Industry 4.0 - Revolutionising Life Science Manufacturing Through Connected Systems & Data
Introduction

The life science industry has a strong legacy in data collection and has been embracing ‘Industry 4.0’ – which we will refer to as Pharma 4.0 in this paper - methodology before the term existed. It has been collecting data in large historian systems for over 40 years. Right now, almost every device in a GMP manufacturing facility collects data and the industry continues to complete projects to physically connect all these devices and systems.

Data collection and visualisation to improve the performance of the manufacturing supply chain has been a goal for the life science industry for a very long time. However, in GMP manufacturing, it is not about being new – it is about using proven solutions and approaches to create never before seen (or possible) quality and reliability standards.

In this paper, Industry 4.0 or ‘Pharma 4.0’ has been fully defined, the industry’s appetite for change established and the technologies and approaches that will facilitate such change evaluated. The role of data throughout all this has been analysed and its importance discussed. For the life science industries, Pharma 4.0 is a radical change that will not be driven by radical investment but by ‘making the most of now.’
Introduction

Defining Pharma 4.0
Pharma 4.0 refers to the new tools and processes that are enabling smart, decentralised production, with intelligent factories, integrated IT systems, the Internet of Things (IoT) and flexible, highly integrated and automated manufacturing systems. It is the latest wave of technological advances that will drive the next phase of pharmaceutical manufacturing by using proven solutions and approaches to decision making to improve quality, reliability and reduce waste.

The Market
There is growing interest among the leaders and decision makers in the pharma industry around Pharma 4.0. What must be discussed and appreciated by those who influence progression in the life science sector is the scope of Pharma 4.0 - it will someday change everything.
When talking about Pharma 4.0, it’s important to move away from discussions about semantic alternatives or incremental changes. Instead, the industry must appreciate that Pharma 4.0 is about overhauling the way the industry thinks and creating processes, practices and services that are completely new.
Pharmaceutical manufacturers face an ever-present need to remain competitive in a marketplace where product portfolios are diversifying, innovative start-ups challenging the status-quo, supply chain partners becoming more integrated and patients more involved in decisions around their care.
Realising the promises of Pharma 4.0 will be the market differentiator for businesses competing in this environment.

Change and Reward with Reduced Patient Risk
Pharma 4.0 is a revolution and with any revolution comes change and ultimately reward for those that adapt the quickest and most effectively. Companies like WhatsApp, Apple and Google fundamentally disrupted, forced change and now lead their respective markets by creating new products and services.
Those businesses that do the same in the pharmaceutical industry will lead the market for years to come.
We’re already seeing some examples of revolutionary new thinking when it comes to digital-to-physical transfer (transferring digital instructions to the physical world). Johnson & Johnson is working with HP Inc. on 3D printing medical devices including contact lenses in community settings. Scale is currently a challenge but it’s only a matter of time before factories are redundant.
The life science industry is reducing risk with the Pharma 4.0 revolution - the new products, processes and services will be cheaper, faster, safer and higher quality than their predecessors.
Appetite for Change

In a survey of business and operational leaders from across the life science sector conducted by Zenith Technologies in 2018, 58% of respondents said that Pharma 4.0 will drive the most change in life sciences over the next five years – more than any other technology area. Interestingly, the same number of respondents said that they are currently most focussed on digitalisation, with only 46% stating that Pharma 4.0 was their current priority.

When asked their motivation for investing in new technology:

- 77% said they want to save money in manufacturing processes
- 69% want to save time
- 62% are aiming for increases in revenue
- Only 19% want to understand patients better

Ultimately, the criteria that drives decision making and investment in the life science industry remains the same - business leaders want to reduce cost, increase efficiency and revenue. This remains true for Pharma 4.0.

What is new, however, is the mindset. The traditional approach in pharma manufacturing to investing in new technology or equipment has been to identify the need and opportunity, procure, install and validate.

With Pharma 4.0,

- 77% of the respondents said they will invest in people to make more of emerging technologies
- 46% said they will do so by improving legacy systems
- 46% said they will leverage third-party support
- And only 42% said they will invest in new systems.

With Pharma 4.0, change will be driven by people interpreting data and reshaping the approach to manufacturing.
Manufacturing Execution Systems (MES) & Automation

The Food and Drug Administration (FDA) provided criteria for the acceptance of electronic records, electronic signatures and handwritten signatures executed to electronic records as equivalent to paper in the Part 11 regulations in 1997. This allowed for the first significant uptake of MES and automation in the pharmaceutical industry. Since then projects have delivered incremental (sometimes significant) improvements in efficiency, quality, reliability and safety. However, in the context of Pharma 4.0, they could effectively eliminate human error and delay from manufacturing – preventing waste and upping efficiency. The financial benefits are significant.

In the Zenith survey, respondents were asked about automation; 42% of participants said they are currently ‘very automated’ and 12% ‘automated wherever possible.’ In five years 50% want to be ‘very automated’ and 23% ‘automated wherever possible.’

The desire for automation is clear as it offers several operational benefits – faster, more reliable and ultimately cheaper processes – but its adoption has been a decades-long and gradual process.

The potential that Pharma 4.0 holds for automation is massive with individual management processes throughout manufacturing expected to become automated.

A simple example is the approach to a temperature gauge giving a higher than expected reading during manufacture. An automated system could detect this reading, interpret event data against previous information and decide upon a course of action and rectify the situation. This would negate the need for an operator to intervene and make an assessment on the required course of action and carry out said action. The time saving for each event will often be minimal, but when scaled across an entire factory or at the enterprise level – the impact becomes significant.

Future developments will also allow machine learning algorithms to adjust manufacturing lines and production scheduling much more quickly than with human intervention. New developments will also pave the way for predictive maintenance and the opportunity to identify and correct issues before they happen.

While MES systems are becoming more widely adopted, they have added more complexity to manufacturing environments. This has brought about implementation challenges. In response, long-term thinking sits at the forefront of every project to ensure that the process is cost-effective and continuously delivers value.

With the shift from paper-based processes to intelligent, electronic systems that will be accelerated by Pharma 4.0, MES systems will give more meaningful business insight, remove room for error, and enable resources to be better used. For example, instead of just measuring the downtime of a piece of equipment for overall equipment effectiveness (OEE), MES can provide batch, cleaning, maintenance and operator inputs as context for the downtime to allow for detailed trend analysis and precise preventative measures to be put in place.

As better approaches to recording and accessing data in real-time are adopted, production both in single plants and across global facilities will be completely revolutionised by increasingly sophisticated and more connected MES systems.
Connecting Everything and Creating Context

The foundation of any change to a manufacturing environment driven by Pharma 4.0 thinking will be contextualised data and connectivity. Every system and piece of equipment needs to be able to record and distribute reliable event data, communicate with other systems and pieces of equipment and subsequently access relevant and reliable data.

Once this connectivity is in place, operational teams have the basis for making better choices, or have the need to make choices removed as self-learning systems do this by interpreting data.

It is imperative that data is contextualised for it to be useful – the integrated technologies need to know what the data is and when it was created. A database with time-stamped data is essential as consistent time data makes every subsequent interpretation and decision simpler and more reliable. If we use the example of the temperature gauge again, when an irregular temperature reading is given, the automated system will look for data around a previous event that mirrors the current one – it simply cannot do this reliably if said data is not accurately time-stamped.

Batch context - By adding context information such as product or recipe names, process phases or batch identification to time-series data in process historians, the value of the data for process engineers is greatly increased.

However, historians are ‘write’ optimised and not ‘read’ optimised, creating a technical constraint as they store and compress new data making extraction and interpretation arduous. Finding the relevant historical event and building the process context around it can be laborious, requiring manual manipulation of data rather than an automated approach.

With the right systems, software and approach in place - operators can find specific batches, filter by products or phases and create and overlay profiles for good and bad batches.

The ability to search data over a specific timeline and visualise all related events in that timeframe quickly and efficiently will allow users (and eventually machines) to predict more precisely what is occurring or what will occur across industrial processes. Human-machine interfaces such as this are one of the many lauded Pharma 4.0 disruptions that will revolutionise pharmaceutical manufacturing.

Communication standards

Communication standards, such as those from the Object Linking and Embedding for Process Control (OPC) Foundation and the FieldComm Group, and data exchange standards from the International Organization for Standardization (ISO) and the International Electrotechnical Commission (IEC) are crucial for making sure devices and systems are designed to communicate with each other.

In addition, standards from the International Society of Automation (ISA) specify engineering design data (e.g. ISA S108 for configuring intelligent devices), and the Capital Facilities Information Handover standard (CFIHOS) standardises product data to facilitate equipment and device acceptance testing and handover.

These standards will be increasingly important as machines and systems communicate directly with each other and make decisions with less human involvement in the coming years.
Big Data

Big data analytics draws data from sources that have traditionally been disconnected and looks for relationships and trends that were previously undetectable. For example, combining production data with that from sales and dispatch systems can streamline production planning.

Enterprise Resource Planning (ERP) tools can already do some of this on a much smaller scale, however they use smaller data sets than a Pharma 4.0 plant will generate so the conclusions and recommendations are comparatively less valid.

The life science industry has been doing big data analysis for over 20 years. However, there are inherent dangers that will be exponentially more problematic when interpreting the larger data sets that will be created by Pharma 4.0 approaches.

Spurious correlations, which are inevitable when dealing with numerous variables and data points, will no doubt seem attractive to operators and engineers but must be ignored to ensure data is used effectively. If a business acts on this data without confidence, the consequences can be very problematic and even detrimental.

It is vital that businesses adopt the data-driven improvement cycle approach – DMAIC.

- Define
- Measure
- Analyse
- Improve
- Control

The only correlations that should be acted upon must be carefully hypothesised, tested and validated. Process engineers must measure a large amount of data with a small number of variables, wait, monitor and define improvements before implementing change and starting the cycle again.

This iterative approach will only be successful if complete, contextualised and accurate data is collected from a fully integrated network of systems and machines.
Disruptive Thinking and Technology

There are a number of systems and technologies that will develop to enable the better gathering and use of data as the pharmaceutical industry embraces Pharma 4.0.

Data Lakes

Big data is stored in a data lake. It is vital that businesses upload the data into the data lake correctly through optimised ingestion practices, otherwise it becomes a data swamp. Ingestion tools are already readily available, allowing for more time to be spent on analysis.

As discussed previously, contextualising data is important - a time stamp makes data ingestion easier and importantly, when records are created at the same time as a batch, the correct ingestion allows time-series and context data to be linked. These ingestion tools can then make accurate suggestions and semi-automate the linking of data.

Edge Devices / Edge Computing

Edge devices collect data and run local analytics on a piece of equipment or process. They store local data for a limited time and only send information to the data lake if there is an event. This keeps the data lake clean of unnecessary information. The resulting data can be used to create insights into performance.

Machine Learning & Digital Twin

Machine learning and artificial intelligence will lead to significant change in manufacturing practices. With ‘deep learning’, computers will train themselves by running scenarios and learning from the outcomes using the massive amounts data available in data lakes with the aim of creating a digital twin.

Using simulations to model a process and running scenarios in this virtual system rather than running experiments on real equipment is already used in pharmaceutical process development. The concept of the digital twin goes beyond traditional modeling simulation to create a generic digital representation of an asset. The twin captures multiple characteristics of the asset from sensor data, and the data can be used for deviation or anomaly detection, prediction, and simulation. The digital twin models can also learn continuously as they adapt to new information.

Building on the DMAIC approach, digital twins will reduce variables by modelling processes, removing a variable and supporting tests for improvement.

Asset Performance Management & Utilisation

Asset performance, throughout its lifecycle, is key to every organisation. When assets can talk to each other and communicate data, engineers can get a better understanding of causes and effects of faults and their impact on performance on a much more detailed scale. Asset performance management tools that can access, interpret and visualise the relevant data in a data lake will offer better predictive asset analytics, risk-based maintenance and condition-based monitoring.

Data can also be used to more effectively monitor utilisation and inform decisions around purchasing extra machines by confirming whether current assets are being fully utilised.

Industrial Apps

Contextualised data in a lake will open the door for the development of clever industrial apps that monitor asset utilisation and performance. These apps will be significantly cheaper than current industrial-scale software, and offer real-time, remote, visual monitoring of assets.
The Future of Production

The life science industry has been slower to adopt cutting-edge technologies than other sectors, however it has spent decades using data to drive operational improvement. Embracing the potential for Pharma 4.0 is going to be critical to future operations of all manufacturers. Fully automated and connected facilities that can create, interpret and act upon reliable data will take advantage of all that digital manufacturing has to offer.

The life science industry has spent many years becoming more energy-efficient and using better materials and equipment to make improvements.

Pharma 4.0 will see the industry connect equipment across plant and enterprises and use better, more reliable and larger volumes of data to revolutionise manufacturing.

Zenith Technologies

Zenith Technologies’ role in the Pharma 4.0 revolution is to help manufacturers connect their systems and equipment and ingest and analyse the data created to inform operational decisions.

This connection and big data-led approach will fundamentally change the way manufacturers operate and ensure a more successful development and production of life changing medicines for patients who need them most.
References

CONTRIBUTORS

Ryan McInerney
MES Project Manager & Technical Consultant
Zenith Technologies

Ryan currently leads the project implementation and the delivery of site services at one of the top 10 pharmaceutical companies in addition to consulting with pharmaceutical companies worldwide on current MES, Historian and IT implementations.

Ryan has over 9 years of experience supporting 4 out of the top 10 pharmaceutical companies in Operations, MES and Process Engineering, giving him direct and current experience with the data analysis techniques and evidence based decision methodologies that are being deployed right now in the pharma industry.

David Staunton
Global Services Director
Zenith Technologies

David is the Global Director of Services at Zenith Technologies and leads the delivery of Automation, MES and Digital services out of Zenith’s 16 offices globally.

David has over 20 years’ experience in delivering Automation, MES and Digital projects and services for some of the largest biopharmaceutical companies in the world.

David lectures in project management on Master’s Programmes in UCD and regularly presents at national and international conferences.

Zenith Technologies
www.zenithtechnologies.com