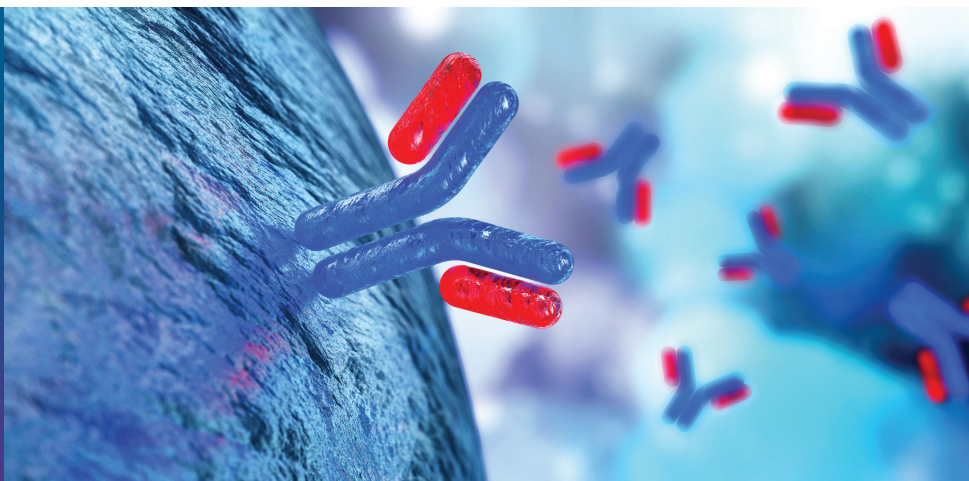


Safe handling of monoclonal antibody based drugs (mABs)



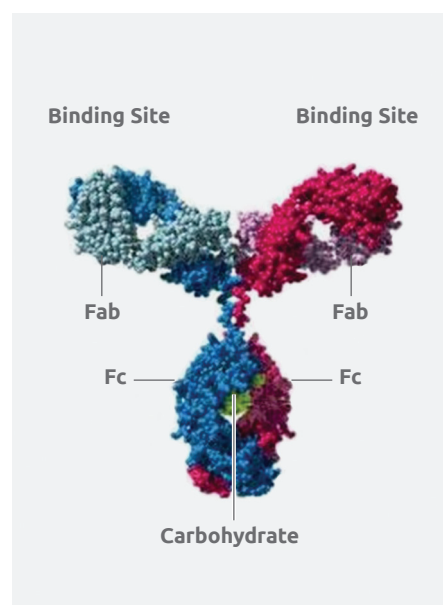
The 2016 NIOSH list of hazardous drugs includes 4 mABs (ado-trastuzumab emtansine, brentuximab vedotin, gemtuzumab ozogamicin, pertuzumab)¹. Also, NIOSH is considering adding the following mABs to the list: Bevacizumab, Blinatumomab, Inotuzumab ozogamicin, Trastuzumab².

It has been argued that the larger molecular weight of hazardous monoclonal antibodies (mABs) may prevent their dermal or nasal absorption via occupational exposure. However, the concern in occupational health is whether these drugs can possibly attain a detectable (not necessarily

therapeutic) level through repeated dermal and/or nasal exposure. Currently, there is no direct evidence to support a particular molecular weight above which a drug cannot achieve a detectable level following repeated occupational exposure.

Therefore, the repeated exposure of healthcare workers to hazardous monoclonal antibodies (mABs) should be kept to a minimum, as a precaution³.

This is an evidence of the growing awareness in the medical community to the occupational risks of mAB drugs.



What is Tevadaptor®?

TEVADAPTOR® is a closed system transfer device used by pharmacists, nurses or other healthcare professionals for safe reconstitution of drugs, including cytotoxic drugs and monoclonal antibodies, for infusion, injection, or instillation, through the use of several protection layers⁴:

- Elastomeric septa that prevent the unintentional release of drug in droplet form⁵
- A hydrophobic and oleophobic 0.2 µm membrane that prevents bacterial contamination by incoming air and the escape of hazardous aerosols and drops⁶
- An active carbon matrix that is highly efficient in adsorption of drug vapors^{7,8}

Advantages of Using Tevadaptor® with mABs

- Protection of the user (pharmacist, nurse): prevents the escape of hazardous drug aerosols and the release of drug in droplet form.
- Protection of the drug from microbial contamination^{6,9}: the 0.2 µm membrane cleans the incoming air thus preventing bacterial contamination of the sterile drug solution.
- Economical savings¹⁰: drug costs, especially for biological drugs, represent

a significant part of the total healthcare spend. According to the study detailed below, by using a CSTD which forms a drug storage container (vial adaptor mounted on a drug vial), multiple withdrawals of a drug over an extended time period can be performed. This enables vial sharing, which leads to reduction of drug wastage and better usage of drugs.

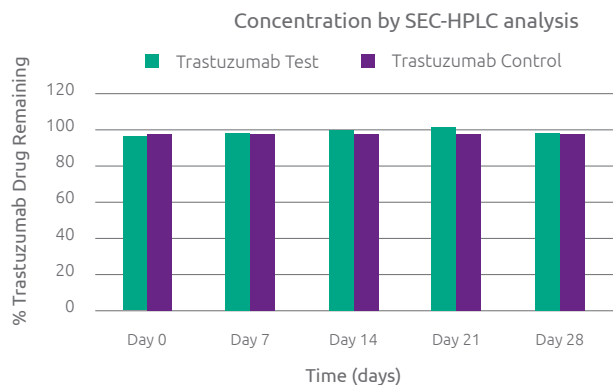
Tevadaptor®'s Compatibility with mAB Drugs

A study was performed in order to show that handling of a mAB based medication using the Tevadaptor® system does not alter the mAB's structure and its biological activity¹¹. The study was performed using single dose vials of Trastuzumab 150 mg that did not contain any preservative. The evaluation was done by connecting Tevadaptor® Vial Adaptors to drug vials, reconstituting according to manufacturer's instructions, and storing for up to 28 days at 2-8°C while protected from light. Sampling was performed by testing Trastuzumab drug vials fitted with Tevadaptor® on days: 0, 7, 14, 21 and day 28. On each testing day, control Trastuzumab vials were freshly prepared by reconstitution using standard needle and syringe. Both test and control Trastuzumab samples were subjected

to a range of physicochemical and biological tests for a full assessment of stability.

No significant differences were observed between test and control samples in all the parameters that were tested:

- Reverse Phase (RP) HPLC
- Size-Exclusion (SEC) HPLC
- Cation Exchange Chromatography
- Capillary Gel Electrophoresis (CE-SDS-PAGE)
- pH
- Biological Activity - Cell Proliferation Assay
- Biological Activity - ELISA
- Sterility Test - all test infusions remained clear and showed no signs of growth.



This study applied a significant number of robust scientific techniques. It presents a compelling body of evidence to support the use of Tevadaptor® with Trastuzumab, as an example of a monoclonal antibody (mAB) drug that can be safely stored within a closed system for up to 28 days at 2-8°C, with no deleterious effect on the drug either from a physicochemical viewpoint or a biological mode of action view.

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