BLUEmountain

HARNESSING THE POWER OF INDUSTRY 4.0 FOR LIFE SCIENCE

Leverage the latest advancements in technologies to drive innovation and deliver improved patient outcomes

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INTRODUCTION

Industry 4.0 is a new host of technology-enabled manufacturing and management processes that is changing the paradigm of industry around the world. The life sciences industry is no exception to the shifting trends. Pharma 4.0™ is the industry-specific term that was redefined by an ISPE special interest group to highlight the innovative technologies that are adopted to ensure the manufacturing and delivery of high-quality pharmaceutical products that are effective and safe. The push to start moving a company towards Industry 4.0 is propelled by sector-specific challenges it faces in the day to day, such as increasing compliance requirements, the ever-growing international competition, and the rising demand for better and safer products to be delivered faster.

Industry 4.0 is regarded as the “Fourth Industrial Revolution” that was first presented in 2011 at the Hannover Fair as the German government's strategy to apply science and risk-based approaches to manufacturing and process intelligence. The term brings together novel technologies such as cloud computing, advanced computing, robotics, artificial intelligence, and the Internet of Things (IoT).

Visualize a pharmaceutical factory with entirely automated tools, computers, and robotics that can identify and rectify critical issues, and perform quality control checks - in other words, a self-contained system that sustains itself without human intervention. This is the vision of Industry 4.0.

Harnessing the power of Industry 4.0 in the life sciences has the potential to drive innovation and transform the way pharmaceutical, biotechnology, and healthcare companies operate.

HISTORY

INDUSTRY 1.0

Medicines were originally botanical, herbal, or mineral and animal preparations collected from the environment and used in forms that were scarcely altered from how they are found in nature. The 19th century saw the transition from unaltered manual preparations to the production of drugs on a wholesale scale using machinery that was able to crush, mill, blend, and press drugs into tablets. One such example is the salicylic acid-containing willow bark, that post-mechanization started to become commercially available as aspirin tablets. Individual pharmacies, and the dye and chemical industry played a great role in developing technologies at the time and kickstarted the pharmaceutical industry. Some of the machines from that time, including pneumatic mills and tablet presses, are still in use even today.

INDUSTRY 2.0

The second industrial revolution took place between the late 19th and early 20th centuries. It became known as the technological revolution. Electricity and electronic machines paved the way for globalization and the advancement of manufacturing technology. Production quantities also increased greatly during this time. Standardization led to consistent quality, potency, and efficiency of manufactured drugs.

Many believe that a large percentage of pharmaceutical manufacturing today still functions at the Industry 2.0 stage.

INDUSTRY 3.0

Industry 3.0 happened sometime in the late 20th century, and it became known as the digital revolution. Computers and communication technologies, including the internet and wireless communication made it possible to establish a high degree of automation to achieve higher product and process quality. With greater automation, remote sensing capabilities, and robotic monitoring, the need for human operators is greatly reduced. It also reduces human exposure to toxic chemicals and diminishes human error.

While many industries are well into Industry 3.0, it is still making its way across the life science industry. The adoption of Industry 3.0 can help the industry tackle its drug shortage problems by improving process control and real-time analytics.

INDUSTRY 4.0

As each industrial revolution has transformed the world, so too will Industry 4.0. This stage enables manufacturing systems to operate in an autonomous, integrated and self-organizing way that is almost free from human involvement. Industry 4.0 forces us to rethink manufacturing paradigms and imagine a world where manufacturing technologies are not only responsive to rapid changes in supply or demand but can also analyze and predict trends in real-time.

PILLARS OF **INDUSTRY 4.0**

Moving from a current manufacturing system to one that has adopted the Industry 4.0 level requires a new way of thinking and operating. It also requires a coordinated effort to ensure the entire system is designed and ready to address everything from product quality to regulatory compliance and data integrity issues. We discuss here the pillars of Industry 4.0 that will enable the transformation journey for the life science industry.

It's All About the Data

In many ways, the basis of Industry 4.0 is data. The amount of data gathered in pharmaceutical manufacturing is staggering, and not traditionally structured. Even medium-sized pharmaceutical companies collect between 500 terabytes to 10 petabytes of data each year. What can it be used for once collected, and what do we do with it once we are done using it?

There are four key problems when it comes to data.

The absence of context:
Numbers and figures mean vastly different things depending on where they come from. 650 milligrams of paracetamol in a tablet is vastly different from 650 milligrams of digitalis. When you only know the figure of 650 milligrams without the context, the information becomes meaningless.

Data entropy:
The further you get from the source of the data, the more the quality of the data degrades. It loses context, and compression can cause a great loss in quality, especially in terms of visual data.

Poorly and variously structured data:
We often think of data as a massive spreadsheet of numbers that is easy to access and use, but this is often not the case. Some data is auditory, and some data is visual. Even when we have well-ordered numbers, how do we organize them into usable rows, columns, or graphs? How can we take this even further into forming meaning and gathering insights from data?

Data overload:
Sometimes, there is simply too much data! Where can it possibly be stored, and how can pharmaceutical industries come up with the hardware to store, retrieve and use this data?

The path to adopting Industry 4.0, is all about how data is collected, organized, and transformed into insights. Data collection is the first step of that process. Once collected data is digitized, it can then be sorted and analyzed as Big Data. Artificial intelligence, which comes next, is able to extract meaning and knowledge from digitized data. Digital maturity is the state of gaining true insight from collected data and turning it into actions. A key ingredient to implementing Industry 4.0 successfully is being able to achieve total digital maturity that transforms reactive operations into integrated digital ecosystems that are proactive and predictive.

The Industrial Internet of Things (IIOT)

The Industrial Internet of Things (IIOT) is a digital, or virtual interconnection of actual physical items and machinery to each other, creating a cyber-physical system.

Imagine that you are traveling home from work and need to make dinner. You have informed your house management system that you'll be making a baked casserole. If you drive a GPS-enabled car, it can recognize when you are exactly fifteen minutes away. At this time, your GPS system could communicate with your kitchen! When you enter the home, the kitchen system has already switched the oven on to preheat, and the casserole is ready to be baked immediately. This is just an example of what the Industrial Internet of Things could look like, but it still paints a vision of an easier, more efficient, less wasteful method of doing things. The Industrial internet of things (IIOT) would take this basic example much further, incorporating it into manufacturing.

Computing devices, sensors, and equipment can be integrated online. Products "talk" back within an IIOT framework, communicating about environmental conditions, quality attributes, use, and performance of products. Machinery would communicate with each other in an integrated system. In a pharmaceutical factory, this could look like a tablet press communicating that it is being underused below its capacity and that the mixing machine should work more quickly.

In life sciences, IIOT can be applied to real-time situations, on an as needed basis. Many believe that we are entering the era of personalized medicine. If information about personalized dosages or drug combinations is communicated with manufacturing equipment through IIOT, personalized medicine becomes a reality in a shorter period of time.

IIOT can massively improve industrial efficiency and capabilities. Different countries have different regulations for products, and one factory may be providing drugs to different countries. Similar to being personalized to an individual, drug manufacturing can be personalized to each set of regulations, making the validation and compliance processes less stressful while being able to reduce waste and address drug shortages on a global scale.

Artificial Intelligence

Artificial intelligence (AI) and Machine Learning (ML) have been buzzwords in the industry for a decade. AI itself exists on a hierarchy, from lower independent capability to higher independent capability. Artificial Neural Networks (ANN) are the lowest rung of AI. These neural networks are physical wiring systems made to mimic human and animal nervous systems in order to create faster processes. The integration of digital data within a computational framework can generate immense insights for the pharmaceutical industry. Yet there exists massive hesitation that prevents its widespread use.

True artificial intelligence incorporates independent thought, not based entirely on the outcome of previous experiences. They can use this independent thought to make decisions normally made by humans, providing data-driven power. AI is a powerful tool for reasoning, problem-solving, learning, and decision making.

Biopharmaceutical applications of AI are varied and promising. AI-based quality control can fine-tune quality decisions each time, refining which products pass the test and which do not. IIOT and AI can also work together to create collaborative robots which work together, and the AI can power efficiency-improving decision making.

Digital Twins

A digital twin is a digital replica of a physical process, through the creation of modeling and simulations. It is a perfect, virtual mimic of a real thing, and can be classified into different types:

- **A component twin** or part twin is the smallest digital twin. It is just one unit or part of a larger manufacturing process or system.
- **Asset twins** involve two or more components. These can be useful in communicating performance data.
- **System or unit twins** use more than one asset.
- **Process twins** provide a holistic overview. It represents systems that work together to create a production facility.

It is easy to imagine a digital twin as a mere simulation, but this is a pale imitation of what it actually is. Digital twins often rely heavily on sensors that collect data to power it. Digital twins and physical objects can work together iteratively to create the best possible version of a component, asset, system or process.

Digital twins represent immense advantages and applications in the life science industry. It can greatly boost research and development. Imagine setting up an experiment. In order to test whether something really works the way you hypothesize, you need replicates. Replicates are expensive and require resources. A digital twin can be used to run infinite replicates over and over. It makes it possible to visualize the entire product life cycle and determine the efficient use of materials. Material harvesting is an integral part of the sustainable vision of a circular economy. For example, digital twins can generate usage possibilities for tablet packaging and other non-hazardous waste. Real trials often involve physically large objects, mechanically complex projects, and expensive equipment. The use of a digital twin eliminates most - if not all, of this wastage.

CHALLENGES OF IMPLEMENTING **INDUSTRY 4.0**

Big Data, Digital twins, AI, and IIOT represent a massive potential for the life science industry to upgrade itself and benefit from the digital transformation. Wastage and expenditure can be reduced, working conditions and sustainability improved, and competitive advantages provided to early adopters of Industry 4.0. However, this is not to say that the adoption is without its hurdles. Here we outline the key challenges a company faces in implementing Industry 4.0.

Regulatory

Current regulatory frameworks in place around the world are not prepared for the advanced technologies that Industry 4.0 brings. Most of the regulations around manufacturing compliance were established around the industry 2.0 stage. Even when new processes promise to ease the regulatory burden and improve product quality, the lack of evidence that regulatory agencies are prepared to implement the required changes makes it a challenge for the industry to ditch conventional systems and adopt advanced technological options.

A large part of the life sciences industry is still transitioning into Industry 3.0 while a good percent of them still function at the Industry 2.0 level. Regulating an industry that is at these two stages has itself proven to be a challenge. Adding a third level of advancement complicates this even further. Regulatory frameworks will need to be adjusted in such a way that they encourage early adopters of new technologies without penalizing those that need additional time to upgrade their systems.

Anticipating these regulatory stumbling blocks can go a long way toward addressing them. International communication with industry leaders can create a set of regulatory processes to address the massive changes that Industry 4.0 will bring. New guidelines are being developed to address the continuous manufacturing of small molecule and biological drugs that will make it easier to achieve global regulatory acceptance for them.

Technical

Industry leaders will also pioneer finding technical challenges by sheer virtue of encountering them. First, they must be uncovered, then they must be rectified.

One of the biggest challenges industry members are running into now is the question of what to do with data, especially once it has been collected and used. Should data be destroyed? If it is not destroyed, what can be done with years and years of data, requiring immense storage capabilities? How can we process and retrieve this amount of data?

Removing humans from the manufacturing equation and replacing them with IIOT and AI systems requires a shift from human-machine interfaces to machine-machine interfaces. Intensive reprogramming each time a new system is connected is impractical. Manufacturers must work with each other to build plug-and-play systems even when components come from different manufacturers.

Other significant risks associated with Industry 4.0 are data vulnerability and cyber-threats. Cyber threats include stealing and misuse of data, particularly secret or sensitive data, as well as hacking systems and rendering them unusable to the owners. Using third-party data stores, retrievers and processors requires a set process to address how and when they can use the data. Companies will need to strengthen their data and systems architecture to reduce the threat of disruptions and data breaches to product manufacturing systems.

Logistical

The innovations which result from Industry 4.0 will require a massive cultural and mindset change. People often fear progress, both from real concerns about hurdles, as well as a concern as to what the future might bring.

The biggest shift that will likely take place is in recruitment. Life science companies actively seek the best biologists, chemists, and engineers. Now, there will be a massive demand for data scientists and software architects. Initially, there may also be a scarcity of available personnel, with the existing workforce being in great demand.

A number of logistical challenges also surround the use of AI. Artificial intelligence requires a lot of data, particularly historical data, to function. Licenses, such as intellectual property rights, surrounding the use of information, stunt the capability of AI. Manufacturers must move away from a closed, secretive business model, and be encouraged to freely share and collaborate with their data. Rather than competition driving innovation, the dawn of Industry 4.0 hints at a more collaborative approach to success.

BENEFITS OF ADOPTING **INDUSTRY 4.0**

Despite all its challenges, the progress and improvement in manufacturing technologies that Industry 4.0 will usher in, is unstoppable, and life science industries will benefit greatly from it. Industry 4.0 presents a number of benefits that can help a company keep pace with and yield an edge over its competition.

1. Tech-enabled systems automatically provide agility and reactivity.
2. It can boost sustainability.
3. Customization is a feature that can be programmed in, allowing specific targets to be met without a new manufacturing chain.
4. Human error and therefore wastage is reduced.
5. Robotics and computing technologies ensure incredible energy efficiency.
6. Approximately two-thirds of drug shortages are from quality issues. Automation within Industry 4.0 can mitigate this, with robotic quality checks.
7. The Human Element: Industry 4.0 promises to greatly improve working conditions. The post-COVID era is also the age of the empowered worker. Resignations are skyrocketing in Europe and the United States. Workers are demanding better wages and pushing back against repetitive jobs, long hours and poor working conditions. The automation and overall efficiency improvements with Industry 4.0 could eliminate unsafe and repetitive jobs and lower worker hours. In addition, workers can be relieved from working with hazardous chemicals and processes.
8. Industry 4.0 provides significant advantages with its data management power and automation capability. The amount of data gathered in pharmaceutical manufacturing is significant. The usual statistical analysis are often lacking when it comes to examining pharmaceutical data. Cloud computing provides required storage and computing capacity instantaneously, resulting in an elastic computing response.

MAKING THE MOVE TOWARDS **INDUSTRY 4.0**

There is considerable excitement around Industry 4.0 in the life science industry. Digital technologies including cloud-based and big-data analytic solutions are rapidly gaining acceptance in the industry. For a company that seeks to improve its efficiency, productivity, and profitability, embracing an Industry 4.0 mindset will facilitate this process. There are a few things to keep in mind.

01

Consider implementing cloud-based solutions.

Cloud-based solutions meet industry requirements for large data storage, computing resources, and AI algorithms, which are crucial for working with big data. The biggest advantage of cloud-based platforms is convenience. Cloud platforms provide auto-backup, and data replication services, and guarantee that data endures. Quality data can be accessed anytime, anywhere around the world. Experts predict that cloud computing solutions will see mass adoption by top life sciences, research and development, and information technology organizations within the next few years. However, compared to other industries, life science organizations have been hesitant to adopt cloud-based solutions mainly due to security and quality concerns.

Quality concerns can be addressed by choosing to work with providers that have established businesses in the industry for years and have a long and reputable history of good practice. To evaluate and choose a service provider, it would also be beneficial to refer to ISPE GAMP guidelines, Britain's MHRA guidance on managing cloud-based services, or The World Health organizations cloud-based service provider agreements. They all suggest choosing providers with life-science-specific certifications.

The concern of security often stops companies from considering a move into cloud-based systems. However, due to the amount of development and implementation of the latest security technologies, current cloud-based solutions are considered more secure than traditional on-premise systems. Moreover, these systems were originally built, tested, and used by the finance and health care industries where data security and privacy are of the utmost importance.

02

Tackling Data Integrity and Compliance

Data integrity relates to the use and maintenance of collected data and is a critical requirement for the FDA's compliance process. ALCOA and GAMP standards are used to ensure data integrity and validation. Organizations must carefully consider vendors looking at their validation and maintenance resources and look to leverage an application designed around GMP compliance and data integrity requirements. Some of the key features to look for in a cloud-based solution to ensure GMP compliance include:

- Easily viewable audit trails
- Unique user logins
- Information capture capability (date, time and signature capture)
- Ability to set different security levels.
- Smart fields and pick lists to reduce data recording errors.
- Automated workflows to ensure steps are not missed.
- Capability to make certain fields required.

03

It is important that the company prioritize achieving digital maturity across all its systems, processes, and people as it looks to establish a future-ready manufacturing process that is predictive, self-correcting, and adaptive.

04

A company must be prepared to look beyond an immediate cost-benefit-based analysis of available tools and digital technologies. Think of them as important initial investments to prepare for a future where these technologies will offer tremendous advantages. Benefits include, more control, fewer errors and product shortages, and increased efficiency, revenue, and profitability.

CONCLUSIONS

Progress is inevitable and so is the reshaping of the life science industry's manufacturing practices through digital transformation, robotics, and autonomous and advanced computerized systems. The promise of Industry 4.0 is to improve sustainability, efficiency, resource utilization, and quality while minimizing product shortages around the world. Despite these advantages, the road to Industry 4.0 adoption can pose significant barriers and for many companies, the approach has been slow and cautious. But digital technologies are here to stay and making the eventual move towards Industry 4.0 will help foster innovation, productivity, and profitability for the life science industry.

Blue Mountain RAM is a platform for the future, enabling companies to support future initiatives by focusing heavily on components of Industry 4.0. The software is designed to specifically help life science companies optimize equipment and process in research and development, and manufacturing, both at present and in future growth.

So, no matter which stage of the Industry 4.0 adoption journey your organization is currently in, Blue Mountain can help to transform your manufacturing process and drive innovation.

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