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Medical devices for safe handling of cytotoxic drugs

The main objectives of these devices are to protect patients against bacterial contamination and healthcare workers against chronic exposure to chemical contamination. Many manufacturers have developed medical devices for the safe reconstitution of cytotoxics.

For many years, the use of chemotherapy has been growing considerably. Because of the increase in this activity and the risk incurred by healthcare workers when handling cytotoxic drugs, safety devices have been developed to improve quality in the preparation of these drugs. Pharmacy technicians also require training.



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Avoidance of needle risks

Avoiding the use of needles achieves several goals. Needles increase the risk of operator exposure to cytotoxic drugs by contact or injection. Moreover, the absence of a needle is a good way to decrease contact with liquid aerosols. These are caused by drug droplets squirting out, when the needle is withdrawn from the vial, if overpressure has been caused during manipulation. For these reasons, ASHP, GERPAC and Europharmat recommend needleless systems if possible. Unfortunately, the use

of air-venting systems is not always possible, e.g. if the vial opening is too small, or for soap solutions. Needles are necessary in such cases. A needle safety transfer device may protect operators against the risk of puncture, but does not decrease the risk of aerosol formation.

Selection criteria for medical devices

Limitation of contamination

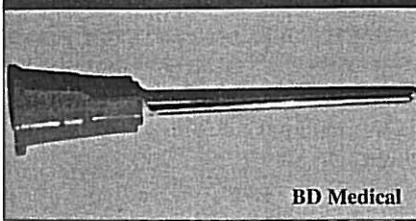
The imperative to limit both microbial and chemical contamination has led to the adoption of closed systems. According to the American Society of Health-System Pharmacists (ASHP), closed-system drug-transfer devices mechanically prevent the transfer of environmental contaminants into the system and the escape of drug or vapour out of the system [1]. This echoes the definition adopted by the National Institute for Occupational Safety and Health (NIOSH) [2]. This definition, taking into account drug vapour, clearly indicates that air-venting devices, even those with a 0.20 μm filter membrane, are not strictly closed-system devices. The recommendations of the GERPAC-Europharmat workgroup (the French isolators users' group - *Les Journées Nationales d'Etudes sur les Dispositifs Médicaux*) based their definition on that of the ASHP, but specified that closed systems should protect the operator against the escape of vapour, liquids and solids [3].

Compliance with these recommendations cannot be considered a substitute for ventilated cabinets or isolators.

Container-contents interactions

It is important to take into account the possible physico-chemical interactions between anticancer drugs and the device. In particular, devices containing plasticisers such as PVC should be avoided as much as possible [4-6]. It is then preferable to use devices made of polyolefins (polyethylene, polypropylene) or polyurethane. In addition, chemical contaminants from the surroundings cross the wall of a device (permeation). It can occur during sterilisation with peracetic acid [7] or hydrogen peroxide. Permeation through medical devices is a potential toxic risk to the patient and the loss of stability of the drug may be revealed by a pH change.

Figure 1: BD Blunt safety transfer device



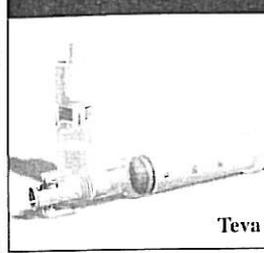
BD Medical

Figure 2: PCHIMX-1



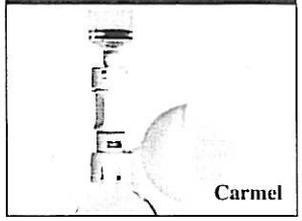
DORAN International

Figure 3: Tevadaptor



Teva

Figure 4: Closed-system device Phaseal



Carmel

Classification of devices

The latest International Society of Oncology Pharmacy Practitioners (ISOPP) standards [8] classify special devices for the reconstitution and administration of cytotoxic drugs as follows:

- (1) Devices to protect the handler of the vial/ampoule
- (2) Devices to protect the operator during preparation
- (3) Devices to protect the administrator during administration of the cytotoxic drug to the patient.

Devices/systems used to transfer the drug solution from a vial to an infusion bag fall in class 2. ISOPP standards specify that manufacturers have to indicate if the device can be used for the entire or only a part of the preparation process, if the device can be used if more than one vial is necessary for a preparation, and if studies demonstrate the ability of the device to reduce or eliminate environmental contamination.

Class 2 devices may be divided into two groups, based on their function: devices to access the primary vial (access and reconstitution devices) and devices to access the infusion bag (dilution devices). For the reconstitution devices, four points have to be strictly controlled: limitation of aerosol formation, asepsis, safe use and the residual volume. For dilution devices, we have to be vigilant on the universality of use, maintenance of asepsis, safe use and minimal chemical contamination.

Access and reconstitution devices [9]

If a needle is required, a safety transfer needle can be used to decrease the risk of needlestick. The Blunt Fill needle (see Figure 1) has a special bevel (45° angle). This bevel is sufficient to penetrate the cap, but ten times the force is needed to puncture the skin or the operator's gloves. Nevertheless, the risk of an aerosol is not reduced.

Spikes are widely used to access the vial. The syringe connection to the spike must be the Luer-lock type for safety. Important criteria include the type of connection (bidirectional valve or not), a single or double channel, the residual volume, or pore size of the air filter (0.45 µm or 0.20 µm). The double channel spikes (Baxter's Chemo-Aide Pin, Codan's Spike, Hospira's CS-51 Spike, B.Braun's Chemo-Spike) incorporate an air vent protected with a 0.22 µm hydrophobic filter. B.Braun's Mini-spike has a 0.45 µm hydrophobic air filter. Hospira's CS-53 spike only has one channel.

Dilution devices

Dilution devices allow access to the bag contents. The selection criteria for these devices are the polymer used for manufacture,

a bidirectional valve to allow needle-free operation, a Luer-lock connection, and the residual volume.

Chemo-set and Connect-Z are two extension sets. They are used with special infusion devices to which they are connected by a bidirectional valve, allowing needle-free manipulation. The Luer lock between the extension set and the infusion set ensures safe transfer of the anticancer drug solution. PCHIMX-1 (see Figure 2) is a recent special extension set. It is a device with two independent entrances made to be connected to two infusion bags. Like the other devices, it allows safe handling because it has a bidirectional valve on the tube that is connected to the cytotoxic drug infusion bag.

Devices called in practice 'closed systems'

The Tevadaptor (see Figure 3) is a 3-part device including a vial adapter, a syringe adapter and an infusion bag adapter. The vial adapter fixes firmly to the vial. It has a dual channel perforator with a hydrophobic 0.22 µm air-filter. The infusion bag adapter contains a perforator with two channels: one for the injection of the cytotoxic drug solution and another for the administration. The syringe adapter allows the transfer of the solution from the vial to the infusion bag using a Luer connection to reinforce safety. Nevertheless, the Tevadaptor cannot be considered, or recommended, as a closed-system device.

PhaSeal from Carmel is the only closed-system device suitable for handling cytotoxic drugs (see Figure 4). It allows the drug to be transferred from the vial to the syringe and then to the infusion bag without any contact between the drug and the environment at any time. This multi-component system uses a double membrane to enclose a specially cut injection cannula as it moves into a drug vial, Luer-lock, or infusion-set connector. Several studies comparing PhaSeal to traditional techniques show a significant reduction in environmental contamination if this device is used [10, 11].

Conclusion

Cytotoxics can be safely reconstituted if aseptic handling is strictly respected and chemical contamination is minimised. Devices decrease the risk of chemical contamination and maintain a good level of asepsis. However, these devices must be used in a clean environment and operators must wear protective clothing and must be regularly trained and evaluated.

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