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WHITE PAPER

RETURN ON INVESTMENT: WHAT IS THE COST OF NOT DOING MES?

Major saving areas with MES / Typical steps to evaluate ROI / MES data infrastructure to enable Pharma 4.0

"If you need to do an ROI study, then perhaps MES is not for you ...!" goes a provocative comment from a consultant when positioning to management the benefits of Manufacturing Execution Systems (MES). In this age of digitization, many pharma and biotech companies still struggle to gain senior level buy-in for investments in manufacturing IT. Whilst corporate IT initiatives such as Enterprise Resource Planning (ERP) are well understood and seen as 'no-brainers', not believing in a Return On Investment (ROI) for manufacturing solutions is a major reason why companies still struggle to eliminate paper GxP records and modernize systems.

Where is the ROI?

To justify an investment typically an assessment is made on the estimated impact on the top and bottom lines of the profit and loss, i.e. what savings, revenue, quality and efficiency gains a new capability will bring. An ROI study, once successful, works out a timeframe that the identified benefits would take to pay back (return) the upfront costs. If we think on ERP systems, companies are rarely conducting formal studies to decide if they need to implement a solution that manages their business finances. Upon reaching a certain scale and complexity a corporate ERP simply becomes expected infrastructure. With ERP it is understood that One View Of The Truth is needed and process owners, financial controllers, investors, accounting auditors and regulators all demand robust systemized controls and records that electronic systems provide for key data and transactions.

Is this not yet true for manufacturing production and quality? Are there no such internal and external drivers and benefits that easily justify level 3 systems (ISA, 2018) such as MES?

Does MES save costs?

Yes! MES digitizes the end-to-end processes in and around manufacturing – from receiving goods to warehousing, through production and packing. There exist great opportunities for building process improvements and efficiency savings across the entire operation and the shop floor into MES. Looking at the following cost components in manufacturing we can identify areas where MES adds benefits and potential for ROI:

Raw and packing materials:

- Type of cost: direct, variable and tracked batch to batch
- Relevant MES functionalities: stopping manual errors occurring with materials at the time they occur

Examples:

- Waste from using incorrect materials or using restricted/expired inventory, results in potential for cost savings due to scrapped/reworked production or in worst case, recalled batches

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Operating expenses:

- Type of cost: indirect, usually fixed on an overall factory level
- Relevant MES functionalities: eliminating or automating processes that require personnel results in potential for cost savings through headcount reduction.

Examples:

- Removal of second person verifiers in material weighing and charging operations due to use of validated systemized material flow controls (EMEA)
- Reduction of persons needed to generate, review and approve data and documentation

Work-in-process (WIP) inventory costs:

- Type of cost: direct, usually variable based on the production throughput
- Relevant MES functionalities: speeding or automating processes that hold up production and making data available for improved scheduling.

Examples:

- Optimizing non-value-added setup, troubleshooting and clearance/tear-down times for production machinery through the use of system controlled equipment status management and more efficient operator SOPs
- Improving cycle times through finite scheduling by integrating planning with real-time plant floor operation status and feedback
- Improving batch review, approval and thus product release times through review by exception and parametric release based on Electronic Batch Recording (EBR)

Quality and compliance costs:

- Type of cost: direct, usually variable based on factory performance
- Relevant MES functionalities: improving and automating data and record controls as required by regulatory authorities, particularly in the area of data integrity by reducing human errors in the entry, usage and storage of data (FDA).

Examples:

- Elimination of paperwork
- Right first time controls of manual data entries
- Automated timestamps and calculations
- Systemized check of person's identity and authority including biometrics
- Integration to other systems for automated data entry
- Electronic archiving of source data

A business case for MES

Industry and client studies as well as post-implementation assessments on MES consistently show a summary of strong and important benefits both due to stronger quality controls and improvements in efficiency of processes and data. The list below is from a multi-site MES deployment at a global pharma multinational corporation and represents a compelling case for MES in pharma and biotech manufacturing:

Reduction of data entry time by	80%
Reduction of batch deviations by	80%
Elimination of lost paperwork by	80%
Reduction of paperwork between shifts by	60%
Reduction of manufacturing cycle time by	35%
Reduction of defects (product quality) by	25%
Reduction of "work in process" by	25%

While the benefits shown are considerable, to take the next step to use these as benchmarks for a specific assessment at a facility can be challenging if the existing processes are not well enough known, recorded and trended. To be able to improve a process you need to already have sufficient data about it, and this must be accurate and match the reality of what happens day to day. A constant struggle in pharma manufacturing is that existing 'data' is at insufficient depth or detail and is often based on 'tribal knowledge' and what is recorded on paper which is inherently unreliable and inaccurate. It can often happen that ROI assessments for level 3 systems are hampered by the very systems intended to be replaced and improved!

Typical steps to run through for a first ROI evaluation of cost/benefit savings would be as follows:

- **Perform interviews** with key management to identify wishes, drivers and objectives, desired capabilities, planned changes and potential risks that will impact the business in future
- **Workshop on** how value of data and capability may change over time based on identified future impacts
- **Analyze existing processes** at non-detailed level, confirm durations of key activities and bottle neck processes by measurement not rumor
- **Establish monetary data** to define value of typical areas of saving such as increased equipment utilization, yield, material scrap rate, WIP, cycle time, quality

defects rework etc., focus on areas where cost/value data is known

- **Talk and onboard** operational staff to highlight perceived opportunities for improvement and to check for feasibility to change processes
- **Select 'low hanging fruit'** which is easiest to implement at greatest possible value for deeper assessment
- **Compare solutions** check against the selected process in standard off-the-shelf level 3 systems and perform user workshops and surveys for buy-in and acceptance
- **Form consensus** on potential for improvements in the process time, accuracy and failure rate and equate findings back to monetary value

Data integrity and the cost of non-compliance

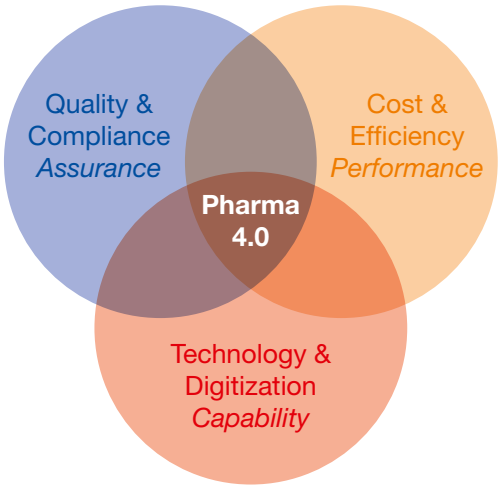
Risk is an important additional item to assess in terms of identifying problems, causes and potential benefits for a business considering large scale IT solution investments. For pharma and biotech companies today the topic of data integrity is receiving the highest attention in the industry due to the risks of failing to meet the latest regulatory expectations. Inspectors policing the largest pharma markets such as the US and Europe are looking in detail at the underlying recording, systems and handling of data, the critical information used to make quality related decisions and generally people's actions and behaviors according to defined processes.

Data integrity is mainly a change in the way that inspections are conducted as the GMPs are the same, however it has raised direct comparisons of how controlled IT tools can be shown to better manage data than the current paper and procedural systems. However, building monetary values for data integrity non-compliance into an ROI study will be difficult to determine from the perspectives of cost, value and benefits as is dealing with a % element of risk. Data integrity can be considered the main reason that for instance Asian pharma companies have started to adopt level 3 systems in the last 5 years. By adding such non-quantitative benefits into an ROI study alongside the 'traditional' cost/performance topics above then with MES we can demonstrate financial gains with significant risk reduction for the business.

Across the pharma and biotech industry a new trend is emerging: companies are setting up initiatives for MES without running any detailed studies at all as understanding has been growing that such systems directly reduce the risks of data integrity and audit failure due to observations on human error. A large pharmaceutical plant in Asia supplying the US market can be responsible for hundreds of millions of dollars a year in revenues that are at potential and constant threat in today's regulatory climate. Even if the mitigation is a small percentage chance for such export plants that risk may be sufficient enough for corporate management and owners to decide to update their technology and better safeguard their data integrity.

Missing the Pharma 4.0 bus

We are starting to see pharma pioneering companies who are moving rapidly towards digitization as a key corporate initiative. These leaders look 'past compliance' instead to a vision of a data driven innovative business that is powered by latest IT tools and opportunities. This future focus looks to leverage technology to make step changes in process capability and to enable new business models. In a very short time such digital pioneers have realized ahead of the industry that they must first adopt IT systems as a data infrastructure and platform for the coming opportunities of the Pharma 4.0 future.
If we look to other industries, those that have stood still as the massive waves of change that digitization brings have been swept away when the world suddenly turns faster and



away from legacy processes and technology. It may be that the largest risk for a pharma or biotech company today is in not developing new products and services following the digital model and to not build core capabilities that enable innovation in the organization at every level. To put it another way, the biggest risk is to 'miss the digital bus'.

Start benefits' case

Return On Investment is still a critical step to pass for decisions in manufacturing IT that require substantial capital, time, change and effort. By performing a detailed benefits' case and assessment real opportunities for quality and efficiency improvements can be identified and the actual reality inside the manufacturing plants can be known. Such bottom-up initiatives are an excellent starting point for the exploration of process improvements that can be made through the adoption of technology, to meet the current GxP requirements, lower the risks of non-compliance and act as an important stepping stone on the digital journey.

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