AGING FACILITIES

IMPLICATIONS/TASK FORCE/APPROACHES

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AGENDA

• IMPLICATIONS
  • Drug Shortage
  • Why
  • Future Capacities

• TASK FORCE
  • Definition
  • Age Related Problems
  • The Task Force & Results

• APPROACHES
  • Corrective Possibilities
  • Hurdles
  • New Tasks
NUMBER OF NEW DRUG SHORTAGES

After a rise it seems the problem is under control

Source: IMS Institute for Healthcare Informatics
The carry-over from previous years still causes a major drug shortage problem.

Source: IMS Institute for Healthcare Informatics
WHAT ARE THE MAJORITY OF DRUG PRODUCTS

**Form Type**
- Injectables: 15%
- Oral: 82%
- Inserts/Implants: 1%
- Rectals, Topical: 1%
- Dermatologics: 1%

**Brand-Generic Type**
- Generic: 83%
- Brand: 11%
- Branded Generic: 4%
- Other-Branded Generic: 2%

**Number of Products by Supplier Count**

Source: IMS Institute for Healthcare Informatics
WHAT ARE THE REASONS?

- Foreign matter in filled product (particulates, fibers etc.)
- Microbial contaminations
- Glass breakage/container closure
- Mislabling/incorrect product filling

Most other causes aggravate the 1st one.

Source: FDA
ECONOMIC DRIVERS CONTRIBUTE

Healthcare Cost Pressure
Generic Competition
Shareholder Satisfaction

COGS Reduction

Single Site
High Throughput
Low Inventory
Reduced Maintenance
Reduced CAPEX
Lower Labor Costs

Drug Shortage

Source: Woodcock, Wosinska
Facility capacity increases are needed to fulfill the rapidly rising demand.
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CURRENT SITUATION – AGING FACILITIES

- A rising scenario, a rising concern
- Can run smoothly, can be a ticking time bomb
- Rapidly aging, when COGS is sole focus
- Major contributor to drug shortage, when the facility is the sole supplier
CURRENT SITUATION – AGING FACILITIES

If processes are not automated, the precision of manual, human driven steps is crucial

Experience
Defined Tasks
Quality Conscious
Dedication
Pride
Long-term Employee
Old wall panel material starts to become contaminated

Risk:
• Quality issues
• Production shut-down
• High remediation costs

The need to decontaminate an entire site

Sources: Sabre Companies
AGE CAN MEAN SUB-OPTIMAL PROCESSES

Risk:
• Quality issues
• Unit operation breakdown
• Supply problems
• Yield losses

Sources: web
AGE CAN MEAN MULTIPLE EXPANSIONS

Risks:
Do we up-grade the quality standards?
Do we have the right personnel/material/waste flow?
Are the air handling systems or utilities up-to-par?

Sources: blog.ispe.org
HOW DO WE PERFORM UP-DATES

Continuous improvements or a seesaw approach; the later being probably motivated by regulators and not own initiatives

Risk:
- Quality issues
- Prolonged upgrade/shut down periods
- High remediation costs

Example:
We do not bring our car to the service when it broke down

Sources: blog.ispe.org
A CASE OF AN AGING FACILITY – BVL

70 Years in service

2011
The FDA found 10 violations of good manufacturing practices during a late 2011 inspection and 48 violations in May 2011

Nov.’11
A recent internal review of documentation indicated that routine preventive maintenance and requalification of some manufacturing equipment did not occur at the specified time interval, and is overdue

Oct.’12
>$300M investment in up-grades

Limited production has resumed

Jul.’14
Sold, the story to be continued...

Dec.’13
SUN Pharma gets under FDA scrutiny

Jun.’13
will concentrate production in the company’s newer, more commercially sustainable facilities. Ben Venue will cease production in one of the company’s older manufacturing facilities and cease aseptic filling operations of drugs manufactured in the company’s oldest manufacturing facility

Jan.’13
announced that it has voluntarily entered into a consent decree with the U.S. Food and Drug Administration (FDA) that relates to current Good Manufacturing Practice requirements.

Sources: Press releases, FDA files

Doxil Drug Shortage
AGING FACILITY ACTIVITIES

Formation of Facility/Process/Analytics Subteams

PDA Aging Facility Workshop 2015
AGING FACILITIES DEFINITIONS

- High process variability
- Depreciation
- HVAC unable to adjust to changes
- High degree of manual activities
- Equipment age
- Number of Incidences
- Poor maintenance
- Improper or outdated analytics
- State of the Art questionable
- Equimt. spare parts availability
- ...
AGING FACILITY DEFINITIONS

• **Facility**: Structure and building wide systems that support manufacturing operations (e.g. wall/ceiling/floor composition and layout, water systems, compressed air systems, clean steam systems, automated facility control systems (including systems such as LIMS, SAP and others), HVAC systems, etc.). Personnel, material and waste flows, overall facility layouts including cleanroom classifications and pressure cascades.

• **Process**: The manufacturing process (e.g. formulation, sterilization, filling, etc.) and related equipment specific to that process (e.g. bio reactors, process vessels, filling lines, lyophilyzers, CIP systems, etc.) Process flows, product transfers and flow of raw materials or components into the process unit operations.

• **Analytics**: In process tests performed during the manufacturing process (e.g. host cell proteins, biuret, conductivity, pH, potency, pre-filtration total microbial count, sterility, etc.) inline testing, process analytical technology tools, sensor technology, signal and test result capture via automation, the resulting statistics and potential corrections. Possible simulation tools, which can mimic specific quality, attribute shifts if changes are made. Sampling points, activities and testing.
AGING FACILITY ACTIVITIES

Formation of Facility/Process/Analytics Subteams

PDA Aging Facility Workshop 2015

PDA Survey and Survey Report
SURVEY RESULT SUMMARY

• Survey showed that most sites and products are older (>11 years = >80%)
• 73% of respondents say the facility runs good or excellent
• Aging is seen as dated technologies, frequent breakdowns, not meeting requirements
• Batch rejection rate is fairly high (>5% of 18% respondents)
• Very low portion of respondents perform in-process analytics or perform improvements
• Regulatory requirements encourage modernization and risk assessments are used extensively
• Improvements are mainly made to facilities, not to process and analytics
• Technology scouting is hardly ever done
AGING FACILITY ACTIVITIES

- Formation of Facility/Process/Analytics Subteams
- PDA Aging Facility Workshop 2015
- PDA Survey and Survey Report
- Assembly of questions by task force members
- Answers of questionnaire
- Points to Consider Document

Revised ➔ Board ballot
Task Force Team assembled 89 questions using the workshop, survey and other member input.
Consolidated Question #1:
What components should be included when evaluating the need to modernize a facility or process and what factors often prevent companies from moving forward with modernization plans?

Touched on in the answer:
Q.08. How would you recognize that your facility is aging, when you are living with it every day?
Q.15. How do you know that your facility is aging?
Q.16. Is there a trigger point which determines that you are having an aging facility?
Q.21. What are the major reasons for not modernizing the facility?
Q.29. Does the underlying infrastructure support process recapitalization (utility distribution piping, electrical distribution, water system, structural elements)?
Q.35. How do we reduce the fear of change?
Q.38. What components should be included in the business case to justify/demonstrate the need for a facility upgrade?
Q.39. Is the risk of not changing greater than the risk of making a change?
Q.71. How can I construct a business case for modernizing an aging facility?
Q.88. How to convince the C-Suite to make necessary changes, what are the benefit propositions and how to bring them concisely forward?
Q.80. When should a company begin considering modernizing a facility?
### Points to Consider for Aging Facilities

**Table of Contents**

I. Introduction ........................................................................................................ 5  
II. Recognizing A Facility is Aging ................................................................. 5  
   Q1. What indicators should be evaluated to determine if a facility or process is aging? 5  
      Facility/Equipment .................................................................................. 5  
      Process/Supply ....................................................................................... 6  
III. Impediments to Modernization ................................................................. 7  
   Q2. What factors often prevent companies from moving forward with modernization plans? 7  
      Regulatory Timing .................................................................................. 7  
      Risk and Cost .......................................................................................... 8  
      Lack of Knowledge .................................................................................. 8  
   Q3. How do to reduce the fear of change? ..................................................... 8  
IV. Business Case for Modernization ............................................................... 9  
   Q4. What components should be included in the business case to demonstrate the need for a facility upgrade? ................................................................. 9  
   Q5. How does a recapitalization plan fit into facility modernization? .......... 9  
   Q6. How viable is the concept of re-purposing existing out-of-service facilities? 9  
   Q7. How many times can a facility be partially renovated? ......................... 10  
V. Strategies for Modernization ...................................................................... 10  
   Q8. What are some strategies for addressing an aging facility? .................. 10  
      Modernizing the Existing Facility .............................................................. 11  
      Maintaining a Facility when the Decision has been made to Build a New One 12  
   Q9. How can analytical instruments be modernized? ...................................... 12  
      Replacement of Existing Equipment using the Same Technology .............. 12  
      Replacement of Existing Equipment with New Technology .................... 13  
   Q10. How can risk management be applied to modernizing a facility or process? 13  
   Q11. How can risk management help determine a cost-effective strategy for process and facility upgrade? ................................................................. 15  
   Q12. What are some strategies for modernizing a process? ......................... 15  
      Strategies for ongoing modernization of a new process or one that has been recently modernized ................................................................. 15  
      Strategies for modernization of an older process that has not been updated routinely ........ 17
AGENDA

• IMPLICATIONS
  • Drug Shortage
  • Why
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POSSIBILITIES – RETROFITTING PROCESSES

Needed conversion
POSSIBILITIES – RETROFITTING PROCESSES

From large scale stainless steel to medium volume single-use

- De-risking
- Higher flexibility
- Faster turn-around
- Closed systems
- Advanced PAT

10kL

2kL
Single-use technology processes create flexibility & speed, but...

...is only as flexible as the surrounding infrastructure!
NEEDED – DEFINING & HARMONIZING

The PDA Task Force PAC IM needs to address change classifications and regulatory actions for example harmonization

What is what, can mean:
- Substantial resources drain
- Lowering the motivation of change/improvement
- Mothballing facilities
NEEDED – NEW APPROACHES
...WE CAME A LONG WAY THOUGH!
THANK YOU!
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