

Antineoplastic Compatibility Studies for Use with Oncology Devices

Introduction

Antineoplastic drugs are common agents that are given during chemotherapy treatment. Such drugs are therefore required to interact with and be administered using specific IV equipment. Traditional IV equipment, including tubing and plastic components, can be affected or degraded by the drug itself. There are two known effects of drug interaction which can both damage the plastic parts and release unwanted chemicals; this is known as "leaching" into the fluid path, which is ultimately delivered to the patient.

Organizations such as NIOSH and USP 797 have recommended the use of specialized IV equipment to help protect the healthcare worker from exposure to chemotherapy agents and to protect the integrity of the drug itself.^{1,2} This paper is aimed at describing both the known drug interactions with specific administration or preparation devices and also the ICU Medical compatibility validation process and results for its oncology preparation and delivery products.

Plastic Integrity Following Drug Interactions

Solid plastic components can be damaged by interaction with solvents agents, such as alcohol. The only known antineoplastic drugs which contain solvents are in the etoposide and paclitaxol classes.^{3,4} Etoposides contain 30% of organic solvent in its undiluted form, while paclitaxol contains 48%. What causes the interaction is twofold: component design and plastic composition. While some plastics like ABS are known to breakdown with exposure to solvents, the actual breakdown is also dependent on the design of the part and how much stress is designed into the part. The solvent acts as a stress reliever, where cracks can occur when the solvent interacts with and relieves the stress in that part. Cracks in the plastic components can cause drug leakage, which is hazardous to the healthcare worker and the environment.

In order to evaluate the integrity of a device after exposure to organic solvents, the following protocol was used. Products were exposed to 30% ethanol alcohol solution by infusing the solution into the assembled device and allowing samples to rest for 24 hours. Following the 24-hour period, the alcohol solution was flushed out of the device and the device was inspected for visual degradation. The device was then placed into standard functional analysis testing according to the product's specification to ensure that no physical or mechanical degradation occurred. This chemical compatibility test is used to validate the appropriateness of any plastic device that may be used in the ICU Medical Oncology product line. Table 1 shows the chemical compatibility of various devices and their associated validation study.

Chemical "Leaching" Following Drug Interaction

Certain chemicals can be released or "leach" from soft plastic components, such as tubing, when exposed to antineoplastic drugs. It is well documented that Di(2-ethylhexyl) phthalate, known as DEHP, can be released from flexible PVC devices, such as IV tubing and bags.⁵ DEHP is a plasticizer that provides flexibility to soft PVC devices and makes them easier to manipulate. Temperature, exposure time and lipid content of the IV solution affect the rate that DEHP will leach into the fluid path and subsequently be delivered to the patient with potentially harmful side effects. The paclitaxol class of chemotherapy drugs contains a high lipid content and can accelerate the leaching process in DEHP-plasticized PVC products.

Advances in medical device design have allowed for the DEHP plasticizer to be removed from PVC devices. The absence of DEHP allows PVC devices to safely be used for the administration of antineoplastics with no potential leaching. ICU Medical has been exclusively manufacturing DEHP-free tubing products for all of its medical devices since 1998. Table 1 provides a listing of ICU devices that are approved for use with anti-neoplastic administration and which do not contain DEHP.

TABLE 1

Device	Validated With Solvent and Lipid-Based Drugs	Contains DEHP Plasticizer	Test Report
Spiros™ Closed Male Connector	YES	NO	07-027t
IV Tubing and Components	YES	NO	07-109t 07-150t 07-155t
Needle-Free Vial Access Spikes	YES	NO	06-130t
Needle-Free Bag Access Spikes	YES	NO	06-130t 07-110t
Genie™ Vial Access Device	YES	NO	07-025t
CLAVE® Needle-Free Connector	YES	NO	SE20-244 06-193t

Summary

ICU Medical has researched the issues of chemical interactions with administration equipment and antineoplastic drugs. The two known effects – cracking of plastic devices and leaching of DEHP plasticizer – can be eliminated with proper product design and validation. ICU exclusively uses DEHP-free components and evaluates all plastic components for use in its Oncology product line. All products which are available in the above mentioned devices or series are validated for use with antineoplastic drugs. Test reports and further information are kept on file at ICU Medical, San Clemente, Calif.

REFERENCES

1. National Institute for Occupational Safety and Health (US). *Prevention of Occupational Exposure to Antineoplastics and Other Hazardous Drugs in Healthcare Settings*. Sep-2004.
2. United States Pharmacopoeia (USP) 797. *Pharmaceutical Compounding, Sterile Preparations*. 2006.
3. Paclitaxol (TAXOL®) Injection. Bristol-Myers Squibb Company, Oncology, Princeton, NJ. *Drug Package Insert*. 2003.
4. Etoposide (TOPOSAR®) Injection. Teva Sicor Pharmaceuticals, Irvine, CA. *Drug Package Insert*. 2005.
5. FDA Public Health Notification: *PVC Devices Containing DEHP Plasticizer*. July 12, 2002.

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