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Chemical Compatibility of ChemoClave™ and ChemoLock™

Thank you for your interest in the ICU Medical ChemoClave and ChemoLock closed system transfer devices (CSTDs). ICU has been innovating CSTD products since 2007 and has extensive experience with medical-grade consumable devices that are exposed to a wide variety of drug formulations.

ICU Medical manufactures all ChemoClave and ChemoLock products exclusively without the use of ortho-phthalates, a class of organic plasticizers frequently used in PVC. These plasticizers can be added in concentrations up to 40% to render the rigid PVC more pliable and suitable for extrusion into components used for IV infusions.[1,2] These ortho-phthalates, particularly the most commonly used form di(2-ethylhexyl) phthalate (DEHP), are linked to developmental and reproductive toxicity, endocrine disruption, and are listed as probable carcinogens.[3,4] These plasticizers do not chemically bind to the PVC backbone and can therefore migrate (leach) out when in contact with certain drug formulations or under certain environmental conditions and travel down into the patient's bloodstream.[5] For instance, high amounts of DEHP were extracted from PVC bags containing paclitaxel, cyclosporine, teniposide, 5-fluorouracil, and quinine.[6] With DEHP being fat soluble, the leaching is particularly enhanced from PVC bags and tubing in the presence of surfactants like Kolliphor EL and Polysorbate, which are commonly used in chemotherapeutic formulations.[7,8] The absence of ortho-phthalates like DEHP in ICU Medical CSTD products protects patients from potential exposure to these chemical plasticizers.

Microbial ingress and sterility integrity have been verified independently for a 7-day period, where under a simulated use protocol, the ChemoClave system was able to maintain complete sterility of the drug.[9-11]

Many of the antineoplastic drugs, such as etoposide and paclitaxel, contain chemical solvents, surfactants, or fat emulsions, which have the potential to damage certain medical plastics. ICU Medical developed the ChemoClave and ChemoLock using medical-grade plastics that are compatible with such drug formulations—since the inception of the product line in 2007. ICU Medical has extensively tested ChemoClave and ChemoLock products with a number of representative drug formulations that demonstrate compatibility for several therapeutic classes.[12-16] These test results are applicable to the following products within the ChemoClave and ChemoLock product lines that use identical materials of construction:

- Spiros™ closed male luer
- Clave™ and MicroClave™ and Neutron™ needlefree connectors
- ChemoClave bag spikes
- ChemoClave vial spikes
- ChemoClave administration sets
- ChemoLock injector
- ChemoLock vial and bag spikes
- ChemoLock administration sets
- Diana™ cassettes and diluent sets

Drug formulations were selected for chemical compatibility testing based on their widespread use, chemical composition, and known potential to interact with or damage plastics. These studies were designed to include both single-dose and multi-dose drugs that allow for extended storage periods, such as Cisplatin (up to 28 days), thus offering the longest potential opportunity for interaction with the devices.

The ChemoClave system, as well as the ChemoLock system that is constructed of materials identical to ChemoClave, were exposed to over 13 antineoplastic drugs in their undiluted form.[12-16] Administration sets were similarly exposed to drug formulations at three times their therapeutic dose in order to simulate the worst-case exposure for administration equipment. Three separate tests were completed including a functional integrity (leak) test, drug stability test, and plastic migration test. The results demonstrate that the ChemoClave and ChemoLock products are compatible with common therapeutic classes for a minimum of 24-hours and a maximum of 28-days for multi-use drugs.

The following table includes a list of drugs that are known to fall into these common therapeutic classes and may therefore be considered compatible with the ChemoClave and ChemoLock systems.

- 5-Fluorouracil
- Aflibercept
- Aldesleukin
- Alemtuzumab
- Amsacrine
- Arsenic trioxide
- Atezolizumab
- Azacitidine
- BCG (Bacillus Calmette-Guérin)
- Belimumab
- Bendamustine HCl
- Bevacizumab (Avastin)
- Bleomycin
- Blinatumomab
- Brentuximab vedotin
- Busulfan
- Cabazitaxel
- Carboplatin
- Carfilzomib
- Carmustine
- Cetuximab
- Cidofovir
- Cisplatin
- Cladribine
- Clofarabine
- Cyclophosphamide
- Cyclosporine
- Cytarabine
- Dacarbazine
- Dactinomycin
- Daunorubicin
- Decitabine
- Deferoxamine
- Denosumab
- Desferal
- Dexrazoxane
- Docetaxel
- Doxorubicin
- Epirubicin
- Eribulin
- Etoposide
- Fludarabine
- Gemcitabine
- Gemtuzumab ozogamicin
- Hydrocortisone
- Idarubicin
- Ifosfamide
- Infliximab
- Interferon alfa-2b
- Intron A
- Ipilimumab
- Irinotecan
- Ixabepilone
- L-Asparaginase
- Leuprolide acetate
- Lipiodol
- Liposomal Daunorubicin & Cytarabine
- Liposomal Doxorubicin
- Liposomal Vincristine
- Melphalan
- Mesna
- Mechlorethamine HCl
- Methotrexate
- Mitomycin
- Mitoxantrone
- Mustine
- Mycophenolate mofetil
- Natalizumab
- Nelarabine
- Ofatumumab
- Omalizumab
- Oxaliplatin
- Paclitaxel
- Paclitaxel (Protein-Bound)
- Panitumumab
- Pegaspargase
- Peginterferon alfa-2a
- Pembrolizumab
- Pemetrexed
- Pentostatin
- Pertuzumab
- Plerixafor
- Prexasertib (LY2606368)
- Porfimer sodium
- Pralatrexate
- Raltitrexed
- Rituximab
- Romidepsin
- Streptozocin
- Tacrolimus
- Temozolomide
- Temsirolimus
- Teniposide
- Testosterone cypionate (DEPO-TESTOSTERONE)
- Thiotepa
- Topotecan
- Tocilizumab
- Trastuzumab
- Trastuzumab emtansine
- Treosulfan
- Triptorelin
- Ustekinumab
- Vedolizumab
- Vinblastine
- Vincristine
- Vindesine
- Vinflunine
- Vinorelbine

Busulfan (Busulfex®) and Amsacrine (AMSA PD®) Specifics: All ChemoClave and ChemoLock products are compatible with the diluted solution of Busulfan at a 0.536 mg/mL concentration, which corresponds to a 0.7 mg/mL concentration in 500 mL of 0.9% sodium chloride, as instructed in the prescribing information.[17,18] Similarly, all ChemoClave and ChemoLock products are compatible with the diluted solution of Amsacrine up to a concentration of about 0.146 mg/mL in 5% dextrose, as instructed in the prescribing information.[19] These concentrations represent the typical administration scenarios used for delivery of Busulfan and Amsacrine to patients. Test results show that ChemoClave and ChemoLock administration sets meet functional requirements following exposure to 0.536 mg/mL Busulfan and 0.146 mg/mL Amsacrine solutions over a 24-hour period and are therefore deemed compatible for administration within that time period to the patient when in the diluted form.

The ChemoClave 13 mm vial spike CH-82, CH-62, and vented vial spike CH-72 are compatible with the undiluted solutions of Busulfan and Amsacrine. No other ChemoClave products are compatible with undiluted Busulfan and Amsacrine solutions. This means that before infusing Busulfan or Amsacrine using a ChemoClave bag spike, the drugs must first be diluted following the recommended methods:

Busulfan: After drawing the drug out of a vial through the CH-82, CH-62, or CH-72 vial spike, connect the drug syringe to the Clave connector on the bag spike, aspirate back a minimum of 6.5 mL of solution from the IV bag into the drug syringe, and re-inject into the IV bag through the Clave bag spike.

Amsacrine: Amsacrine STOCK SOLUTION should be prepared as per prescribing information.[19] After drawing the STOCK SOLUTION out of the vial through the CH-82, CH-62, or CH-72 vial spike, connect the drug syringe to the Clave connector on the bag spike, aspirate back a minimum of 6.5 mL of solution into the drug syringe, and re-inject into the IV bag through the Clave bag spike.

The ChemoLock 13 mm vial spike CL-82, CL-62, and vented CL-72 and CL2000S syringe injector are compatible with undiluted Busulfan and Amsacrine for a maximum duration of 1 hour. No other ChemoLock products are compatible with undiluted Busulfan and Amsacrine. This means that before infusing Busulfan or Amsacrine using a ChemoLock bag spike, the drugs must first be diluted using the following recommended methods:

Busulfan: After drawing the drug out of a vial through a CL-82, CL-62, or CL-72 vial spike and CL2000S syringe injector, connect the CL2000S to the port connector on the bag spike, aspirate back a minimum of 6.5 mL of solution from the IV bag into the drug syringe, and re-inject into the IV bag through the port bag spike.

Amsacrine: The Amsacrine STOCK SOLUTION should be prepared as per prescribing information.[19] After drawing the STOCK SOLUTION out of the vial through the CL-82, CL-62, or CL-72 vial spike and CL2000S syringe injector, connect the CL2000S to the port connector on the bag spike, aspirate back a minimum of 6.5 mL of solution into the drug syringe, and re-inject into the IV bag through the Clave bag spike.

Thank you again for your continued support of ICU Medical CSTDs. For further questions or concerns, please visit our website at www.icumed.com or contact your local sales representative.

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