Safety Considerations When Evaluating How to Provide Compounded Sterile Products

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Speaker Disclosure

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Decisions

- When considering compounded sterile products you have 3 choices:
  - Outsource to a local or national compounding pharmacy
  - Have the hospital pharmacy prepare
  - Have the staff on the patient care units prepare

- Regardless of the choice, ISMP believes that sterile compounding is a high-risk process with serious patient safety implications that require considerable effort and attention
Compounding Sterility Issues

- There have been considerable sterility issues with compounded sterile products from all sources:
  - 1975: “Nationwide epidemic of sepsis caused by contaminated intravenous products”\(^1\)
  - FDA: 200 adverse events reported involving 71 compounded sterile products since 1990, some of them with “devastating repercussions”\(^2\)
  - 1990-2012: At least 24 incidents of contaminated pharmacy-prepared products from all sources reported nationally infecting over 900 patients and resulting in 92 deaths\(^3\)

USP Chapter <797>

- The definitive standard since 2004 to ensure sterility of pharmacy-compounded sterile drugs
- Only 17 states require compliance\(^4\)
  - In a survey of US hospitals in 2011, 65% say they comply with USP <797> clean room requirements\(^5\)
  - Less than 17% of hospitals comply with all requirements\(^6\)
IV Compounding Errors

- However, compounding errors in pharmacy-prepared products from all sources have occurred as well:
  - 2009: 30% of surveyed hospitals experienced a patient event involving a compounding error within the prior 5 years\(^7\)
  - A 5-hospital observational study found a mean daily error rate of 9% (highest for complex solutions like TPN – 22-37%)\(^8\)
  - 2005-2011: Serious cases of sterile compounding errors involving 15 patients, 8 of which died, reported due to:
    - wrong concentration/strength of the product dispensed (overdose)\(^9-13\)
    - wrong product or diluent used in compounding\(^14,15\)
    - product mislabeling by the pharmacy\(^16\)

2011 Guidelines to Reduce IV Compounding Errors

Safety of Compounding Source

• Second Consensus Development Conference on the Safety of Intravenous Drug Delivery Systems - 2008

• Consensus panel ranking of safety (highest=7):  
  – Manufacturer ready-to-use (6.0)  
  – Point-of-care activated (4.6)  
  – Outsourced ready-to-use (4.5)  
  – Pharmacy-compounded (4.2)  
  – Non-pharmacy compounded at point-of-care (1.8)

Why ISMP believes Manufacturer Prepared Premixed, Prefilled Products are Safer?

• FDA requirements under cGMP require enhanced sterility conditions and testing prior to release of the product for both accuracy and sterility – ensuring better accuracy and sterility

• FDA manufacturer vs. FDA registered compounding – the difference
A Standard of Practice

• ASHP Summit 2008 (based on Consensus Panel):
  – Use commercially available, ready-to-administer i.v. medications if available\(^\text{19}\)
  – Dispense i.v. medications and admixtures in ready-to-administer form (i.e., a form that requires no manipulation prior to administration)\(^\text{19}\)

• ISMP Summit 2011 (based on Consensus Panel):
  – When available, commercially–prepared, premixed IV products that meet the patient’s needs, are used over manually compounded sterile products\(^\text{17}\)

TJC Requirements\(^\text{20}\)

• **MM.03.01.01, EP 10:** Medications in patient care areas are available in the most ready-to-administer forms commercially available or, if feasible, in unit-doses that have been repackaged by the pharmacy or a licensed repackager.

• **MM.03.01.03, EP 3:** Whenever possible, emergency medications are available in unit-dose, age-specific, and ready-to-administer forms.

• **MM.05.01.11, EP 4:** Medications are dispensed in the most ready-to-administer forms commercially available or, if feasible, in unit doses that have been repackaged by the pharmacy or licensed repackager.
Safety of Non-Pharmacy Sterile Product Preparation

• CDC estimates in the last 5 years, 26 outbreaks of serious infections have occurred related to unsafe injection practices on patient care units, involving more than 95,000 patients.\textsuperscript{21}
• 2007 review: 592 preventable infections and 62 deaths due to contaminated MDVs in hospitals.\textsuperscript{22}
• 2008 hospital-based study: found bacterial contamination in 5.6% of the 637 MDVs sampled.\textsuperscript{23}

TJC Requirements

• \textbf{MM.05.01.07, EP 1:} A pharmacist, or pharmacy staff under the supervision of a pharmacist, compounds or admixes all compounded sterile preparations except in urgent situations in which a delay could harm the patient or when the product’s stability is short.

  \hspace{2em}– 2011 ASHP Study indicated that 14.7% of IV doses are prepared by the nurse.\textsuperscript{5}
What This Means

• Both hospital pharmacies and outsourced sterile compounding have caused patient harm due to sterility issues and medication errors with sterile compounding
  – There are high and low performers in both groups
  – Little regulatory oversight over outsourced compounders
  – Biggest predictor of quality is compliance with USP <797> and the ISMP Guidelines for SAFE Preparation of Sterile Compounds\textsuperscript{17,24}
  – Both are safer than point-of-care preparation of CSPs

What ISMP Proposes

• Point-of-care preparation of sterile products should be minimized as much as possible
• Regardless of outsourced vs. in-house preparation:
  – The use of all commercially-available premixed, prefilled products from a manufacturer should always be utilized over compounded products
  – There is a need for senior leadership understanding of risk and support (including budgetary support) for the use of safe sterile compounds
Key Elements of Making Your Decision
Insource vs. Outsource

• Will it allow you to provide more ready-to-use products and avoid point-of-care preparation?
• Do you have the environment, resources, or expertise for sterile compounding?
  – Full compliance with USP <797>\textsuperscript{24}
  – Permanent vs. temporary need (e.g. drug shortages, staffing)

Key Elements of Making Your Decision
Insource vs. Outsource

• Can your staff be better allocated for patient safety programs?
  – Medication reconciliation, anticoagulation management, pharmacist participation on rounds, community liaison program
• Which can provide a better labeled, safer product?
• Have you properly vetted your outsource provider as being high quality?

(for more, see ASHP Guidelines on Outsourcing Sterile Compounding\textsuperscript{25})
Improving the Safety of In-house Preparation

• Adherence to all aspects of USP <797>\textsuperscript{24}
• Adherence to ISMP Guidelines for the SAFE Preparation of Sterile Compounds\textsuperscript{17}
• Use of dedicated, trained, (certified?) staff
• Automation

Use of Automation

• 2011 survey of U.S. hospitals showed that only:\textsuperscript{5}
  – 20.4% - automated TPN compounders
  – 12.5% - automated syringe filling device
  – 11.9% - bar-code verification during preparation
  – 3.6% - remote video supervision of IV technician preparation (IV workflow software, e.g. DoseEdge)
  – 2.5% - stand-alone robotic device
• Technology to measure specific gravity, final weight, photometric analyzers – rare
The Use of Outsourced Vendors

• 70.9% of hospitals outsource sterile compounding (fully or partially) according to a 2011 ASHP survey

• From legal and Joint Commission perspective, the hospital is responsible for the services provided to its patients under contract.

Joint Commission Requirements for Contracted Providers

• Contracted services must adhere to all applicable TJC standards
  – “The same level of care should be delivered to patients regardless of whether services are provided directly by the hospital or through contractual agreement.”
  – For Example:
    • MM.05.01.09 – Medication labels – standard format/content
    • HR.01.06.01 – Staff competencies assessed

• Contracted providers can be evaluated for compliance during the hospital survey
  – Can include a site visit
**LD.04.09.01**

Care, treatment, and services provided through contractual agreement are provided safely and effectively.

- **EP 1:** Clinical leaders and medical staff provide advice on sources of contracted services
- **EP 2:** Hospital describes, in writing, the nature and scope of services provided under contract
- **EP 3:** Designated leaders approve contracts
- **EP 4:** Establish performance expectations for the contracted service

- **EP 5:** Communicate the expectations in writing to the provider of the contracted services
  - Need not be in contract, can be addendum or separate document
- **EP 6:** Evaluate these services in relation to the established expectations
- **EP 7:** Take steps to improve these services when the expectations are not met
- **EP 8:** Maintains continuity of care/services when contract terminated/renegotiated

**CMS:** Governing body is responsible for oversight and monitoring of these requirements.
Summary of Joint Commission Requirements for Contracted Providers

• Contracted services must adhere to all applicable TJC standards
• Selected with clinical leader/medical staff input
• Contract approved by governing body
• Development, communication, and on-going evaluation of written performance expectations
  — Governing body must review and approve ongoing evaluation

Selection of an Outsourced Vendor

• Initial review (if not done yet, do so!) and ongoing evaluation
• Components:
  — Document review
  — Due diligence
  — On-site visit
  — Evaluation
  — Contract
  — On-going monitoring
Document Review

- Request and review vendor-provided information
  - See ASHP Guidelines on Outsourcing Sterile Compounding
    - Basic Information
      - e.g., hours, phone#, prices
    - Copies of Documents
      - e.g. licenses, sample batch report, liability insurance
    - Attestation and Self-Assessment
      - “on file and available for review”
    - Outside independent reports

Vendor Document Review

- May not get everything requested
  - Information too voluminous to send
  - Confidentiality concerns
- If you don’t, make sure:
  - They give a reason why
  - They will allow you to view on-site
Due Diligence

• Hospital review of “public domain” data that are not obtained from the vendor
  – Primary source verification of licensure (Rx & RPh)
  – Disciplinary actions/ “Cease and Desist Orders”
  – Product recalls, if FDA registered
  – Accreditation status, if applicable
  – Consumer complaints (BBB, web)

Purpose

• Purpose of Document Review/Due Diligence:
  – Preliminary screening
  – Planning on-site visit
  – *Never as a replacement for an on-site visit!*
On-Site Visit

• Done by qualified individual(s) and DOP
  – USP 797, Facilities Mgt, Infection Control, Data Analysis, Culture of Safety
  – Use consultant(s) if no expertise in-house
  – In-depth interview of other hospitals who did a thorough review recently *(only if can’t do above)*

• Planned – use a checklist

*(see ASHP Advantage tips for conducting site visits)*

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On-Site Visit

• Purpose: observation, interviews and review of documents not previously sent
  – Compliance with USP <797> and ISMP Guidelines for the SAFE Preparation of Sterile Compounds
    • *No sterile compounder who does not meet these basic standards should be considered acceptable*
  – Overall training and competence of staff
    • “learning culture” present
  – Whether beyond-use dating is based on acceptable stability data
  – Use of technology to improve the safety of compounding
On-Site Visit

- Presence of a safety culture in the organization
  - Appropriate use of quality control data, medication error reporting, lack of tolerance to near-misses, having just-culture, lack of intimidation, etc.
- Appropriate product packaging and labeling
  - Compatible bar code on label with readability checked before sending out, use of TALLman lettering, label easily read in any direction, etc.
- Appropriate resources
- Delivery and service capabilities
  - Including an emergency preparedness plan

Evaluation

- Multidisciplinary group
  - Everyone on site visit plus infection control, risk management, patient care staff, performance improvement, pharmacy leadership
- Set performance expectations (for contract)
  - Absolute vs. desirable
- Evaluate against performance expectations
  - Does vs. capability to do
  - Compare to in-house capabilities/ability
Contract/Written Agreement

• Contract
  – Their contract vs. yours
    • If theirs, be sure to include an addendum
  – Contract should specify what data you need for ongoing monitoring (i.e., dashboard)
    • QC data, Medication Error data
  – Contract should specify what penalties if expectations not met, including termination
  – Pharmacy input in wording of contract
  – Send your written valuation and contract to governing body for approval

On-Going Evaluation

• Assign pharmacist to monitor
  – Quarterly review
    • Requested data from vendor
    • Internal data
      – Medication errors, service issues
    • Public domain sites for disciplinary actions/complaints, same ownership
  – Re-verify license at time of renewal
  – Comprehensive review every 2-3 years (w/site visit)
  – Present report to governing body
In Summary

- Outsourced sterile compounders provide a valuable service to hospitals and are no better or worse than hospital pharmacies with good and bad performers in each group.
- Hospital pharmacies are responsible for the quality of CSPs whether prepared in-house or outsourced.
- Hospitals need to evaluate in-house processes vs. outsourced vendors to determine safest approach.
- Compliance with USP <797> (or cGMP) and ISMP Guidelines for the SAFE Preparation of Sterile Compounds are absolute requirements.
- A good review process for outsourced vendors includes: document review, due diligence, site visit, evaluation, a good contract and ongoing monitoring of services.

"Change Is Hard"

"... this is the way we have always done it."
Questions and Discussion

References

3. Sterile compounding tragedy is a symptom of a broken system on many levels. ISMP Medication Safety Alert. 2012 (Oct 18);17(21):1-4.
11. Fatal 1,000-fold overdoses can occur, particularly to neonates, by transposing mcg and mg. ISMP Medication Safety Alert. 2007(Sep 6);12(18):1-4.
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