Distek ezfill+ Cleaning Verification

Objective:

The ezfill+ is designed to heat, degas, and accurately dispense dissolution media from 250 – 1000 ml. To provide optimal performance and to minimize the risk of carryover, especially when changing media, the following sequence should be followed for all aqueous based media.

1. Execute a single “WASH” cycle using the desired media and discard
2. Dispense desired number of vessels
3. Execute a “WASH” cycle (1 – 4 times)

Note: It is recommended that at least a single “WASH” cycle should be executed prior to every use and anytime the system has been sitting idle for more than 45 minutes.

Note: The number of “WASH” cycles needed are determined based on the media that was previously used and the media to be used. For example, a media containing surfactants would require several “WASH” cycles to adequately remove any residual surfactant-based media. It is recommended to execute two “WASH” cycles by default and four or more for surfactant-based medias based on the concentration of surfactant used.

Proposed Procedure

To establish the effectiveness of the “WASH” cycle follow the following test procedure for each media type to be used.

1. Prepare the desired dissolution media
2. Execute a “WASH” cycle.
3. Dispense several vessels worth of media
4. Execute a “WASH” cycle(s) with DI Water
5. Dispense a vessel of DI water
6. Run an appropriate analytical technique to determine if any carryover from the previous media is present
7. If the analytical results do not meet your carryover specification, increase the “WASH” cycle by 1 and repeat until the level of carryover is below your specifications.

Below is an example of such a cleaning validation study. Although the ezfill+ is not normally intended to dispense media containing active ingredients, a solution with a compound such as caffeine can be used to establish the amount of

carryover inherent in the system. Deionized water (DI) with caffeine in a concentration of 0.016 mg/ml added is an ideal surrogate media A. This concentration corresponds to approximately 0.8 AU absorbance at 273 nm using a 10 mm pathlength cuvette. Pure DI water is then used as Media B. Sample data of the amount of residual caffeine measured using such solutions after corresponding number of "WASH" cycles are shown in Table 1.

Repetition	% Carryover	
	Wash 1	Wash 2
1	0.61%	ND
2	0.38%	ND
3	0.33%	ND

Table 1: Residual caffeine measured after corresponding number of "WASH" cycles

The definition of the acceptable amount of carryover (contaminant) from the previous media A to the current media B (contaminated) per volume dispensed is set by policy of each company. However, even a very aggressive safety factor of carryover less than 1 part in a 1000 (0.1%) was achieved in this example with only 2 wash cycles.

References

Nassani, M. (2005). Cleaning Validation in the Pharmaceutical Industry. *Journal of Validation Technology*. Retrieved from https://pdfs.semanticscholar.org/106e/17f0a0abf4dc7583231f9f254d5a8debd0d5.pdf.