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Background and Importance

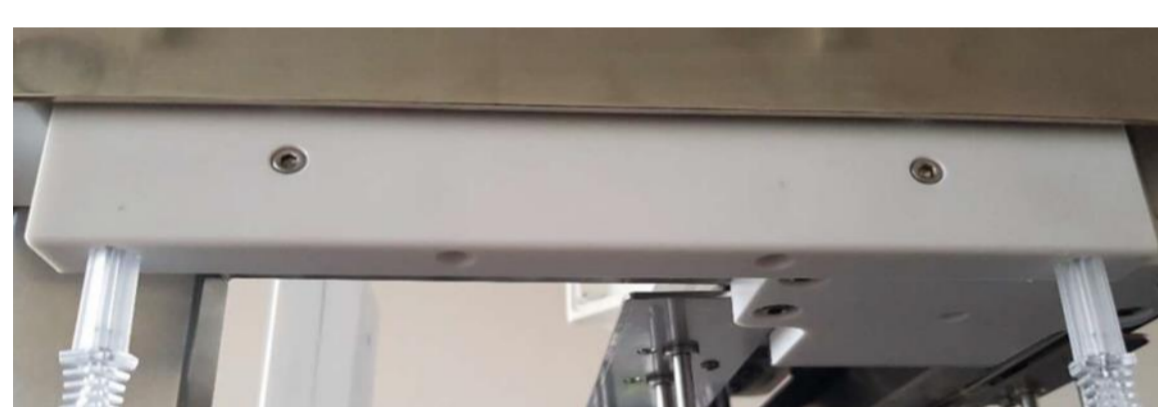
At the Pharmacy in Heidelberg University Hospital the Smartcompounder Chemo (Smartcompounders, Enschede, NL) has been used since 2019. The device is designed for an automated, batch-associated preparation of infusion solutions or elastomeric pumps inside a safety workbench or an isolator (CR Class A). Pre- and post-processing of the runs is performed manually by pharmaceutical staff. For preprocessing, spikes are connected to the vials, which are tied to holders as well as the infusion bags. QR codes of vial- and bag- holders have to be scanned for identification and holders will then be connected to the device.

Aim and Objectives

Residual surface contaminations with antineoplastic drugs on robot parts, holders as well as gloves and infusion bags were detected by wipe tests to assess the efficiency of our internal cleaning strategy.



Pic. 1 Holders with infusion bags connected at the front of the device, holders with vials at the back. Syringe fixing position on the left, robot head on the right.



Pic. 2 Syringe fixing position



Pic. 3 Vial holder



Pic. 4 Robot head



Pic. 5 Bag holder

Materials and Methods

In July and September 2022 we performed wipe tests, which were provided and analyzed by the Institut für Umwelt & Energie, Technik & Analytik (IUTA, Duisburg, Germany) in accordance to previously published and accredited methods. Before and after one preparation run of Gemcitabine and one of Paclitaxel up to 3 samples were taken from the following potentially exposed surfaces: Gloves after loading and unloading, robot head (Pic. 4), syringe fixing position (Pic. 2), vial holder (Pic. 3), bag holder (Pic. 5) and infusion bags (only after preparation). After analyzing the first sample set, cleaning procedures were adapted followed by a second sample set, which was identical except of adding two wipe samples of each vial surface of Gemcitabine (Hexal, Holzkirchen) and Paclitaxel (Ever, Jena) before loading.

Results

All wipe tests had been analyzed for detection of Paclitaxel and Gemcitabine surface contamination (Table 1). Paclitaxel was not detectable in any of the two sets. The first sample set showed Gemcitabine residues on gloves after loading as well as unloading (2 of 2 samples), syringe fixing position and robot head before and after the run (1 sample respectively), vial holder before and after the run (3 of 3 samples), bag holder after the run (1 of 3 samples). The second sample set showed Gemcitabine residues on gloves after loading (1 sample) and unloading (2 samples), syringe fixing position before and after the run (1 sample), bag holder after unloading (1 of 3 samples), and one infusion bag with minimal residue ($< 0,1 \text{ ng/cm}^2$).

	Jul 22		Sep 22	
	Before preparation	After preparation	Before preparation	After preparation
Gemcitabine HEXAL - Vial 1	/	/	< 3 ng/sample	/
Gemcitabine HEXAL - Vial 2	/	/	6,3 ng/sample	/
Paclitaxel EVER - Vial 1	/	/	< 3 ng/sample	/
Paclitaxel EVER - Vial 2	/	/	< 3 ng/sample	/
Gloves after Loading/unloading Gemcitabine	17 ng/sample	4400 ng/sample	< 3 ng/sample	15 ng/sample
Gloves nach Loading/unloading Paclitaxel	< 3 ng/sample	< 3 ng/sample	35 ng/sample	4,3 ng/sample
Syringe fixing position	0,46 ng/cm ²	0,33 ng/cm ²	2,4 ng/cm ²	5,7 ng/cm ²
Robot head	1,9 ng/cm ²	3 ng/cm ²	< 3 ng/Probe	< 3 ng/Probe
Holder 1 Vial Gemcitabine	< 0,1 ng/cm ²	3000 ng/cm ²	< 0,1 ng/cm ²	< 0,1 ng/cm ²
Holder 1 Vial Paclitaxel	< 0,1 ng/cm ²	< 0,1 ng/cm ²	< 0,1 ng/cm ²	< 0,1 ng/cm ²
Holder 2 Vial Gemcitabine	4,8 ng/cm ²	5,2 ng/cm ²	< 0,1 ng/cm ²	< 0,1 ng/cm ²
Holder 2 Vial Paclitaxel	< 0,1 ng/cm ²	< 0,1 ng/cm ²	< 0,1 ng/cm ²	< 0,1 ng/cm ²
Holder 3 Vial Gemcitabine	0,64 ng/cm ²	7,7 ng/cm ²	< 0,1 ng/cm ²	< 0,1 ng/cm ²
Holder 3 Vial Paclitaxel	< 0,1 ng/cm ²	< 0,1 ng/cm ²	< 0,1 ng/cm ²	< 0,1 ng/cm ²
Holder 1 Infusion bag Gemcitabine	< 0,1 ng/cm ²	1,1 ng/cm ²	< 0,1 ng/cm ²	< 0,1 ng/cm ²
Holder 1 Infusion bag Paclitaxel	< 0,1 ng/cm ²	< 0,1 ng/cm ²	< 0,1 ng/cm ²	0,34 ng/cm ²
Holder 2 Infusion bag Gemcitabine	< 0,1 ng/cm ²	< 0,1 ng/cm ²	< 0,1 ng/cm ²	< 0,1 ng/cm ²
Holder 2 Infusion bag Paclitaxel	< 0,1 ng/cm ²	< 0,1 ng/cm ²	< 0,1 ng/cm ²	< 0,1 ng/cm ²
Holder 3 Infusion bag Gemcitabine	< 0,1 ng/cm ²	27 ng/cm ²	< 0,1 ng/cm ²	< 0,1 ng/cm ²
Holder 3 Infusion bag Paclitaxel	< 0,1 ng/cm ²	< 0,1 ng/cm ²	< 0,1 ng/cm ²	< 0,1 ng/cm ²
Finished Infusion bag 1	/	< 0,004 ng/cm ²	/	0,01 ng/cm ²
Finished Infusion bag 2	/	< 0,004 ng/cm ²	/	< 0,004 ng/cm ²

Tab. 1: Results of Gemcitabine samples

Conclusion and Relevance

Compared to Gemcitabine there was no residue detectable for Paclitaxel. This might be explained by the much higher viscosity of Paclitaxel, which could have hampered spreading of the drug (less droplets and aerosoles).

After having seen residues of Gemcitabine on parts of the robot as well as gloves in the first sample set results, we adapted our cleaning processes of holders and robot parts. This led to only a few positive samples (6 vs 13) in the second set with even lower values at almost all locations. Samples from the surface of the vials showed left residues from the production process, which could have led to glove contamination. Prepared infusion bags showed – importantly - no relevant contamination from the production process.