

## WHITE PAPER

# SAFE TOXIC DRUG ADMIXTURE AND REDUCTION OF CONTAMINATION WITH CLOSED SYSTEM DEVICES (MINI-SPIKE® 2 CHEMO, PURESITE AND CYTO-SET®/ CYTO-SET® MIX)

### BACKGROUND

In parallel to the increase in the administration of antineoplastic drugs, there has been an increase in the number of preparations in pharmacy departments for individualised patient-related therapy. Particular attention should be paid to the preparation and administration of cytotoxic drugs. It is recognised that many cytotoxic drugs present a risk to occupational health and exhibit mutagenic, teratogenic and carcinogenic properties<sup>1-3</sup>.

Several health care professionals may be exposed to these risks during their working day<sup>3</sup>. They may be exposed to cytotoxic drugs during the preparation, transport, compounding, and administration, as well as during waste handling<sup>4</sup>. The presence of cytotoxic drug residues has also been proven by environmental monitoring of pharmacy working surfaces<sup>1-4</sup>. Despite “clean working” and handling according to the guidelines on controlling occupational exposure to hazardous drugs, contamination on working surfaces and working places can be detected<sup>5</sup>. Wiping samples collected from working surfaces and places is recommended to identify contaminations. These samples are analysed by liquid or gas chromatography. Clinical studies detected cytotoxic drugs on up to 75% of surfaces explored in pharmacy departments<sup>6</sup>. Exposure to hazardous drugs occurs mainly through powders, leakages and aerosols<sup>1</sup>.

Risk management and the adoption of preventive measures, such as engineering and administrative controls and the proper use of specially designed “protective devices”, are crucial issues to reduce healthcare professional exposure to cytotoxic drugs.

### PURPOSE

The aim of the prospective “La Fe” study by García et al. was to compare the performance of Mini-Spike® 2 Chemo and Puresite versus Phaseal™ in a pharmacy department during the presence of two cytotoxic drugs<sup>1</sup>. A second study conducted by Meier et al. was focused on the analysis, control and reduction of contamination in the workplace during handling of ten cytotoxic drugs. Mini-Spike® 2 Chemo was used for the preparation, Puresite and Cyto-Set®/Cyto-Set® Mix as transfer and administration devices<sup>2</sup>.

### METHODS

García et al.<sup>1</sup> evaluated the presence of cyclophosphamide (CYP) and 5-fluorouracil (5-FU) at three sampling times: baseline, after a decontamination procedure and six months after use of a “protective device” for CYP and 5-FU compounding. To test compounding time, four different nurses followed the same compounding protocol with each device. They tested a total of 90 sites in the pharmacy compounding area and explored the same 30 locations at each sampling time. These locations included different points in the biological safety cabinets, floors in front of the cabinet, inside surfaces of Sterile Access Systems, countertops, transfer trays,

external vial surfaces, and negative controls. The detection limits for the analysis of CYP and 5-FU were 0.1 and 5.0 ng/ml of recovery solution, respectively.

Testing was carried out using an independent laboratory and wipe testing kit. CYP was analysed on a gas chromatography-mass spectrometry tandem (GC-MSMS) system and 5-FU was performed on a High-Pressure Liquid Chromatography system with UV detection.

In addition, a questionnaire to obtain feedback from the nurses was developed.

Meier et al.<sup>2</sup> examined cytotoxic drug preparations on 180 working days. During the observation times, three samples were analysed. By means of wipe samples, taken on five representative locations (refrigerator door, working places in clean rooms and storage spaces, under the extractor fan, on the floor), and use of a Pharma Monitor® Kit, the frequency of cytotoxic drug contamination was explored. On every day, 814 samples were tested. The samples were evaluated by liquid chromatography with tandem mass spectroscopy (LC-MS/MS). Ten cytotoxic drugs were used: 5-FU, cyclophosphamide, ifosfamide, gemcitabine, epirubicine, topotecane, irinotecan, doxorubicin, methotrexate, and etoposide. The analytical detection limit was 0.1 ng/cm<sup>2</sup>.

Both research groups defined a compounding protocol which included the preparation, the administration and cleaning procedure.

## RESULTS

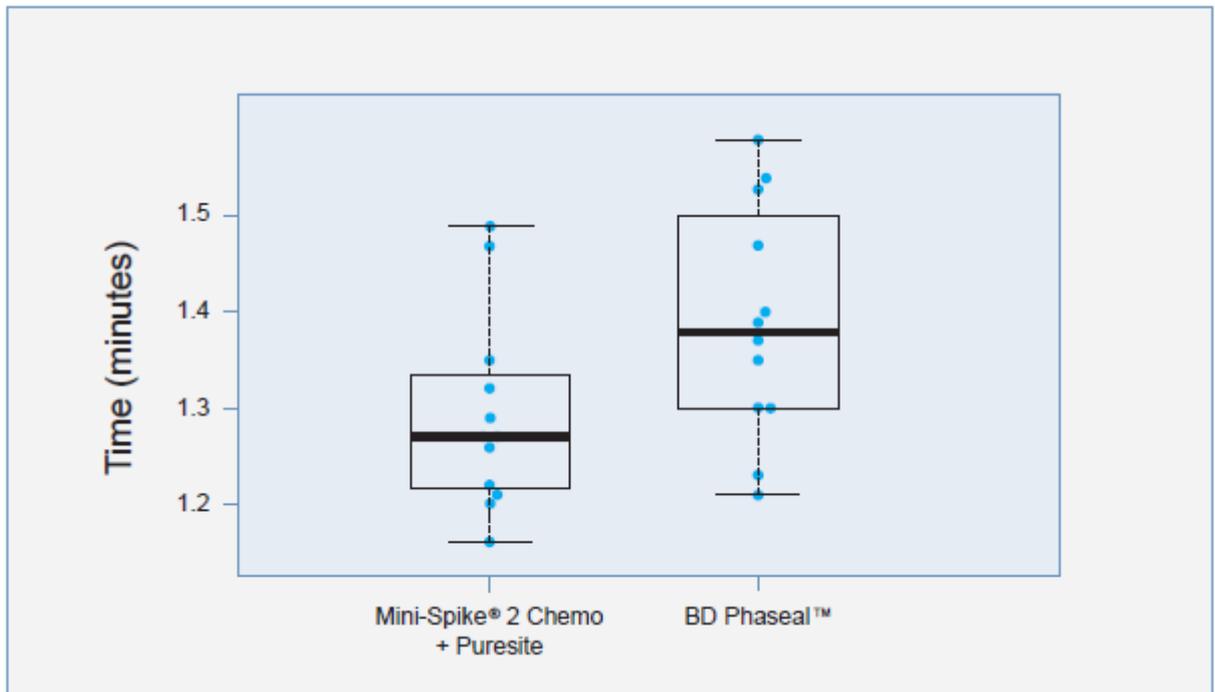
García et al. find no statistically significant differences in the median contamination surface levels between basal and final sampling times. However, they observed a statistically significant difference of 10 seconds on compounding times; nurses compounded more rapidly with Mini-Spike® 2 Chemo + Puresite (Figure 1). The satisfaction survey favours Mini-Spike® 2 Chemo + Puresite in terms of ease of use and learning curve, as well as in the number of components of the device<sup>1</sup>.

By means of a series of measures (closed infusion and transfer devices as well as consistently and regularly cleaning), the study by Meier et al. showed a reduced number of contaminated wipe samples from 19% (n=153) at the beginning to 14% (n=110) at the study end. This corresponds to a reduction of 28% (Figure 2). Wipe samples with cytotoxic drug concentrations over 10 ng/cm<sup>2</sup> were not found in the third observation period<sup>2</sup>.

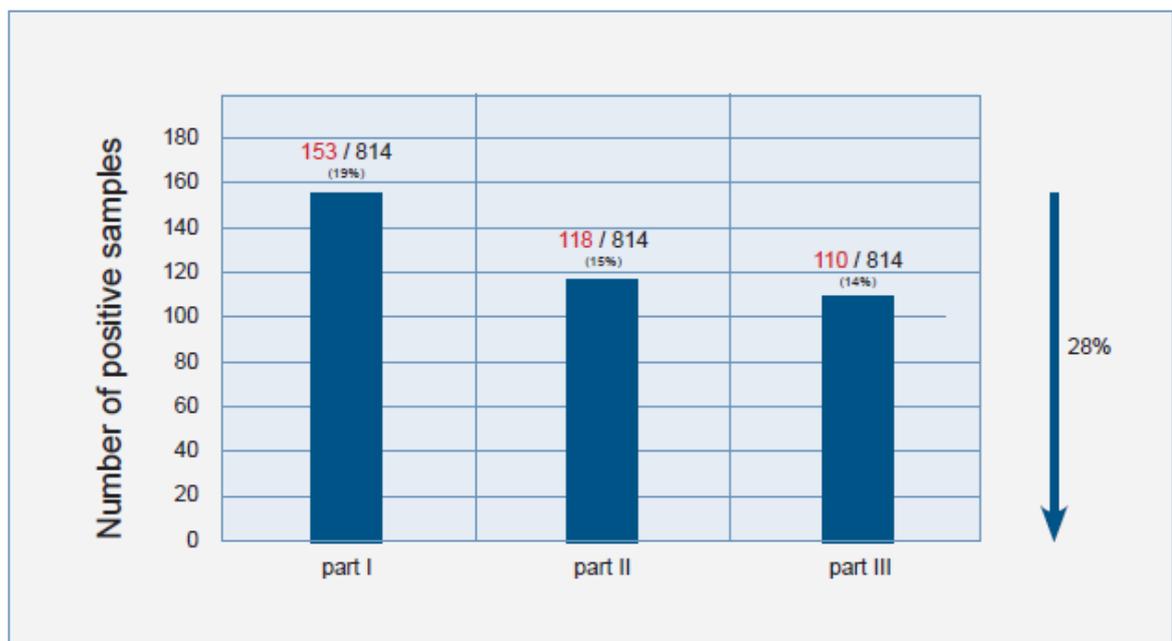
## CONCLUSION

- Equivalent contamination protection can be reached through closed transfer and dispensing devices (PureSite and Mini-Spike® 2 Chemo) in comparison to the closed transfer device (PhaSeal™).
- However, compounding times, ease of use and learning curves favoured PureSite and Mini-Spike® 2 Chemo.
- Through a closed infusion system (Cyto-Set®), a closed transfer device (PureSite), a closed dispensing pin (Mini-Spike® 2 Chemo), and consistent and regular cleaning, significant improvements for employee protection can be achieved.

**Figure 1:** Compounding time with Mini-Spike® 2 Chemo + Puresite and Phaseal™



**Figure 2:** Number of positive contaminated wipe samples



## REFERENCES

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