, cyclophosphamide is only being used as proof of concept. [3]

Protocol

1. Wipe down device with and surrounding countertop with PeridoxRTU consistent with protocol tested by Contec:
    a. Wipe irregular surfaces, then flat surfaces with PeridoxRTU (3-minute dwell)
    b. Wipe irregular surfaces, then flat surfaces with PeridoxRTU (no dwell required)
    c. Wipe irregular then flat surfaces with 70% IPA to remove residues and allow to dry

2. Follow formula as below:

Cyclophosphamide 10mg/mL Oral Suspension	
Cyclophosphamide 25mg Capsules*	40ea
Syrspend SF	q.s. 100mL

* Cyclophosphamide 25mg Capsules manufactured by Cipla (NDC 69097-516-07)

Don a single pair of chemo gloves and count out Cyclophosphamide 25mg Capsules and measure out 85% Syrspend SF oral suspension. Add Syrspend SF to PM140 milling bottle before pouring in capsules. Dispose of gloves appropriately. Mix on FagronLab™ PM140 for 6 minutes until a homogenous suspension forms. QS to final volume with Syrspend SF and shake.

3. With a fresh set of gloves, remove wipes from the environmental wipe test kit. Follow kit instructions to prepare wipes.
4. Wipe down 6 areas, using a fresh set of gloves for each wipe, to avoid cross contamination:
    a. The external lid of the PM140 device
    b. The sides of the PM140 device
    c. A 1ftx1ft square in front of the device
    d. A 1ftx1ft square behind the device
    e. 1ftx1ft square on either side of device
5. Package the used wipes as directed by kit instructions, being sure to clearly label which wipe number corresponds with which area wiped.
6. Return to ChemoGlo for quantitation and detection of cyclophosphamide

Pass: No cyclophosphamide detected: The lower limits of detection of the cyclophosphamide test are 10.0 ng/ft2 and 0.01 ng/cm2.

Fail: Cyclophosphamide detected

Result and Conclusion

The final result after mixing was a homogenous blue suspension with no visible agglomerations or particulates. Testing from ChemoGLO revealed that cyclophosphamide was below the detectable limit on all surfaces tested, indicating that the process of adding whole unopened capsules to an oral suspension vehicle and mixing in the FagronLab PM140 was sufficient to prevent contamination of the surrounding area with hazardous drug residue.

Looking for more information? Reach out to the FACTS team at facts.support@fagronacademy.us