USP 800: Beyond the Basics
Part II

Stronger Together

Memorial Cancer Institute
MEMORIAL REGIONAL HOSPITAL | MEMORIAL HOSPITAL WEST
MEMORIAL AVENTURA GROUP

Marie Louis-Jeune, PharmD, BCPS
Pharmacy Quality and Safety Coordinator
Memorial Cancer Institute
November 9, 2019

Bibliography

Memorial Cancer Institute
MEMORIAL REGIONAL HOSPITAL | MEMORIAL HOSPITAL WEST
MEMORIAL AVENTURA GROUP

Marie Louis-Jeune completed her undergraduate experience obtaining a Bachelor of Science in Exercise Science from Florida State University in 2009. Marie then went on to earn her Doctor of Pharmacy degree from South University School of Pharmacy in Savannah, Georgia in 2012. Following pharmacy school, she joined Memorial Regional Hospital completing a PGY-1 in Pharmacy Practice. Post residency, Marie transitioned into a Clinical Pharmacist role at Joe DiMaggio Children's Hospital. During this time, she obtained her Board Certification in Pharmacotherapy and worked in various specialties including PICU and Hematology/Oncology. Marie then went on to complete a PGY-2 residency in Health-System Pharmacy Administration. During this time, she completed the ASHP Pharmacy Leadership Academy. She also served as the 2015-2016 Treasurer for the Florida Hospital Orlando Residency Program and was a 2015-2016 Communications and Awards Committee member of the Pharmacy Administration Resident Collaboration. Post residency, Marie transitioned into the Pharmacy Sterile Compounding Supervisor role at Memorial Cancer Institute in 2016. Her role evolved into the Pharmacy Operations Manager in 2017 and during this time she completed the ASHP Medication Safety Certificate. She is currently, since 2018, the Pharmacy Safety and Quality Coordinator. Marie is a member of FSHP and FLASCO.

Disclosure

Memorial Cancer Institute
MEMORIAL REGIONAL HOSPITAL | MEMORIAL HOSPITAL WEST
MEMORIAL AVENTURA GROUP

I do not have any commercial interest, financial relationships, or conflicts of interest to disclose in regards to the content of this presentation.

Objectives

Memorial Cancer Institute
MEMORIAL REGIONAL HOSPITAL | MEMORIAL HOSPITAL WEST
MEMORIAL AVENTURA GROUP

- Explain USP 800 recommendations on environmental sampling and medical surveillance
- Understand the key components of selecting a certification vendor
- **Discuss USP 800 recommendations, ASCO's position and NIOSH future goals on CSTDs**
- **Review recommendations on evaluating CSTDs**
- **Identify the financial impact of implementing and utilizing CSTDs**

Abbreviations

Memorial Cancer Institute
MEMORIAL REGIONAL HOSPITAL | MEMORIAL HOSPITAL WEST
MEMORIAL AVENTURA GROUP

- ASCO: American Society of Clinical Oncology
- CI: Confidence Interval
- CSTD: Closed System Transfer Devices
- GPO: Group Purchasing Organization
- GRADE: Grading of Recommendations Assessment, Development and Evaluation
- HD: Hazardous Drug
- MD: Mean Difference
- NIOSH: National Institute for Occupational Safety and Health
- ROBINS-I tool: **r**isk **o**f **b**ias **i**n **n**on-randomized **s**tudies of **i**nterventions tool
- RR: Risk Ratio
- USP: United States Pharmacopeia

CSTD

Memorial Cancer Institute
MEMORIAL REGIONAL HOSPITAL | MEMORIAL HOSPITAL WEST
MEMORIAL AVENTURA GROUP

USP 800

ASCO

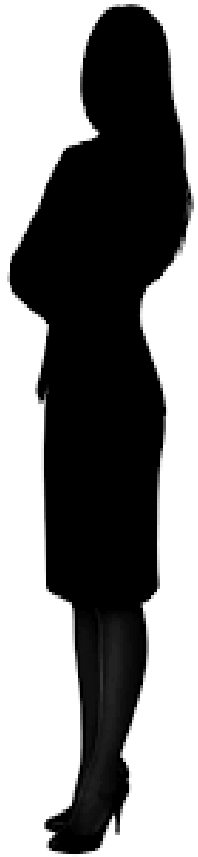
NIOSH

USP 800

- CSTD: Supplemental engineering control

Recommendation

- CSTDs should be used when compounding HDs.
- CSTDs *must* be used when administering HDs.
- Carefully evaluate performance claims associated with available CSTDs based on independent, peer-reviewed studies and demonstrated containment reduction.



ASCO

Position Statement

- A testing protocol for CSTDs is needed.
- There is a need for a process to identify and certify effective CSTDs.

Qualifying statement

- CSTDs plus safe handling of HDs versus safe handling alone for reducing exposure to infusional HDs in healthcare staff

CSTDs plus safe handling of HDs versus safe handling alone for reducing exposure to infusional HDs in healthcare staff

Objective

- Assess the effects of CSTD of infusional HD plus safe handling versus safe handling alone for reducing staff exposure to infusional HDs and risk of staff contamination.

Selection criteria

- Included comparative studies of any study design that compared CSTD plus safe handling versus safe handling alone for infusional HDs.
  - Irrespective of language, blinding, or publication status

CSTDs plus safe handling of HDs versus safe handling alone for reducing exposure to infusional HDs in healthcare staff

Data collection and analysis

- Two review authors independently identified trials and extracted data.
- Calculated the RR and MD with 95% CI.
- Assessed risk of bias according to the ROBINS-I tool.
- Assessed the quality of the evidence using GRADE.

CSTDs plus safe handling of HDs versus safe handling alone for reducing exposure to infusional HDs in healthcare staff

Results

- 24 observational cluster studies (359 hospitals)
- No randomized controlled trials identified
  - Description of control groups were varied
  - 22 studies: intervention and control used by pharmacist and/or technician
  - 2 studies: intervention and control used by **nursing**, pharmacist or technicians
- 22 studies provided data on one or more outcomes
- CTSD used in the studies
  - CSTD A (13 studies)
  - CSTD B (1 study)
  - CSTD C (1 study)
  - CSTD A & B (1 study)
  - Varied (5 studies)
  - Not stated (2 studies)

Closed-system transfer device safe handling versus safe handling alone for reducing healthcare staff exposure to infusional hazardous drugs: exposure and contamination				
Outcomes	Safe handling alone	CSTD + safe handling	Relative effects (95% CI)	Quality of the evidence (GRADE)
Exposure (urine tests for exposure)				
Cyclophosphamide	917 per 1000	761 per 1000 (422 to 1393)	RR 0.83 (0.46 to 1.52)	**Very low**
Cyclophosphamide or ifosfamide	714 per 1000	64 per 1000 (0 to 1000)	RR 0.09 (0.00 to 2.79)	**Very low**
Cyclophosphamide, ifosfamide, or gemcitabine	There were no participants with exposure in either group.			**Very low**
Other measures of exposure	None of the studies report on blood tests or other measures of exposure to infusional hazardous drugs.			

Closed-system transfer device safe handling versus safe handling alone for reducing healthcare staff exposure to infusional hazardous drugs: exposure and contamination				
Outcomes	Safe handling alone	CSTD + safe handling	Relative effects (95% CI)	Quality of the evidence (GRADE)
Surface contamination (proportion of surfaces contaminated): ***Pharmacy areas***				
Cyclophosphamide, ifosfamide, methotrexate, 5-fluorouracil, cytarabine, gemcitabine	102-507 per 1000	90-451 per 1000	RR 0.65-0.96 (include 1)	**Very low**
Irinotecan, docetaxel, paclitaxel, vinorelbine, ganciclovir, multiple drugs	There is no evidence of difference in the proportion of samples contaminated with drug in patient-care areas between CSTD plus safe handling and safe handling alone.			**Very low**

Closed-system transfer device safe handling versus safe handling alone for reducing healthcare staff exposure to infusional hazardous drugs: exposure and contamination				
Outcomes	Safe handling alone	CSTD + safe handling	Relative effects (95% CI)	Quality of the evidence (GRADE)
Surface contamination (proportion of surfaces contaminated): ***Patient-care areas***				
Cyclophosphamide	440 per 1000	444 per 1000 (378 to 519)	RR 1.01 (0.86 to 1.18)	**Very low**
Ifosfamide	71 per 1000	102 per 1000 (64 to 161)	RR 1.44 (0.91 to 2.28)	**Very low**
Methotrexate	25 per 1000	25 per 1000 (14 to 46)	RR 1.00 (0.55 to 1.85)	**Very low**
5-fluorouracil, cytarabine, gemcitabine, irinotecan, docetaxel, paclitaxel, vinorelbine, multiple drugs	There is no evidence of difference in the proportion of samples contaminated with drug in patient-care areas between CSTD plus safe handling and safe handling alone.			**Very low**

Closed-system transfer device safe handling versus safe handling alone for reducing healthcare staff exposure to infusional hazardous drugs: exposure and contamination

Outcomes	Safe handling alone	CSTD + safe handling	Relative effects (95% CI)	Quality of the evidence (GRADE)
Surface contamination (quantity of surface contamination (pg/ cm^2)): ***Pharmacy areas***				
Cyclophosphamide	124.30 pg/ cm^2	49.34 pg/ cm^2 lower	MD −49.34 pg/ cm^2 (−84.11 to −14.56)	**Very low**
Ifosfamide	10.8 pg/ cm^2	0.32 pg/ cm^2 lower	MD −0.32 pg/ cm^2 (−6.58 to 5.94)	**Very low**
Methotrexate	18.23 pg/ cm^2	3.09 pg/ cm^2 lower	MD −3.09 pg/ cm^2 (−13.80 to 7.61)	**Very low**
5-fluorouracil	8720.5 pg/ cm^2	257.87 pg/ cm^2 higher	MD 257.87 (−459.65 to 975.38)	**Very low**
Cytarabine, gemcitabine, and irinotecan	There is no evidence of difference in the amount of drug in pharmacy areas between CSTD plus safe handling and safe handling alone.			**Very low**

Closed-system transfer device safe handling versus safe handling alone for reducing healthcare staff exposure to infusional hazardous drugs: exposure and contamination				
Outcomes	Safe handling alone	CSTD + safe handling	Relative effects (95% CI)	Quality of the evidence (GRADE)
Surface contamination (quantity of surface contamination (pg/ cm^2)): ***Patient-care areas***				
Cyclophosphamide	168 pg/ cm^2	13.34 pg/ cm^2 lower	MD −13.34 pg/ cm^2 (−36.01 to 9.32)	**Very low**
Ifosfamide	4.59 pg/ cm^2	3.59 pg/ cm^2 higher	MD 3.59 pg/ cm^2 (−3.45 to 10.63)	**Very low**
Methotrexate	1.42 pg/ cm^2	0.10 pg/ cm^2 higher	MD 0.10 pg/ cm^2 (−0.57 to 0.78)	**Very low**
5-fluorouracil, cytarabine, gemcitabine, and irinotecan	There is no evidence of difference in the amount of drug in patient-care areas between CSTD plus safe handling and safe handling alone.			**Very low**
Other measures of contamination	None of the studies report on atmospheric contamination.			

ASCO

Qualifying Statement

- Review of evidence for CSTDs did not find any published studies that evaluated health outcomes but rather found studies of surrogate markers.
  - Antineoplastic drugs in urine, surface contamination, and containment levels of drugs in controlled laboratory settings
- Largely industry-sponsored body of evidence was of low quality.
- Need for third party to develop neutral testing method to determine efficacy of CSTDs.

ASCO

Qualifying statement

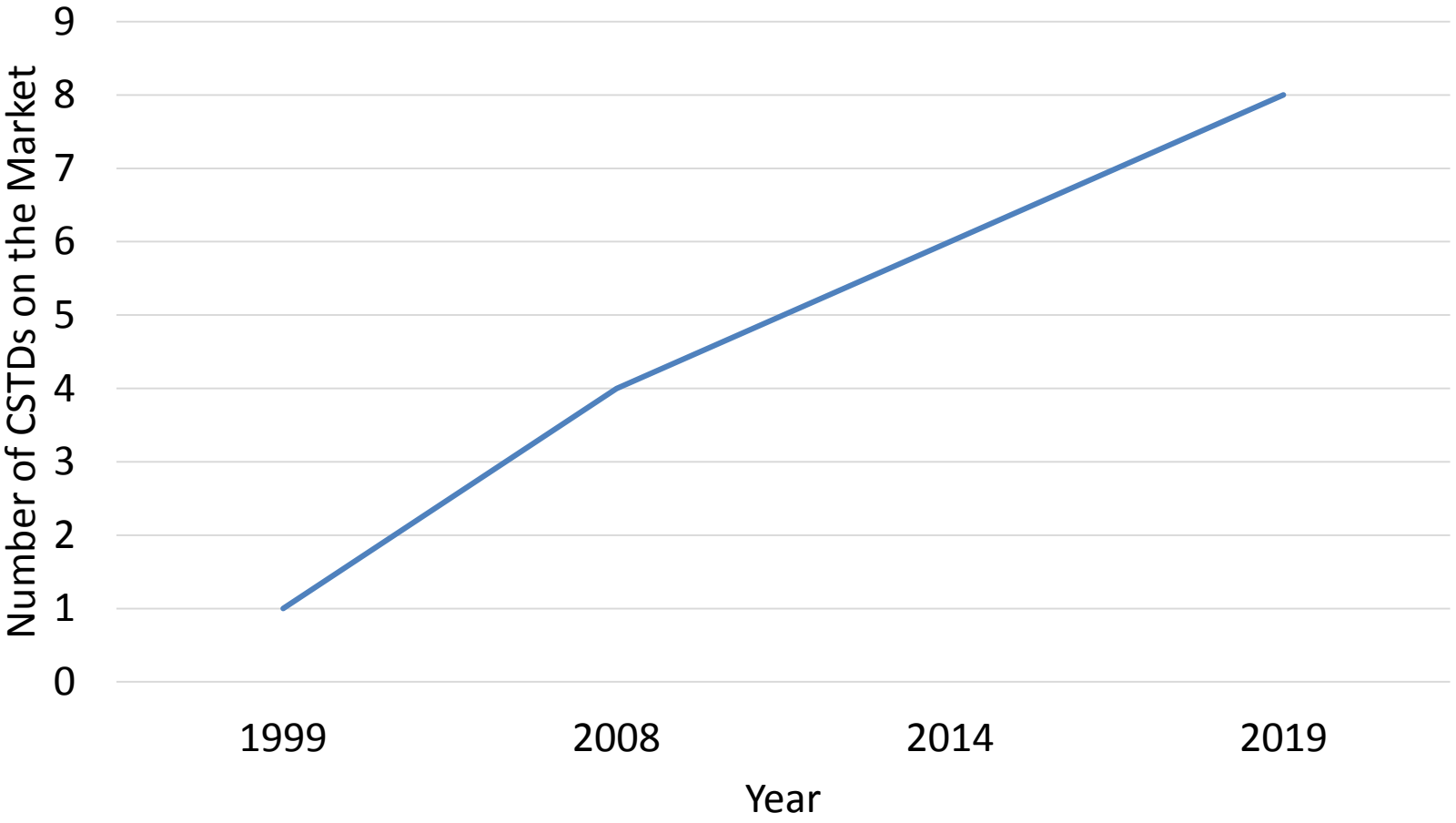
- NIOSH in process of developing an independent vapor containment performance protocol for CSTDs in health care settings.
- ASCO standards will be revised to incorporate the NIOSH CSTD testing protocol when it becomes available.
- NIOSH encouraged to develop a certification process so that practices can identify effective CSTDs.

NIOSH

Performance Test Protocol for CSTDs

- Collaborative effort between healthcare industry representatives and NIOSH researchers.
- Healthcare industry request for independently developed containment test protocol.
- 2004 NIOSH Alert released while limited models of CSTDs in market.
  - Recent increase in CSTDs models in market

CSTDs on the Market



NIOSH

Performance Test Protocol for CSTDs

- Purpose is to challenge a CSTD's ability to function as a closed system that restricts drug mass (vapor or liquid) from crossing the system boundary and escaping into the surrounding environment.
  - Not to demonstrate CSTDs are effective in reducing hazardous drug surface contamination.

NIOSH

Performance Test Protocol for CSTDs

- CSTD performance standards in regards to sterile practice for patient protection exist.
- CSTD performance standards in regards to drug containment ***do not*** exist.
- Consumers have no worker-protection performance basis to make their selection of a CSTD.
- May be inclined to select a product based on acquisition costs and uncertain claims of protective performance.

NIOSH

Performance Test Protocol for CSTDs

- Upon publication, manufacturers of CSTDs and consumers will be able to use and refer to this protocol, enabling consumers to conduct meaningful comparisons between products and subsequently choose products based upon their demonstrated ability to perform as closed systems.

Lessons Learned

NIOSH requires the use of CSTDs when transferring hazardous drugs from primary packaging to infusion bags, bottles, or pumps.

True or False

Lessons Learned

NIOSH requires the use of CSTDs when transferring hazardous drugs from primary packaging to infusion bags, bottles, or pumps.

False

CSTD

Memorial Cancer Institute
MEMORIAL REGIONAL HOSPITAL | MEMORIAL HOSPITAL WEST
MEMORIAL AVENTURA GROUP

USP 800

Carefully evaluate performance claims.

ASCO

A testing protocol and process to identify and certify effective CSTDs is needed. Standards will be revised to incorporate NIOSH protocol when it becomes available.

NIOSH

Performance test protocol for CSTDs to assist with product selection based upon ability to perform as closed systems.

Lessons Learned

NIOSH is in the process of developing an independent vapor containment performance protocol for CSTDs in health care settings and the ASCO standards will be revised to incorporate these testing protocol once available.

True or False

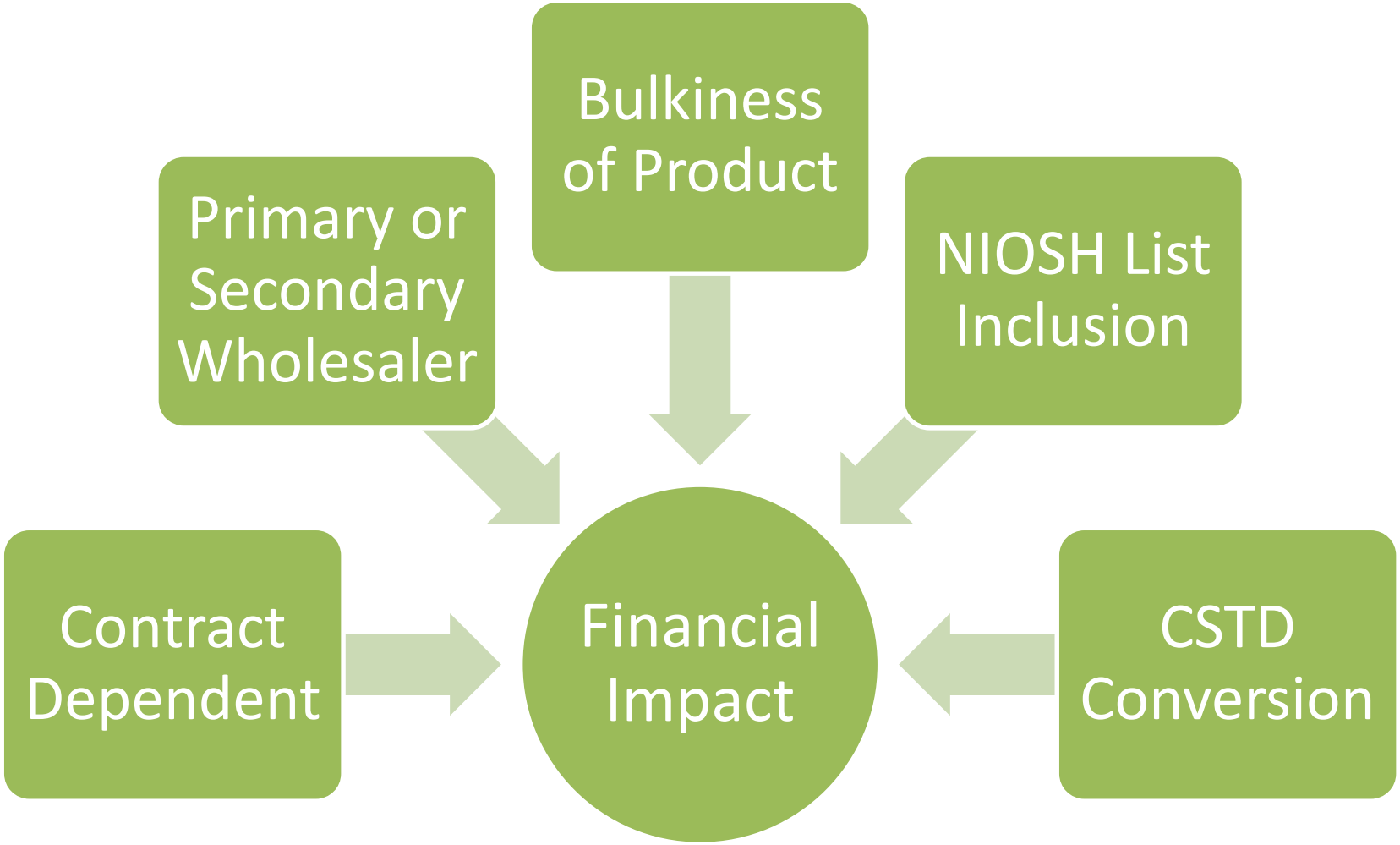
Lessons Learned

NIOSH is in the process of developing an independent vapor containment performance protocol for CSTDs in health care settings and the ASCO standards will be revised to incorporate these testing protocol once available.

True

Financial Impact

Memorial Cancer Institute
MEMORIAL REGIONAL HOSPITAL | MEMORIAL HOSPITAL WEST
MEMORIAL AVENTURA GROUP



Contract Dependent

Memorial Cancer Institute
MEMORIAL REGIONAL HOSPITAL | MEMORIAL HOSPITAL WEST
MEMORIAL AVENTURA GROUP

Pricing

- Supplier's listed price
- Agreement period
  - Availability to extend the agreement period/term
- Instant rebate
  - Sole Source Agreement
- Medicare and Medicaid Anti-Kickback statue
- Direct purchases from Supplier vs. Wholesaler
  - Purchases from supplier requires additional payment for carrier and shipping

Contract Dependent

Memorial Cancer Institute
MEMORIAL REGIONAL HOSPITAL | MEMORIAL HOSPITAL WEST
MEMORIAL AVENTURA GROUP

Customer's utilization commitment

- Identifies percentage requirement of utilization for CSTD products
- Customer may be asked to provide proof of purchases for all similar products during the applicable period
- At risk of increasing customers product pricing to tier level under customer's current GPO agreement
- Increase in price also affect by GPO membership

Wholesaler

Memorial Cancer Institute
MEMORIAL REGIONAL HOSPITAL | MEMORIAL HOSPITAL WEST
MEMORIAL AVENTURA GROUP

Item Description	Primary Wholesaler Price	Secondary Wholesaler Price	Savings/Loss
Bag access port	$90.00	$100.00	($10.00)
CSTD Male Leur	$100.00	$120.00	($20.00)
Vial adapter A	$1,600.00	$1,800.00	($200.00)
Vial adapter B	$21,000.00	$24,000.00	($3,000.00)
Vial adapter C	$1,500.00	$1,600.00	($100.00)
Secondary CSTD filtered line	$4,500.00	$5,000.00	($500.00)
Secondary CSTD line	$2,500.00	$4,000.00	($1,500.00)
CSTD spike adapter	$250.00	$400.00	($150.00)
CSTD 10 mL syringe	$1,600.00	$1,700.00	($100.00)
CSTD 20 mL syringe	$2,400.00	$2,600.00	($200.00)
CSTD 30 mL syringe	$2,000.00	$2,500.00	($500.00)
CSTD 3 mL syringe	$2,000.00	$2,200.00	($200.00)
CSTD 5 mL syringe	$4,000.00	$4,100.00	($100.00)
CSTD 60 mL syringe	$1,900.00	$2,000.00	($100.00)
		TOTAL	($6,680.00)

Bulkiness of Product

Memorial Cancer Institute
MEMORIAL REGIONAL HOSPITAL | MEMORIAL HOSPITAL WEST
MEMORIAL AVENTURA GROUP

Storage space

- Minimize ordering and PAR level
- Potential for drop shipment if inventory not managed appropriately

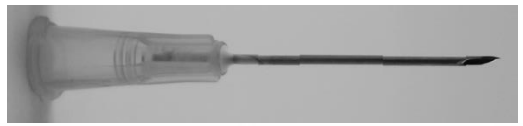
Request more frequent hazardous bin pick up or order more bins

Identify amount of space in room held for pick up

Bulkiness of Product

Memorial Cancer Institute
MEMORIAL REGIONAL HOSPITAL I MEMORIAL HOSPITAL WEST
MEMORIAL AVENTURA GROUP

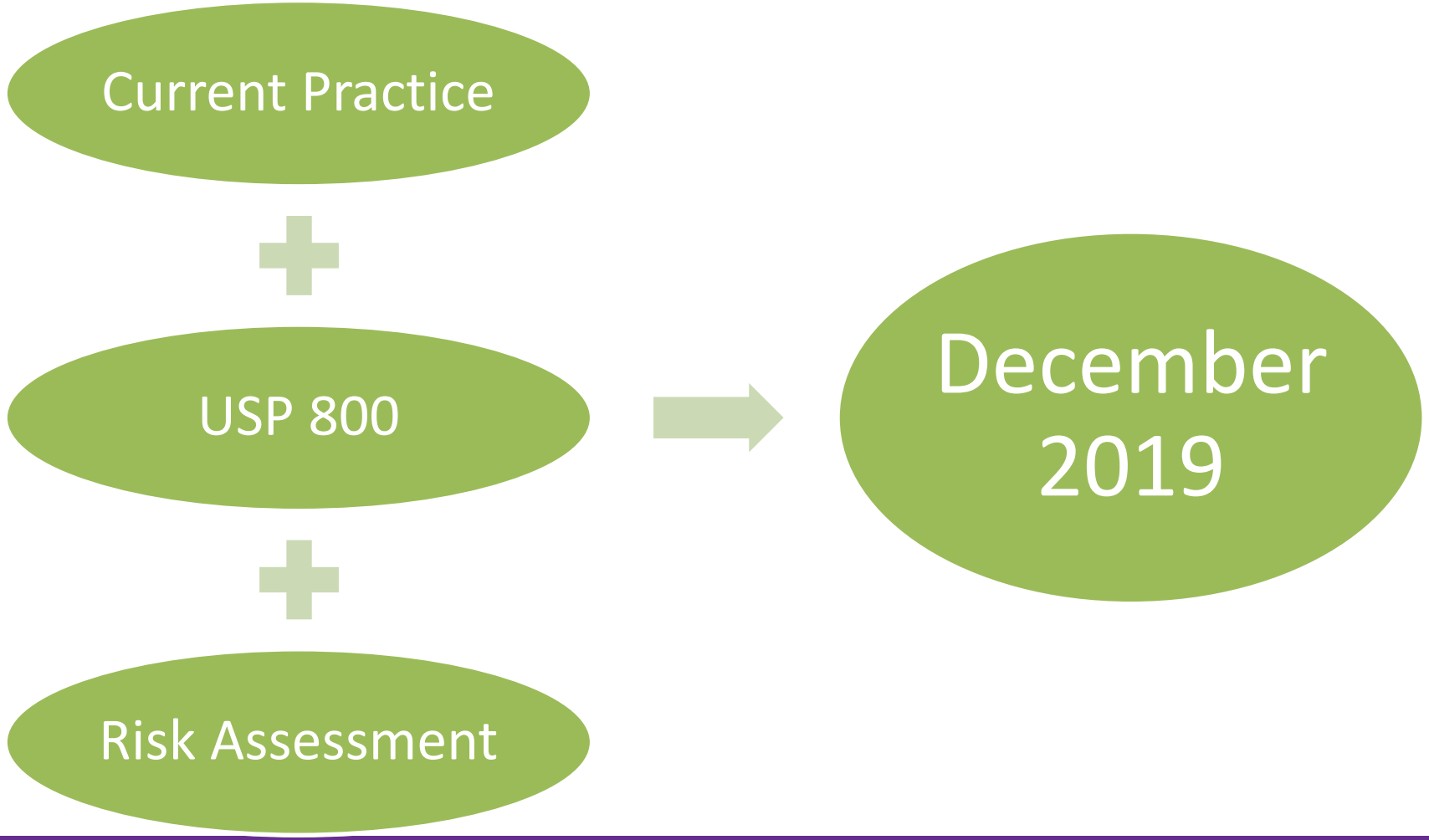
VS



Stronger Together

NIOSH List Inclusion

Memorial Cancer Institute
MEMORIAL REGIONAL HOSPITAL | MEMORIAL HOSPITAL WEST
MEMORIAL AVENTURA GROUP



NIOSH List Inclusion

Memorial Cancer Institute
MEMORIAL REGIONAL HOSPITAL | MEMORIAL HOSPITAL WEST
MEMORIAL AVENTURA GROUP

Antineoplastic drugs	Cytotoxic; Meet one or more NIOSH criteria for HDs; Additional reproductive toxicities to men and women; Occupational hazard to healthcare workers
	Brentuximab, carboplatin, vinblastine
Non-antineoplastic drugs	Meet one or more NIOSH criteria for HDs; Some represent reproductive occupational hazard; Varying degrees of occupational exposure risk
	Dexrazoxane, ganciclovir, phenytoin, tacrolimus
Non-antineoplastic drugs WITH reproductive effects	Primarily meet NIOSH criteria for reproductive hazards; Potential reproductive occupational hazard; Varying degrees of occupational exposure risk
	Oxytocin, valproate, zonisamide

CSTD Conversion

Memorial Cancer Institute
MEMORIAL REGIONAL HOSPITAL | MEMORIAL HOSPITAL WEST
MEMORIAL AVENTURA GROUP

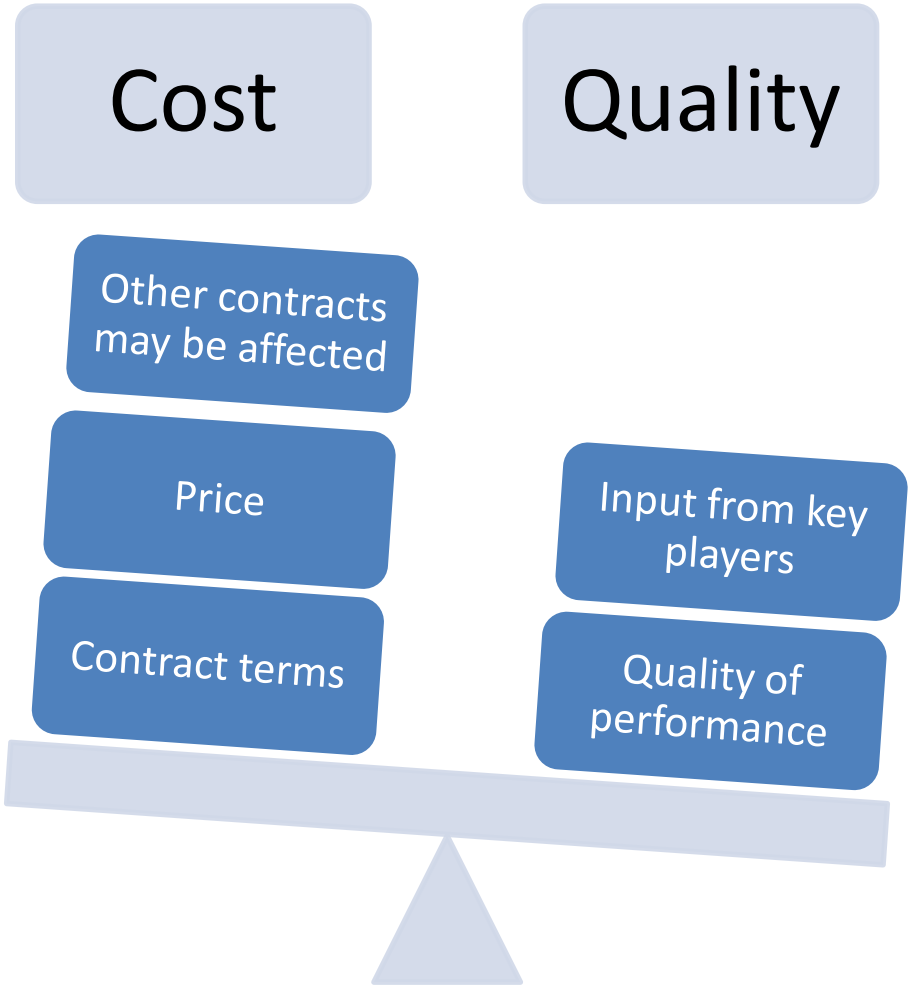
Purchase CSTD Purchase Data
January - September 2019

ALPHABETIC ORDER

ITEM DESCRIPTION	Hospital A	Hospital B	Hospital C	Hospital D	GRAND TOTAL	ANNUALIZED
Bag access port	$300.00	$50.00	$3,000.00	$30,000.00	$33,350.00	$44,466.67
CSTD Male Leur	$20.00	$200.00	$4,000.00	$28,000.00	$32,220.00	$42,960.00
Vial adapter A			$5,000.00	$26,000.00	$31,000.00	$41,333.33
Vial adapter B	$200.00	$2,000.00	$6,000.00	$24,000.00	$32,200.00	$42,933.33
Vial adapter C	$201.00	$2,001.00	$7,000.00	$22,000.00	$31,202.00	$41,602.67
Secondary CSTD filtered line	$202.00	$2,002.00	$8,000.00	$20,000.00	$30,204.00	$40,272.00
Secondary CSTD line			$9,000.00	$18,000.00	$27,000.00	$36,000.00
CSTD spike adapter			$10,000.00	$16,000.00	$26,000.00	$34,666.67
CSTD 10 mL syringe	$600.00		$11,000.00	$14,000.00	$25,600.00	$34,133.33
CSTD 20 mL syringe		$400.00	$12,000.00	$12,000.00	$24,400.00	$32,533.33
CSTD 30 mL syringe	$700.00		$13,000.00	$10,000.00	$23,700.00	$31,600.00
CSTD 3 mL syringe	$300.00	$100.00	$14,000.00	$8,000.00	$22,400.00	$29,866.67
CSTD 5 mL syringe			$15,000.00	$6,000.00	$21,000.00	$28,000.00
CSTD 60 mL syringe			$16,000.00	$4,000.00	$20,000.00	$26,666.67
GRAND TOTAL	$2,523.00	$6,753.00	$133,000.00	$238,000.00	$380,276.00	$507,034.67

CSTD Conversion

Memorial Cancer Institute
MEMORIAL REGIONAL HOSPITAL | MEMORIAL HOSPITAL WEST
MEMORIAL AVENTURA GROUP



CSTD Conversion

Memorial Cancer Institute
MEMORIAL REGIONAL HOSPITAL I MEMORIAL HOSPITAL WEST
MEMORIAL AVENTURA GROUP

CSTD Brand Name (Circle): CSTD A CSTD B CSTD C CSTD D CSTD E

Employee Name: _____ Contact Number: _____

1) During administration of most chemotherapy, the preparation is attached to a secondary line and y-sited to a primary line. Can you show us how the full dose would be administered without pulling from the primary line especially when the dose calls for a filtered secondary line?
    a. Rationale: Many issues arise including delay in infusion with this setup which leads to the patient receiving only the fluid attached to the primary line until the issue is identified.

Response:_____
_____

2) Have you received any complaints or product failure reports regarding leakage or malfunction during compounding and infusion? If so, how many and what were the reports or complaints"
    a. Rational: leakage identified between the secondary line bonded on to the CSTD in addition to the secondary line y-sited to the primary line.

Response:_____
_____

3) For a primary infusion of chemotherapy, is a specific brand of an IV connector required with us of the CSTD?
    Response:_____

CSTD Conversion

Memorial Cancer Institute
MEMORIAL REGIONAL HOSPITAL I MEMORIAL HOSPITAL WEST
MEMORIAL AVENTURA GROUP

Evaluation Question	Evaluation Score 1 Least	2	3	4	5 Highly
Transparency regarding issues experienced at other sites live with their CSTD					
Ease of use for preparation/compounding					
Ease of use during administration					
Bulkiness of equipment for discarding yellow bin					
Safety and perceived ability to contain hazardous vapors					
Ability of CSTD to be used for multiple parenteral routes (SQ/IM, bladder irrigation, IT, IV)					
Recommendation of implementing this CSTD within our system					

Summary

Memorial Cancer Institute
MEMORIAL REGIONAL HOSPITAL | MEMORIAL HOSPITAL WEST
MEMORIAL AVENTURA GROUP

- A testing protocol and process to identify and certify effective CSTDs is needed.
- Standards will be revised to incorporate NIOSH protocol when it becomes available.
- CSTD financial impact is multifactorial including the contract terms and NIOSH list of inclusion.
- Quality may outweigh cost during CSTD implementation or conversion.
- Prior to implementation of the testing protocol, site specific evaluation should include frontline staff and prior knowledge base of workflow issues with the CSTD in question.

Acknowledgement

Memorial Cancer Institute
MEMORIAL REGIONAL HOSPITAL | MEMORIAL HOSPITAL WEST
MEMORIAL AVENTURA GROUP

Financial Impact

Alan H. Mutnick, PharmD, FASHP
Director- Pharmacy Contracting
Memorial Healthcare System

References

Memorial Cancer Institute
MEMORIAL REGIONAL HOSPITAL | MEMORIAL HOSPITAL WEST
MEMORIAL AVENTURA GROUP

1. USP Chapter <800> Hazardous Drugs – Handling in Healthcare Settings. United States Pharmacopeia 42-National Formulary 37.; 2019.
2. Celano P, et al. Safe Handling of Hazardous Drugs: ASCO Standards. J Clin Oncol 37:598-609, 2019.
3. Gurusamy KS, Best LM, Tanguay C, et al: 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 3:CD012860, 2018.
4. National Institute for Occupational Safety and Health: NIOSH Alert: Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings. https://www.cdc.gov/niosh/docs/2004-165/pdfs/2004-165.pdf. Accessed August 28, 2019.
5. National Institute for Occupational Safety and Health: A Performance Test Protocol for Closed System Transfer Devices Used During Pharmacy Compounding and Administration of Hazardous Drugs. https://www.cdc.gov/niosh/docket/review/docket288a/pdfs/APerformanceTestProtocolforClosedSystemTransferDevices.pdf. Accessed September 3, 2019.
6. Connor TH, MacKenzie BA, DeBord DG, Trout DB, O'Callaghan JP. NIOSH list of antineoplastic and other hazardous drugs in healthcare settings, 2016. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, Publication Number 2016-161.
7. Jacobson JO, Polovich M, McNiff KK, et al: American Society of Clinical Oncology/Oncology Nursing Society chemotherapy administration safety standards. J Clin Oncol 27: 5469-5475, 2009