We Owe It to Patients To Embrace a Modern Quality System

“An ounce of prevention is worth a pound of cure” – Benjamin Franklin

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Conference on Quality in the Space and Defense Industries
Serving Patients Is a Privilege…

This privilege comes with significant responsibilities.
The Current Industry Quality System Is Outdated

Foundation formed in the early 1900’s

Developed in response to tragic events

Globalization has caused fragmentation and patchwork of requirements

GMPs tacitly promote a “test and inspect in quality” approach

So what does an ideal quality system look like?
Results of a Typical Pharmaceutical Quality Management Systems

- Multiple internal reviews and rework
- Unpredictable, inconsistent output
- Continuous fixes to product and processes
- Confusing SOPs and inefficient processes
- People dependent quality
- Relies on extensive inspection and testing
- No formal risk program

‘Too slow’ and ‘Sales Prevention’ or ‘Too many recalls’ and ‘Not Keeping up with Science’
An Ideal

Quality System

Is Simple, Robust and Sustainable
Quality System

A Well Designed QMS Promotes Accountability, Transparency and Continuous Improvement
A Simple Example of Simple, Robust and Sustainable

What Does SOP Mean?

Standard Operating Procedures

OR

Stacks Of Paper
A Simple Example of Simple, Robust and Sustainable

| Written for the User’s Benefit | Clear, Concise and Accurate | Uses Pictures and Symbols | Uses Proven Tools such as Information Mapping |

A Good Standard Operating Procedure

**S**tandard **O**perating **P**rocedures

**S**tacks **O**f **P**aper

OR
Consequences of Poor Quality Can Be Significant

- Harms patients
- Incurs regulatory sanctions
- Loss of business
- Incurs Liability
- Decreases Productivity
- Increases cost

These ramifications are not insignificant and must not be viewed as a “cost of doing business”
Why Have Others Implemented an Effective Modern QMS?

<table>
<thead>
<tr>
<th>Industry</th>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>Semi-Conductor Industry</td>
<td>Survival</td>
</tr>
<tr>
<td>Consumer Electronics</td>
<td>Reduce defects</td>
</tr>
<tr>
<td>Automotive Industry</td>
<td>Competitive advantage</td>
</tr>
</tbody>
</table>

A common thread was to satisfy the customer and achieve a competitive advantage.
The US Nuclear Navy Also Implemented an Ideal QMS

- Clear, concise and accurate procedures
- Repeat back process
- Not fully automated
- Immediate, irreversible with significant consequences
- Qualifications required
- Train on what to do, what can go wrong and how to respond
Victims of success

High barriers to entry and change

Isolation from economic downturns

Accept variability

What Keeps the Pharma Industry From Changing?

There Has Not Been Sufficient Pain Creating Pressure to Force Us to Change

If it isn’t broke don’t fix it

Fear of gaining regulatory approval

Inspect and test in quality approach

Blind compliance
Successful companies will batten down the hatches today to weather the storm tomorrow.
How to Develop an Ideal Quality Management System

Rome was not built in a day, and building an effective QMS is a journey that never ends.

- Create a culture of quality
- Promote the benefits of quality
- Tailor the message for the audience
- Gain executive support
- Work cross-functionally
- Drive operational excellence
- Implement new techniques and technologies
Where to Start

Implement Management Review

Focus on CAPA (Corrective Action, Preventive Action)

Identify, track and control variation

Obtain process, product knowledge and understanding

Conduct risk assessments to focus effort
Management Needs to Know When Stuff Happens

The outcome of management review…

a. Improvements

b. Resources

c. Revisions to quality policy and objectives

d. Timely and effective communication of the results of the management review

Remember serving patients is a privilege
A Simple CAPA System That Is Commonly Used Today

However this is not enough for an effective and efficient CAPA system.
An Advanced CAPA System Will

Must look for and address weak signals

- Provide feedback throughout the lifecycle of a project
- Respond to data trending and holistic data reviews
- Requires an Exception
- Implements a corrective action
- Happens in manufacturing
- Initiates an Investigation
- Utilizes a risk based approach
- Determines root cause
- Address industry and regulatory surveillance
- Document continuous improvement projects
- Implement CAPA earlier in the development process

Implement CAPA earlier in the development process
Three Other Important Things to do

- Identify, track and control variation
- Obtain process, product knowledge and understanding
- Conduct risk assessments to focus effort
<table>
<thead>
<tr>
<th>Current Quality Management System</th>
<th>Ideal Quality Management System</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple internal reviews and “re-dos”</td>
<td>Get it right the first time</td>
</tr>
<tr>
<td>Unpredictable, inconsistent output</td>
<td>Consistency in quality</td>
</tr>
<tr>
<td>Continuous fixes to product and processes</td>
<td>Build in Quality from the start</td>
</tr>
<tr>
<td>Confusing SOPs and inefficient processes</td>
<td>Clear SOPs and more simple and robust process</td>
</tr>
<tr>
<td>People dependent quality</td>
<td>Overall culture of quality</td>
</tr>
<tr>
<td>Relies on extensive inspection and testing</td>
<td>Leverages process knowledge and understanding</td>
</tr>
<tr>
<td>No formal risk program</td>
<td>Addresses risks leading to fewer issues</td>
</tr>
<tr>
<td>‘Too slow,’ ‘Risk Averse,’ ‘Not Risk Averse Enough’</td>
<td>Satisfied customers</td>
</tr>
</tbody>
</table>
What to Expect When You Succeed

The Power of Error Reduction
Improved Quality and Lower Cost

Reduced Errors

<table>
<thead>
<tr>
<th>Year</th>
<th>Cumulative Savings (M)</th>
<th>Errors per Lot</th>
</tr>
</thead>
<tbody>
<tr>
<td>2006</td>
<td>$0</td>
<td>2.0</td>
</tr>
<tr>
<td>2007</td>
<td>$50</td>
<td>0.5</td>
</tr>
<tr>
<td>2008</td>
<td>$100</td>
<td>0.0</td>
</tr>
<tr>
<td>2009</td>
<td>$150</td>
<td>95%</td>
</tr>
<tr>
<td>2010</td>
<td>$100</td>
<td>0.0</td>
</tr>
<tr>
<td>2011</td>
<td>$150</td>
<td>0.0</td>
</tr>
<tr>
<td>2012</td>
<td>$150</td>
<td>0.0</td>
</tr>
</tbody>
</table>

Cumulative Savings (M) Since 2006

Errors per Lot

Year
What to Expect When You Succeed

Reduced Errors

Faster Cycle Times

Disposition Cycle Time

Days

Drug Substance

Drug Product

2006

2012

64%

64%
What to Expect When You Succeed

- Less Scrap, Rework and Rejects
- Faster Cycle Times
- Reduced Errors

Scrap Reduction

- Year: 2006
- Dollars: 300
- Year: 2012
- Dollars: 6

92% Scrap Reduction
What to Expect When You Succeed

- Reduced Errors
- Faster Cycle Times
- Less Scrap, Rework and Rejects
- Lower Cost
- Robust, Reliable Supply

And we supplied every patient, every time!
Serving Patients Is a Privilege…

We must be there for every patient, every time