




**Management Case Study:**  
Systematic Approach to Health System  
Compounding in the New Era of Safety Concerns,  
Drug Shortages and Regulatory Changes

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1:45 p.m. – 2:15 p.m.

**Virginia Mason Medical Center**

- An integrated not for profit healthcare system
  - 336 bed tertiary-care teaching hospital
  - 8 primary care and specialty clinic sites throughout the Puget Sound Area
- 450 employed physicians
- 5,000+ employees
- Leader in patient safety, quality and application of lean principles to healthcare delivery



**Overview**


- Purpose
  - Describes one approach to managing sterile injectable drug shortages and address the tension between meeting patient care needs and ensuring product integrity
  - Case study of injectable papaverine drug shortage
- Goal
  - To be transparent with our experience
  - Patient safety and quality come first
- Disclosure
  - I am not a 797 expert

**Learning Objectives**

- Understand implications of the changing compounding landscape in light of safety concerns, drug shortages and regulatory changes
- Explain one system's approach towards addressing a sterile compounding situation using the medication use process and plan-do-study-act cycle
- Identify two considerations when selecting alternative to injectable papaverine for intraoperative use

**There are ...**

- **Things we know that we know**
- **Known unknowns**
  - Things we now know we don't know.
- **Unknown unknowns**
  - Things we don't know we don't know
- **The absence of evidence is not evidence of absence**
  - Simply because you do not have evidence that something exists does not mean that you have evidence that it doesn't exist.



Donald Rumsfeld, Press Conference at NATO Headquarters, Brussels, Belgium, June 6, 2002

**Methods**

- **Environmental Scan**
- **Gap Analysis**
- **Risk Assessment**
- **Tools**
  - Invoice/purchase reports
  - Multi-modal communication
  - State board and national organization resources
  - First-hand observation of process and indications
  - Primary literature, evidence
  - Ongoing plan-do-study-act (PDSA) cycles

### Environmental Scan

- Increased focus on compounding by all stakeholders
- Lack of clarity surrounding definitions
- Concurrent drug shortages
- Increasing regulatory activity and significant degree of practice variation
- Tension between meeting patient care needs and ensuring product integrity

### Timeline

Early Oct 2012	Mid Oct 2012	Late Oct 2012
<ul style="list-style-type: none"> <li>Public Health NECC memo</li> <li>WA facilities identified having NECC products</li> </ul>	<ul style="list-style-type: none"> <li>FDA publishes erroneous NECC list</li> <li>Ameridose closes</li> <li>Gap analysis</li> <li>Compound work ↑</li> </ul>	<ul style="list-style-type: none"> <li>Ameridose recall</li> <li>Ongoing gap analysis</li> <li>Alternatives</li> <li>Internal policy change</li> </ul>
<h4>Nov - Dec 2012</h4> <ul style="list-style-type: none"> <li>Site visits</li> <li>Validating internal sterility/batch testing</li> <li>Cont. environmental scan</li> </ul>		

**Other:**


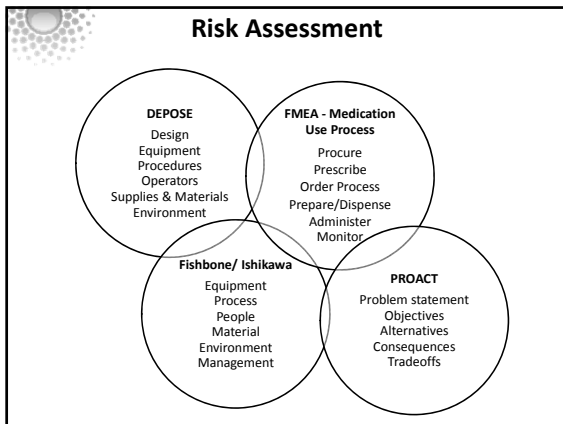
- Vendor CQI evaluation
- Ongoing drug shortages
- CDC One & Done campaign (multi-patient/dose vials)
- 60 Minutes

### Timeline

Jan 2013	Feb 2013	March – April 2013
<ul style="list-style-type: none"> <li>Papaverine shortage</li> <li>BOP prohibited "office use"</li> </ul>	<ul style="list-style-type: none"> <li>BOP revised "office use"</li> <li>HB 1800 introduced</li> </ul>	<ul style="list-style-type: none"> <li>High risk compounding work plan</li> <li>Capital request for powder hood</li> </ul>
May 2013	Ongoing	
<ul style="list-style-type: none"> <li>Governor Inslee signed HB 1800</li> <li>Powder hood installed</li> </ul>	<ul style="list-style-type: none"> <li>Weekly notice of compounding pharmacy closures</li> <li>Drug shortages</li> <li>Legislative activity</li> </ul>	


### Compounding Gap Analysis

- Capture internally, externally prepared products
- Identify gaps in therapy and potential alternatives
  - Started October 2012, living document
  - Tool for communicating with executives
  - Sterile, non-sterile
  - Incorporated "office-use" list

### Risk Assessment: Papaverine injection

Select/Procure	Prescribe/Order	Order Processing	Prepare/Dispense	Administer	Monitor
<ul style="list-style-type: none"> <li>Manuf v. bulk non-sterile powder</li> <li>Compounding pharmacies advertise</li> <li>Grey market pharmacies</li> <li>No "brown bagging"</li> </ul>	<ul style="list-style-type: none"> <li>Used by Cardiothoracic, Vascular, Plastics, Urology, Transplant</li> <li>Alternatives</li> </ul>	<ul style="list-style-type: none"> <li>Paper</li> <li>Preference card</li> <li>Lack expertise</li> <li>"Office use" regulations</li> </ul>	<ul style="list-style-type: none"> <li>No internal equipment, procedures for sterilizing</li> <li>Internal decision: no high risk compounds from outside pharmacies</li> </ul>	<ul style="list-style-type: none"> <li>Vein bath, irrigation</li> <li>In office and patient home administration</li> <li>Diagnostic injection in ultra-sound</li> </ul>	<ul style="list-style-type: none"> <li>Evaluate effectiveness of alternatives</li> <li>Patient awareness of compounding pharmacies</li> </ul>



### Risk Assessment: Papaverine injection

**Select/ Procure**

- Manuf v. bulk non-sterile powder
- Compounding pharmacies advertise
- Grey market pharmacies
- No "brown bagging"

- Supply status
- Supply options
  - Alternatives
  - Compounded
  - Supply chain options
  - Emergency/reserves
- Clear policy on medication distribution practices

### Risk Assessment: Papaverine injection

**Prescribe/ Order**

- Used by Cardiothoracic, Vascular, Plastics, Urology, Transplant
- Alternatives

- Understand intended pharmacological and operational application
  - Intraoperative – Vasodilation
  - Office/Home – Erectile Dysfunction
- Recognize implications
- Understand stakeholders' concerns
  - Surgeon, Physician, Nurse
  - Manager
  - Patient
- pH – Compatibility - Availability – Expense
- Investigate alternatives
  - Literature search
  - Engage providers

### Risk Assessment: Papaverine injection

**Order Processing**

- Paper
- Preference card
- Lack expertise
- "Office use" regulations

- Understand implications of origin and vehicle for ordering
  - Align with new processes
- Regulatory and policy boundaries

### Risk Assessment: Papaverine injection

**Preparation/ Dispensing**

- No internal equipment, procedures for sterilizing
- Internal decision: no high risk compounds from outside pharmacies

Consider the ..

- Who?
- What?
- Where?
- When?
- How?

**Administer**

- Vein bath, irrigation
- In office and patient home administration
- Diagnostic injection in ultra-sound

### Risk Assessment: Papaverine injection

**Monitor**

- Evaluate effectiveness of alternatives
- Patient awareness of compounding pharmacies

- Gather/invite input into how the alternative or process changes are going
  - Various sources
  - Communication
  - Outcomes
- Plan – Do – Study – Act

### Intraoperative Papaverine Alternatives

**Initial Trial**

- Nitroglycerin 4 mcg/mL in 50 mL NS syringes
- Surgeons reported experiencing more vasospasm

**Practice-based considerations**

- Mechanism of action, onset
- pH – Compatibility - Availability – Expense
- Understanding type of procedure

### Alternatives to Nitroglycerin

Options	Notes
Verapamil	pH: 4-6.5; heparin compatible; available
Diltiazem	pH: 3.7-4.1; heparin variable compatibility; available
Nicardipine	pH: 3.5 ; likely not heparin compatible, available
Nitroglycerin	pH: 3-6.5; heparin compatible; available
Lidocaine	Conflicting literature or specific application
Adenosine	Limited supply
Papaverine	pH: 3-5; Unavailable

- Engage physicians in finding evidence to support practice
  - Specific surgery search terms
- Yu et al 2011 survey
  - Top 2: papaverine and verapamil
  - Empiric (42%), habit (21%), it works (16%)
- Wei He et al. 2008
  - Cocktail to address multiple vasoconstrictors

### Nitroglycerin and Nicardipine Cocktail

Wei He et al.	Nitroglycerin 5mg + niCARDipine 5mg in 0.9% NaCl 250ml
<ul style="list-style-type: none"> <li>Nicardipine 5mg</li> <li>Nitroglycerin 5mg                             <ul style="list-style-type: none"> <li>glyceryl trinitrate</li> </ul> </li> <li>8.4% NaHCO3 0.3 mL</li> <li>Normosol – R solution 300ml                             <ul style="list-style-type: none"> <li>Similar to Lactated Ringers minus calcium plus magnesium                                     <ul style="list-style-type: none"> <li>Theorized to be close to plasma but compatibility concerns</li> </ul> </li> </ul> </li> <li>pH of 7.1</li> </ul>	<ul style="list-style-type: none"> <li>Non-PVC bags</li> <li>Normal saline v. Normosol-R</li> <li>Not buffered                             <ul style="list-style-type: none"> <li>Tried and tested pH with one buffered bag buffered</li> <li>pH of drugs and diluents vary batch to batch</li> </ul> </li> <li>Surgery observation of vasodilation                             <ul style="list-style-type: none"> <li>Report, instant feedback, clear picture of indication</li> </ul> </li> </ul>

### Key Learnings

- Be proactive, thorough, humble
- Seek to understand
  - Ask questions, over communicate, involve key stakeholders, simulate
- Prepare for the worst but fail forward
- Know what you don't know and look for the unknown


### Summary

- In the absence of commercial products designed to meet patient care needs
  - Assess current state of internal and external compounding
  - Identify and incorporate potential risk and mitigation strategies
  - Develop processes and policies to keep patients safe
  - Engage stakeholders early and understand their needs
  - “Go See”
  - Be ready to make the “right decision”

### References


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### Health care systems need to only consider official FDA statements when determining the safest and best way to deliver patient care.




**A** True

**B** False

Using the medication use process framework is an effective and systematic way to describe a situation and engage stakeholders. 

**A** True

**B** False

Intraoperative vasodilators must be at physiologic pH in order to be effective. 

**A** True

**B** False