BUD Wading Through the Weeds: Part 1

Cancer Care Ontario Recommendations

Potential Strategies to Extend Beyond-Use Date

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Disclosures

- Advisory Boards:
  - Abbvie, Amgen, Astellas, Celgene, Innovative OncoSolutions, Janssen, Hoffman-La Roche, Novartis, Pfizer, Purdue Pharma, Shire
- Speaker/Consulting Fees:
  - Apobiologix, Hoffmann-La Roche

Objectives

- Describe the NAPRA Model Standards for Pharmacy Compounding of Hazardous and Non-Hazardous Sterile Preparations
- Discuss the potential financial impact of beyond-use date (BUD) in a publicly funded health care system
- Review the key components of Cancer Care Ontario's Beyond-Use Date Recommendations Report

CCO Recommendations Disclaimer

Notes on Use of this Recommendations Report

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NAPRA Model Standards

- Aim is to provide pharmacy personnel with standards, in order to guarantee the overall quality and safety of sterile preparations
- Separate documents for hazardous and non-hazardous sterile preparations
- Based on USP-NF Chapters <797>, <800> and ASSTSAS* Prevention Guide-safe handling of hazardous drugs (2008)
- Core components:
  - Requirements for a sterile compounding service
  - Product and preparation requirements, including BUD
  - Quality Assurance Program

NAPRA: National Association of Pharmacy Regulatory Authorities
*** Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales**

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CCO BUD Mitigation Strategy

- Systemic Treatment Program struck a working group in Dec, 2016
  - Membership: physicians, regional directors, pharmacists, pharmacy technicians, CCO representatives (chair)
- 11% of 59 facilities reported assigning a 6-hour BUD for single-dose vials
- Most facilities use hospital reference guides, published stability literature or manufacturer's recommendations to establish BUD
- A few facilities have adopted other measures to extend BUD

Financial Impact of 6-hour BUD

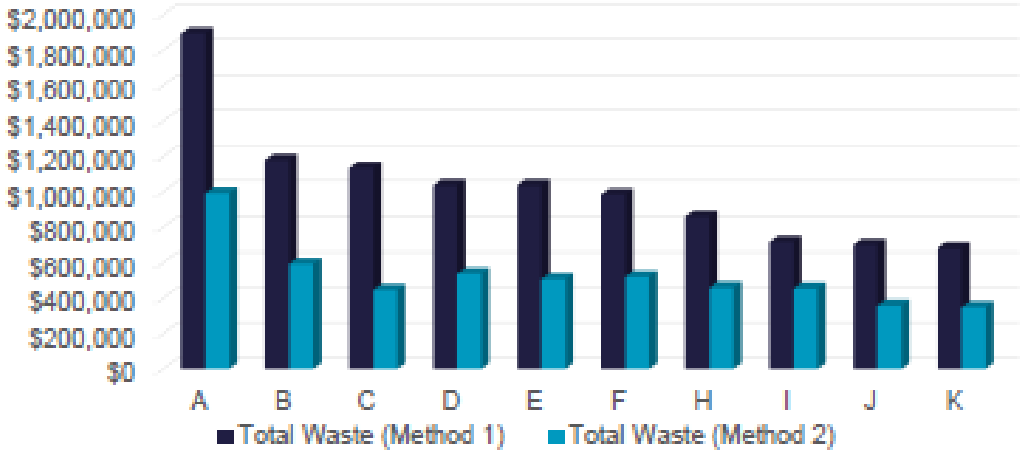
- CCO utilized eClaims™ data (January to June 2016) for 26 NDFP drugs that are single-use vials to model potential wastage[1]
- Assumptions:
  - all sites have access to all available vial sizes
  - contents of vials may be shared
  - doses for all patients are prepared at the same time
  - Single dose vial contents were true to stated quantity per manufacturer
- Limitations: single month of pembrolizumab data

1. Redwood, E. J Clin Oncol March 2017; 35_(8) suppl: 13

Financial Impact of 6-hour BUD

Results

Table 1: Drug Waste Cost Estimate – By Facility

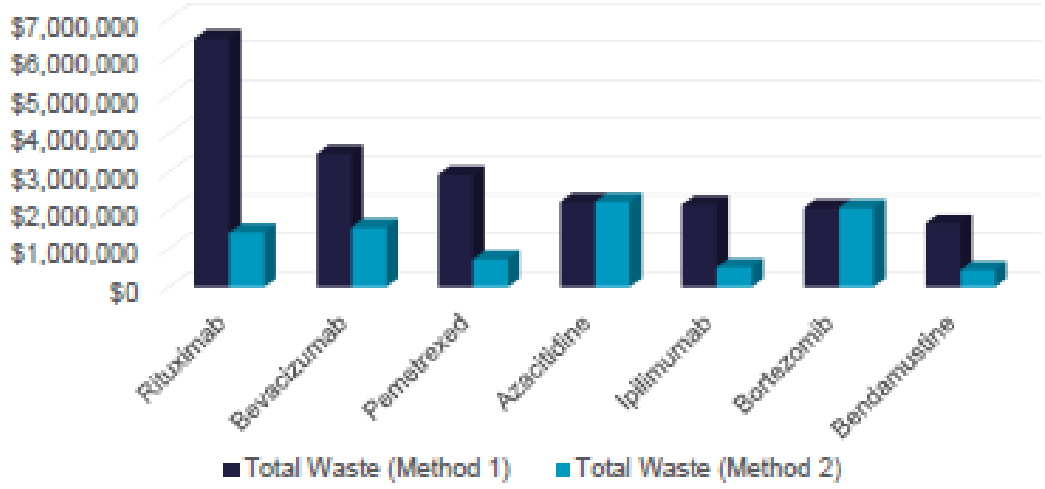


The 10 facilities with the highest waste estimates are summarized in Table 1. The total waste estimates for all facilities are $25,927,861 (method 1) and $12,945,353 (method 2). All estimates are represented in Canadian dollars.

Method 1: used the largest vial size matched to the closest amount of drug required.
Method 2: used the optimal vial size mix, when there are multiple vial sizes.

Waste estimates were also calculated by drug. The highest waste drugs are only available in larger dose vials (ex.100 and 500 mg for rituximab) and could result in more waste than drugs with more size options or less variance between sizes.

Table 2: Drug Waste Cost Estimate - By Drug



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Financial Impact of BUD - Summary

- Adoption of 6-hr BUD for single-dose vials will add $13-26M to provincial expenditures for cancer drugs
- As immuno-oncology drugs enter public funding landscape, impact will be even greater
- Drug waste is not funded through PDRP*

*PDRP Provincial Drug Reimbursement Programs

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BUD Mitigation Strategy Working Group

- Focus of work: extending BUD of single-use vials; not CSPs
- Four approaches identified that may have system impact:
  - Closed system drug-transfer devices (CSTDs)
  - Dose rounding
  - Facility-level sterility testing
  - Automated robotic dispensing units

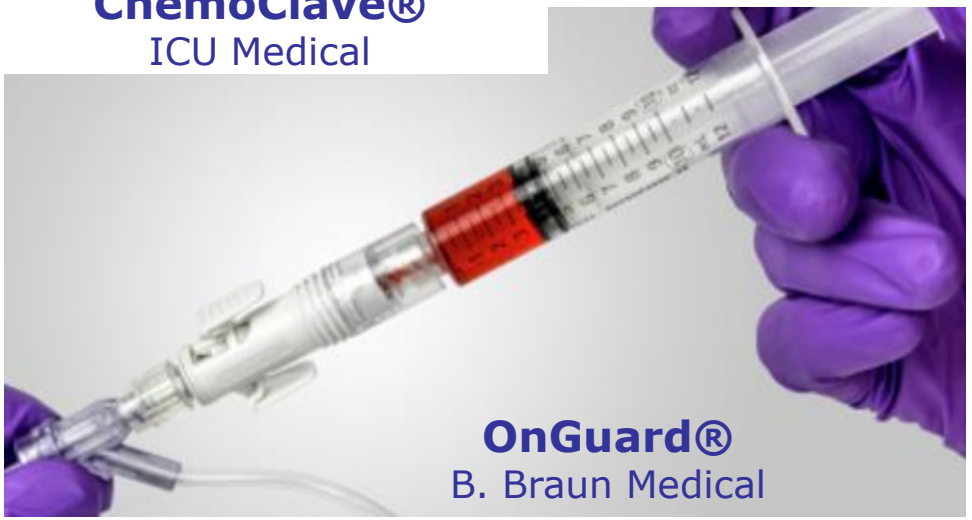
Closed System Drug-Transfer Devices

Equashield®
(Equashield Medical)

ChemoClave®
ICU Medical

PhaSeal®
BD Medical

Texium®
BD Medical



OnGuard®
B. Braun Medical

Closed System Drug –Transfer Devices

CSTDs may be used with single-dose vials to extend the current BUD of 6 hours, if supported by facility level sterility testing, but should not exceed 7 days

- Multiple studies have shown the viability of CSTDs for maintaining sterility for up to 7 days[2-5]
- The extended BUD of the single-use vials (using nutrient or culture media as outlined in NAPRA) should be supported by the results of facility-level sterility testing
- Minimal testing frequency of annually is suggested. Repeat testing ensures that personnel, processes and devices are continually evaluated

2. De Prijck KD. Letters in Applied Microbiology. 2008;47:543-8
3. McMichael DM. Am J Pharm Benefits. 2011;3:9-16
4. Carey ET. Am J Pharm Benefits. 2011;3:311-18
5. Ho KV. J Hematol Oncol Pharm. 2016;6:46-50

Closed System Drug-Transfer Devices (CSTDs)

- NIOSH Definition:

  A closed system drug transfer device or "CSTD" is a drug transfer device that mechanically prohibits the transfer of environmental contaminants into a system and the escape of hazardous drug or vapor concentrations outside the system.[1]

- NAPRA does not reference CSTDs at all
- USP<797> and USP<800>
  - CSTDs are considered supplementary engineering controls, but USP states that in facilities that prepare a low volume of HDs, the use of two tiers of containment (e.g. CSTD within a BSC or CACI that is located in a non-negative pressure room) is acceptable
  - USP<800> states: CSTDs **must** be used for administration of antineoplastic HDs when the dosage form allows.

1. https://www.cdc.gov/niosh/topics/hazdrug/sampling.html

Dose Rounding

A strategy of dose rounding may be used to reduce drug wastage associated with single-dose vials

- A dose rounding strategy to within 10% of the calculated dose, based on vial size availability, may be considered
  - Should be guided by patient-specific and disease-related facors, goals(s) of treatment and expected toxicities
  - Applies to both traditional cytotoxics and monoclonal antibodies and other biologic agents
  - Same threshold may be utilized for adjuvant/curative and palliative therapies
- HOPA* position statement endorses a similar dose rounding threshold[6]

*HOPA Hematology Oncology Pharmacy Association

6. Bott AM. Dose Rounding of Biologic and Cytotoxic Anticancer Agents 2017 October retrieved from http://www.hoparx.org/

Facility –Level Sterility Testing

Extending the BUD of single-dose vials should only be implemented when supported by facility-level sterility testing.

- A formal testing protocol should be established and validated at the local level to ensure ongoing sterility of extending the sterility of extending the BUD beyond 6 hours
- Departments of Pharmacy and Microbiology should collaborate, based on institutional SOPs or outsource these procedures to USP-adherent commercial laboratory providers

Automated Robotic Dispensing Units (ARDUs)

ARDUs may be used to extend the BUD of single-dose vials if local testing consistently demonstrates ongoing sterility under the specified storage conditions.

- No published evidence to date that directly supports the use of ARDUs to extend the BUD of single-dose vials in accordance with NAPRA Model Standards
- ARDUs can be used as BSCs to maintain the sterility of single-dose vials
- A formal testing protocol should be established and validated at the local level to support this approach

Other Mitigation Strategies

- **Dose Banding**
  - defined as a system whereby drug doses calculated by any method are grouped and rounded to a set of predefined standard doses
  - May be considered for select drugs to contribute to system efficiencies, reduce wait times and minimize drug wastage
  - Chatelut *et al*[7] compared dose banding with individualized BSA dosing and fixed dosing according to pharmacokinetic criteria for six commonly utilized chemotherapeutic drugs. They concluded that dose banding resulted in no significant difference in inter-individual plasma exposure.
- **Non-same day models or scheduling strategies**
- **Vial size purchase options**

7. Chatelut E. Br J Cancer 2012;107:1100-6

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