Implications of Discarded Weight-Based Drugs

The National Academies of SCIENCES ENGINEERING MEDICINE

Pharmaceutical Compounding & Dispensing

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Agenda

1. Causes of Pharmaceutical Waste
2. Strategies and Best Practices
3. Drug Shortages and Waste

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Pharmaceutical Waste

1. **Incomplete use of package**
   Multiple dosage forms
2. **FDA-labeling parameters**
   Storage conditions and excursions
3. **Beyond-use dates**
   Compounded preparations
4. **Expired product**
   Manufacturer-labeled expiration dates
5. **Preparation**
   Errors in preparation or compounding, coring
6. **Lost product**
   Drops, breaks, spills, leaks

Incomplete use of package

Sterile injectable container types

Single-dose

- No antimicrobial effectiveness testing
- Designed for single patient as a single injection or infusion

Multiple-dose

- Meets antimicrobial effectiveness testing
- Contains more than one dose

Single-patient-use

- Meets antimicrobial effectiveness testing
- Contains more than one dose
- Intended for a single patient

FDA Guidance for Industry[1]

October 2018

1. U.S. Food and Drug Administration. (2018). *Selection of the Appropriate Package Type Terms and Recommendations for Labeling Injectable Medical Products Packaged in Multiple-Dose, Single-Dose, and Single-Patient-Use Containers for Human Use – Guidance for Industry.* Retrieved from https://www.fda.gov/media/117883/download

Incomplete use of package

Regulation of single-dose containers

FDA and CDC

- Use for a single dose for a single patient and discard unused portion

USP

- General Chapter <797> Pharmaceutical Compounding—Sterile Preparations
- Single-dose vials punctured in ISO 5 environment may be used for up to six hours if stored in ISO 5 environment

CMS

- Recognizes USP <797>

Single-dose containers:

- **Vials**
- **Ampules**
- **Prefilled syringes**

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Incomplete use of package

Single-dose containers: strategies and best practices

Batching preparations

- Preparation of doses at the same time

Dose rounding and banding

- Rounding to nearest predetermined unit
- Banding all patients within range to the same dose

Drug-vial optimization

- Use of closed-system transfer device to extend six-hour <797> limit

Goals

- **Use full vial within six hours**
- **Extend six-hour limit**

Strategies and best practices:
Batching preparations

Weight-based doses; preparations that do not use full vial content

- Standardized administration times for existing orders[1]
  - Daptomycin – annualized savings of ~1,110 vials and ~$250,000

- Use of cheaper package sizes (price per mg)[1]
  - Caspofungin – annualized savings of ~572 vials and ~$60,000

- Anticipatory batching using full vial to prepare multiple doses[2]
  - Isoproterenol – annualized savings of ~$600,000

Limitations

- Discontinued or altered orders – consider timing of batch
- Beyond-use dating of anticipatory preparations

1. Goff DA , Bauer KA, Reed EE, Stevenson KB, Taylor JJ, West JE. Is the "low-hanging fruit" worth picking for antimicrobial stewardship programs? *Clin Infect Dis.* 2012;55:587–92.
2. Toerper MF, Veltri MA, Hamrock E, Mollenkopf NL, Holt K, Levin S. Medication waste reduction in pediatric pharmacy batch processes. *J Pediatr Pharmacol Ther*. 2014;19(2):111–117.

Strategies and best practices:
Rounding and dose banding

Weight-based doses

- Banding of three oncology agents: bevacizumab, trastuzumab, rituximab[1]
  - Annualized savings from rounding down: $770,556
  - Can successfully prevent waste if rounded to a whole vial or usable remaining volume

- Simulated rounding to nearest vial size of seven monoclonal antibodies[2]
  - Of 237 doses, 28.7% rounded down; 71.3% rounded up
  - Rounded dose percent change from order ranged from 1.4% to 20%
  - Theoretical annualized savings from rounding down: $83,595.53

Limitations

- Payer policies related to FDA-approved or coverage-determined dose relative to dose administered
- Nearest vial size may be lower or higher than acceptable range for rounding

1. Fahey OG, Koth SM, Bergsbaken JJ, Jones HA, Trapskin PJ. Automated parenteral chemotherapy dose-banding to improve patient safety and decrease drug cots. *J Onc Pharm Pract*. 2020;26(2):345-350.
2. Lindsey S, Parsons LB, Figg LR, Rhodes J. Evaluation of dosing strategies of biologic agents and the theoretical impact of dose rounding. *J Onc Pharm Pract*. 2018;24:47-55.

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Strategies and best practices:
Drug-vial optimization (DVO)

Closed-system transfer device (CSTD)

- Vial adapter used to prevent exposure to hazardous drugs by either physical barrier or filtration
  - Peer-review studies demonstrate that some barrier-type CSTDs prevent microbial growth when affixed to vials[1,2]
- Annual cost of drug waste reduced from $770,900 in 2011 to $49,000 in 2018 after DVO implementation[3]
- Savings of $96,348.70 during 50-day DVO implementation on 21 antineoplastic drugs

Limitations

- FDA 510(k) clearances state "prevention of microbial ingress" or related language
  - Does not specifically approve extension of vial dating
- Regulators and accreditors currently do not allow the practice

1. McMichael DM, Jefferson DM, Carey ET, Forrey RA, Spivey SM, Mulvaney JM, Jorgenson JA, Haughs RD. Utility of the PhaSeal closed system drug transfer device. *Am J Pharm Benefits*. 2011;3(1):9-16.
2. Carey ET, Forrey RA, Haughs D, Jefferson DM, Jorgenson JA, McMichael DM, Mulvaney JM, Spivey SM. Second look at utilization of a closed-system transfer device (PhaSeal). *Am J Pharm Benefits.* 2011;3(6):311-318.
3. Amerine LB, Savage SW, Rowe EC, Daniels R, Valgus JM, Redding R, Eckel SF. Implementation of drug vial optimization to reduce drug waste. ACCC-cancer.org March-April 2019
4. Edwards MS, Solimando DA, Grollman FR, Pang JL, Chasick AH, Hightman CM, Johnson AD, Mickens MG, Preston LM. Cost savings realized by use of PhaSeal closed-system transfer device for preparation of antineoplastic agents. *J Oncol Pharm Pract.* 2013;19(4):338-47.

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FDA-labeling limitations

Commercially manufactured products and preparations according to manufacturer labeling

Describes how product should be stored

- Temperature
- Light exposure

Often includes dating for excursions and for preparations

- Storage limits at room temperature
- Storage limits for preparations

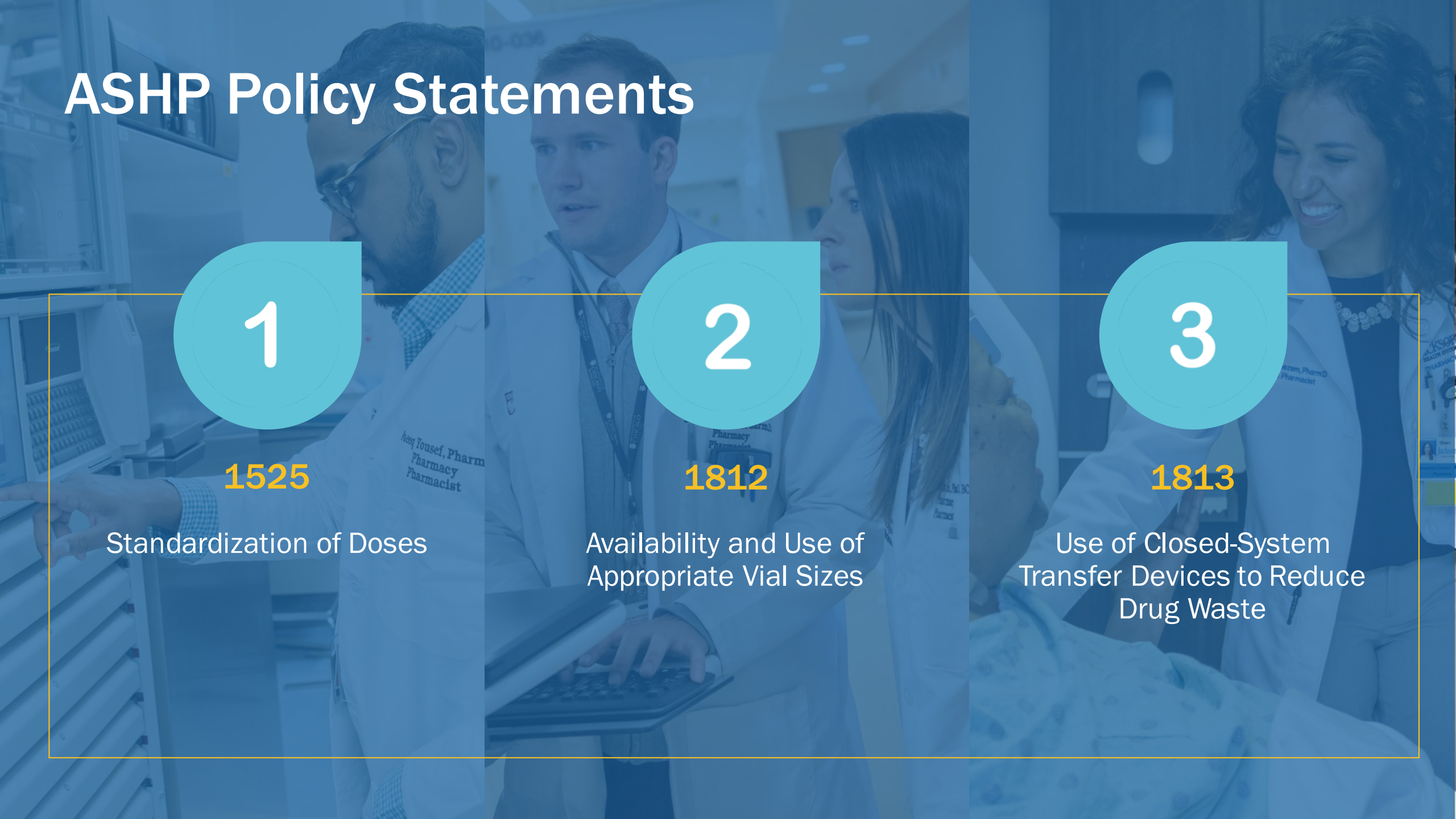
Peer-review literature establishing extended dating using stability-indicating assays not recognized by regulators and accreditors

Waste as a result of FDA-approved product labeling

Drug shortages and waste

- 276 drugs in ASHP Drug Shortages Database as of April 1, 2020
  - Commonly generic drugs with about 40% sterile injectables
  - Single-dose injectables recently in short supply:
    - Antineoplastic agents
    - Analgesics and sedatives
    - Neuromuscular blockers
    - Antimicrobial agents
  - Regulations, standards, and accreditor policies may lead to unnecessary waste of these drugs

ASHP Policy Statements



1

1525

Standardization of Doses

2

1812

Availability and Use of Appropriate Vial Sizes

3

1813

Use of Closed-System Transfer Devices to Reduce Drug Waste

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