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Activity Objectives

- Explain factors that led to the compounding crisis in October 2012, including lessons learned
- Describe provisions of the Pharmaceutical Quality, Security and Accountability Act (S.959)
- Determine practical approaches for evaluating the pharmacy department's and outsourced compounding pharmacy's compliance with USP Chapter <797>

Activity Objectives

- Describe safety considerations unique to hazardous sterile i.v. preparations
- Describe the role of standardization in all areas of the health system as a means of ensuring i.v. safety
- List potential changes to current processes that could prevent future compounding crises

U.S. Illnesses and Deaths Associated with Compounded Medications-2001-2013

- 20 Pharmacy Compounding Errors
- 1022 Adverse Events
  - 75 deaths
  - New England Compounding Pharmacy: 733 cases and 53 deaths; fungal meningitis and other infections
- Causes
  - Primarily contamination
  - Miscalculations

The Pew Charitable Trusts. Pharmacy Sterile Compounding Summit: Summary of a Stakeholder Meeting. (URL in ref list)

The Pharmaceutical Quality, Security and Accountability Act (S. 959)

- Creation of "compounding manufacturer" regulated by FDA
  - Compounds preparations without or in advance of a prescription
  - Must have a licensed pharmacist directly supervising compounding operations
  - Register with FDA and report drugs sold every 6 months
  - Undergo FDA inspection
  - Report adverse events
  - Label products as compounded drugs and "not for resale"; cannot be sold to wholesalers
  - Cannot be licensed as pharmacies

The Pharmaceutical Quality, Security and Accountability Act (S. 959)

- Hospitals and health-systems are considered "traditional compounders" regulated at state level
- Allows for creation of drugs that cannot be compounded including non-sterile medications
- Creates "track and trace" provisions for electronic tracking to improve supply chain integrity

In the Wake of the Compounding Crisis: Lessons Learned

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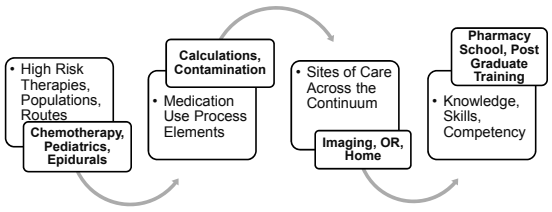
Objectives

- Delineate risk points involving sterile compounded products across the medication use process
- Determine locations where sterile products are given
- Provide recommendations to ensure safety and quality of sterile compounding
- Describe lessons learned from sterile compounding events

Sterile Compounding Complexity and Vulnerability



Risk Points in the Medication Use Process

Selection and Procurement	• Drug Shortages-31 cancer drugs and expect ↑ • Recalls • Concentrations
Prescribing	• Variable orders , dose units and concentrations
Storage	• Beyond Use Dating • Storage outside of Pharmacy
Preparation	• Facility ·Labels ·Outsourcing • Checking processes ·Technology ·Calculations • Personnel competency and compliance
Administering	• Order vs Label vs MAR vs Infusion pump library • Calculations • Concentration vs rate • Point of care activation of IVs

See enlargement p. 34

Risk Points in the Medication Use Process

Risk points include

a. Variable concentrations
b. Drug shortages
c. Labels
d. Staff competency
e. a, c, d
f. All of the above

Errors in Aseptic Product Preparation in UK Hospital Pharmacies, 2004-7

- Rate: 0.49%; 4691 voluntary reports/958,532 products
- Incident reports: majority were near misses; 24 detected during or after administration
- 40% of errors involved adult chemotherapy
- 34.2% of errors due to labeling error
- Impact on patient outcomes
  - 68.6% of errors would not impact patient outcome
  - 18.4% minor impact
  - 0.1% (4 reports of near misses) potentially catastrophic

Bateman R et al. *BMJQS*. 2010; 19:1-6.

Errors in Aseptic Product Preparation in UK Hospital Pharmacies, 2004-7

- Pediatric cytotoxic and parenteral nutrition products were associated with greater levels of perceived patient harm
- Causes
  - Individual staff error (78.1%)
  - Distraction/interruption (4.3%)
  - Workload/staffing (6.3%)
  - Inadequate training (3.7%)

Observational Study of Accuracy in Compounding I.V. Admixtures at 5 Hospitals

- Observations for 5 days at each pharmacy
- Overall mean error rate was 9% (145 /1679 doses), excluding ready-to-use products
  - Mean error rates for individual pharmacies: 6% to 10%
- Wrong-dose errors were the most common type of error
- 2/100 errors were judged to be potentially clinically important based on potential for patient harm
- Observation is the gold standard for evaluating safety of processes

Flynn EA et al. *Am J Health-Syst Pharm*. 1997; 54:904-12.

California Compounding Regulations

- Sterile compounding self-assessment: Required upon pharmacy licensure, change of pharmacist-in-charge, and biannually (odd years)
- Requirement for a documented, ongoing quality assurance program that monitors personnel performance, equipment, and facilities.
- Comprehensive regulations specifically address:

Facility	Policies and procedures
Training and competency	Quality assurance
Recordkeeping	Labeling
Master formulas	Handling cytotoxics
Attire	Preparation from non-sterile powder
Process validation	Quantitative analysis

California Code of Regulations. Title 16 Section 1735. (URL in ref list)
California State Board of Pharmacy. Compounding Drug Products. (URL in ref list)

Do you know all of the sites where sterile products are given?

Health-System Sites of Care

- Traditional Patient Care Units
- Inpatient and Outpatient Procedural and Diagnostic Areas
  - Cath lab
  - Operating Rooms
  - Interventional Radiology
  - Imaging
  - Pain Management
  - Dialysis
- Ambulatory clinics

Sites of Care Across the Continuum

- Home
- Physician offices
- Skilled nursing facilities
- Ambulatory surgery centers
- Pain management clinics

Locations for Sterile Product Administration

Sites of sterile product administration include:

a. Imaging
b. Home
c. Interventional radiology
d. All of the above

Controversies in Sterile Compounding Support the Need for Professional Practice Standards

- Single dose vials
- Overfill
- I.V. preparation activation in pharmacy vs patient care units
- Closed-system transfer devices and beyond use dating
- Priming

Inpatient Challenges with Patient's Own Medications

- Patients on intrathecal pain formulations made with non-sterile powder that run out
- Pulmonary hypertension infusions-patient's own compounding
- Patient receiving parenteral medications from restricted distribution channels that are brought in from home

Knowledge, Skills, Competency

- Only 1 in 6 graduates of pharmacy schools are adequately prepared to perform sterile compounding
  - Evaluation of accuracy of compounding of 2 simple solutions by pharmacy students
    - Solution 1: Only 54% of students prepared medications within 10% of desired concentration; 46% had errors ranging from <75% to >200% of the desired concentration.
    - Solution 2: 78% of students prepared medications within +/-10% of desired concentration, wide range of concentration errors (-89% to 269%).
- Sterile compounding is not an area of focus in most post-graduate training programs
- Technician training programs include sterile compounding, however, hands-on training is not in-depth

Kadi A et al. *Am J Pharm Ed.* 2005; 69:508-15.

Model Sterile Compounding Curriculum

Pediatrics	**Volumes, concentrations, osmolarity**
Chemotherapy	**Doses, regimens, supportive care, routes, rates, hydration, rescue medications**
TPN	**Additives, incompatibilities, osmolarity, automated compounders**
ISMP	**Newsletters and self assessment**
Electrolytes	**Doses, concentration, central vs. peripheral administration**
High-alert Medications	**Rates, routes, concentrations**
Pain Management	**Infusions, PCA and epidurals, opioid dose equivalence, non-sterile powder, concentrations, rates**

See enlargement p. 34

Pharmacy Sterile Compounding Summit

- Needs identified
  - Evidence-based beyond use dating
  - Standardization of orders for compounded sterile products (CSPs)
  - Education and training to improve personnel competency
  - Increase in quality of lab testing
  - Evidence-based, standardized assessment tool for pharmacy inspectors

The Pew Charitable Trusts. Pharmacy Sterile Compounding Summit: Summary of a Stakeholder Meeting. (URL in ref list).

Training and Competency

Training and monitoring ongoing competency of staff is essential to ensure safety and quality of sterile compounded products.

a. True
b. False

I.V. Compounding Risk Assessment

- How are staff trained initially and what is the ongoing process to ensure staff competency?
- How often are staff observed to determine compliance with safe compounding processes?
- Is only one sterile product prepared at a time?
- What quantitative methods are available to validate the accuracy of compounded preparations?

I.V. Compounding Risk Assessment

- What is the process for checking high-alert/high-risk medications?
  - Are pre-checks performed by the pharmacist?
- Do labels support safe compounding? Safe administration?
- What is the process for checking pharmaceutical calculations?
- How often are onsite evaluations of outsource pharmacies conducted?

Professional Imperatives

- Training/Certification/Licensure: All pharmacists and technicians engaged in sterile compounding should be educated, trained for proficiency, certified and licensed to perform this activity
- Ongoing training: Pharmacists and technicians should be required to engage in periodic refresh training to ensure (through testing and verification of preparations) that they sustain knowledge, skills, and abilities

Myers CM. *Am J Health-Syst Pharm*. 2013; 70:e41-54.

Professional Imperatives

- Need for evaluation of current practices across all settings
  - Although tragedies have occurred in large scale compounding pharmacies, "would increased surveillance of hospital and home infusion compounding reveal heretofore undetected lapses that need attention?"
  - "It is time for a systematic assessment of the nature and the dimensions of the problems in every type of setting where sterile compounding occurs."

Myers CM. *Am J Health-Syst Pharm*. 2013; 70:e41-54.

Lessons Learned

- Sterile Compounding is a specialty area that demands advanced knowledge and skills
- Safe use of sterile medications requires assessing risks across the entire medication-use process and throughout the settings where these compounds are administered
- Periodic evaluation of outsourcing processes is essential
- Observation methodology should be utilized to ensure adherence with safe sterile compounding processes

Ensuring Quality and Safety of CSPs

Creating a Culture of Safety: Ensuring the Safe Preparation of Sterile I.V. Products in the Current Environment

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Associate Director of Pharmacy and Infusion Services
The Ohio State University Comprehensive Cancer Center- Arthur G. James Cancer Hospital and Richard J. Solove Research Institute
Columbus, Ohio

Objectives

- Describe strategies that pharmacy departments can employ to cope with increased workload in sterile i.v. preparation and compounding
- Identify practical approaches for evaluating the pharmacy department's and outsourced compounding pharmacy's readiness and compliance with USP Chapter <797>
- Understand the safety considerations unique to hazardous sterile i.v. preparations

Background

- Workload in sterile product preparation areas increased with USP <797>
  - Increased cleaning requirements
  - More elaborate garbing and gowning procedures
  - Complex end-product sterility testing
- Staffing based on production volume may not have changed
  - Decreased efficiency vs. increased workload

Common Breaches in Sterile Technique

- Staff may take shortcuts when compounding
  - Compromising aseptic technique
  - Reusing syringes and vials while compounding
  - Omitting the disinfection steps
    - Gloves every 30 minutes
    - Spraying vials with sterile 70% IPA vs. using alcohol pads
  - Shadowing the critical sites

Strategies for Increased Workload

- Frozen pre-mixed products
- Vial and bag systems
- Outsourcing

Frozen Pre-Mixed Products

PROs	CONs
• Decreased waste • Decreased compounding time • Manufacturer bar coded to facilitate bar code medication administration (BCMA)	• Increased cost • Increased space and time to thaw

Vial and Bag Systems

PROs	CONs
• Decreased waste • Decreased turn around time (stored in patient care areas) • Manufacturer bar coded to facilitate BCMA	• Increased direct cost for device • Potential for error during administration (inactivated vial)

Outsourcing of Compounded Sterile Preparations (CSPs)

Outsourcing of CSPs

- Often used for complex or high risk sterile preparations
- Increased cost
- Liability for the hospital
  - May be the same as the source
- Decreased control over quality assurance

Quality Assurance for Outsourced CSPs

- ASHP Foundation *Outsourcing Sterile Products Preparation: Contractor Assessment Tool*
  - http://www.ashpfoundation.org/sterileproductstool
- Must perform site visits, cannot allow self assessment
  - Tool includes several "Site Visit" questions
- Direct observation of aseptic technique and cleaning is better than reviewing documentation

ASHP Research and Education Foundation. Outsourcing Sterile Products Preparation: Contractor Assessment Tool (URL in ref list)

Quality Assurance of Outsourced CSPs

- Include random and regular announced and unannounced site visits in the contract
  - If resources are not available to perform the visits, consider collaborating with other customers to do alternating visits
- Speak to the outsourcers certifying contractors
  - May be able to give a detailed history of any issues at the facility

Quality Assurance for Insourced CSPs

- Use this same tool for internal operations as well
- Identify neutral party (e.g., another pharmacy leader, epidemiologist, or accreditation lead) to perform the assessment
- Lack of USP <797> compliant facilities does not excuse poor technique
  - "If we don't have a clean room, why should we wear gowns and gloves"

Outsourcing Challenges

Which of the following is a challenge of outsourcing CSPs?

a. Decreased hospital cost per CSP
b. Quality assurance of CSPs
c. Increased workload
d. Decreased hospital liability
e. a and b

Common Challenges with Hazardous Drugs

HD Preparation Demographics

How many Hazardous Drug CSPs does your hospital prepare daily?

a. 0-5
b. 6-20
c. 21-50
d. 51-100
e. 100+

Training Considerations for Hazardous Drugs (HD) as CSPs

- HD as CSPs involve the most complex manipulations of sterile products
- Must maintain negative pressure within the vials at all times
  - Observe the hood for spray after compounding
  - Ask the technicians on the following shift if there is spray left in the PEC

Measuring and Rounding of HD Doses

- Weight-based dosing is often used with HDs
  - May result in doses to two or three decimal places (especially for investigational drugs)
  - These low doses may not be measureable
- Develop a chart for syringe size selection for each preparation dose range
  - May want to include on production label if possible

Priming of Preparations

- HD preparations can create environmental contamination if spiked and primed by nursing
  - Vandenbroucke showed 25% leakage rate upon administration of an HD
- Best practice documents state that pharmacy should prime HD in a PEC
  - ONS Safe Handling of Hazardous Drugs
  - ASHP Guidelines on Handling Hazardous Drugs
  - NIOSH Alert 2004-165

Vandenbroucke J. *EJHP Practice*. 2001; 7(2):60-8.
NIOSH Alert: Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings. (URL in ref list).

Priming of Preparations

- Collaborate with nursing to standardize tubing
  - Secondary set for most HD preparations
  - Primary set for HD preparations where a reaction may occur
  - Special sets (e.g., low sorbing for paclitaxel) where appropriate
- Create a priming chart for pharmacy and nursing cross-referencing HD and tubing
- Consider adding tubing information to pharmacy production or product labels

Sample HD Priming Chart

Drug Generic Name & Form	Trade Name	*Hazardous Drug Group	IV Tubing Set
Aldesleukin	Proleukin	3	Secondary 2C7461
Alemtuzumab	Campath	3	Syringe/IVPB 2426-0500
Arsenic	Trisenox	3	Secondary 2C7461
Asparaginase	Elspar	3	Syringe
Azacitidine	Vidaza	3	Syringe/IVPB 2C7461
Azathioprine (malignant indications)	Imuran	3	Primary 2426-0500
Azathioprine (non-malignant indications)	Imuran	1	Primary 2426-0500

See enlargement p. 35

Administration Set Selection

For which i.v. admixtures would a primary set be most appropriate?

a. Phase 1 study of an investigational agent
b. Intermittent i.v. antibiotic
c. Rituximab
d. Paclitaxel
e. a and c

Priming of Preparations

Do's	Don'ts
• Attach infusion set, prime with base solution, then add drug –OR- • Attach infusion set, add drug, then backflow prime with diluent	• Prime after HD has been added to bag – Unless: • Required by investigational study (e.g., pharmacokinetics) • Part of a desensitization protocol (e.g., carboplatin) • Required for a titration

Reconstitution and Overfill

- Standardize reconstitution procedures
  - Reconstitute from the bag
  - Reconstitute using a separate source of diluent (SWFI, BSNS, etc.)
  - Determine when equivalent volume must be removed from final container (e.g., sodium bicarbonate drips)
- Account for overfill and total volume in the preparation consistently
  - HD
  - Continuous infusions
    - Pressors, heparin, insulin, antiarrhythmics

Proceedings from the ISMP Sterile Preparation Compounding Safety Summit: Guidelines for SAFE Preparation of Sterile Compounds. (URL in ref list).

Additive Volume Offset

What is the appropriate threshold after which volume equal to the additives should be removed from a CSP during compounding?

a. Any amount
b. 5%
c. 10%
d. 50 mL
e. None of the above

Reconstitution and Overfill

- Standardize compounding of exact volume preparations
  - Use syringes/dispensing pump to fill an empty bag
- Validate that the correct preparation technique is used every time
  - Reconstitution- ensure diluent vials are presented with the empty drug vial
  - Total volume- ensure the volume of the preparation additives are correctly represented
  - Exact volume- ensure the syringes used to draw up the base solution are present and volume verified

Drug Vial Optimization (DVO)

- DVO is the use of a single-dose vial for the preparation of multiple preparations
- Consider batching preparations together and standardizing administration times for expensive medications
  - e.g., anti-infectives, long-acting insulins
- Closed-System drug Transfer Devices (CSTDs)
  - Recent FDA 510(k) approval for one device
  - Others have submitted

Closed System Transfer Device DVO Considerations

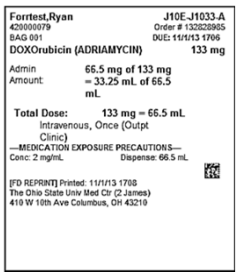
PROs	CONs
• Studies have been published showing sterility using a CSTD at seven days • FDA has approved the 510(k) for at least one product • Decreased waste and significant cost savings may be realized	• Proper aseptic technique is essential for sterility with any CSTD • FDA 510(k) process lacks rigor of drug approval process • Uncertain liability for use of SDVs outside of manufacturer labeling

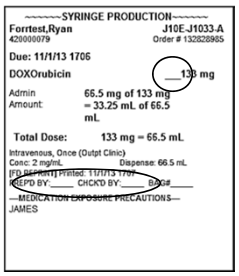
McMichael D et al. *Am J Pharm Benefits*. 2011; 3(1):9-16.
Carey ET et al. *Am J Pharm Benefits.* 2011; 3(6):311-8.

Labels

- Always use a production label with sufficient detail for the compounder
  - Name, volume, and dose of each component
  - Base solution volume
  - Set to be used for priming
  - Special instructions for preparation or auxiliary labeling
- Print a production label for each dose
  - 1:1 ratio helps to ensure instructions are available for each dose when printing a batch
- Require compounders to use the production label and save it for pharmacist verification

Labels


Forrtest,Ryan J10E-J1033-A
420000079 Order # 132828965
BAG 001 DUE: 11/1/13 1706
DOXOrubicin (ADRIAMYCIN) 133 mg
Admin Amount: 66.5 mg of 133 mg = 33.25 mL of 66.5 mL
Total Dose: 133 mg = 66.5 mL
Intravenous, Once (Outpt Clinic)
---MEDICATION EXPOSURE PRECAUTIONS---
Conc: 2 mg/mL Dispense: 66.5 mL
[FD REPRINT] Printed: 11/1/13 1708
The Ohio State Univ Med Ctr (2 James)
410 W 10th Ave Columbus, OH 43210


~~~~~~SYRINGE PRODUCTION~~~~~~
Forrtest,Ryan J10E-J1033-A
420000079 Order # 132828965
Due: 11/1/13 1706
DOXOrubicin 133 mg
Admin Amount: 66.5 mg of 133 mg = 33.25 mL of 66.5 mL
Total Dose: 133 mg = 66.5 mL
Intravenous, Once (Outpt Clinic)
Conc: 2 mg/mL Dispense: 66.5 mL
[FD REPRINT] Printed: 11/1/13 1709
CHECPD BY:_____ CHCKD BY:_____ BAG#_____
---MEDICATION EXPOSURE PRECAUTIONS---
JAMES

See enlargement p. 35
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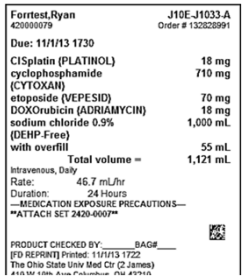
Labels



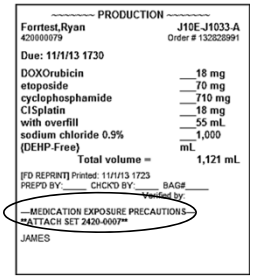
Forrtest,Ryan J10E-J1033-A
420000079 Order # 132828991

Due: 11/1/13 1730

CISplatin (PLATINOL)	18 mg
cyclophosphamide (CYTOXAN)	710 mg
etoposide (VEPESID)	70 mg
DOXOrubicin (ADRIAMYCIN)	18 mg
sodium chloride 0.9% (DEHP-Free)	1,000 mL
with overfill	55 mL
Total volume =	1,121 mL

Intravenous, Daily
Rate: 46.7 mL/hr
Duration: 24 Hours
—MEDICATION EXPOSURE PRECAUTIONS—
ATTACH SET 2420-0007

PRODUCT CHECKED BY:_____BAG#____
[FD REPRINT] Printed: 11/1/13 1722
The Ohio State Univ Med Ctr (2 James)



~~~~~~~ PRODUCTION ~~~~~~~
Forrtest,Ryan J10E-J1033-A
420000079 Order # 132828991

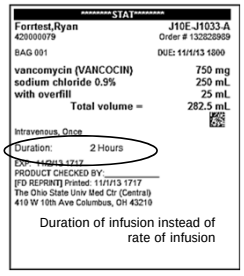
Due: 11/1/13 1730

DOXOrubicin	___18 mg
etoposide	___70 mg
cyclophosphamide	___710 mg
CISplatin	___18 mg
with overfill	___55 mL
sodium chloride 0.9% (DEHP-Free)	___1,000 mL
Total volume =	1,121 mL

[FD REPRINT] Printed: 11/1/13 1723
PREP'D BY:_____ CHCK'D BY:_____ BAG#____
Verified by:
—MEDICATION EXPOSURE PRECAUTIONS—
ATTACH SET 2420-0007
JAMES

See enlargement p. 36

Labels



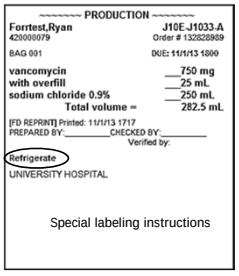
********STAT********
Forrtest,Ryan J10E-J1033-A
420000079 Order # 132828989

BAG 001 DUE: 11/1/13 1800

vancomycin (VANCOCIN)	750 mg
sodium chloride 0.9%	250 mL
with overfill	25 mL
Total volume =	282.5 mL

Intravenous, Once
Duration: 2 Hours
EXP: 11/2/13 1717
PRODUCT CHECKED BY:_____
[FD REPRINT] Printed: 11/1/13 1717
The Ohio State Univ Med Ctr (Central)
410 W 10th Ave Columbus, OH 43210

Duration of infusion instead of rate of infusion



~~~~~~~ PRODUCTION ~~~~~~~
Forrtest,Ryan J10E-J1033-A
420000079 Order # 132828989

BAG 001 DUE: 11/1/13 1800

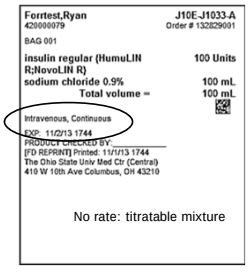
vancomycin	___750 mg
with overfill	___25 mL
sodium chloride 0.9%	___250 mL
Total volume =	282.5 mL

[FD REPRINT] Printed: 11/1/13 1717
PREPARED BY:_____CHECKED BY:_____
Verified by:
Refrigerate
UNIVERSITY HOSPITAL

Special labeling instructions

See enlargement p. 36

Labels



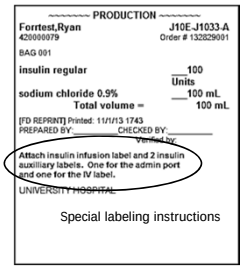
Forrtest,Ryan J10E-J1033-A
420000079 Order # 132829001

BAG 001

insulin regular (HumuLIN R;NovoLIN R)	100 Units
sodium chloride 0.9%	100 mL
Total volume =	100 mL

Intravenous, Continuous
EXP: 11/2/13 1744
PRODUCT CHECKED BY:_____
[FD REPRINT] Printed: 11/1/13 1744
The Ohio State Univ Med Ctr (Central)
410 W 10th Ave Columbus, OH 43210

No rate: titratable mixture



~~~~~~~ PRODUCTION ~~~~~~~
Forrtest,Ryan J10E-J1033-A
420000079 Order # 132829001

BAG 001

insulin regular	___100 Units
sodium chloride 0.9%	___100 mL
Total volume =	100 mL

[FD REPRINT] Printed: 11/1/13 1743
PREPARED BY:_____CHECKED BY:_____
Verified by:
Attach insulin infusion label and 2 insulin auxiliary labels. One for the admin port and one for the IV label.
UNIVERSITY HOSPITAL

Special labeling instructions

See enlargement p. 37
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Nursing Considerations for HD CSPs

Programming of Pumps

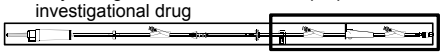
- Nursing needs clear direction and standardization on how to program the pump
  - Enter the volume on the label
  - Enter a volume less than that of the label
    - So the pump will stop before air is detected
    - Allows the nurse to observe the final infusion
  - Enter the rate on the label and stop after the infuse over time
    - Potentially under-doses the patient for intermittent i.v. infusions

Flushing of Preparations

- I.V. tubing may contain 10-25 mL of volume
- Must consider total volume of container when choosing
- Secondary sets:
  - Should specify which port is used on the primary line (i.e., above the pump)
- Primary sets:
  - More complicated flushing procedures

Flushing of Preparations

- Primary set flushing:
  - Stopping pump when air is just above the pump means under infusion ~10-15 mL
    - May be significant if a low volume preparation or an investigational drug



  - Flushing with base solution in port below the pump may result in a bolus dose
    - Example: Pump rate @ 10 mL/hr; I.V. set contains 6 mL below the pump
  - Hang secondary flush bag by gravity

See enlargement p. 37

Discontinuation of I.V. HDs

- Administration set should be assembled so that the entire set can be removed after administration is complete
  - Easier in the outpatient setting
  - Leave the HD IVPB connected until all ports are full
- CSTD use will allow the nurse to safely disconnect a HD

Flushing of Preparations

Primary and secondary sets are flushed the same way after administration of a HD.

a. True
b. False

Conclusions

- There are many considerations for ensuring the safety of CSPs.
- Outsourced CSPs may be an answer to workload challenges, but they require due diligence.
- HD as CSPs have their own safety concerns that must be considered.
- Standardization of processes within pharmacy and nursing is necessary for safety.

Looking Ahead: Potential Changes and the Role of Standardization in Prevention of Future Mishaps

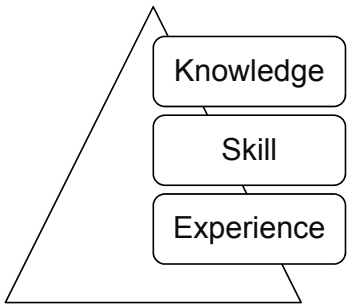
Patricia C. Kienle, M.P.A., B.S.Pharm., FASHP
Director, Accreditation and Medication Safety
Cardinal Health Innovative Delivery Solutions
Laflin, Pennsylvania

What's Most Important?

Which of the following is the most important element in creating a safe sterile compounding system?

a. Knowledge
b. Skill
c. Experience

Balance of Elements



What We Know

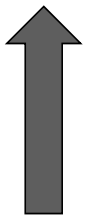
- Standards
- Best practices
- Compounding tragedy of 2012
- USP
- ASHP and others
- Public information

Elements to Prevent Mishaps

- Follow standards
- Improve best practices
- Include key quality tenets in our processes

Standardization

- Manufactured products
- Outsourced compounds
- Batches mixed in-house
- One-offs
  - Clinical need
  - Inertia



ASHP I.V. Safety Summit

Proposed Actions Regulatory and Statutory

- Require nationally standardized infusion concentrations
- Require total content and volume on i.v. preparations
- Require standardization and distinct connections for enteral, i.v., epidural, and intrathecal administration devices
- Request expedited FDA approval for additional concentrations

Proposed Actions Industry

- Manufacture infusions of commonly used medications in a range of standardized concentrations appropriate to selected populations

ISMP Sterile Preparation Compounding Safety Summit

- Proceedings from the ISMP Sterile Preparation Compounding Safety Summit: Guidelines for SAFE Preparation of Sterile Compounds

URL in ref list

ISMP Consensus Statements

- Establish SOPs with sufficient detail
- Standardize work flow processes
  - Quality control
  - Process change control
  - Documentation
- Use commercially-available premixes
- Standardize base solutions used
- Establish standard formulas

Standardization

- Products and preparations
- Personnel
- Medication administration

Products and Preparations

- Identify national and organizational standards
  - Drugs
  - Base solutions
  - Concentrations
- Question why your standard differs from others

High Risk I.V. Med Dose Limits

- Medication
- Dosing stops
  - Minimum
  - Soft
  - Hard
- Safety recommendations

URL in ref list

Locations of CSPs

- Inpatient nursing units
- Procedural areas
  - Surgical services
  - Cardiac cath lab
  - Interventional radiology
- Ambulatory areas
  - Dialysis
  - Ophthalmology

Standardizing Heparin

How many standard heparin concentrations do you have in your organization?

a. One
b. Two
c. More than two

Heparin

- Heparin 25,000 units in 250 mL or 500 mL
- Heparin 1,000 units in 500 mL
- Other?

Standardizing Oxytocin

Our organization has standardized oxytocin as …

a. 20 units in 1000 mL
b. 30 units in 500 mL
c. Something else
d. No standard established

Professional Standards

- Specialty medical associations provide guidance for some procedures
- ACOG: Optimizing Protocols in Obstetrics
- Are you aware of the procedures used in your organization?

The American Congress of Obstetricians and Gynecologists. Optimizing Protocols in Obstetrics: Oxytocin for Induction. (URL in ref list)

Imaging Areas

- Cardiac cath lab
- Interventional Radiology
- Nuclear Medicine
  - Radiopharmaceuticals
  - Adjunct medications
- Heparin for flush
- Nitroglycerin
- Sincalide
- Dobutamine

Other Procedural Areas

- Intravenous and other routes
- Dialysis
  - Preparation of heparin syringes for packing catheters
- Ophthalmology
  - Mixing multiple ophthalmic solutions for administration to multiple patients

Personnel

- Competence
  - Training
  - Ability to comply with organizational-specific expectations
- Standards → your policies and procedures
- Incorporate
  - USP and state standards
  - Best practices
  - Forms that match policies

Key Elements to Include

- Compounding supervisor
  - Provides oversight and monitoring
  - Limits process variation
- Completion of USP <797> required tests
  - Media fill
  - Gloved fingertip sampling
  - Surface sampling

Medication Administration

Med Use Cycle

- Order entry
- Order review
- Dispensing
  - I.V. labels match MAR view
- Administration
  - Drug libraries
  - Smart pump screens
  - Volume to be infused (VTBI)

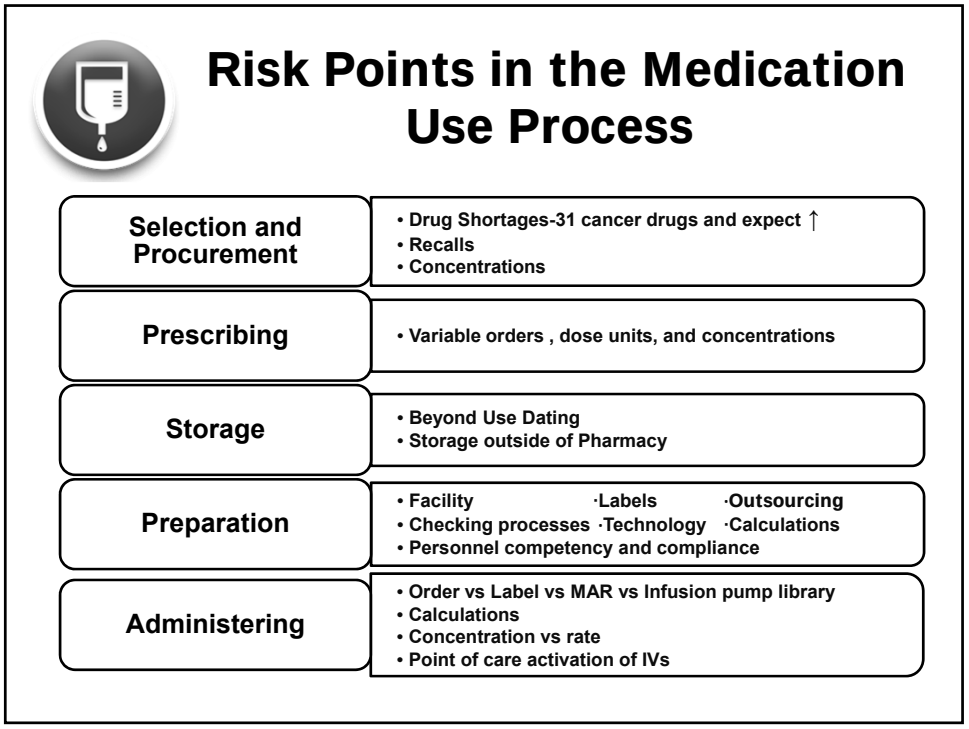
Action Steps

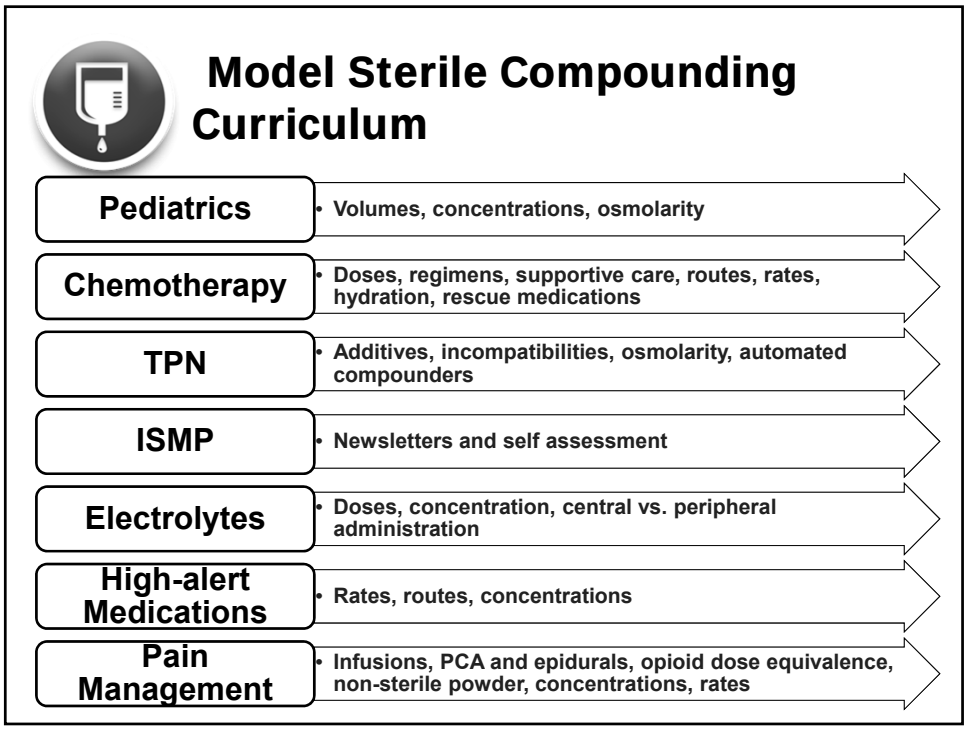
- Determine standards for common meds
- Investigate CSP preparation and use in all areas of your health system
- Lock down policies, procedures, and forms
- Examine all med-related documents to ensure consistency
- Structure sterile preparation process

What's Next?

- Elevate sterile compounding to the key service it represents
- Infuse safety and efficacy into new technology
- Assess potential failure modes when new processes are introduced

Contemporary sterile compounding services are essential elements for the safety of our patients

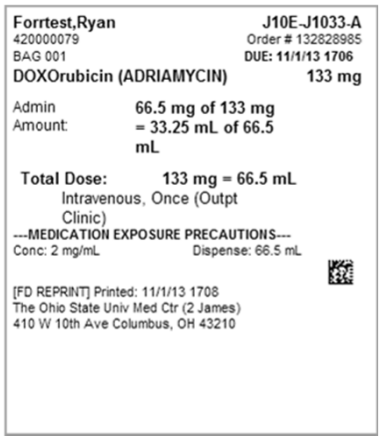

Risk Points in the Medication Use Process
Selection and Procurement
• Drug Shortages-31 cancer drugs and expect ↑
• Recalls
• Concentrations
Prescribing
• Variable orders , dose units, and concentrations
Storage
• Beyond Use Dating
• Storage outside of Pharmacy
Preparation
• Facility ·Labels ·Outsourcing
• Checking processes ·Technology ·Calculations
• Personnel competency and compliance
Administering
• Order vs Label vs MAR vs Infusion pump library
• Calculations
• Concentration vs rate
• Point of care activation of IVs

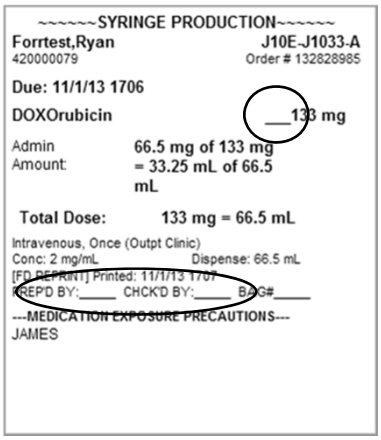

Model Sterile Compounding Curriculum
Pediatrics
• Volumes, concentrations, osmolarity
Chemotherapy
• Doses, regimens, supportive care, routes, rates, hydration, rescue medications
TPN
• Additives, incompatibilities, osmolarity, automated compounders
ISMP
• Newsletters and self assessment
Electrolytes
• Doses, concentration, central vs. peripheral administration
High-alert Medications
• Rates, routes, concentrations
Pain Management
• Infusions, PCA and epidurals, opioid dose equivalence, non-sterile powder, concentrations, rates

Sample HD Priming Chart

Drug Generic Name & Form	Trade Name	*Hazardous Drug Group	IV Tubing Set
Aldesleukin	Proleukin	3	Secondary 2C7461
Alemtuzumab	Campath	3	Syringe/IVPB 2426-0500
Arsenic	Trisenox	3	Secondary 2C7461
Asparaginase	Elspar	3	Syringe
Azacitidine	Vidaza	3	Syringe/IVPB 2C7461
Azathioprine (malignant indications)	Imuran	3	Primary 2426-0500
Azathioprine (non-malignant indications)	Imuran	1	Primary 2426-0500

Labels


Forrtest,Ryan J10E-J1033-A
420000079 Order # 132828985
BAG 001 DUE: 11/1/13 1706
DOXOrubicin (ADRIAMYCIN) 133 mg
Admin Amount: 66.5 mg of 133 mg = 33.25 mL of 66.5 mL
Total Dose: 133 mg = 66.5 mL
Intravenous, Once (Outpt Clinic)
---MEDICATION EXPOSURE PRECAUTIONS---
Conc: 2 mg/mL Dispense: 66.5 mL
[FD REPRINT] Printed: 11/1/13 1708
The Ohio State Univ Med Ctr (2 James)
410 W 10th Ave Columbus, OH 43210


~~~~~~SYRINGE PRODUCTION~~~~~~
Forrtest,Ryan J10E-J1033-A
420000079 Order # 132828985
Due: 11/1/13 1706
DOXOrubicin ___133 mg
Admin Amount: 66.5 mg of 133 mg = 33.25 mL of 66.5 mL
Total Dose: 133 mg = 66.5 mL
Intravenous, Once (Outpt Clinic)
Conc: 2 mg/mL Dispense: 66.5 mL
[FD REPRINT] Printed: 11/1/13 1707
PREP'D BY:____ CHCK'D BY:____ BAG#____
---MEDICATION EXPOSURE PRECAUTIONS---
JAMES
~~~~~~

Labels

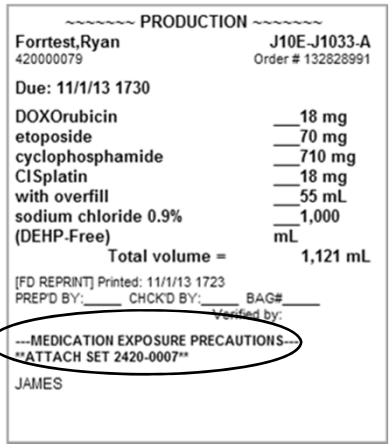
Forrtest,Ryan J10E-J1033-A
420000079 Order # 132828991

Due: 11/1/13 1730

CISplatin (PLATINOL)	18 mg
cyclophosphamide (CYTOXAN)	710 mg
etoposide (VEPESID)	70 mg
DOXOrubicin (ADRIAMYCIN)	18 mg
sodium chloride 0.9% (DEHP-Free)	1,000 mL
with overfill	55 mL
Total volume =	1,121 mL

Intravenous, Daily
Rate: 46.7 mL/hr
Duration: 24 Hours
---MEDICATION EXPOSURE PRECAUTIONS---
ATTACH SET 2420-0007

PRODUCT CHECKED BY:_____BAG#___
[FD REPRINT] Printed: 11/1/13 1722
The Ohio State Univ Med Ctr (2 James)
410 W 10th Ave Columbus, OH 43210



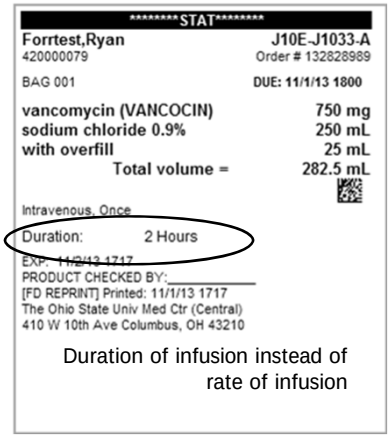
~~~~~~~ PRODUCTION ~~~~~~~
Forrtest,Ryan J10E-J1033-A
420000079 Order # 132828991

Due: 11/1/13 1730

DOXOrubicin	___18 mg
etoposide	___70 mg
cyclophosphamide	___710 mg
CISplatin	___18 mg
with overfill	___55 mL
sodium chloride 0.9% (DEHP-Free)	___1,000 mL
Total volume =	1,121 mL

[FD REPRINT] Printed: 11/1/13 1723
PREP'D BY:_____ CHCK'D BY:_____ BAG#_____
Verified by:
---MEDICATION EXPOSURE PRECAUTIONS---
ATTACH SET 2420-0007
JAMES

Labels



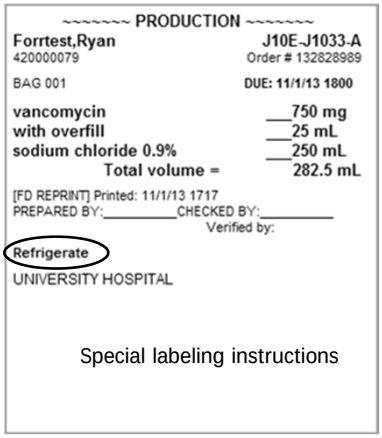
********STAT********
Forrtest,Ryan J10E-J1033-A
420000079 Order # 132828989

BAG 001 DUE: 11/1/13 1800

vancomycin (VANCOCIN)	750 mg
sodium chloride 0.9%	250 mL
with overfill	25 mL
Total volume =	282.5 mL

Intravenous, Once
Duration: 2 Hours
EXP: 11/2/13 1717
PRODUCT CHECKED BY:_____
[FD REPRINT] Printed: 11/1/13 1717
The Ohio State Univ Med Ctr (Central)
410 W 10th Ave Columbus, OH 43210

Duration of infusion instead of rate of infusion



~~~~~~~ PRODUCTION ~~~~~~~
Forrtest,Ryan J10E-J1033-A
420000079 Order # 132828989

BAG 001 DUE: 11/1/13 1800

vancomycin	___750 mg
with overfill	___25 mL
sodium chloride 0.9%	___250 mL
Total volume =	282.5 mL

[FD REPRINT] Printed: 11/1/13 1717
PREPARED BY:_____CHECKED BY:_____
Verified by:
Refrigerate
UNIVERSITY HOSPITAL

Special labeling instructions

Labels

Forrtest,Ryan J10E-J1033-A
420000079 Order # 132829001
BAG 001
insulin regular (HumuLIN R;NovoLIN R) 100 Units
sodium chloride 0.9% 100 mL
Total volume = 100 mL
Intravenous, Continuous
EXP: 11/2/13 1744
PRODUCT CHECKED BY:_____
[FD REPRINT] Printed: 11/1/13 1744
The Ohio State Univ Med Ctr (Central)
410 W 10th Ave Columbus, OH 43210

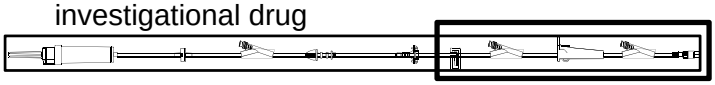
No rate: titratable mixture

~~~~~~~ PRODUCTION ~~~~~~~
Forrtest,Ryan J10E-J1033-A
420000079 Order # 132829001
BAG 001
insulin regular ___100 Units
sodium chloride 0.9% ___100 mL
Total volume = 100 mL
[FD REPRINT] Printed: 11/1/13 1743
PREPARED BY:_____CHECKED BY:_____
Verified by:
Attach insulin infusion label and 2 insulin auxilliary labels. One for the admin port and one for the IV label.
UNIVERSITY HOSPITAL

Special labeling instructions

Flushing of Preparations

- Primary set flushing:
  - Stopping pump when air is just above the pump means under infusion ~10-15 mL
    - May be significant if a low volume preparation or an investigational drug



  - Flushing with base solution in port below the pump may result in a bolus dose
    - Example: Pump rate @ 10 mL/hr; I.V. set contains 6 mL below the pump
  - Hang secondary flush bag by gravity
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