Drug resistance of materials used in Corvida Halo® Closed System Transfer Device

OBJECTIVE:

Demonstrate that materials within the fluid (drug) path do not fail when exposed to the most aggressive drug solvents commonly used in chemotherapy drugs. In addition, demonstrate that after exposure to these solvents, there are no hazardous chemicals that leach from the materials in the fluid path.

TEST METHOD:

A comprehensive list of chemotherapy drugs was reviewed to identify the solvents most likely to have a deleterious effect on the materials within the fluid path. This could include plastic degradation and/or toxic chemicals to leach from the device. Materials used in Halo® that are in the fluid path include: stainless steel, polyisoprene rubber, and high density polyethylene. The solvents considered included: dimethylsulfoxide, dimethyl formamide, ethanol, dehydrated alcohol, methanol, isobutyl alcohol, N,N-dimethylacetamide, polyethylene glycol, cremaphor EL, polysorbate 80, methylamine, sodium hydroxide, water, ether, HCl, sodium citrate. Of these solvents, those with the likelihood of impact to the plastic include: N,N-dimethylacetamide, polyethylene glycol, cremaphor EL, and polysorbate 80. The pH adjusted 0.9% saline represented the worst case for the stainless steel.

The test was performed in three phases by a third party lab, Aspen Research, experienced in Extractables and Leachables testing. The first phase was a leachable screening study where the device was used with four solvents representing the worst case for each class, including a polar aqueous solvent (0.9% saline pH3 HCl), polar organic solvent (33% dimethylacetamide (DMA)), intermediate polar solvent (50% ethanol), non-polar solvent (hexane). Note: although hexane is much more severe that any drug solvent, it is commonly used as an extreme challenge condition for potential toxic leachants from plastics. The test procedure for Phase I was as follows:

1. A Halo® Closed Vial Adaptor was attached to a vial containing 5ml of the test solvent
2. The test solvent was drawn from the vial into the syringe; components remain connected and were conditioned for 72 hours at 37°C. Approximately every 12 hours, the solvents were transferred back and forth to insure the fluid path remain wetted with the solvent throughout the entire 72 hours
3. Following the 72 hour exposure, the solvents were removed from the device and analyzed using GC/MS and MPLC-DAD-TOFMS for organic extracables and by ICP/MS for metals. Any extractants were analyzed for potential toxicity.

The second phase involved using the Halo® CSTD to transfer each of the chosen study drugs. The three chosen study drugs were based on those containing those solvents most likely to affect the materials within the fluid path. These drugs included: Toposar, Busulfex, and Paclitaxel[4]. Two sets of Halo® components were used for each drug trial. The procedure for Phase II was as follows:

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1. Halo® Closed Vial Adaptor was attached to drug vial
2. Halo® Closed Syringe Adaptor was attached to a standard syringe
3. The Closed Syringe Adaptor was connected to the Closed Vial Adaptor and 1ml was drawn into the syringe. The components remained connected for 1 hour, allowing the entire fluid path to be exposed to the drug.
4. The Closed Syringe Adaptor was disconnected from the Closed Vial Adaptor
5. The Closed Syringe Adaptor was reconnected to the Closed Vial Adaptor and the drug was returned to the original drug vial
6. Steps 3 through 5 were repeated 7 times for a total of 14 manipulations (connection/disconnections)over an 8 hour period
7. Following the 14 manipulations, the test devices were pressure tested to a minimum of 15 psi under water to detect any leaks from the devices.

The final phase, Phase III, was to transfer the selected drugs following the same procedure used with the solvents in Phase I. Following these transfers, the drugs were analyzed to identify toxic leachables.

RESULTS:

All devices throughout all three phases performed without any failures. There were no air leaks during the pressure test performed in Phase II. All chemical leachables and extractants for phase I and III were analyzed by an independent, board certified Toxicologist and found to present no safety concern.

CONCLUSION:

This series of tests demonstrate that even after Halo® devices are exposed to drugs over extended periods at elevated temperatures (up to 72 hours at 37°C) and subjected to 14 manipulations, they are capable of containing fluid and vapors. The materials within the Halo® components have been shown to be compatible with even the most aggressive drug solvents, including dimethylacetamide, that has been contraindicated for other CSTDs currently on the market.

Reference:

1. Extractables Screening of Chemotherapy Drug Transfer Device, Aspen Project No. A48867
2. Pressure Testing of Chemotherapy Drug Transfer Device, Aspen Project No. A49213
3. Leachables Screening of Chemotherapy Drug Transfer Device, Aspen Project No. A48867
4. Each drug contained the following:
    a. Toposar: each ml contains: 2mg citric acid, 30mg benzyl alcohol, 80 mg modified polysorbate 80/tween 80, 650 mg polyethylene glycol 300, and 30.5% alcohol
    b. Busulfex: each 10mL vial contains 60mg busulfan (246 g/mole) dissolved in N,N-dimethylacetamide (DMA) 33% v/v and polyethylene glycol 400, 67% v/v
    c. Paclitaxel: each ml contains: 6 mg paclitaxel, 527 mg purified Cremophor EL (polyoxyethylated castor oil), 49.7% dehydrated alcohol

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