

ChemoClave™ Closed System Transfer Device (CSTD) Surface Wipe Study Using Methotrexate (MTX) as a Marker

Report of a study commissioned by ICU Medical Inc. and conducted by and at RJ Lee Group, Inc.,
Greene County, PA

Background

ChemoClave is a needlefree closed system drug transfer device that meets the definition recognized by USP <800> as “a drug transfer device that mechanically prohibits the transfer of environmental contaminants into the system and the escape of the hazardous drug or vapor concentrations outside the system.”^{1,2} To validate a CSTD’s ability to “prohibit the escape of hazardous drug concentrations outside the system,” surface wipe test methods have been developed and commissioned by ICU Medical Inc.

The US Food and Drug Administration (FDA) accepts surface wipe studies as part of the 510(k) premarket clearance for closed system transfer devices. Surface wipe test results are included in the documentation submitted to the FDA to obtain 510(k) clearance for the ChemoClave (K173477) CSTD with the following indications for use: The ChemoClave is a needlefree Closed System Transfer Device (CSTD) that mechanically prohibits the transfer of environmental contaminants, including bacterial and airborne contaminants into the system, and the escape of drug or vapor concentrations outside the system during drug preparation and administration, thereby minimizing exposure of individuals, healthcare personnel and the environment to hazardous drugs.³

Objective

The purpose of the surface wipe study was to evaluate the ChemoClave CSTD for containment of hazardous drugs through a surface wipe analysis while performing compounding tasks using methotrexate as the hazardous drug marker.

Methods

The study was conducted at RJ Lee Group (RJLG) laboratory, where all tasks were performed in a Class II biological safety cabinet (BSC) in a Class 100 cleanroom. Before the study, four (4) separate surfaces of the BSC work area, measuring approximately 400 centimeters squared (cm²) were demarcated: two (2) separate surfaces of the BSC workbench (left and right of middle); the BSC grill (middle); and the BSC airfoil (middle).

Hazardous Drug Marker

Methotrexate was selected as the hazardous drug marker for its common use in the clinical setting and the availability of a sensitive analytical method to detect trace levels of the chemical. Vials of liquid MTX for injection, USP, 1 g/40 mL (Teva, Pharmaceuticals, Lot.13F21KA) were acquired for the study.

Pre-study

MTX vial decontamination

To minimize the concern that vial contamination could impact the study, all MTX vials were decontaminated and tested before use. The multi-step decontamination procedure was intended to deactivate and remove traces of MTX from surfaces. The procedure included separate applications of detergent containing sodium hypochlorite and sodium thiosulfate/benzyl alcohol followed by wiping with lint-free towels and rinsing. After drying, composite wipe samples were collected from vials, and the results were obtained to verify that no detectable levels were present.

BSC decontamination

Before each CSTD evaluation, the demarcated work area surfaces within the BSC were decontaminated using the procedure described above for the vial decontamination, and wipe samples were collected from the BSC workbench (left and right), grill, and airfoil.

Training of CSTDs

A certified pharmacy technician performed all simulated compounding tasks using personal protective equipment (PPE) and was trained in the use of the CSTD system following the system's directions for use (DFU).

Sample Size

The study evaluated three (3) individual trials of the ChemoClave CSTD, where the CSTD was accessed multiple times. The sample size represents the practice of normal hazardous drug compounding procedures and is in alignment with the FDA's review for hazardous drug containment for CSTDs with the ONB clearance.

Field Blanks

Field blank samples were collected for quality control purposes.

Procedure

For the CSTD system evaluation, three (3) individual trials were performed. For each individual trial, the pharmacy technician donned a new pair of nitrile outer gloves and performed all compounding activities inside the BSC within the demarcated areas. The technician placed four (4) IV bags, each containing 0.9% sodium chloride solution with the CSTD on the BSC workbench with the access ports inside the demarcated area (two on the left side and two on the right side). Four (4) vials of MTX were placed within the demarcated area and accessed using the compatible CSTD.

One by one, the technician would draw off three (3) individual volumes of 12 mL of MTX drug from each of four (4) vials and then push them into an IV bag, disconnecting and reconnecting after each individual transfer. During each trial, four (4) vials were used for each of the four (4) IV bags, totaling 12 transfers, 144 mL, and 3.6 grams (g) MTX. The simulated compounding procedure was completed in accordance with the CSTD Instructions for Use.

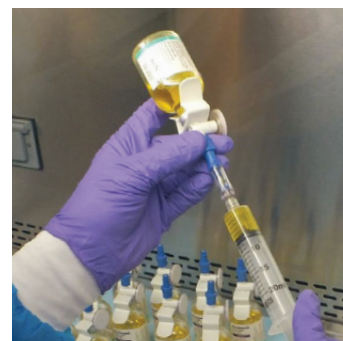


Photo 1. ICU Medical ChemoClave system, vial access.

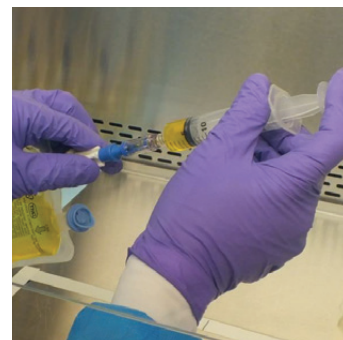


Photo 2. ICU Medical ChemoClave system, IV bag access.

Following each trial, wipe samples were collected from each of the pre-determined wipe locations using wipe sampling media (kits) assembled by RJLG. All samples were collected by a Certified Industrial Hygienist (CIH) with RJLG following standard techniques using the wipe sampling media (kits) assembled by RJLG.

The samples obtained during the study were stored at or below negative 70°C before laboratory analysis.

Following each trial, wipe samples were collected from the following locations:

Technician's gloves

BSC workbench left and right

BSC grill

BSC airfoil



Photo 3. Wipe sample collected from BSC workbench (left).

Analysis

The wipe samples were prepared and analyzed according to internal proprietary methods using a liquid chromatograph that was equipped with dual-mass spectrometers (LC-MS/MS). Samples were processed at the laboratory in compliance with Good Laboratory Practice (GLP) protocols (ref. 21 CFR Part 58) and Primera's Bioanalytical Method Validation Standard Operating Procedure SOP-PASC-0501. The laboratory analysis Limit of Quantitation (LOQ) was 10 nanograms (ng) per sample. For surface wipe samples, the results were reported as ng per centimeter squared (cm²).

Data Analysis Provided by

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Laboratory Analysis Provided by

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Table 1. Summary of ICU Medical ChemoClave Trials

Sample ID	Surface	Area, cm ²	MTX, ng	MTX conc., ng/cm ²	Comments
5297661	Field blank	na	nd	na	
5297662	Workbench left	400	nd	<0.025	Decontamination, Pre-Trial Sampling
5297663	Workbench right	400	nd	<0.025	
5297664	Grill	400	nd	<0.025	
5297665	Airfoil	400	nd	<0.025	
5297666	Gloves	–	nd	na	
5297668	Workbench left	400	nd	<0.025	ChemoClave, Trial 1
5297669	Workbench right	400	nd	<0.025	
5297670	Grill	400	nd	<0.025	
5297671	Airfoil	400	nd	<0.025	
5297672	Gloves	–	nd	na	
5297673	Workbench left	400	nd	<0.025	ChemoClave, Trial 2
5297674	Workbench right	400	nd	<0.025	
5297675	Grill	400	nd	<0.025	
5297676	Airfoil	400	nd	<0.025	
5297677	Gloves	–	nd	na	
5297678	Workbench left	400	nd	<0.025	ChemoClave, Trial 3
5297679	Workbench right	400	nd	<0.025	
5297680	Grill	400	nd	<0.025	
5297681	Airfoil	400	nd	<0.025	

na – not applicable

nd – not detected (<10 ng/sample)

Results

Data provided according to an analytical report from RJLG show the wipe samples collected from vials following the initial decontamination procedure and before use in the study were free of detectable MTX. MTX was not detected on any of the surface samples obtained before any of the work trials. Following trials with the ChemoClave CSTDs, no MTX was detected on any of the working surfaces or the technician's gloves.

Conclusion

Results of the surface wipe study suggest the ChemoClave CSTD was effective in preventing detectable surface contamination during three separate trials of simulated compounding activities with known amounts of methotrexate.

References

1. The United States Pharmacopeial Convention. USP General Chapter <800> Hazardous Drugs – Handling in Healthcare Settings. Chapter 14 Administering. 2017.
2. National Institute for Occupational Safety and Health (NIOSH): A Performance Test Protocol for Closed System Transfer Devices Used During Pharmacy Compounding and Administration of Hazardous Drugs. NIOSH Docket Number 288-A.
3. U.S. Food and Drug Administration (FDA): https://www.accessdata.fda.gov/cdrh_docs/pdf13/K131549.pdf. Accessed January 20, 2023.