

FROST & SULLIVAN

# Pharmaceuticals Manufacturing

The power of data and market trends impacting pharmaceutical manufacturing and R&D facilities



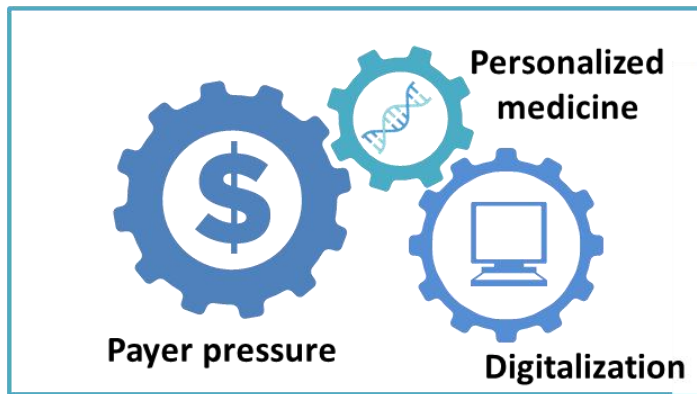
000111000111000111

## Contents

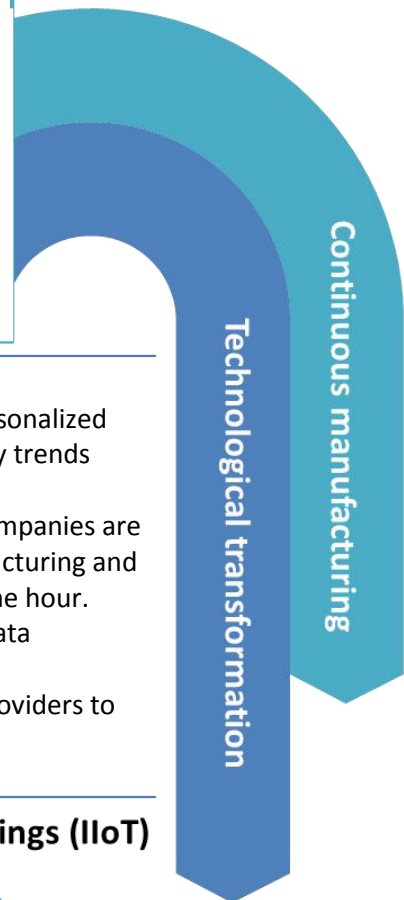
1. Executive Summary.....	3
2. Introduction .....	4
3. Key Trends in Pharmaceutical Industry.....	5
Rising Cost Pressure Propelling Growth in Outcome Based Reimbursement and Outsourcing.....	5
Quest for Novel Treatments Leading to Rise in Drug Complexity and Personalized Medicine.....	5
Expanding Digital Footprint .....	6
4. Focus on Pharmaceutical Manufacturing – streamlining operations to enhance production efficiency.....	7
Rapid Transitioning to Continuous Manufacturing.....	7
Technological Transformation Generates Huge Data-Related Growth Opportunities .....	8
Best Practice on Data Management and Data Storage .....	11
5. Focus on Labs – Adopting Advanced Technologies such as Modular Manufacturing and IIoT to Boost Production .....	12
Rise in Modular Manufacturing .....	12
Increasing Adoption of Industrial Internet of Things (IIoT) .....	14
Computerized Maintenance Management System Aiding 4.0 Manufacturing Transition.....	18
Rising Adoption of Electronic Batch Records Accelerating Time to Market.....	18
6. Conclusion.....	19

# 1. Executive Summary

## Trends shaping pharmaceutical industry

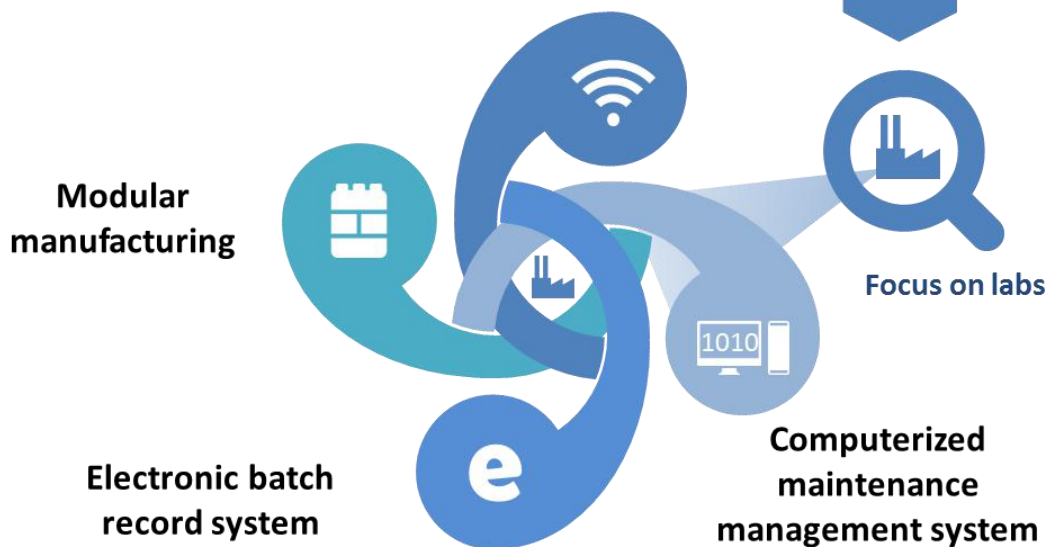


## Impact on pharmaceutical manufacturing



- Rising payer pressure, the move towards more complex personalized medicine and increasing adoption of digital solutions are key trends shaping the global pharmaceutical industry
- To align themselves to the global trends, pharmaceutical companies are optimizing their operations. Adoption of continuous manufacturing and a complete technological transformation are the needs of the hour.
- 2017 witnessed multiple regulatory updates pertaining to data management, security, access and validation.
- Pharma companies are actively partnering with specialist providers to enhance data security and validation, especially in cloud.

## Industrial internet of things (IIoT)



## 2. Introduction

The global pharmaceutical industry is witnessing a surge in CEO confidence from US tax reforms, turbulent equity markets, and the strengthening global economy. The growth of the pharmaceutical industry is boosted by healthcare digitalization and democratization, creating an explosion in patient data, and the emergence of value-based reimbursement models. The convergence of biopharmaceuticals, drug delivery devices, and companion diagnostics—enabled by digital connectivity—is driving regulatory and commercial changes in many exciting ways for the industry.

Recently, the US Food and Drug Administration (FDA) released several guideline documents, which are likely to increase the adoption of digital technologies in pharmaceutical manufacturing. These guidelines provide frameworks for electronic submission of clinical data and manufacturing establishment information, while laying down expectations for maintaining data integrity and compliance with good manufacturing practices (GMP).

This has encouraged pharmaceutical companies to adopt advanced processes such as Industrial Internet of Things (IIoT), modular manufacturing, electronic batch record systems and computerized maintenance management systems that employ sensors and advanced analytics.

The objective of this paper is to outline the key transformational trends in the pharmaceutical industry and assess their impact on pharmaceutical manufacturing and research and development (R&D) facilities. The paper tracks the various strategies adopted by pharmaceutical companies to enhance their manufacturing capabilities and technological footprint – with a special focus on labs. It aims to demonstrate the role that improved building management solutions can play in achieving cost effectiveness, improving energy efficiency, and boosting the sustainability of the pharmaceutical industry's production processes.

### **3. Key Trends in Pharmaceutical Industry**

The pharmaceutical industry is facing a number of key challenges and transformational changes that will determine its future development: Rising costs, the move towards more complex personalized medicine and the increasing adoption of digital solutions are all key trends shaping the industry.

#### **Rising Cost Pressure Propelling Growth in Outcome Based Reimbursement and Outsourcing**

Globally, governments are struggling to meet the increasing demand for advanced treatments from an ageing population. The result is increased pharmaceutical expenditure which is forecast to increase by 6.5% per year to 2022, when global expenditure will exceed \$1 trillion<sup>1</sup>.

Escalating drug prices have meant insurance providers and government agencies are focusing on outcome-based reimbursement of drugs. Governments are also encouraging the adoption of low cost biosimilars<sup>2</sup>, as alternatives, where possible, to costly biologic drugs.

The pressure to curb rising drug prices is forcing pharmaceutical companies to look at different avenues for increasing their operational efficiency and reducing expenditure. This is resulting in an increase in outsourcing, especially in the manufacturing of drugs. Due to evolving manufacturing practices, which requires the manufacturing of high value, low volume drugs, pharmaceutical companies are increasingly viewing Contract Manufacturing Organization (CMO) providers as strategic partners. They can assist in boosting their technical capability and provide manufacturing support across regions whilst also delivering the flexibility and reliability that the suppliers themselves would expect.

#### **Quest for Novel Treatments Leading to Rise in Drug Complexity and Personalized Medicine**

To compete in a crowded market, pharmaceutical manufacturers are exploring novel biologic<sup>3</sup> compounds and therapeutic targets. In 2017, the US FDA approved a record number of drugs (46 new approvals) of which, 22 were biologics.<sup>4</sup> Pharmaceutical companies such as Roche, Amgen, Sanofi, AbbVie and Novo Nordisk are increasingly focusing on biologics due to a growing demand for innovative therapies and rising patent cliffs. Consequently, the ability to rapidly ramp-up production facilities is a key success factor.

---

<sup>1</sup> Frost & Sullivan

<sup>2</sup> A biosimilars is a copy of an approved biological drug (see footnote below) in the market. Biological drugs are protected for a certain period of time through patent laws, which prevent any company to make a copy of them. However, once patents expire, companies are free to make biosimilars, and launch them at a lower price to the biological drug. Biosimilars are clinically demonstrated to be similar and interchangeable with approved biological drug.

<sup>3</sup> Biologic drug is a medicine that has been made using a living system such as a cell or a microorganism. It is generally a large and complex molecule. E.g. insulin, blood component, vaccine etc.

<sup>4</sup> US FDA

## **Expanding Digital Footprint**

Initially considered as a laggard, the global pharmaceuticals industry is catching up on the adoption of digital solutions. Digital data is transforming operations across the pharmaceutical value chain, right from drug discovery to post marketing surveillance.

The adoption of digital sensors in clinical trials is on the rise. They are being used to analyze patient data and help in patient recruitment and retention. They are also being utilized for tracking patient experience in clinical trials and guiding trial design.

## **4. Focus on Pharmaceutical Manufacturing – streamlining operations to enhance production efficiency**

The pharmaceutical industry is navigating a challenging path. It needs to improve operational efficiency in order to reduce costs and protect margins, whilst also ensuring the quality and safety of pharmaceuticals. As part of achieving these goals, it must innovate and increase the utilization of digital solutions. However, all of this must be done within the frameworks provided by regulatory agencies, particularly to ensure that data is correctly recorded and securely stored at all points in the process, including the building's environmental conditions.

### **Rapid Transitioning to Continuous Manufacturing**

The need to manufacture drugs cost effectively, in a safer, faster and more sustainable manner is propelling pharmaceutical companies to gradually transition to continuous manufacturing processes, meaning that pharmaceutical buildings must be operational 24 hours per day, 365 days per year.

Currently, most drugs are manufactured using batch processing, which involves multiple steps. Product is collected after each step, evaluated for different parameters conforming to quality, before using it as a raw material for the next step.

Continuous processing, on the contrary, uses a continuous stream of raw materials, furnishing finished products at a constant rate. Through the use of sensors, an active feedback mechanism reduces the need of manual handling, increasing overall safety in production. The process results in less waste, leading to a lower ecological footprint, reduced inventory and lower capital costs, making the process cost effective.

### **Regulatory stance**

Regulatory agencies are encouraging manufacturers to transition to continuous manufacturing. The FDA was one of the first regulatory agencies that recommended adoption of continuous manufacturing.

*“Right now, manufacturing experts from the 1950s would easily recognize the pharmaceutical manufacturing processes of today. It is predicted that manufacturing will change in the next 25 years as current manufacturing practices are abandoned in favor of cleaner, flexible, more efficient continuous manufacturing.”* Janet Woodcock, Director, FDA Center for Drug Evaluation and Research

The European Medicines Agency (EMA) adopted a similar stance and recognized that continuous manufacturing dossiers are likely to be more complex. It recommended early dialogue with the agency, especially for legacy products transferred from batch to continuous manufacturing. The agency supports the industry through scientific advice, process analytical technology (PAT) teams, subject matter expert office, and the Innovation Task Force. As per the EMA *“The current regulatory framework is adequate to allow*

*continuous manufacturing. No specific guideline currently available, but existing guidelines are supportive.”*

### **Case examples**

Vertex was the first pharmaceutical company to get approval for using continuous manufacturing in 2015 from the FDA and EMA, for its fixed-dose combination tablet product, Orkambi, used for the treatment of cystic fibrosis. Janssen’s tablet for treating HIV, Prezista was the first supplemental FDA approval (2016) for changing from an established batch process to a continuous manufacturing process. It resulted in a significant reduction in operational requirements, with the usage of 2 rooms instead of 7 for batch process. Also, production timelines were reduced to 1 day, instead of up to 2 weeks for batch.<sup>5</sup>

### **Challenges and solutions**

One of the most significant challenges was being able to determine the clinical efficacy of an active ingredient online. This has changed with the emergence of highly specialized technological tools and software solutions that enable data collection directly in the process. Tools for analysis improve the manufacturer’s understanding and control of the process, increase process quality and reduce the risk of losing products due to nonconformity. This increases the utilization of operational assets by 30% to 40%; and a product that previously took one or even two months in production is finished in a few days. Ensuring proper control of room assets is vital to achieving these efficiency gains. HVAC systems and other process equipment must be optimized to ensure peak operational performance.

## **Technological Transformation Generates Huge Data-Related Growth Opportunities**

Pharmaceutical companies are facing unprecedented growth in data. Pharma’s transition from paper to digital, across the value chain, has added a tremendous volume of data to its IT system. With rising usage of sensors in production and in the building, as well as the adoption of Industrial Internet of Things (IIoT) practices in manufacturing, the volume of data generated is expected to register an exponential growth.

To encourage innovation and increase adoption of new technological solutions, regulatory agencies are proactively providing guidance to the industry. Recently, the FDA has released several guideline documents, all of which indicate more reliance on electronic data.

### **Regulatory updates**

Recently released documents by the FDA to steer the pharmaceutical industry towards optimized use of data, included the following:

---

<sup>5</sup> Global DataPoint



- Providing regulatory submissions in electronic format—submission of manufacturing establishment information
- Current expectations and guidance, including data integrity and compliance with Current Good Manufacturing Practices (cGMP)

These are likely to have an influence on the way data is managed and stored by pharmaceutical companies.

### **Current expectations and guidance, including data integrity and compliance with cGMP**

This is one of the key guidance documents released by the FDA in 2017. It details the FDA’s expectations on the storage and management of data by pharmaceutical companies. The FDA published the document in light of rising incidences of violations involving data integrity observed during cGMP inspections.

As per the guideline, data integrity requires that data is attributable, legible, contemporaneous, original or true copy and accurate. The following are required to maintain data integrity:

- *“Backup data are exact and complete, and secure from alteration, inadvertent erasures, or loss*
- *Data be stored to prevent deterioration or loss*
- *Activities be documented at the time of performance and that laboratory controls be scientifically sound*
- *True copies or other accurate reproductions of the original records; and complete information, complete data derived from all tests, complete record of all data, and complete records of all tests performed”*

All of these have implications for the building management and control systems.

### **Data access, management and security**

As per good manufacturing practices (GMP), any data created as part of a record must be evaluated by the quality unit as part of release criteria and maintained for GMP purposes. Electronic data generated to fulfill GMP requirements should include relevant metadata. This is defined as contextual information required for understanding data that will be required to reconstruct a GMP activity. All computerized systems in pharmaceutical manufacturing and research, must meet the following conditions:

- *“Should have sufficient controls to prevent unauthorized access or changes to data. There should be controls to prevent omissions in data (e.g., system turned off and data not captured). There should be a record of any data change made, the previous entry, who made the change, and when the change was made*

- *If system breakdowns or failures would result in the permanent loss of records, a back-up system should be provided. A means of ensuring data protection should be established for all computerized systems*
- *Appropriate installation and operational qualifications should demonstrate the suitability of computer hardware and software to perform assigned tasks*
- *Incidents related to computerized systems that could affect the quality of intermediates or Active Pharmaceutical Ingredients (API) or the reliability of records or test results should be recorded and investigated”*

### **Key implication**

As a regulatory requirement, pharmaceutical manufacturers are required to store environmental parameters such as temperature, humidity, pressure and airborne particle counts over a period of up to 30 years from production to packaging and storage of the drugs. Pharmaceutical companies can benefit from working with vendors, which provide field devices, controllers and building management systems that are used to generate, collect, monitor, report, analyze and store such data. A level of confidence now exists in the industry that such data can now be securely stored in the cloud for safe retrieval at a later stage.

### **Data validation**

Computer systems validation are regulated in the US by the FDA rule on Electronic Records/Signatures (21 CFR Part 11) and in the EU by the European Medicine Agency's Guidelines to Good Manufacturing Practice - Annex 11. Key regulatory requirements state that when computers or automated data processing systems are used as part of production or the quality system, a pharmaceutical manufacturer is required to validate computer software for its intended use according to an established protocol. Also, all the electronic records should be signed with electronic signatures; e-signatures have the same legal standing as a person's handwritten signature.

A number of pharmaceutical companies are gradually shifting to cloud computing, wherein the data is stored and managed through an off-site server or the cloud. This includes vital production process and building control data. For instance, Kyowa Hakko Kirin, a manufacturer of prescription drugs, had transferred almost 40% of the data from the company's physical data centers to the Amazon Web Services Cloud, as of September 2015.<sup>6</sup>

However, to date, regulatory agencies have not released any guidance document governing data validation on clouds. In the absence of any guidance, creating validation documentation as per a company's internal standard operating procedures (SOPs) is key for deploying cloud-based solutions. In case of an inspection, a company must be able to demonstrate the validation of the software as per its internal SOPs. The best placed

---

<sup>6</sup> Amazon Web Services Cloud

company to provide this is the system supplier, which can provide automated validation reports, using real time analytics on different performance parameters. The result is a validation report in a few days, rather than 4-8 months, the time which is usually required for validation of on-premise software solutions, which is a significant efficiency gain. Validating documents through clouds allows pharmaceutical firms to decrease the time spent on regulatory review, helping to boost productivity, to gain operational efficiency and to increase speed-to-market.

## Best Practice on Data Management and Data Storage

The pharmaceutical industry requires a robust set of best practices to ensure protection of data as, in addition to patient data, it needs to protect its self-generated data, including intellectual property and operational parameters. The pharmaceutical industry is an attractive target for hackers, who actively fish for intellectual property. In June 2017, a cyber-attack on Merck resulted in a temporary shutdown of the human papilloma virus vaccine Gardasil 9 production, which resulted in a loss of greater than \$300 million.<sup>7</sup>

The following best practices can assist pharmaceutical companies in developing a secure environment for data management and storage:

- **People management:** In any organization, people are the key to regulate processes. It is important to implement strict authentication policies and checkpoints – across users, devices and the network – to avoid misuse of information. Companies should deploy tools that can provide increased security by combining workflows in access control, intrusion detection and video surveillance. A building management solution provider should be able to provide a flexible and scalable platform that supports a variety of communication protocols and IT standards providing improved operational safety at lower running costs.
- **Policies, training and advanced reporting tools:** People should be regularly trained on a company's compliance policies. Training programs that give examples of possible scenarios are simple yet effective in raising awareness and empowering personnel. In pharmaceutical production, quality control personnel should be trained to conduct regular review of operations and practices to identify any data anomalies. *“One of the simplest, most effective things company leaders can do to stop data integrity problems in their tracks is putting a quality person directly into the manufacturing area to detect and address problems in real time.”*<sup>8</sup> - Jose Gutierrez, Consultant at the FDA Group. Pharmaceutical companies should employ sensors and tools that provide real time information on different parameters such as energy usage and power consumption. Such tools can assist in early identification of problems, leading to timely rectification.

---

<sup>7</sup> TechRepublic

<sup>8</sup> J. Gutierrez, FDA

- **Cyber security:** Pharmaceutical companies need to consider a holistic security approach. Assessing risk and understanding a company's vulnerabilities should be the first step. This should be followed by having an updated inventory of systems, networks and dataflow. A company should have multiple layers of protection, using tools such as anomaly-detection software and authentication software. Information technology and operations technology engineers should work together to build layers of defense using diverse technologies, at multiple levels of the industrial and building automation and control systems. All the incorporated cyber security solutions shall be certified to international standards series IEC 62443.

## 5. Focus on Labs – Adopting Advanced Technologies such as Modular Manufacturing and IIoT to Boost Production

In addition to the broader trends shaping pharmaceutical manufacturing, drilling down further, reveals that pharmaceutical labs are gradually adopting advanced technologies such as modular manufacturing and IIoT. Through the adoption of these technologies pharmaceutical firms aim to boost their production efficiency, to increase the speed to market, to reduce their carbon footprint and to enhance the safety and integrity of their production processes.

### Rise in Modular Manufacturing

Modular manufacturing or 'factory in a box' is the latest trend in the pharmaceutical manufacturing sector. In the advent of personalized medicines, which have an uncertain demand, CMOs and pharmaceutical manufacturers are actively utilizing single-use systems in modular manufacturing to achieve flexibility in production planning. Genentech, Lilly, and Merck are all exploring such systems. Key drivers propelling labs towards modular manufacturing include the following:

#### **Faster time to market**

Modular manufacturing gives the flexibility of connecting multiple pieces of equipment through the use of sensors to provide an integrated and robust production system. Transparency in production processes due to the availability of machine status data helps in the efficient monitoring of operations and to avoid downtime – leading to a faster time to market.

#### **Need to expand global footprint**

Entering new markets, especially in emerging countries, requires significant investment in the set-up of manufacturing facilities. A key barrier faced is the arrangement of a qualified engineering team and equipment providers. Modular manufacturing helps to overcome this barrier by providing standardized structures, all over the world. A company can use the same modules and equipment in an emerging economy like China as it uses in a developed

country like the US, without the hassle of arranging specialists for the set-up of manufacturing facilities.

### **Manufacture low volume personalized medication**

The adoption of a business model geared to provide low volume-high value drugs requires smart manufacturing strategies. Modular manufacturing gives the industry the flexibility to establish multiple small units at low cost, across different locations.

### **Shorter production timeline can help in speed to market in a low cost and sustainable manner**

The need to accelerate production while reducing cost of goods sold and manufacturing drugs in an environment friendly manner, is providing a big push to the adoption of modular manufacturing. Modular manufacturing often involves the use of single-use equipment, which results in cost savings and reduces carbon footprint thanks to the avoidance of equipment cleaning and re-sterilization throughout the manufacturing process.

### **Regulatory stance**

Regulatory agencies do not differentiate between regular manufacturing and modular manufacturing. In both cases GMP requirements must be followed, with each batch having the same specifications, quality, efficacy, safety and reproducibility. Labs need to ensure that material used to construct different parts of the modular lab including walls, floor and ceilings meet quality standards laid down by regulatory agencies. In addition, modular structures should meet local standards related to climate control and earthquake resistance.

### **Case examples**



Pfizer is the leader in modular manufacturing. In order to develop modular manufacturing capabilities, it has established Portable, Continuous, Miniature, and Modular (PCCM) manufacturing units in Belgium, Germany and Texas (US).<sup>9</sup> Modular pods developed here are shipped to a warehouse, where they can be assembled to function as a complete production unit.

*As per Phillip R. Nixon, VP, Pfizer, "Complete manufacturing facilities can be deployed in less than 12 months using the PCMM model. PODs can be assembled and deployed in inexpensive warehouse space, which reduces the site cost for a manufacturing facility. There is plenty of vacant warehouse space available around the world, or pharma companies can build new warehouse facilities relatively inexpensively. PCMM units can be disassembled and redeployed, if business conditions change. One of the initial applications of PCMM*

---

<sup>9</sup> Pharmaceutical Online, BIOPRO Baden-Württemberg

*technology within Pfizer will be to transfer new chemical entity products from its R&D site to launch and commercial sites with virtually no scale up or tech transfer. This will enable the company to accelerate its process development cycle and time-to-market.”*

### **Key challenge and solution**

Modular manufacturing requires a flexible and mobile research infrastructure along with measurement, automation and control solutions that can easily adapt to any situation. Changes to the room layout have influence on temperature, humidity and pressure, but also on the lighting and blind concept and last but not least, the energy consumption billing allocation formula.

Pharmaceutical companies need to partner with vendors that can offer total room automation, including economical fume hood sash management, for a safe and secure operation and reduced energy consumption.

### **Increasing Adoption of IIoT**

IIoT is making in-roads in pharmaceutical manufacturing. The pharmaceutical industry is gradually adopting IIoT technologies, most of which are already mature in other industries and have proven effective in improving the efficiency of complex manufacturing operations. Leveraging lessons from this should help companies improve their financial and operational performance.

### **IIoT enhances operational efficiency**

Digital technologies have become an essential component of the manufacturing industry in automating operations, streamlining processes and integrating the different manufacturing departments that are otherwise not adequately connected. IIoT technologies will enable manufacturers to gain a 360-degree view of their plant operations, with the ability to drill down to any level of detail at any stage of product development. This essentially means that data can be accessed at just the click of a mouse or a tap of the screen.

### **Promotes use of paperless environment, reducing carbon footprint**

The benefits of IIoT in pharmaceutical manufacturing are similar to those in other industry verticals. The distinguishing advantage, however, is that IIoT help pharmaceutical manufacturers ensure proper documentation during production for compliance reasons. This may involve terabytes of data being stored and processed in the cloud, as traditional methods of data storage get completely phased out. Introduction of IIoT in the pharmaceutical sector also means making a fundamental shift towards outcome-based, targeted therapies, characterized by a more individualized production method.

IIoT plays an important role in the continuous monitoring of connected factory equipment and personnel. This real-time tracking can help to improve the effectiveness of factory processes by enabling informed decisions through digitally enhanced and data-driven

services. The other important benefit of IIoT in pharmaceutical manufacturing is the modular construction of pharmaceutical production plants, including “plug-and-play” integration of both production and building automation systems. This leads to a lower time-to-market of pharmaceuticals.

### **Connected sensors yield more meaningful data**

The pharmaceutical industry has extremely sensitive storage conditions. The manufactured products typically are of high value and have a short storage life. At times, improper demand forecasting can lead to stockpiling of drugs for up to 6 months. Medicines need to be stored under prescribed storage temperatures, moisture and sterility conditions. This makes it imperative to use approved monitoring and control systems that can validate the storage conditions and keep the drugs viable.

### **Regulatory viewpoint**

The pharmaceutical industry is one of the most regulated manufacturing industries. The industry demands a clear understanding of manufacturing processes and strict adherence to stringent regulatory standards that guide these processes. Any change introduced in the production process of a product has to be registered with regulatory agencies for each affected product. However, the adoption of IIoT should not face regulatory obstacles, unless a company changes a production process in ways that impact product quality. Adding sensors to a machine for collecting data and monitoring operations does not entail the modification of the machine or the process. Rather, it will facilitate meeting regulatory guidelines which mandate the collection of all information about machines, people, and materials involved in pharmaceutical manufacturing.

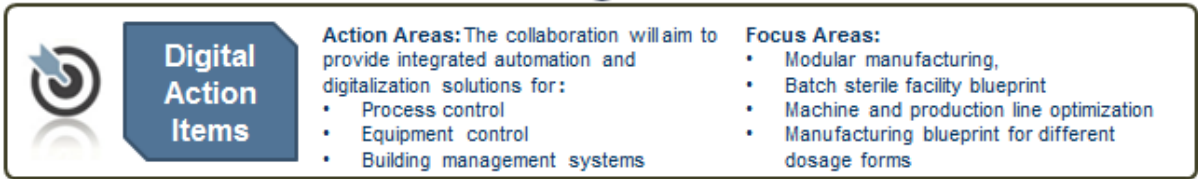
### **Case examples**



GSK has partnered with Siemens to enhance manufacturing on four key facets: efficiency, productivity, safety, and quality.<sup>10</sup>

---

<sup>10</sup> Company Website, Frost & Sullivan







Merck and Janssen are two other early adopters of IIoT. While Merck is trying to connect disparate data sources, such as supply and demand data, and use historical forecasts and predictive algorithms to drive production based on accurate demand scenarios<sup>11</sup>, Janssen is overhauling its manufacturing processes to enhance efficiency in production<sup>12</sup>.

*“The supply chain of the future should fully rely on digital solutions. Our vision is to have a self-driving supply chain powered by artificial intelligence. As Tesla has developed self-driving cars, we want a self-driving supply chain without pilots. We want to join with a few selected partners to develop tailored solutions in terms of technology, and together we can discover how to leverage the technology to drive our business better.”* Alessandro de Luca, Chief Information Officer, Healthcare Business Sector, Merck

*“We’ll be able to put raw materials in at one end and through the steps of mixing, blending and compressing the materials into tablets, through sensor technology that’s embedded in the equipment; we’ll be able to perform the testing online, in real-time. Our use of IoT-enabled manufacturing opens up a much greater world of flexibility, a dramatic reduction in cycle time, and allows us to use our people resources more efficiently.”* Kathryn E. Wengel, Worldwide Vice President & Chief Supply Chain Officer, Johnson & Johnson

### **Key challenge and solution**

Traditionally, the pharmaceutical sector has been a laggard when it comes to the adoption of technology. IIoT requires the installation of multiple hardware and software components for establishing a robust system. Engaging with multiple suppliers can result in unnecessary complications in vendor management. A pharmaceutical company looking to adopt an IIoT platform should engage with a supplier that can provide end-to-end IIoT solutions. Suppliers should be able to connect all the products, plants, systems and machines, to enable the capture of the wealth of data generated by the IIoT system.

IIoT has become an integral part of manufacturing and therefore it is only natural that the pharmaceutical industry should look to adopting it at the earliest opportunity. This will involve manufacturing companies taking important decisions, such as phasing out legacy systems. The IIoT may be in a nascent stage of development, but its impact on pharmaceutical manufacturing is certainly indisputable.

---

<sup>11</sup> Pharm Exec

<sup>12</sup> IndustryWeek

## **Computerized Maintenance Management System Aiding 4.0 Manufacturing Transition**

Downtime as a result of a fault in production can cause losses to pharmaceutical manufacturers. Key factors leading to downtime include poor maintenance (resulting in internal technical faults), misconduct by employees and external damage. Technical faults can be predicted by maintenance software before they happen and cause the machine to breakdown. This is achieved through analysis of data generated by sensors in machines, on various parameters such as vibration, lubrication, noise and bearing temperatures. A comprehensive maintenance strategy is also pivotal to ensure an error-free production and safe drugs.

To have an effective preventive maintenance program in place, pharmaceutical firms started to utilize industry 4.0-inspired Computerized Maintenance Management System (CMMS). The CMMS collects and analyzes data collected through sensors using predictive algorithms to compose predictive maintenance plans. It also assists in the issuance of work orders, scheduling interventions and controlling the execution of preventive maintenance tasks. Transition from corrective to preventive maintenance provides the following benefits:

- Enhanced production efficiency
- Increased machinery performance and life, increasing return on investment
- Reduced maintenance costs
- Reduced downtime and asset failure
- Avoiding operational failure helps to maintain quality and safety of drugs

## **Rising Adoption of Electronic Batch Records Reducing Time-to-Market**

Paper based batch record systems are prone to error resulting from manual reporting of readings. A single human error can delay the release of an entire batch as a regulatory inspector can question the quality of a batch in case of mismatch in production metrics and a company's standard operating procedures.

Electronic master batch record management systems can integrate the manufacturing execution system and the process control system to provide automated documentation of production data. Paperless manufacturing ensures efficient quality assurance. Every step and every raw material can be monitored, tracked and recorded during the production. The systems coordinate the real-time control processes on each level, synchronize the process steps, and exchange parameter values. Reviews are conducted with the help of exception rules that identify and document deviations. The process promotes quality and reduces cost by eliminating errors, reducing scrap and avoiding process delays. It also helps in meeting regulatory compliance requirements with adequate cGMP features and with complete manufacturing traceability.

An electronic master batch record management system offers the following advantages over a paper based batch record system:

- Adoption of electronic master batch record management system results in up to 75% reduction in human errors leading to reduction in investigations and waste<sup>13</sup>
- It provides instant access to archived batch records leading to faster investigation and audit times
- Time spent by production personnel on handling documents is reduced by up to 30%<sup>14</sup>

*“When you work with paper you have to wait for someone to review the paper. Armed with real-time process information, qualified personnel can conduct batch quality review during manufacturing rather than after. An electronic batch record solution is the GPS of manufacturing operations. It guides the user to the desired destination, finds the shortest trip, alerts one to dangers, and feeds them back in real time.”* Jerome Repiton, Head of Product Supply Operational Excellence, Ferring Pharmaceuticals

## 6. Conclusion

With increasing emphasis on improving operational efficiency through technology upgrades, pharmaceutical companies can hope to ease the increasing pressure on their bottom line figures, arising due to the rising complexity in their business environment. Technological advancements in pharmaceutical manufacturing require partnership with multiple suppliers that can assist on several fronts, including sensor deployment, data storage, system and site access and management. Another important aspect is the building automation management, wherein important parameters such as temperature, humidity, and sterility of pharmaceutical production facilities and research labs can be closely maintained and monitored.

However, engaging with multiple suppliers for each site can lead to unnecessary complications, both from a technical and from a business management perspective. Problems could emerge while integrating different vendor tools or negotiating multiple supplier contracts. In conclusion, it is recommended that pharmaceutical companies engage with a single or a small number of large suppliers that can provide end-to-end services – from integrated building automation solutions to data management and access tools.

---

<sup>13</sup> Sustainable Design and Manufacturing - Springer

<sup>14</sup> Sustainable Design and Manufacturing - Springer

Frost & Sullivan, the Growth Partnership Company, works in collaboration with clients to leverage visionary innovation that addresses the global challenges and related growth opportunities that will make or break today's market participants. For more than 50 years, we have been developing growth strategies for the Global 1000, emerging businesses, the public sector and the investment community. Is your organization prepared for the next profound wave of industry convergence, disruptive technologies, increasing competitive intensity, Mega Trends, breakthrough best practices, changing customer dynamics and emerging economies?

For information regarding Frost & Sullivan's technology snapshot, please write to:

[info@frost.com](mailto:info@frost.com)

[www.frost.com](http://www.frost.com)