

CADTH RAPID RESPONSE REPORT: REFERENCE LIST

# Closed-System Drug- Transfer Devices for Chemotherapeutic Drugs: Safety and Guidelines

Service Line: Rapid Response Service  
Version: 1.0  
Publication Date: December 8, 2020  
Report Length: 9 Pages

**Authors:** Yan Li, Charlene Argáez

**Cite As:** *Closed-System Drug-Transfer Devices for Chemotherapeutic Drugs: Safety and Guidelines*. Ottawa: CADTH; 2020 Dec. (CADTH rapid response report: reference list).

**Disclaimer:** The information in this document is intended to help Canadian health care decision-makers, health care professionals, health systems leaders, and policy-makers make well-informed decisions and thereby improve the quality of health care services. While patients and others may access this document, the document is made available for informational purposes only and no representations or warranties are made with respect to its fitness for any particular purpose. The information in this document should not be used as a substitute for professional medical advice or as a substitute for the application of clinical judgment in respect of the care of a particular patient or other professional judgment in any decision-making process. The Canadian Agency for Drugs and Technologies in Health (CADTH) does not endorse any information, drugs, therapies, treatments, products, processes, or services.

While care has been taken to ensure that the information prepared by CADTH in this document is accurate, complete, and up-to-date as at the applicable date the material was first published by CADTH, CADTH does not make any guarantees to that effect. CADTH does not guarantee and is not responsible for the quality, currency, propriety, accuracy, or reasonableness of any statements, information, or conclusions contained in any third-party materials used in preparing this document. The views and opinions of third parties published in this document do not necessarily state or reflect those of CADTH.

CADTH is not responsible for any errors, omissions, injury, loss, or damage arising from or relating to the use (or misuse) of any information, statements, or conclusions contained in or implied by the contents of this document or any of the source materials.

This document may contain links to third-party websites. CADTH does not have control over the content of such sites. Use of third-party sites is governed by the third-party website owners' own terms and conditions set out for such sites. CADTH does not make any guarantee with respect to any information contained on such third-party sites and CADTH is not responsible for any injury, loss, or damage suffered as a result of using such third-party sites. CADTH has no responsibility for the collection, use, and disclosure of personal information by third-party sites.

Subject to the aforementioned limitations, the views expressed herein do not necessarily reflect the views of Health Canada, Canada's provincial or territorial governments, other CADTH funders, or any third-party supplier of information.

This document is prepared and intended for use in the context of the Canadian health care system. The use of this document outside of Canada is done so at the user's own risk.

This disclaimer and any questions or matters of any nature arising from or relating to the content or use (or misuse) of this document will be governed by and interpreted in accordance with the laws of the Province of Ontario and the laws of Canada applicable therein, and all proceedings shall be subject to the exclusive jurisdiction of the courts of the Province of Ontario, Canada.

The copyright and other intellectual property rights in this document are owned by CADTH and its licensors. These rights are protected by the Canadian *Copyright Act* and other national and international laws and agreements. Users are permitted to make copies of this document for non-commercial purposes only, provided it is not modified when reproduced and appropriate credit is given to CADTH and its licensors.

**About CADTH:** CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

**Funding:** CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

Questions or requests for information about this report can be directed to [requests@cadth.ca](mailto:requests@cadth.ca)

## Research Questions

1. What is the safety of closed-system drug-transfer devices for the handling of chemotherapeutic drugs?
2. What are the evidence-based guidelines regarding the use of closed-system drug-transfer devices for the handling of chemotherapeutic drugs?

## Key Findings

Two health technology assessments, one systematic review with meta-analysis, and two evidence-based guidelines were identified regarding the safety or use of closed-system drug-transfer devices for the handling of chemotherapeutic drugs.

## Methods

### Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including Medline via OVID and CINAHL via EBSCO, the Cochrane Library, the University of York Centre for Reviews and Dissemination (CRD) databases, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine’s MeSH (Medical Subject Headings), and keywords. The main search concept was closed system drug-transfer devices. No filters were applied to limit the retrieval by study type. The search was also limited to English language documents published between January 1, 2015 and November 30, 2020. Internet links are provided where available.

### Selection Criteria

One reviewer screened literature search results (titles and abstracts) and selected publications according to the inclusion criteria presented in Table 1. Full texts of study publications were not reviewed. Open access full-text versions of evidence-based guidelines were reviewed when abstracts were not available.

**Table 1: Selection Criteria**

<b>Population</b>	Individuals receiving, administering, or at risk of being unintentionally exposed to chemotherapeutic drugs  Subgroup of interest: Individuals who are pregnant, lactating or trying to conceive
<b>Intervention</b>	CSTDs
<b>Comparator</b>	Q1: Alternative methods for transferring drugs (e.g., personal protective equipment, biohazard safety cabinet); other CSTDs (including PhaSeal, ChemoClave Genie and Spiros, Texium, OnGuard, and Equashield) Q2: Not applicable

<b>Outcomes</b>	Q1: Safety (e.g., unintended drug exposure, adverse events, harms) Q2: Recommendations regarding best practices (e.g., guidance regarding when closed-system drug transfer devices should be used; whether CSTDs are safe for individuals who are pregnant, lactating or trying to conceive)
<b>Study Designs</b>	Health technology assessments, systematic reviews, randomized controlled trials, non-randomized studies, evidence-based guidelines

CSTD = closed-system drug-transfer device.

## Results

Two health technology assessments<sup>1-2</sup> and one systematic review<sup>3</sup> with meta-analysis were identified regarding the safety of closed-system drug-transfer devices for the handling of chemotherapeutic drugs. Furthermore, two evidence-based guidelines<sup>4-5</sup> were identified regarding the use of closed-system drug-transfer devices for the handling of chemotherapeutic drugs.

Additional references of potential interest that did not meet the inclusion criteria are provided in the appendix.

### Health Technology Assessments

1. Garate L, Gutiérrez A, López-Argumedo M, et al. [Closed vs open systems for the preparation and administration of cytostatic and other hazardous drugs (NIOSH Group 1): analysis of the scientific evidence, costs and organisational requirements]. Vitoria-Gasteiz: Departamento de Salud, Gobierno Vasco, Vitoria-Gasteiz (Basque Office for Health Technology Assessment (OSTEBA)); 2019 Dec: [https://www.euskadi.eus/web01-a2aznscp/es/k75aWebPublicacionesWar/k75aObtenerPublicacionDigitalServlet?R01HNoPortal=true&N\\_LIBR=052485&N\\_EDIC=0001&C\\_IDIOM=es&FORMATO=.pdf](https://www.euskadi.eus/web01-a2aznscp/es/k75aWebPublicacionesWar/k75aObtenerPublicacionDigitalServlet?R01HNoPortal=true&N_LIBR=052485&N_EDIC=0001&C_IDIOM=es&FORMATO=.pdf) (full-text in Spanish; structured summary in English, p23-26). Accessed 2020 Dec 07.
2. Health Improvement Scotland. Closed-system transfer-devices for limiting exposure to cytotoxic anti-cancer drugs in healthcare professionals, patients and visitors [*Evidence Synthesis 06*]. Edinburgh, Scotland: Health Improvement Scotland; 2019 Oct: [http://www.healthcareimprovementscotland.org/our\\_work/technologies\\_and\\_medicines/topics\\_assessed/es\\_06.aspx](http://www.healthcareimprovementscotland.org/our_work/technologies_and_medicines/topics_assessed/es_06.aspx) Accessed 2020 Dec 07.

### Systematic Reviews and Meta-analyses

3. Gurusamy KS, Best LM, Tanguay C, Lennan E, Korva M, Bussieres JF. Closed-system drug-transfer devices plus safe handling of hazardous drugs versus safe handling alone for reducing exposure to infusional hazardous drugs in healthcare staff. *Cochrane Database Syst Rev*. 2018 Mar 27;3:CD012860. [PubMed: PM29582940](https://pubmed.ncbi.nlm.nih.gov/29582940/)

### Guidelines and Recommendations

4. Celano P, Fausel CA, Kennedy EB, et al. Safe handling of hazardous drugs: ASCO standards. *J Clin Oncol*. 2019 Mar;37(7):598-609. [PubMed: PM30620670](https://pubmed.ncbi.nlm.nih.gov/30620670/)

5. Easty A, Coakley N, Cheng R, et al. Safe handling of cytotoxics. Toronto (ON): Cancer Care Ontario; 2018 Jun.  
See: *RECOMMENDATION 5: CYOTOXIC DRUG PREPARATION* (p. 10),  
*RECOMMENDATION 8: DRUG ADMINISTRATION* (p. 14)

## Appendix — Further Information

### Previous CADTH Reports

6. Young C, Farrah K. Closed-system transfer devices for the handling of hazardous drugs: clinical effectiveness, cost-effectiveness, and guidelines [*CADTH rapid response report: reference list*]. Ottawa (ON): CADTH; 2017 Aug: <https://www.cadth.ca/sites/default/files/pdf/htis/2017/RA0918%20Closed%20System%20Transfer%20Device%20Final.pdf> Accessed 2020 Dec 07.
7. Closed-system transfer devices for the handling of hazardous drugs: a review of the clinical and cost-effectiveness and guidelines [*CADTH rapid response report: summary with critical appraisal*]. Ottawa (ON): CADTH; 2015 May: <https://www.cadth.ca/sites/default/files/pdf/htis/may-2015/RC0658%20Closed%20System%20Transfer%20Device%20Final.pdf> Accessed 2020 Dec 07.
8. Closed-system transfer devices for the handling of hazardous drugs: clinical and cost-effectiveness and guidelines [*CADTH rapid response report: reference list*]. Ottawa (ON): CADTH; 2015 Mar: <https://www.cadth.ca/sites/default/files/pdf/htis/apr-2015/RA0747%20Closed%20System%20Transfer%20Final.pdf> Accessed 2020 Dec 07.

### Randomized Controlled Trial – Alternative Outcomes

9. Simon N, Vasseur M, Pinturaud M, et al. Effectiveness of a closed-system transfer device in reducing surface contamination in a new antineoplastic drug-compounding unit: a prospective, controlled, parallel study. *PLoS ONE [Electronic Resource]*. 2016;11(7):e0159052. [PubMed: PM27391697](https://pubmed.ncbi.nlm.nih.gov/27391697/)

### Non-Randomized Studies

#### *Alternative/Unclear Substance within CSTD*

10. Halloush S, et al. Evaluating Six Commercially Available Closed-System Drug-Transfer Devices Against NIOSH's 2015 Draft Vapor Protocol. *Hosp Pharm*. 2020;55(6):391-399. <https://journals.sagepub.com/doi/abs/10.1177/0018578719848730>
11. Vuelta-Arce M, Chiapella-Mico C, Mestre-Prad MT, et al. Comprehensive tackling to the safe handling of hazardous drugs: a multidisciplinary approach to clinical practice. *Int J Occup Med Environ Health*. 2020 Sep 17;33(5):621-634. [PubMed: PM32716012](https://pubmed.ncbi.nlm.nih.gov/32716012/)
12. Forshay CM, Streeter SO, Salch SA, Eckel SF. Application of the 2015 proposed NIOSH vapor containment performance protocol for closed system transfer devices used during pharmacy compounding and administration of hazardous drugs. *J Oncol Pharm Pract*. 2019 Jul;25(5):1160-1166. [PubMed: PM30041583](https://pubmed.ncbi.nlm.nih.gov/30041583/)

13. Sessink PJM, Nyulasi T, Haraldsson ELM, Rebic B. Reduction of Contamination with Antibiotics on Surfaces and in Environmental Air in Three European Hospitals Following Implementation of a Closed-System Drug transfer Device. *Ann Work Expo Health*. 2019 Apr;63(4):459-467.  
[PubMed: PM30852616](#)

14. Garrigue P, Montana M, Ventre C, et al. Safe Cytotoxic Drug Preparation Using Closed-system Transfer Device: Technical and Practical Evaluation of a New Device (Vialshield/Texium) Comparatively to a Reference One (PhaSeal). *Int J Pharm Compound*. 2016 Mar-Apr;20(2):148-154.  
[PubMed: PM27323425](#)

#### Alternative Comparator

15. Vasseur M, Simon N, Picher C, et al. A decontamination process adding a tensioactive agent and isopropanol to a closed-system drug transfer device for better control of isolator contamination. A prospective, parallel study. *PLoS ONE [Electronic Resource]*. 2018;13(8):e0201335.  
[PubMed: PM30089139](#)

#### Alternative Outcomes

16. Marler-Hausen T, Holt C, Headley C, Sessink P. Use of a closed-system drug transfer device reduces contamination with doxorubicin during bolus injection. *Br J Nurs*. 2020 May 28;29(10):S15-S21.  
[PubMed: PM32463759](#)
17. Salch SA, Zamboni WC, Zamboni BA, Eckel SF. Patterns and characteristics associated with surface contamination of hazardous drugs in hospital pharmacies. *Am J Health Syst Pharm*. 2019 Apr 17;76(9):591-598.  
[PubMed: PM31361828](#)
18. Bartel SB, Tyler TG, Power LA. Multicenter evaluation of a new closed system drug-transfer device in reducing surface contamination by antineoplastic hazardous drugs. *Am J Health Syst Pharm*. 2018 Feb;75(4):199-211.  
[PubMed: PM29339374](#)
19. Garcia SV, Clerigues NV, Ferrer VF, Briz EL, Andres JLP. Use and handling safety of Mini-Spike 2 R chemo and puresite for safe chemotherapy compounding in a hospital pharmacy. *Regul Toxicol Pharmacol*. 2018 Dec;100:1-6.  
[PubMed: PM30296468](#)
20. Valero S, Lopez-Briz E, Vila N, Solana A, Melero M, Poveda JL. Pre and post intervention study of antineoplastic drugs contamination surface levels at a Pharmacy Department Compounding Area using a closed system drug transfer device and a decontamination process. *Regul Toxicol Pharmacol*. 2018 Jun;95:1-7.  
[PubMed: PM29510165](#)
21. Vyas N, Turner A, Clark JM, Sewell GJ. Evaluation of a closed-system cytotoxic transfer device in a pharmaceutical isolator. *J Oncol Pharm Pract*. 2016 Feb;22(1):10-19.  
[PubMed: PM25073678](#)

## Guidelines – Unclear Methodology

22. Alberta Health Services, Covenant Health. Cytotoxic drug manual administration and handling guidelines. *Version 3.5*. Edmonton (AB): Alberta Health Services; 2018.
23. Anglin P, Briggs V, Charbonneau F, et al. Cancer Care Ontario beyond-use date: recommendations report. Toronto (ON): Cancer Care Ontario; 2018 Mar: <https://www.cancercareontario.ca/sites/ccocancercare/files/guidelines/full/BUD%20Recommendations%20Report%20final.pdf> Accessed 2020 Dec 07.

## Review Articles

24. Eisenberg S. Hazardous Drugs and USP <800>: Implications for Nurses. *Clin J Oncol Nurs*. 2017 Apr 01;21(2):179-187. [PubMed: PM28315550](#)
25. Martin Lancharro P, De Castro-Acuna Iglesias N, Gonzalez-Barcala FJ, Moure Gonzalez JD. Evidence of exposure to cytostatic drugs in healthcare staff: a review of recent literature. *Farm*. 2016 Nov 01;40(n06):604-621. [PubMed: PM27894231](#)

## Policy Documents

26. Duke Occupational and Environmental Safety Office. Safe handling of hazardous drugs [supplement V]. Durham (NC): Duke University; 2020 May: <https://www.safety.duke.edu/sites/default/files/V-HazardousDrugs.pdf> Accessed 2020 Dec 07.
27. Alberta Health Services. Hazardous medication Personal Protective Equipment (PPE) guide and list. *Version 1.7*. Edmonton (AB): Alberta Health Services; 2019 Jun: <https://www.albertahealthservices.ca/assets/info/hp/pharm/if-hp-pharm-hazardous-medications-ppe-guide.pdf> Accessed 2020 Dec 07.
28. Regina Qu'Appelle Region, Nursing Procedure Committee. Hazardous drugs administration & handling [nursing procedure]. Saskatoon (SK): Saskatchewan Health Authority; 2016 Feb: <http://www.rqhealth.ca/service-lines/clinical-quality-professional-practice/files/H.30.pdf> Accessed 2020 Dec 07.
29. Sessink PJM, Sewell G, Vandenbroucke J, et al. Preventing occupational exposure to cytotoxic and other hazardous drugs [European policy recommendations]. Brussels, Belgium: European Parliament; 2016 May: [https://www.europeanbiosafetynetwork.eu/wp-content/uploads/2016/05/Exposure-to-Cytotoxic-Drugs\\_Recommendation\\_DINA4\\_10-03-16.pdf](https://www.europeanbiosafetynetwork.eu/wp-content/uploads/2016/05/Exposure-to-Cytotoxic-Drugs_Recommendation_DINA4_10-03-16.pdf) Accessed 2020 Dec 07.
30. Cancer Care Manitoba. Safe handling of hazardous medications (cytotoxic and non-Cytotoxic) [policy]. Winnipeg (MB): Winnipeg Regional Health Authority; 2015 Oct: <https://mpa.in1touch.org/uploaded/web/Legislation/110%20160%20010%20-%20Oct%202015.pdf> Accessed 2020 Dec 07.



## Additional References

31. Besheer A, Burton L, Galas RJ, Jr., et al. An industry perspective on compatibility assessment of closed system drug-transfer devices for biologics. *J Pharm Sci.* 2020 Oct 28;S0022-3549(20)30663-8.  
[PubMed: PM33127425](#)
32. Fazel S, Keefe A, Palmer A, et al. Comparison of policy levers for the safe handling of antineoplastic agents in Alberta, Manitoba, and British Columbia. Vancouver (BC): CAREX Canada, Simon Fraser University; 2020 Feb:  
[https://www.carexcanada.ca/CAREX\\_ANTINEOPLASTIC\\_POLICY\\_LEVER\\_COMPARISON\\_FEB\\_2020.pdf](https://www.carexcanada.ca/CAREX_ANTINEOPLASTIC_POLICY_LEVER_COMPARISON_FEB_2020.pdf) Accessed 2020 Dec 07.
33. Sreedhara A, Zamiri C, Goswami S, et al. Challenges of using closed system transfer devices with biological drug products: an industry perspective. *J Pharm Sci.* 2020 Jan;109(1):22-29.  
[PubMed: PM31697946](#)
34. Centers for Disease Control and Prevention (CDC). Closed System Drug-Transfer Device (CSTD) research: overview; 2019 Jan.  
<https://www.cdc.gov/niosh/topics/hazdrug/CSTD.html> Accessed 2020 Dec 07.
35. Mathias PI, MacKenzie BA, Toennis CA, Connor TH. Survey of guidelines and current practices for safe handling of antineoplastic and other hazardous drugs used in 24 countries. *J Oncol Pharm Pract.* 2019 Jan;25(1):148-162.  
[PubMed: PM28841099](#)
36. Field A, Hughes G, Rowland S. A strategy for formulating regulation on CSTDs. *Br J Nurs.* 2017 Sep 06;26(Sup16b):S15-S22.  
[PubMed: PM28981323](#)
37. Kunneva L. Closed system drug transfer devices for chemotherapy. *Nursing.* 2016 Jan;46(1):67-68.  
[PubMed: PM26692315](#)