

Aging Facilities – The Challenge Continue For Pharma/Biotech

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Agenda

- Background
 - 2015 PDA Survey on Aging facilities
 - 2017 points to consider for aging facilities
 - Recent facts about Drug Shortages
- Common issues still affecting industry
- Other considerations
- Summary
- Q&A

Background



Background – FDA observations

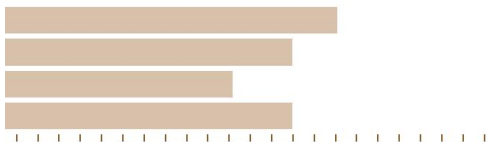
- A rising scenario, a rising concern
- Can run smoothly, BUT can be a ticking time bomb
- Rapidly aging, when COGS is sole focus
- Major contributor to drug shortage, when the facility is the sole supplier



- Increase in product shortages due to compliance issues
- High dependency on manual/ Human driven processes
- Sub-optimal or obsolete facilities and processes
- Tendency to expand facilities rather than green fields – patching approach
- Strong focus on Cost rather than Quality/Compliance

2015 – PDA Aging Facilities Survey

PDA Survey



2015 Aging Facilities



- Most sites and products are older (>11 years = >80%)
- 73% 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 perform in-process analytics or perform improvements
- Regulatory requirements to encourage modernization and risk assessments are used extensively
- Improvements mainly to facilities, not process /analytics
- Technology scouting is hardly ever done

Same topics since 2017

Points to Consider for Aging Facilities

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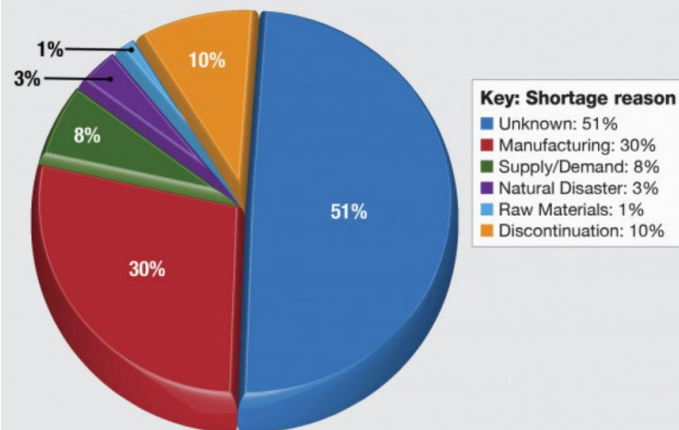


- How to recognize my facility is aging
- What are the limitations or Impediments to Modernization
- How we justify the Business Case for Modernization
- What is the right strategy for Modernization
- How I define or mitigate the Impact of Changing Standards
- How we can slow the Aging Process
- What are the changes in Regulatory environment and how can we minimize impact

Drug Shortages continue as a major cause

Reasons for Shortages as Determined by UUDIS Investigation (2018)*

It is often unclear why shortages occur. Drug manufacturers are not required to report reasons for supply disruptions to FDA or any other governing body. In 2018, the causes of just over half (51%) of active shortages that UUDIS followed were unknown.

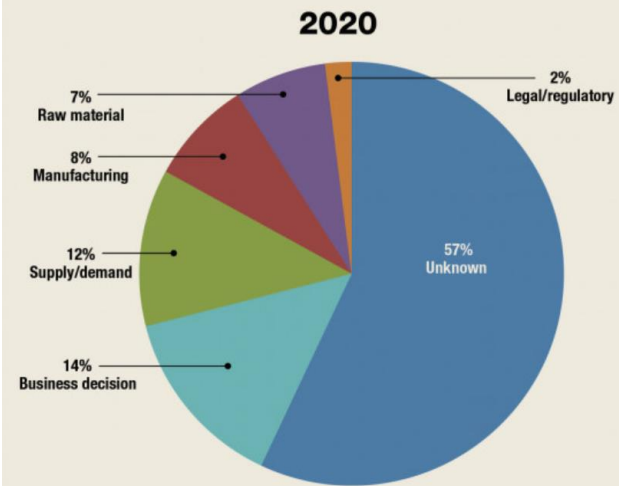


<https://www.pppmag.com/article/2501>



Reasons for Shortages as Reported by Manufacturers During UUDIS Investigation

For the most part, it is unclear why drug shortages occur. However, natural disasters and the COVID-19 pandemic partially accounted for deficits in 2020.



<https://www.pppmag.com/article/2764>

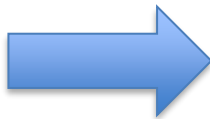
Factors to consider for Aging Facilities



How to recognize Aging facilities

Indicators to evaluate:

- Regulatory/Quality trends
- Facility/Equipment relevance
- Process/supply resiliency



Examples:

- decrease in lot acceptance rate
- increase in recalls
- physical deterioration of systems,
- obsolete technologies
- aging process with outdated raw materials.

What are the limitations or Impediments to Modernization

Limiting Factors:

- Regulatory Timing
- Long Return on Investment (ROI) or high costs
- Lack of Knowledge



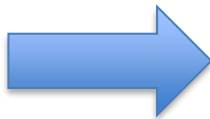
Mitigation ideas:

- Assess product lifecycle and if business wise to modernize or close/transfer
- Develop a global regulatory acceptance strategy

How we justify the Business Case for Modernization

Considerations:

- Investments needed for improvement and change
- Manufacturing interruptions
- Inventory build
- Hours of labor



Opportunities:

- Review and evaluation of consequences
- Quantify regulatory and business benefits – Missing opportunities
- Combination of Compliance with Business sense - \$ at risk

What is the right strategy for Modernization?

Strategies:

- Modernize Actual facility
- Decommission and build a new one



Considerations:

- Need of a comprehensive gap and cost/benefit analysis
 - ability to meet cGMP /safety requirements
 - alignment with current and forecasted demand,
 - cost of modernization
 - facility downtime
 - operational cost

How I define or mitigate the Impact of Changing Standards?

Issues:

- Same technology or new
- Automated vs Manual
- Same output or more
- Short term vs long term vision



Strategies:

- Revised international standards and regulations affect modernization.
- Perform a gap analysis to evaluate compliance with revisions.
- Expectations of regulators and auditors: implementation plan to address gaps

How can we slow the Aging Process?

- Enhanced predictive maintenance program can slow the aging process.
- Enhanced process controls and/or process analytical technology can extend the life of aging process equipment.
- Risk management can help implement an effective maintenance program.

Regulatory implications

- Post-approval change reporting impacts facility and process modernization.
- Engaging regulatory authorities is important when modernizing a process or facility.
- Use of comparability protocols can facilitate changes related to modernization.



FDA perspective



Aging Facilities: An FDA Perspective

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Supervisor Consumer Safety Officer/Pharma 3
Office of Regulatory Affairs (ORA)

PDA MO Valley Chapter Meeting (Oct 5, 2017)

- Are there high risks or the potential for high risks of not meeting cGMPs?
- Are your systems and equipment adequate to prevent contamination, to eliminate potential mix-ups?
- Do you experience errors that maybe were okay 10 or 15 years ago, but would not be acceptable under today's standards?
- Are you experiencing an uptick in errors?
- What programs does your firm have in place to ensure that the facility and processes continue to operate properly? (e.g., Change Control, CAPA)

What about Safety?

- Aging affects the condition and integrity of all process equipment, facilities, and infrastructure.
- Prolonged exposure to normal operating conditions and occasional upsets can cause equipment to deteriorate, making it more prone to failure.
- Many plants now operate at rates and conditions not anticipated during construction.
- Aging is not necessarily related to the actual age of the facility or piece of equipment. It is about how well the facility or equipment has been operated and maintained, which requires constant vigilance by personnel.

SUMMARY



Aging facilities – a continuous opportunity

- Aging/Old \neq Noncompliant (Necessarily) .
 - It is how well is maintained and updated.
- Modernization plans must be facility-specific.
- Common challenges:
 - Financial and operational resources
 - Continuous change in technologies and regulatory expectations
- More than just Quality output – Safety/Compliance need to be considered

