

Performance of the ONGUARD™ CMS with TEVADAPTOR™ Components

Introduction

Antineoplastic drugs are toxic not only to cancerous tissue, but to healthy organs as well. Long-term contact with such drugs was shown to have mutagenic, and even cancer-promoting effects.^{1,2} Therefore, a number of devices have become available to enhance healthcare worker safety in handling such drugs. The term "closed system" has been used excessively in conjunction with cytotoxic drug handling systems. A thermodynamically closed system is one confined within boundaries through which no matter or energy pass.³ This obviously cannot define a usable drug transfer device. Therefore, a more practical definition is necessary, the most comprehensive being that offered by NIOSH: "A drug transfer device that mechanically prohibits the transfer of environmental contaminants into the system and the escape of hazardous drug or vapor concentrations outside the system".⁴ Therefore, a "Closed System Drug-Transfer Device" (CSTD), as defined by NIOSH, must be shown to conform to both aspects of this definition. It will be shown in the following that the ONGUARD™ Contained Medication System (CMS) with TEVADAPTOR components complies with the NIOSH definition by ensuring that no toxic species escape into the environment (containment) and no environmental contaminants contact the drug (sterility maintenance).

System Description and Performance

The ONGUARD CMS is comprised of the following TEVADAPTOR components: Syringe Adaptor, Vial Adaptor, Connecting Set, Spike Port Adaptor and Luer Lock Adaptor. The two primary components are the TEVADAPTOR Vial Adaptor and TEVADAPTOR Syringe Adaptor. The Vial Adaptor is designed to provide pressure equalization within the drug vial during admixture procedures. The Syringe Adaptor has a mechanism ensuring passive needle tip sealing and needle stick prevention during connection and disconnection of the system's elements. In addition, the Connecting Set and Luer Lock Adaptor enable IV drip and IV push administration. All system components utilize elastomeric seals that prevent fluid escape and are designed to provide audible and tactile confirmation of secure connections between the dedicated devices.

Prevention of Hazardous Species Escape (Containment)

The Vial Adaptor contains a unique composite of the TOXI-GUARD™ activated charcoal drug binding matrix and a hydrophobic 0.2 micron sterilizing grade membrane. A combination of retention mechanisms including filtration, impaction, electrostatic interactions and adsorption ensures toxic species containment,^{5,6} while allowing sterilized air to enter the vial. The effectiveness of this design was demonstrated in a definitive third-party study⁷ supported by TEVA Medical Ltd. in which the Vial Adaptor was challenged by high concentrations of cytotoxic drug vapor and particles. In this study a large volume of nitrogen (about 1,000 times more than the volume of air transferred in actual use) was passed to flow through drug-containing vials while the vials were maintained at 50°C to increase drug volatility. The effluent nitrogen was passed through a collecting trap maintained at -70°C. An analytical method utilizing liquid chromatography and mass spectrometry (LC/MS/MS) sensitive to <1 nanogram of drug was used to quantify the drug species within each sample.

The following tested drugs were chosen to represent widely used antineoplastics:

- Cyclophosphamide: Highly volatile, small molecule organic
- Carboplatin: Small molecule organometallic
- Doxorubicin HCl: Medium molecule organic
- Etoposide: Large molecule organic

For each drug a control was run using Vial Adaptors devoid of the TOXI-GUARD matrix and 0.2 micron membrane composite. As expected for the control, considerable amounts of drug exited the system and were identified and measured. For all test samples no toxic species were detected at the nanogram level.

Prevention of Contaminate Ingress (Sterility Maintenance)

Third-party rigorous testing was performed to demonstrate the integrity of TEVADAPTOR devices connected to vials and IV fluid bags against bacterial ingress.⁸ Vials and IV bags containing sterile water or 5% glucose were assembled with a Vial Adaptor and Connecting Set respectively. Each was sampled periodically, using the Syringe Adaptor. Collected samples were transferred to both a tryptic soy broth (TSB) growth medium and a fluid thioglycollate medium (FTM). The assembled test units were left in a non-sterile area between consecutive samplings. All gathered samples were incubated and evaluated for the presence of microorganisms. While every inoculated control sample of TSB and FTM demonstrated growth as expected, no growth was observed from any of the actual test samples in either growth medium for the duration of the test.

Chemical Compatibility

Components were challenged by immersion for 48 hours in aggressive solvents and cytotoxic drug systems.⁹ These included methotrexate (high pH), paclitaxel (organic-surfactant solvent system), and etoposide (organic solvent). In no case was any mechanical or functional damage observed to these components.

Conclusion

The ONGUARD Contained Medication System with TEVADAPTOR components effectively prevents both the ingress of environmental contaminant into the drug containers, and the spread of hazardous drug species (solid, liquid, aerosol and vapor) out of the drug containers into the environment and therefore conforms to both aspects of the NIOSH definition of a CSTD. The validity of this claim is supported by the use of cytotoxic drugs for testing as opposed to drug simulates.

References

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