Crucial Considerations to Ensure the Safety of I.V. Therapy

Presented as a Midday Symposium and Live Webcast at the 48th ASHP Midyear Clinical Meeting and Exhibition

Tuesday, December 10, 2013
Orlando, Florida

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Agenda

11:30 a.m. – 11:40 a.m.  **Welcome and Introductions**  
Rita Shane, Pharm.D., FASHP, FCSHP, *Activity Chair*

11:40 a.m. – 12:15 p.m.  **In the Wake of the Compounding Crisis: Lessons Learned**  
Rita Shane, Pharm.D., FASHP, FCSHP

12:15 p.m. – 12:45 p.m.  **Creating a Culture of Safety: Ensuring the Safe Preparation of Sterile I.V. Products in the Current Environment**  
Ryan A. Forrey, Pharm.D., M.S.

12:45 p.m. – 1:15 p.m.  **Looking Ahead: Potential Changes and the Role of Standardization in the Prevention of Future Mishaps**  
Patricia C. Kienle, M.P.A., B.S.Pharm., FASHP

1:15 p.m. – 1:30 p.m.  **Faculty Discussion and Audience Questions**

Faculty

Rita Shane, Pharm.D., FASHP, FCSHP, *Activity Chair*  
Director, Pharmacy Services  
Cedars-Sinai Medical Center  
Assistant Dean, Clinical Pharmacy  
UCLA School of Pharmacy  
Los Angeles, California

Ryan A. Forrey, Pharm.D., M.S.  
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

Patricia C. Kienle, M.P.A., B.S.Pharm., FASHP  
Director, Accreditation and Medication Safety  
Cardinal Health Innovative Pharmacy Solutions  
Laflin, Pennsylvania
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- Ryan A. Forrey, Pharm.D., M.S., has been a customer advisory board participant for InfuSystem.
- Patricia C. Kienle, M.P.A., B.S.Pharm., FASHP, is an employee and stockholder of Cardinal Health.

The following faculty and planners report no relationships pertinent to this activity:

- Rita Shane, Pharm.D., FASHP, FCSHP
- Kristi Hofer, Pharm.D.
- Catherine Klein, B.S.Pharm

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Crucial Considerations to Ensure the Safety of I.V. Therapy

Activity Overview

I.V. safety is an ongoing concern in the health system. This educational activity will review factors, including increased complexity of parenteral medications across health-system settings and the inordinate number of drug shortages, which contributed to the compounding crisis last year. Practical approaches to managing increased workload in sterile i.v. preparation and compounding will be reviewed. Additionally, ensuring a patient-centered approach to i.v. therapy safety is essential as patients transition across different levels of care both within and outside the acute care setting. Standardization of i.v. therapies is a crucial strategy to improve i.v. safety. The activity will conclude with a discussion of possible changes to current processes that might prevent future catastrophes.

Learning Objectives

At the conclusion of this application-based educational activity, participants should be able to

- 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 readiness and compliance with USP Chapter <797> standards.
- Describe the 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.
Continuing Education Accreditation

The American Society of Health-System Pharmacists is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education. This activity provides 2 hours (0.2 CEUs) of continuing pharmacy education credit (ACPE activity # 0204-0000-13-485-L05-P).

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3. Click on My Learning Activities. Then click on 2013 – Midyear Clinical Meeting & Exhibition (Orlando, FL) under Conferences.

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6. Click on the name of a session and complete the requirements for the session.

7. Click Claim Credit for your profession. It is important that you select the correct profession.
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**Pharmacists and Pharmacy Technicians:** To process your CE on the eLearning Portal, you must enter your NABP e-Profile ID and birth month and date. After you have entered this information once it is saved for future CE processing. You may obtain your eProfile ID at www.nabp.net.

*There may be different directions for workshops and review courses.*

| Date of Activity: Tuesday December 10, 2013 | Attendance Code: M _ _ _ _ _ | CPE Hours: 2.0 |

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[www.asphadvantage.com/2cpe-iv](http://www.asphadvantage.com/2cpe-iv)
Rita Shane, Pharm.D., FASHP, FCSHP
Director, Pharmacy Services
Cedars-Sinai Medical Center
Assistant Dean, Clinical Pharmacy
UCSF School of Pharmacy
Los Angeles, California

Rita Shane, Pharm.D., FASHP, FCSHP, is Director of Pharmacy Services at Cedars-Sinai Medical Center, a 950-bed acute, tertiary care, teaching institution in Los Angeles, California, and Assistant Dean, Clinical Pharmacy Services, at the University of California, San Francisco (UCSF), School of Pharmacy.

Dr. Shane has been recognized for her passion for the profession. Most recently, she received the 2012 Harvey A. K. Whitney Award. She is also the recipient of the 2007 California Society of Health-System Pharmacists (CSHP) Pharmacist of the Year Award and the 2007 Distinguished Service Award from the American Society of Health-System Pharmacists (ASHP) Section of Pharmacy Practice Managers. Dr. Shane was the 2005 recipient of the ASHP Distinguished Leadership Award and the 1995 recipient of the John Webb Visiting Professorship in Hospital Pharmacy for management excellence.

Dr. Shane is a co-investigator in two research studies in collaboration with the UCSF School of Pharmacy and approved by the California State Board of Pharmacy to demonstrate the safety and importance of allowing technicians to check technician-filled medication cassettes in hospitals. She also worked collaboratively with CSHP to author language in support of this regulatory change which was approved by the State of California effective in January 2007. Dr. Shane was co-investigator of a 2000 National Patient Safety Foundation Research Award to study the impact of dedicated medication nurses on the rate of medication administration errors in a randomized, controlled trial, the results of which were subsequently published in the Archives of Internal Medicine.

Dr. Shane recently served as the United States facilitator at the Global Conference on the Future of Hospital Pharmacy held during the 68th Congress of the International Pharmaceutical Federation and was responsible for reviewing the international literature on the subject of medication administration. She is an investigator in a multicenter study of medications errors recovered by emergency department pharmacists which was published in the Annals of Emergency Medicine. Throughout her career, Dr. Shane has participated on committees and task forces at the state and national level. She recently was a member of the American Hospital Association Committee on Health Professions and the National Quality Forum Patient Safety Advisory Committee. She is the ASHP representative to The Joint Commission Hospital Professional Technical Committee. She has presented at local, state, national, and international meetings and has published a number of papers in the pharmacy literature including one of the background papers for the recent ASHP Pharmacy Practice Model Summit.
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

Rita Shane, Pharm.D., FASHP, FCSHP
Director, Pharmacy Services
Cedars-Sinai Medical Center
Assistant Dean, Clinical Pharmacy
UCSF School of Pharmacy

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
  - Personal 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. 21

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
  - 88.6% of errors would not impact patient outcome
  - 18.4% minor impact
  - 0.1% (4 reports of near misses) potentially catastrophic

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


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
- Dialysis
- Imaging
- Pain Management
- 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


Model Sterile Compounding Curriculum

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

See enlargement p. 21

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

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.


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.”


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

- Leadership
- Personnel
- Processes
- Facility/Environment
- Training
- Monitoring
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
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Preparation
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- Labels
- Outsourcing
- Checking processes
- Technology
- Calculations
- Personnel competency and compliance

Administering
- Order vs Label vs MAR vs Infusion pump library
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Pediatrics
- Volumes, concentrations, osmolarity

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- Doses, regimens, supportive care, routes, rates, hydration, rescue medications

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- Doses, concentration, central vs. peripheral administration

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- Infusions, PCA and epidurals, opioid dose equivalence, non-sterile powder, concentrations, rates
Ryan A. Forrey, Pharm.D., M.S.
Associate Director of Pharmacy
The Ohio State University Comprehensive Cancer Center
James Cancer Hospital and Solove Research Institute
Clinical Assistant Professor
College of Pharmacy
The Ohio State University
Columbus, Ohio

Ryan A. Forrey, Pharm.D., M.S., is Associate Director, Department of Pharmacy, at The Ohio State University Comprehensive Cancer Center-James Cancer Hospital and Solove Research Institute (OSUCCC-James), and Clinical Assistant Professor at The Ohio State University (OSU) College of Pharmacy, Columbus, Ohio. He received his Doctor of Pharmacy degree from the University of Arizona College of Pharmacy and completed a PGY1 and PGY2 combined residency in health-system pharmacy and Masters of Science in health-system pharmacy administration at The Ohio State University.

Dr. Forrey has published articles in the field of clinical pharmacy, with emphasis on medication errors and prevention and the safe handling of hazardous drugs. He has presented on numerous topics, including USP Chapter <797>, hazardous medication handling and preparation, pharmaceutical waste management, and other related issues affecting pharmacy practice today. In his position at OSU, he is responsible for the pharmacy operations of the inpatient cancer hospital and five hospital-based ambulatory chemotherapy infusion clinics. These sterile product areas prepare over 65,000 doses of chemotherapy annually.

Dr. Forrey also teaches graduate-level courses in pharmacy management and clean room design at the OSU College of Pharmacy, and serves as a preceptor for the Health-System Pharmacy Administration Residency Program at The Ohio State University Wexner Medical Center. He actively participates in professional pharmacy organizations at the local, state, and national levels, and has served on several executive committees of national and state organizations.
Creating a Culture of Safety: Ensuring the Safe Preparation of Sterile I.V. Products in the Current Environment

Ryan A. Forrey, Pharm.D., M.S.
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

<table>
<thead>
<tr>
<th>PROs</th>
<th>CONs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased waste</td>
<td>Increased cost</td>
</tr>
<tr>
<td>Decreased compounding time</td>
<td>Increased space and time to thaw</td>
</tr>
<tr>
<td>Manufacturer bar coded to facilitate bar code medication administration (BCMA)</td>
<td></td>
</tr>
</tbody>
</table>
Vial and Bag Systems

**PROs**
- Decreased waste
- Decreased turn around time (stored in patient care areas)
- Manufacturer bar coded to facilitate BCMA

**CONs**
- Increased direct cost for device
- Potential for error during administration (inactivated vial)

Outsourcing of Compounded Sterile Preparations (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

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

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

<table>
<thead>
<tr>
<th>Drug Generic Name &amp; Form</th>
<th>Trade Name</th>
<th>*Hazardous Drug Group</th>
<th>IV Tubing Set</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aldesleukin</td>
<td>Proleukin</td>
<td>3</td>
<td>Secondary 2C7461</td>
</tr>
<tr>
<td>Alemtuzumab</td>
<td>Campath</td>
<td>3</td>
<td>Syringe/IVP 2426-0500</td>
</tr>
<tr>
<td>Arsenic</td>
<td>Tresmox</td>
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<td>Secondary 2C7461</td>
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<td>Vidaza</td>
<td>3</td>
<td>Syringe/IVP 2426-0500</td>
</tr>
<tr>
<td>Azathioprine (malignant indications)</td>
<td>Imuran</td>
<td>3</td>
<td>Primary 2426-0950</td>
</tr>
<tr>
<td>Azathioprine (non-malignant indications)</td>
<td>Imuran</td>
<td>1</td>
<td>Primary 2426-0950</td>
</tr>
</tbody>
</table>

See enlargement p. 37

### 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**
- Attach infusion set, prime with base solution, then add drug –OR–
- Attach infusion set, add drug, then backflow prime with diluent

**Don’ts**
- 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

**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**
- 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

**CONs**
- 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

Labels

• Always use a production label with sufficient detail for the compounding:
  – 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

See enlargement p. 37

See enlargement p. 38
Labels

Duration of infusion instead of rate of infusion

Special labeling instructions

See enlargement p. 38

Labels

No rate: titratable mixture

Special labeling instructions

See enlargement p. 39

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 IVs

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. 39
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.
Sample HD Priming Chart

<table>
<thead>
<tr>
<th>Drug Generic Name &amp; Form</th>
<th>Trade Name</th>
<th>*Hazardous Drug Group</th>
<th>IV Tubing Set</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aldesleukin</td>
<td>Proleukin</td>
<td>3</td>
<td>Secondary 2C7461</td>
</tr>
<tr>
<td>Alemtuzumab</td>
<td>Campath</td>
<td>3</td>
<td>Syringe/IVPB 2426-0500</td>
</tr>
<tr>
<td>Arsenic</td>
<td>Trisenox</td>
<td>3</td>
<td>Secondary 2C7461</td>
</tr>
<tr>
<td>Asparaginase</td>
<td>Elspar</td>
<td>3</td>
<td>Syringe</td>
</tr>
<tr>
<td>Azacitidine</td>
<td>Vidaza</td>
<td>3</td>
<td>Syringe/IVPB 2C7461</td>
</tr>
<tr>
<td>Azathioprine (malignant indications)</td>
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</tr>
</tbody>
</table>

Labels

[Foto of labels with text and barcodes]
Special labeling instructions

Duration of infusion instead of rate of infusion
**Flushed 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
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Patricia C. Kienle, M.P.A., B.S.Pharm., FASHP
Director, Accreditation and Medication Safety
Cardinal Health Innovative Delivery Solutions
Laflin, Pennsylvania

Patricia C. Kienle, M.P.A., B.S.Pharm., FASHP, is Director of Accreditation and Medication Safety for Cardinal Health Innovative Delivery Solutions. She is a member of the United States Pharmacopeial Convention (USP) Expert Committee on Compounding and Chair of the Subcommittee and Expert Panel on Hazardous Drugs.

Ms. Kienle received her Bachelor of Science in pharmacy degree from the Philadelphia College of Pharmacy and Science and Master of Public Administration from Marywood University in Scranton, Pennsylvania. She completed an Executive Fellowship in Patient Safety from Virginia Commonwealth University and is an Adjunct Associate Professor at Wilkes University in Wilkes-Barre, Pennsylvania.

Ms. Kienle is an American Society of Health-System Pharmacists (ASHP) Fellow, Pennsylvania Society of Hospital Pharmacists (PSHP) Pharmacist of the Year, and recipient of the Distinguished Achievement Award in Hospital and Institutional Practice from the American Pharmaceutical Association Academy of Pharmacy Practice and Management.


Ms. Kienle has served on the ASHP Board of Directors and as PSHP President. She has also served as a member of the Pharmacotherapy Specialty Council of the Board of Pharmaceutical Specialties, Hospital Professional and Technical Advisory Committee of the Joint Commission, and Board of Governors of the National Patient Safety Foundation.
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

Knowledge
Skill
Experience
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
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

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

**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?

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.
Crucial Considerations to Ensure the Safety of I.V. Therapy

Selected References


California Code of Regulations. Title 16 Section 1735. www.dir.ca.gov/dlse/ccr.htm (accessed 2013 Oct 22)


Myers CM. History of sterile compounding in U.S. hospitals: Learning from the tragic lessons of the past. Am J Health-Syst Pharm. 2013; 70:e41-54


Self-Assessment Questions

The presentation self-assessment questions are listed here for your convenience. Note the correct answers for future reference.

1. Risk points in the medication use process include
   a. Variable concentrations
   b. Drug shortages
   c. Labels
   d. Staff competency
   e. a, c, d
   f. All of the above

2. Sites of sterile product administration include:
   a. Imaging
   b. Home
   c. Interventional radiology
   d. All of the above

3. Training and monitoring ongoing competency of staff is essential to ensure safety and quality of sterile compounded products.
   a. True
   b. False

4. 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
5. 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

6. 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

7. Primary and secondary sets are flushed the same way after administration of a HD.
   a. True
   b. False

8. Which of the following is the most important element in creating a safe sterile compounding system?
   a. Knowledge
   b. Skill
   c. Experience