The Evolution of I.V. Safety: What Improvements Have Been Made Since the 2008 Safety Summit?

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Learning Objectives

- Describe key recommendations from recent I.V. Safety Summits
- Identify types of errors associated with i.v. medication
- Identify challenges associated with emerging therapies given by the i.v. route
- Describe strategies for ensuring the safety of outsourced medications

I.V. Therapies are High-Risk

<table>
<thead>
<tr>
<th>High-risk Therapies</th>
<th>Chemistry Therapies</th>
</tr>
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<tbody>
<tr>
<td>Chemotherapies</td>
<td>High-alert Medications</td>
</tr>
<tr>
<td>Patient-controlled analgesia (PCA)</td>
<td>Intraarticular</td>
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<td>High-risk Routes</td>
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<td>Intrathecal Ophthalmic</td>
<td>Intrathecal</td>
</tr>
<tr>
<td>Intravenous Medications</td>
<td>Volume considerations</td>
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TPNs: Multiple additives, Compatibility Use of automated compounders

Order Entry

Sources of I.V. Errors

- Drug selection
- Concentration
- Weight or Body Surface Area
- Dose units
- Route, rate

Compounding

- Contamination
- Math errors
- Post-checks vs Pre-checks
- Labeling

Administration

- Route, rate
- Math errors
- Human Factors
- Technology bypassed or overridden for Smart Pumps, BCMA
- Independent double checks not performed

2008 ASHP I.V. Safety Summit

Formulary/Medication-Use Policy
- Standard concentrations
- Use commercially available products
- Comprehensive I.V. medication administration policies

Prescribing
- Standard I.V. med orders including diluents, concentrations
- Standard dosing protocols for high alert & emergency meds

Storage
- Stock commercially available product for emergency use
- Limit concentrations of I.V. meds on patient care units

Preparation/Dispensing
- Dispense I.V. medications ready to administer
- Standard procedures for compounding, USP Chapter <797>
- Competencies for staff

Administering
- Independent double checks
- Standard processes: 2 patient identifiers, line labeling
- Smart pumps

I.V. medication administration errors involve all of the following except:

A. Wrong route
B. Bypassing alerts on smart pumps
C. Lack of independent checks
D. Compounding
### FDA and Compounding
- **Medical Center Pharmacy v. Mukasey, 2008**
  - The Fifth Circuit concluded that compounded drugs are “new drugs” …within the meaning of the FDCA and therefore are subject to regulation by the FDA.
- **Pushback from compounding pharmacies**
- **Universal requirements not implemented**
- **Distinction between compounding based on patient-specific prescription vs non-patient specific compounding in advance of prescription**

U.S. FDA. Guidance, Compliance, and Regulatory Information. URL in Ref List.

### Meningitis Outbreak - New England Compounding Pharmacy October 2012
- **Contaminated epidural methylprednisolone and potentially cardioplegia and other products**
  - 344 cases of meningitis, stroke, or CNS infection; 25 deaths (as of 10/27/12; cdc.gov)
  - Product recall involving over 3000 line items
- **FDA Inspection-Form 483 (fda.gov)**
  - 83 vials with greenish black matter
  - Non-sterile powder used
  - Lapses in cleanroom processes
- **Move by Congress to introduce legislation to enhance FDA authority related to compounding**

### 2011 ISMP Sterile Preparation Compounding Safety Summit

<table>
<thead>
<tr>
<th>Consensus Statements</th>
<th>Summary of Key Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quality Management Processes</td>
<td>Compounding Outsourcing Automated I.V. Compounders Drug Conservation Multidose Vials Drug Shortage Mgmt</td>
</tr>
<tr>
<td>Staff Management Training &amp; education National certification program sterile compounding specialists</td>
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</tr>
<tr>
<td>Storage</td>
<td>Space Labeling of bins</td>
</tr>
</tbody>
</table>

### Recommendations from recent I.V. Safety Summits include use of prechecks.

A. True
B. False

### Current I.V. Compounding Landscape 2011 ASHP Survey
- **USP Chapter <797> Compliant Cleanroom: 65.2%**
- **I.V. Robots: 2.5% (chemotherapy: 0.1%)**
- **Remote video supervisor of technicians: 3.6%**
- **Bar code verification during i.v. compounding: 11.9%**
- **Automated TPN Compounders: 20.4%**
- **Validation technology: not assessed**
- **Partial or complete outsourcing: 70.9%**
  - PCA and epidural analgesia: 73.3%
  - Increased outsourcing due to drug shortages, limited concentrations of products, and to extend dating for sterile products

ASHP Guidelines on Outsourcing Sterile Compounding Services

- Request for proposal
- Site visit
  - Review of training materials
  - Review of personnel files
  - USP Chapter <797> compliance
  - Beyond-use dating references
- Quarterly reports of quality assurance program
- Annual onsite evaluation
- Outsourcing Sterile Products Preparation-Contractor Assessment Tool


Strategies for safe outsourcing include all of the following except:

A. Routine site visits
B. Observation of compounding processes
C. Review of staff training records
D. Use of outsourcing for compounding in lieu of commercially available products

Current Technology Landscape and I.V. Safety: Prescribing and Administration

- CPOE: 34.2%
- Electronic MAR: 67.3%
- BCMA: 50.2%
- Smart infusion pumps: 67.9%

Advances:

- Commercially available pump library
- Smart Pump-Electronic Medical Record Integration
  - Requires wireless capability
  - Importance of 2-way integration
  - RN needs to scan one I.V. preparation at a time


Sources of Risk

Smart Pumps in Pediatrics

- Weight-based dose entered: 20 units/kg/h
- Weight is 2kg but 20kg is entered in error
- Smart pump displays 20 units/kg/h
- Lack of continuous weight display
- Infusion rate of 400 units/h instead of 40 units/h
- Unintended consequence: correct weight-based rate, wrong weight → 10-fold error


Pediatric Pump Display
Lack of I.V. Knowledge and Skills
- I.V. medication therapy is not an area of focus in pharmacy training¹
  - Survey on sterile preparations in U.S. pharmacy schools: 13% of
    schools reported “adequate training in compounding sterile
    preparations”²
- Evaluation of accuracy of compounding 2 simple solutions by
  pharmacy students²
  - Solution 1: only 54% of students prepared the medications within 10% of
    desired concentration; 46% had errors ranging from <75% to >200% of
    the desired concentration
  - Solution 2: 78% of students within 10% of the desired concentration; however, the range of concentration errors was greater (-89% to 269%).


I.V. Medication Administration Errors
- Prospective observational study of 107 nurses and 568 I.V.
  administrations
  - 69.7% had at least one clinical error; 25.5% were serious
  - 4 error types (wrong intravenous rate, mixture, volume, and
    drug incompatibility) accounted for 91.7% of errors.
  - Wrong rate: 95 of 101 serious errors.
  - Error rates and severity decreased with clinical experience.
    - Each year of experience, up to 6 years, reduced the risk of error by 10.9% and
      serious error by 18.5%.
  - Administration by bolus was associated with a 312% increased
    risk of error


I.V. Therapy Innovation and Challenges
- Growth of parenteral biologics and other
  specialty pharmaceuticals for chronic diseases
  - Biologics for chronic disease: approx. 400 specialty
    medications across 25 therapeutic categories; primarily injectable medications
  - Patient’s own I.V. therapy +/- infusion device
- Growth in intrathecal pain management and
  use of non-sterile powders
- Cellular immunotherapy for cancer and other
  diseases

Draft ASHP Guidelines on Preventing Medication Errors
  with Chemotherapy and Biotherapy
- Provides comprehensive guidelines across medication use
  system focusing on competency
- Overall chemotherapy error rate of 8.1 errors/100 clinic visits
  - 7.1% of adult clinic visits
  - 18.8% of pediatric clinic visits
  - Errors across all steps of medication use process; most
    common: administration (56%) and ordering (36%) errors
- CPOE for chemotherapy not widely adopted; can introduce new
  errors
- American Society of Clinical Oncology (ASCO) and the Oncology
  Nursing Society (ONS) guidelines

URL in Ref List.

Intrathecal Pain Management
- Drug delivery systems (pump and catheter) that deliver small
  quantities of analgesic intrathecally
- Indicated for chronic, intractable pain; severe spasticity
- Off-label use of medications: clonidine, ketamine
- Non-sterile powder used in compounding
- Safety issues
  - Infections, respiratory depression, neurologic injury, paralysis, inflammatory mass
  - Catheter complications: disconnection, fracture, leak, migration, kinks, granulomas

Chronic I.V. Therapies and Transitions of Care
- The “new” patient’s own medication: patient’s own
  injectable +/- infusion device
  - Biologics for chronic disease
  - Intrathecal analgesia
- Product integrity and liability
  - Stability
  - Sterility
  - Counterfeit
- Preparation considerations
  - Pharmacy staff competency in infusion devices and other
    drug delivery systems
**Chronic I.V. Therapies and Transitions of Care**

- Preparation considerations
  - Non-sterile powder compounding
- Administration considerations
  - Nursing knowledge of infusion device operation
  - Patient competency for self-administration
    - Nursing ability to assess patient competency-TJC requirement
- Patient’s Own Infusion Device
  - Preventive maintenance
  - Infection control considerations
- Coordination of patient-specific medications and supplies across transitions of care

**Immunotherapy**

- Research advances in treatment of cancer and immune disorders
  - Biological response modifiers
  - Cancer vaccines
  - Gene therapy
  - Non-specific immunomodulating agents, e.g. BCG
- New competencies
  - Storage, Preparation, Dispensing, Monitoring
- Facility requirements

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**Why Focusing on I.V. Medication Safety is an Imperative**

- Sterile Compounding is a specialty area
- Safe use of i.v. medications requires knowledge and skills across the entire med-use process
- Technology and automation: need to balance benefits with unintended consequences
- Ensuring safety of outsourcing is essential
- Research advances will increase complexity
- Human factors are at the core of safe i.v. medication use

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National Cancer Institute. Fact Sheet: Biological therapies for cancer. URL in Ref List.
Meeting the Challenge of I.V. Safety

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Learning Objectives

- Examine existing i.v. technology to determine which technologies best support i.v. staff and provide patient safety
- Review i.v. technology in terms of how it works and if it can be “worked around”
- List the deficiencies in some i.v. technology that may compromise product and patient safety

Back to Basics: I.V. Compounding

• We cannot improve i.v. safety if we don’t accept the basics
  – Knowledge and skills are required in the I.V. Room
  – I.V. skills are NOT innate or intuitive
  – MONITORING is required in the I.V. room
  – There is no substitute for well-trained and experienced i.v. technicians and PHARMACISTS
  – Technology and automation are only TOOLS

What are the Compounding Challenges of I.V. Safety?

• Sterility
• Accuracy

What Meets the Challenges of I.V. Safety?

• People?
• Technology/automation?
• People using technology and automation?

What Meets the Challenges of I.V. Safety?

Well-trained staff properly using well-designed technology
MAGIC and myths!

- There are no magic rooms in the pharmacy!
- There are no magic boxes in the I.V. Room!
- There are no magicians in the I.V. Room!

Myth: “Clean” Rooms

- The architects only determine “clean” by design
- Staff and work practices determine if it is “clean” in use

True or False?

As long as sterile preparations are compounded in an ISO 7 “Clean Room” they will ALWAYS be sterile.

What if I have a “magic” box in my clean room?

Challenges to the “magic” boxes

- Cleaning
- Maintenance
- Technique
Challenges to the “magic” boxes (also known as isolators)
- Gloves - pinholes and changing
- Sleeves - damage to gasket or material
- Cleaning - requires tools
  - What can’t I reach?
  - Can I open the front?

The “magic” may be broken!
- Gloves must be changed frequently – not all damage is this obvious!
- Check for pinholes
- The sleeves and gaskets may also be damaged
- There may be pinholes in the sleeves

What about accuracy?
- What meets the challenge of accuracy?
- Technology?
- Automation?

What works?
What can be worked around?

Case Study: Compounding Error
Six doses of 10mL IV cotrimoxazole in 100mL D5W are needed for BMT patients on a PCP prophylaxis regimen. There are a number of partial 30mL, amber multi-dose vials left over from earlier compounding. The compounder decides to use these vials for compounding the required doses.

Challenges?
- Batching with open drug vials is a serious risk both for sterility and accuracy
- Shortages of drugs makes using open vials imperative
- Technology has gaps for batching and for using partial-filled vials
Manual compounding: This is in the “hood”

This is what is presented to be checked

This is the problem

Will technology solve the problem?
- Bar Code Verification in the Clean Room?
- I.V. Workflow Software?
- I.V. Robotics?
- Other?

Bar Code Verification for preparation in Clean Room?
- YES - IF EACH vial is scanned
- NO - IF ONE vial is scanned 5 times!

I.V. Workflow Software
DoseEdge™ - I.V. Soft® - ScriptPro Telepharmacy
- Interface with pharmacy system
- Barcode verification of drug vials
- Photo capture of vials, labels, etc.
- Remote checking based on photos
Considerations

<table>
<thead>
<tr>
<th>Accuracy</th>
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<tbody>
<tr>
<td>● Barcode each vial or 1?</td>
</tr>
<tr>
<td>● Image captures ONLY what is photographed – 1 vial or 5 vials?</td>
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<tr>
<td>● Remote checker only sees images that are captured</td>
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<tr>
<td>● Dose is done before verified</td>
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<table>
<thead>
<tr>
<th>Sterility</th>
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<tbody>
<tr>
<td>● Placement in PEC airflow</td>
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<tr>
<td>● Touch contamination</td>
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<tr>
<td>● Lapses in aseptic technique are not captured</td>
</tr>
<tr>
<td>● HD touch contamination and technique lapses</td>
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I.V. Workflow Software?

- YES - IF compounder follows the rules
- NO – IF not
- Using multiple partial-filled vials is difficult for technology
- Camera only records what is shown

I.V. Robotics?

- Image capture technology ONLY shows what is photographed
- Lapses in compounding technique are NOT captured
- Short-cuts and “work-arounds” are NOT captured

I.V. Robotics are most likely to avoid the error

- Barcode and image capture of all items
- Exact processes
- No “work arounds”
- Will only use robot-punctured partial vials
- Gravimetric methods
- Remote checker verifies all compounding steps

BUT ...

- Robots are NOT “plug and play”
- Robots are Class II Medical Devices
Class II Medical Devices

- BOTH are Class II Medical Devices and BOTH use the FDA 510K process to get to market.
- The FDA does not “approve” Class II Medical Devices the same way it approves drugs.

Can robots make mistakes?

- YES - if given the wrong information
  - Drug databases must be accurate
  - Density input must be accurate
  - Calculation/concentration input must be accurate
- If errors in databases, MANY doses are affected

Other Technology – The “Final” Check?

- USP Chapter <797>, Boards of Pharmacy, and others are recommending end product testing for ACCURACY
- New technology allows testing in the I.V. Room
  - CDEX - Valimed G4
  - SEA Medical – IV Check

ValiMed G4

- The ValiMed G4 drug validation system identifies drug strengths and volume-by-weight in real-time, validating proper dose, diluents, and concentration of high-risk compounded medications and treatment solutions.
- This “catches” errors that may be missed with other technologies.

IV Check

- IV Check measures i.v. samples anywhere i.v. medications are prepared, and instantly reports the drug, dose, and diluent present to validate i.v. preparations.
- IV Check allows pharmacy technicians and pharmacists to verify the drug, concentration, and diluent of i.v. preparations during the compounding process to reduce the drug and time wasted in re-compounding wrong doses.

Poor Job Performance

- No one goes into the I.V. Room planning to make a mistake
  - Knowledge deficit
  - Inadequate training
  - Not enough time
  - Too many interruptions
  - Changing priorities
Human Factors are at the Core of Safe I.V. Medication Use

- Hire the smile and train the skill
  - Training those who compound, check, and administer i.v. medications is critical for patient and worker safety; and for safety for the immediate and surrounding environment
  - This would apply to bugs and drugs
  - Select workers who care, are reliable, and follow rules

Character and personal force are the only investments that are worth anything

Walt Whitman
Back to Basics: Innovative Strategies for Teaching the Principles of Safe Medication Compounding

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Objective
- Describe educational methods that can be used to train pharmacists about safe i.v. preparation

Introduction to Purdue University College of Pharmacy
- Each class (P1 → P4) has ~160 students
- Current curriculum includes 2-credit hour Parenteral Products course
  - Spring semester of P3 year
  - Instruction on preparation of sterile i.v. admixtures
  - Emphasis on USP Chapter <797> regulations
  - I.V. Room environment requirements, including proper attire

The Problem
- Cleanroom training of pharmacy students occurs mainly in classroom
- Four laboratory sessions to practice “hands-on” exercises
  - Five individual tabletop hoods
  - Required to wear sterile gloves
  - Focus on product manipulation only
- Only 2 hospitals in the West Lafayette, IN area with i.v. cleanrooms

The Problem
- Student feedback showed lack of comfort when performing appropriate i.v. procedures
- Many students never step foot in a cleanroom prior to APPE rotations
- Many students are unfamiliar with hospital labeling and packaging
- Lack of physical space and funds to build a cleanroom on campus
- Cost to maintain a USP Chapter <797> compliant space as standards change

The Goal
- Develop an interactive environment which allows students to gain comfort and confidence with the layout and special procedures associated with an i.v. cleanroom as well as products
- Design cleanroom so it would be adaptable for various scenarios and changing standards as well as USP Chapter <797> compliant
- Make learning enjoyable
### The Solution

- Proposal for “Development of Virtual Reality USP Chapter <797> Compliant Clean Room”
  - $70,000 educational innovation grant from Purdue University
- Partner with Envision Center for Data Perceptualization at Purdue to create a virtual cleanroom
  - Three computer technology students
  - The pharmacy students
  - Version one designed over the course of a year after visiting multiple Indiana cleanrooms
  - Validated as USP Chapter <797> compliant by member of coordinating committee

### The Technology

- Multi-wall immersive environment which works on wall sized panels as well as a portable display system
- Equipment involved
  - 3-D glasses
  - Wireless controller for navigation (AKA joystick)
  - Head tracking device to adjust the view of the student

### The Lab Session

**Learning Objectives**
- List USP Chapter <797> standards for a cleanroom
- State the proper attire for a cleanroom
- Describe the physical layout and basic cleanroom procedures
- Identify safety issues within a cleanroom
- Evaluate an actual intravenous medication order for accuracy
- Select the appropriate product(s) for i.v. preparation
- Generate recommendations for prescribers, as appropriate
The Lab Session

- Virtual Cleanroom Exercise
  - Tour of the cleanroom
  - Review of environmental processes and procedures
  - Safety issues and product preparation

<table>
<thead>
<tr>
<th>Anteroom</th>
<th>Chemotherapy Room</th>
<th>Clean Room</th>
</tr>
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<tbody>
<tr>
<td>Trissel’s Handbook</td>
<td>Spill on Floor</td>
<td>Drink in Refrigerator</td>
</tr>
<tr>
<td>ADD-vantage Bags</td>
<td>Vancomycin Bottle in Hood</td>
<td>Overflowing Sharps Container</td>
</tr>
<tr>
<td>Linezolid Vial</td>
<td>Cigarette in Hood</td>
<td>Cardboard Boxes</td>
</tr>
<tr>
<td>Large Volume IVF</td>
<td>Syringe Laying on Edge of Hood</td>
<td>Stock Bottle Blocking Syringe in Hood</td>
</tr>
</tbody>
</table>

The Lab Session

- **Heparin 25,000 units in 100 mL, infuse over 1 hour**
  - Did the physician write this order appropriately?
  - Does this medication need to be reconstituted before dilution? If so, how?
  - What is a normal concentration for this preparation following dilution?
  - If there are multiple products/strengths available, which is the most appropriate? Why?

The Lab Session

- **Heparin 25,000 units in 100 mL, infuse over 1 hour**
  - How much active drug should be used and how is this quantified based on the chosen product?
  - Which diluent is most appropriate for use with this medication? How much?
  - Are there any infusion rate requirements for this medication? If so, what are they?
  - Are there any special storage requirements for this product?

The Lab Session

- Results
  - 96% of students participated
  - 59% had no prior I.V. Room experience
  - 88% agreed or strongly agreed the lab met their expectations
  - When resurveyed at end of the APPE experience, 92% of students who participated felt the virtual environment was helpful to their understanding prior to the real experience

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<thead>
<tr>
<th>Statement</th>
<th>Pre-Assessment</th>
<th>Post-Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication errors can significantly impact patient outcomes</td>
<td>96% A/SA</td>
<td>96% A/SA</td>
</tr>
<tr>
<td>The likelihood of a skilled pharmacist making an error is low</td>
<td>57% D/SD</td>
<td>64% D/SD</td>
</tr>
<tr>
<td>My potential for making an error upon entering practice is low</td>
<td>73% D/SD</td>
<td>73% D/SD</td>
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</table>
The Lab Session

• Results

<table>
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<tr>
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<th>Post-Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>I perceive medication errors to be more significant after completing this lab</td>
<td>N/A</td>
<td>75% A/SA</td>
</tr>
<tr>
<td>My experience in the virtual clean room has enhanced my understanding of clean room procedures</td>
<td>N/A</td>
<td>88% A/SA</td>
</tr>
<tr>
<td>The problem assigned for this lab reinforced my understanding of order processing within the clean room setting</td>
<td>N/A</td>
<td>90% A/SA</td>
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• Feedback

– “...very hands-on and provided a realistic example of clean room standards and violations.”
– “I got a great appreciation of what a clean room actually is. I think in a real clean room I would be overwhelmed with things and wouldn’t appreciate them as much.”
– “The 3-D technology is fun and... whenever you can get out of the classroom to learn is positive.”

The Virtual Cleanroom

• Time for a tour!
  – Anteroom
  – Chemo prep room
  – I.V. Room
  – What’s wrong with this picture?
  – I.V. product preparation assignment

Anteroom
The 2012 Landscape of I.V. Medication Safety: Processes, Tools, and Training

Anteroom

Chemo Room

I.V. Room

I.V. Room

I.V. Room

What's Wrong?
What’s Wrong?

I.V. Product Selection

Future Plans

- Continue to incorporate virtual clean room into training of P3 students
- Enhance virtual clean room experience for P2 students (prior to hospital IPPE)
- Session to be mandatory
- Enhance inventory and add compounding technology
- Enhance programming for use with interactive glove and other technology
- Develop laptop and web-based platform for supplemental instruction
- Virtual community pharmacy and ICU

Recommendations for Staff Training

- Mix the methods (didactic, simulation, hands-on)
- Make it practical
- Integrate accurate examples with those containing errors
- Do not stop the learning process if a gross error is occurring (exception: stepwise procedures)
- Incorporate common sense

Conclusion

- Unique solution developed for a complex problem
- Allowed students to gain hands-on training in a virtual environment modeled from actual cleanrooms throughout Indiana
  - Majority of students felt their confidence with and understanding of i.v. cleanrooms had improved as a result
- Progressive and effective way to provide an introduction to an i.v. cleanroom and its common components, aseptic procedures, USP Chapter <797> requirements, and medication safety
Visit the Virtual Cleanroom

- http://www.boilerpharmacyvirtualcleanroom.com

- The content of this link simulates a virtual cleanroom experience, including identification of:
  – Components of the cleanroom environment
  – Safety hazards within the cleanroom setting

2012 Landscape of I.V. Medication Safety

- Human factors continue to be at the root of harmful events related to i.v. medications
- Expect significant changes in regulatory requirements for sterile compounding at national and state levels
- Training of pharmacy staff in sterile compounding is an imperative and needs to be integrated into pharmacy education and post-graduate training
- I.V. technology continues to evolve and safe use requires significant knowledge, skills, and diligence
- I.V. errors can occur at any step of the medication use process
- I.V. Medication Management should be considered as an area for specialty development