



# USE OF CLOSED SYSTEM TRANSFER DEVICES WITH INVESTIGATIONAL DRUG PRODUCTS

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## **Background and Importance**

Investigational drug products (IDP) should be treated as hazardous drugs (HD) as it is not frequent to have hazard studies available or the information about safety is usually insufficient. This is a handicap for pharmacists, who must guarantee the safety of professionals during the handling, preparation and administration of IDP as well as drug quality.

Recommendations by NIOSH and USP include the use of closed system transfer devices (CSTDs) in the healthcare setting to reduce occupational exposure to HD.

Frequently there is a lack of information about the potential impact of using CSTDs on product quality. This may be a challenge when they are used with IDP, especially with monoclonal antibodies (mAb) and drug-conjugated mAb.

## Aim and Objetives

To review the scientific evidence related to the use of CSTDs when compounding and administering IDPs, in order to determine the main challenges related to its use and to establish the use criteria in daily practice.

#### **Materials and Methods**

A comprehensive search in Medline (PubMed) database was performed. The search strategy was based on a combination of the following terms: closed system transfer devices, drug development and biological products (meSH term). We included studies evaluating CSTD, safe handling and drug quality.

CSTD was defined as a drug transfer device that prohibits the transfer of contaminants into the system and the escape of HD.

#### Results

We included 7 articles (one systematic review, four reviews and two prospective studies) that showed the following critical issues and challenges:

There are several comercially available CSTDs

Marketed CSTDs have different material of constuction that comes in contact with HD

There is not a consistent strategy for compatibility testing of CSTDs with IDP

There is an absence of consensus among pharmacists regarding CSTD

High incidence of insoluble fine particles related to silicone oil droplets has been detected during preparation of HD with CSTDs

The incidence of insoluble fine particles with **mAb** was higher than with other cytotoxic anticancer agents

Drug loss and poor quality product due to adsorption onto CSTD materials have been reported

Stability issues could threaten patient safety

CSTD from
different
manufacturers
have a wide
range of holdup
volume

CSTDs holdup
volume range from
0,04 to 1 mL

The holdup volume has an impact on deliverable drug dose, especially in low volume-dose IDP

Taking into account holdup volume is crucial in clinical trials

### **Conclusion and Relevance**

- Variety of components in CSTDs can potentially lead to incompatibility issues, physical and chemical instabilities
- There is insufficient information to exclude safety concerns for IDP leading to broad use of CSTDs according to guidelines.
- There is an urgent need to increase knowledge about the hazard of new therapies and to assess CSTDs impact on product quality, clinical trial outcome and patient safety.