Drug Shortages –
PDA’s Approach to Prevention and Management

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Presentation to Animal Pharmaceuticals Supply Chain Interruption

By

Christopher J. Smalley

Compounding Pharmacist Advisor
Agenda

• Introduction
• Why Does a Drug Shortage Occur?
• Examples
• PDA’s Approach to Prevention and Management
• QRM – Quality Risk Management
• Risk Levels and Risk Priority
• Drug Shortage Prevention and Response Plan
• Introduction to Workshop
Why Does a Drug Shortage Occur?

Is it a ‘good’ shortage if Sales exceed Marketing forecasts?
Why Does a Drug Shortage Occur?

Is Someone ‘Gaming’ the System?
Why Does a Drug Shortage Occur?

Is it Not Worthwhile Making?  
(Business Decision)
Why Does a Drug Shortage Occur?

Would a Shortage Occur During a New Product Launch?
PDA’s Approach to Prevention and Management of Drug Shortages
Sources of Risks of Shortage

Anywhere in the Value Chain

• Potential Risk to
  – API
    • Unreliable Source
    • Poor Specifications Resulting in Rework
  – Aging Facility
    • Unreliable Equipment
    • Unreliable Utilities
    • Regulatory Issues
# QRM – Risk Ranking

<table>
<thead>
<tr>
<th>Risk Ranking</th>
<th>Risk to Patients (product quality and/or product availability)</th>
<th>Risk to GMP Compliance</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High</strong></td>
<td>• Irreparable patient harm or death&lt;br&gt;• <em>Shortage of a medically necessary (life supporting or life sustaining) product</em></td>
<td>• Consent decree or warning letter&lt;br&gt;• Withdrawal of GMP certificate or manufacturing authorization&lt;br&gt;• Critical health authority observations or repeat inspection observations&lt;br&gt;• Systemic breakdown of GMP systems&lt;br&gt;• Recall</td>
</tr>
<tr>
<td><strong>Medium</strong></td>
<td>• Reversible patient harm&lt;br&gt;• <em>Shortage of product used for acute short-term or chronic long-term product indications</em></td>
<td>• Major health authority observations&lt;br&gt;• High complaint rate</td>
</tr>
<tr>
<td><strong>Low</strong></td>
<td>• No product or patient impact&lt;br&gt;• <em>No shortage or multiple sources available for products that are not medically necessary</em></td>
<td>• Minor observations&lt;br&gt;• Minor departures from GMPs</td>
</tr>
</tbody>
</table>
The Process

The Matrices should be applicable to all circumstances –

• Your firm may chose to evaluate the risk definitions

• The Key is:
  – Identify the highest risk (Priorities)
  – Take steps to reduce that risk (Mitigate)
# QRM – Impact to the Patient

<table>
<thead>
<tr>
<th>Therapeutic Use &amp; Consequences if Product not Available</th>
<th>Availability of Alternatives</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No Alternatives Available</td>
<td>Alternative Products Available: Similar Therapy</td>
</tr>
<tr>
<td>Medically Necessary Product, Life supporting or Life sustaining</td>
<td>Fatal or severe irreversible harm if the patient is not treated with the product</td>
<td>Risk Level A</td>
</tr>
<tr>
<td>Acute short term or chronic long term</td>
<td>Severe harm but reversible if patient is not treated with the product</td>
<td>Risk Level A</td>
</tr>
<tr>
<td>Other indications</td>
<td>Inconvenience if patient is not treated with the product</td>
<td>Risk Level B</td>
</tr>
</tbody>
</table>
The Process

A Couple of Slide Back –

• Matrix described risk in terms of risk to the patient and risk to cGMP compliance
• Going forward, our focus will be on the risk to the patient
  • Addressing risk to the patient is not an excuse to short-cut GMPs
# QRM – Risk Levels

<table>
<thead>
<tr>
<th>Product</th>
<th>Therapeutic Use</th>
<th>Consequences if Product not Available</th>
<th>Availability of Alternatives</th>
<th>Risk Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Targeted biologics for oncology treatment</td>
<td>Medically necessary product, life supporting or life sustaining</td>
<td>Death or severe irreversible harm</td>
<td>No alternatives available</td>
<td>Risk level A</td>
</tr>
<tr>
<td>(Trastuzumab)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antibiotics</td>
<td>Medically necessary product, life supporting or life sustaining</td>
<td>Death or severe irreversible harm</td>
<td>Alternative products available: similar therapy</td>
<td>Risk level A</td>
</tr>
<tr>
<td>(Azithromycin or Ciprofloxacin)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes treatment</td>
<td>Medically necessary product, life supporting or life sustaining</td>
<td>Death or severe irreversible harm</td>
<td>Alternative products available: similar therapy</td>
<td>Risk level A</td>
</tr>
<tr>
<td>(Insulin)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congestive heart failure medicine</td>
<td>Medically necessary product, life supporting or life sustaining</td>
<td>Death or severe irreversible harm</td>
<td>Exact product available but in other presentations</td>
<td>Risk level B</td>
</tr>
<tr>
<td>(Digoxin)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epilepsy medicine</td>
<td>Acute short-term or chronic long-term condition</td>
<td>Severe, reversible harm</td>
<td>Alternative products available: similar therapy</td>
<td>Risk level B</td>
</tr>
<tr>
<td>(Diazepam)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plasma protein therapies</td>
<td>Acute short-term or chronic long-term condition</td>
<td>Severe, reversible harm</td>
<td>Exact product available but in other presentations</td>
<td>Risk level C</td>
</tr>
<tr>
<td>OTC Cough suppressants</td>
<td>Minor indications</td>
<td>Inconvenience</td>
<td>Alternative products available: similar therapy</td>
<td>Risk level C</td>
</tr>
<tr>
<td>(Robitussin)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The Process

This is where your products fit into the matrix. Based on the therapeutic use, consequence if a shortage occurs, and availability of alternatives, a Risk Level is assigned.
# QRM – Risk Priority

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>Likelihood of Shortage</th>
<th>High</th>
<th>Moderate</th>
<th>Low</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk Level A</td>
<td>Risk Priority Level 1</td>
<td>Risk Priority Level 1</td>
<td>Risk Priority Level 2</td>
<td></td>
</tr>
<tr>
<td>Risk Level B</td>
<td>Risk Priority Level 1</td>
<td>Risk Priority Level 2</td>
<td>Risk Priority Level 3</td>
<td></td>
</tr>
<tr>
<td>Risk Level C</td>
<td>Risk Priority Level 2</td>
<td>Risk Priority Level 3</td>
<td>Risk Priority Level 3</td>
<td></td>
</tr>
</tbody>
</table>
QRM – Risk Triage

1. Define impact to patient
   - Medically Necessary Product, Life supporting or Life sustaining
   - Acute short term or chronic long term
   - Other indications

<table>
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<tr>
<th>Availability of Alternatives</th>
<th>No Alternatives Available</th>
<th>Alternative Products Available: Similar Therapy</th>
<th>Exact Product Available but in Other Presentations</th>
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</thead>
<tbody>
<tr>
<td>Risk Level A</td>
<td>Risk Level A</td>
<td>Risk Level B</td>
<td></td>
</tr>
<tr>
<td>Risk Level A</td>
<td>Risk Level B</td>
<td>Risk Level C</td>
<td></td>
</tr>
<tr>
<td>Risk Level B</td>
<td>Risk Level C</td>
<td>Risk Level C</td>
<td></td>
</tr>
</tbody>
</table>

2. At each risk level consider the likelihood of a drug shortage, and define priority

3. Define priority

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>Risk Priority Level 1</th>
<th>Risk Priority Level 2</th>
<th>Risk Priority Level 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk Level A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risk Level B</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risk Level C</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Validation. Delivered.
The Process

That Risk Level, A, B or C, then is matched up with information from your Risk Assessment

• Is the risk of the shortage
  – High
  – Medium
  – Low

• What is the resulting Risk Priority?
# QRM - Risk Controls

<table>
<thead>
<tr>
<th>Risk Priority</th>
<th>Suggested Controls</th>
</tr>
</thead>
</table>
| **Level 1**   | • Appropriate inventory and safety stock management  
               • Multi site sourcing with higher manufacturing capacity reserves  
               • Supplier management controls (see sec. 5.4 of TR54)  
               • Supply chain/transportation line security, business continuity and communication plan  
               • Extended Value Stream Mapping (VSM) |
| **Level 2**   | • Consider multi site sourcing  
               • Value Stream Mapping (VSM)  
               • Proactive inventory management  
               • Process capability and robustness exercised (with Quality Metrics) |
| **Level 3**   | • Generally accepted risk level |
The Process

The Risk Priority shows where your firm should focus its resources

• Suggested controls to mitigate risk
• Remember – what is done from a new product launch?
Drug Shortage Prevention and Response Plan

1. Identify risks
   - List of drug shortage risks and potential sources
     - Drug shortage risk register

2. Assess impact
   - Which patient population could be impacted? How?

3. Control Plan
   - What E2E controls will be implemented to ensure
     - proactive "resilience and flexibility"
     - "return to normal operations" in the event of a shortage

4. Communication Plan
   - What, who, when and how, e.g.
     - HAs: visibility to product risk register, control plan and triggers for HA/HCP notification
     - HCPs: alignment on which patients to prioritize in the event of a shortage

What risk indicating triggers will ensure ongoing monitoring, e.g.
- new product indication
- new market approval
- approval of a new alternate product or new unlicensed product
- shortage of an alternate product
- new risks to product quality/availability
- shutdown of a facility or withdrawal of GMP certificate
- below inventory/safety stock level targets
- usage volumes
Introduction to Workshop

Based on the Worksheets from the Technical Report

• You can chose to use a product from one of your firms
  – Best results for practice are for ‘legacy’ products

• Alternatively, you can create Product ‘X’ and create a scenario
  – A product that lands in Risk Priority Level 3 will not provide much experience using the tool

• Use additional paper to describe the reasons for selecting the ‘Probability of Shortage’
Questions
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