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Article

What is Pharma 4.0? Why is it important and how it will enable the factory of the future?

Extract and further conversation on a keynote presentation given to the Interphex Japan by David Margetts on 27th June 2018, Tokyo

要旨:

アイオーティー(IoT)やインダストリー4.0という言葉を聞いたことがある人の多くは、こうしたテクノロジー主導の取り組みが、従来からの製造方法、設備機器、そしてプロセスにすでに急激な変化を起こしていることにも気付いているかもしれない。インダストリー4.0は医薬品産業にとってどのような関連性があり、我々はそれをどうやって実現していくのだろうか？　こうしたコンセプトに沿ったチャレンジの一つに、ロボット化、自動化、インターネット接続された埋込型センサー、統合型エンタープライズソフトェアなどが一つの複雑な未来型の複合体システムとなって我々のプロセスで動き、リアルタイムで自らが判断し、人が現在関与することで決まるロジックも変更してくれるような姿を”最終形“として思い描くようなことがある。こうした驚くべき構想を把握することは容易ではない。特に医薬品産業では、我々は重要な医薬品を製造するための製造プロセス管理やソフトウェアによる試験管理を通して厳格なGMP要件を常に満たさなければならないため、そのような急激な変化は受け入れがたい。本稿では、Pharma 4.0構想とは何かについて掘り下げて解説し、ある企業が未来の工場の実現に向かってすでに手掛けているいくつかのステップを紹介する。

Abstract:

Many people will have heard of the Internet of Things (IoT) and Industry 4.0 and perhaps are aware that these technology driven initiatives are already starting to disrupt traditional manufacturing methods, equipment's and processes. But how relevant is Industry 4.0 for the pharmaceutical industry and how we will get there?

One challenge with these concepts is that we think of them in their 'end state', where a complex and futuristic combination of robotics, automation, embedded internet connected sensors and integrated enterprise software are running our manufacturing and making decisions in real time and replacing logic that is currently determined through human involvement. This amazing vision can be difficult to grasp and specifically in the pharmaceutical industry then such dramatic disruption can be uncomfortable as we must meet the stringent requirements of the GMP regulations through careful control on our operations, and careful testing and control over software that is used to produce critical medicines.

This article seeks to break down and introduce what the Pharma 4.0 initiative is about and explain the steps that companies are already taking today to advance along the journey towards the factory of the future.

So what is Pharma 4.0?

In reality today, then Industry 4.0 is still in its infancy across the world and there are no strict definitions of what it means and what the results will be for a specific industry. The term itself however is helpful to capture the overall development of manufacturing in the modern age to connect deeply the physical process and equipment with data and information systems. The goal is to gain the huge benefits associated with digitization such as improved control, visibility, understanding, prediction and feedback into manufacturing and ultimately enable software to make automatic responses so that higher levels of performance are reached above those possible with today's manual and semi manual management of operations. Potentially, the last stages of this data journey will require advanced types of computation such as artificial intelligence (AI) that can evaluate the much larger data sets that will be available through integration and be able to learn and adapt our operations in real time to the changing conditions and longer term trends.

Pharma 4.0 is our industry's interpretation of Industry 4.0, and it represents a shift from focusing on producing to a fixed specification to a systemized method of continuous evaluation and control so that our processes are self-adjusting based on running data and the information connected from systems all around the operation. This concept builds on the principles of Quality By Design (QbD) and Process Analytical Technology (PAT) that started over a decade ago in the industry, but until recently we simply did not have the information from electronic systems to make the data accessible for such advanced control. The Pharma 4.0 world will really become a reality when we have the base data platforms in place and they are integrated both to tools and devices that work alongside human operators for greater usability and awareness, and above to software able to enquire into data for self-learning and highlight, propose and take action on improvements and changes for the current running production. The benefits of Pharma 4.0 capabilities will be considerable, and not just limited to efficiency but through the great elimination of manual intervention and passing the human limits of assessing data then will enable higher levels of quality - this objective is of course particularly important in pharmaceutical manufacturing.

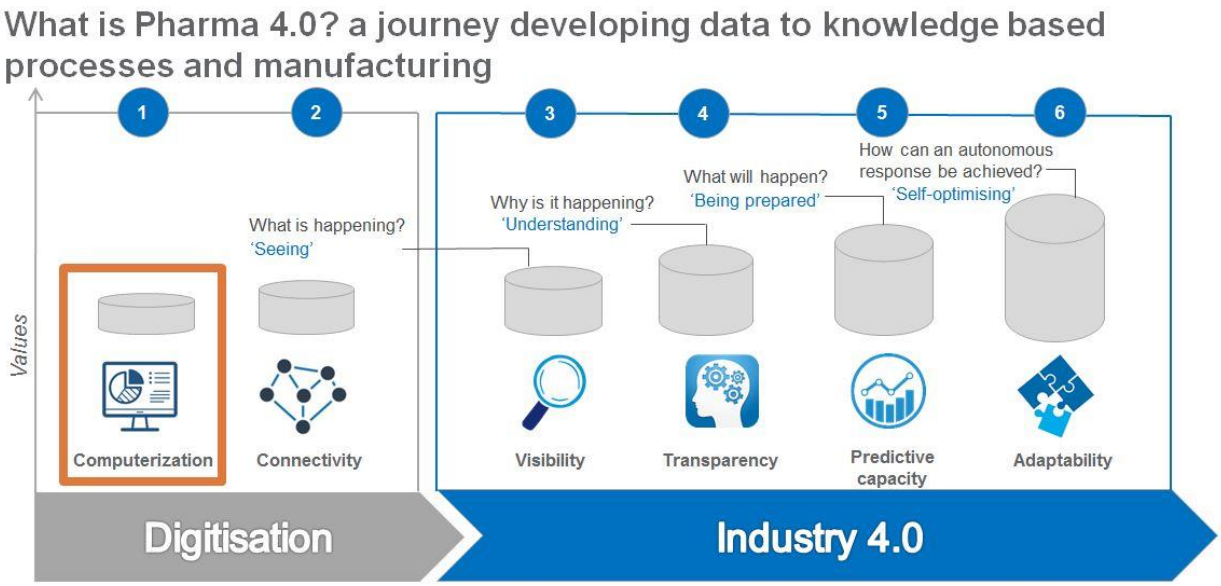

Figure 1: What is Pharma 4.0?

The progression in figure 1 shows that at the heart of Industry/Pharma 4.0 is a drive to modernise and systemise the collation and usage of data for information and knowledge. The highlighted box draws attention to the point that today most of the Pharma industry has not yet completed the computerization step as paper systems are still prevalent, replacing this legacy is a key pre-requisite to the more advanced use of data.

The starting point for Pharma 4.0 is Industry 3.0!

For the average Asian company then the modern technology being discussed as part of Pharma 4.0 can look difficult, costly and far from reach. However, there are step by step approaches to the design and implementation of IT systems that make this easier to adopt and today pharma specific and ready software is highly mature and readily available. A structured and logical sequence to the introduction of these platforms is needed that focuses on the current needs and pains of the business, those that will gain the highest priority benefits first for today, and put in place the capabilities required for tomorrow. A good reference to understand a modern enterprise IT landscape from are the models defined by the International Society of Automation (ISA) (ISA, 2018). ISA starts by defining IT systems to their use in specific layers of a manufacturing company.

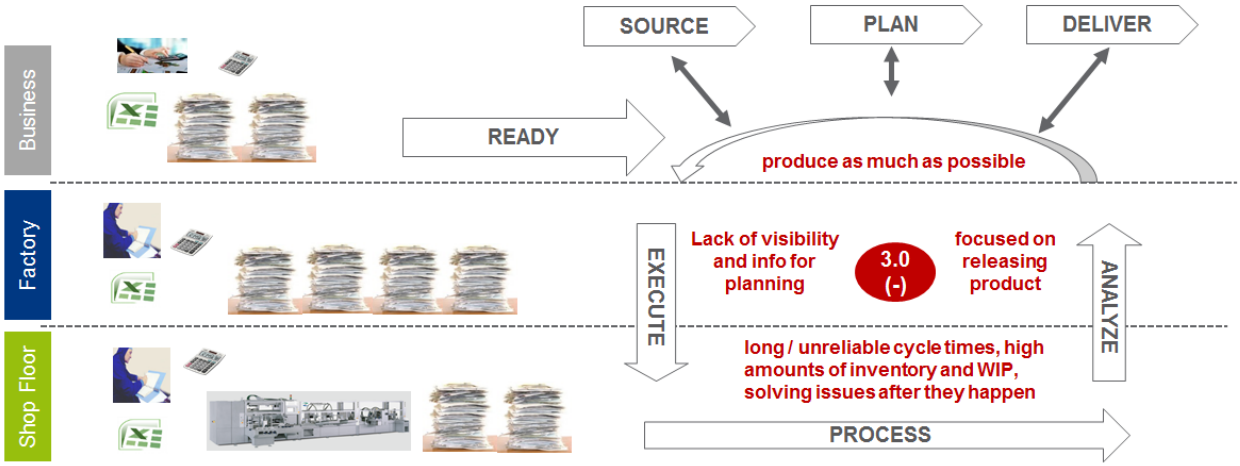

Figure 2: Today's information reality for many Pharma companies

Figure 2 shows where the main supply chain and manufacturing processes sit in the levels of the organization; to keep this simple let's call these levels; Business, Factory and Shop Floor. For companies without any IT systems in place then the lack of electronic information systems causes a large set of challenges, for example,

- Ineffective planning
- Unknown manufacturing performance
- Unknown quality performance
- Little visibility into operations
- A focus on releasing the available product based on insufficient or unreliable data
- No information with which to improve the business

For most companies at least on some level and area, they are still relying on paper to produce the right product at the right quality and cost, but paper systems are often the root cause of many issues in operations related to a lack of timely or accurate information.

The current reality for many production and quality managers is that they are only able to roughly manage the production demands, they must work under constant stress to release product and spend most time fire-fighting issues. They do not have the information to solve the root causes of problems and address sufficiently negative trends and unreliable cycle times. We have to consider this scenario as a not even Industry 3.0 capable operation. So how can we start moving towards Pharma 4.0?

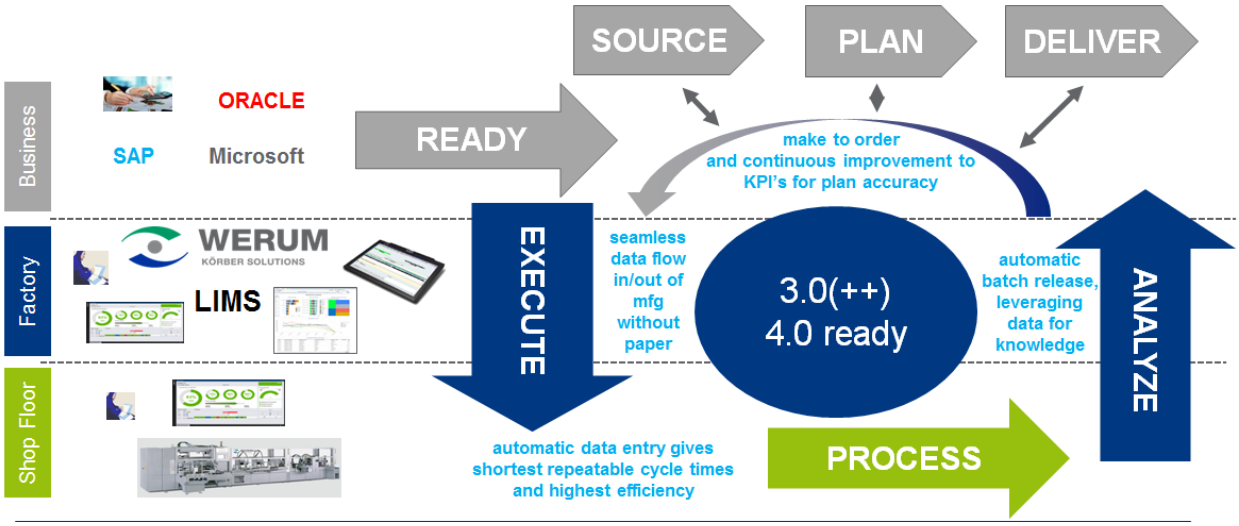

Figure 3: Putting in place basic IT platforms to be ready for Pharma 4.0

Figure 3 shows an evolved IT landscape where the company has implemented in a top down approach an Enterprise Resource Planning (ERP) system to make improvements and automation of the wider supply chain processes and connect these in and out of the production sites. At the factory level then Manufacturing Execution Systems (MES) and Laboratory Information Management Systems (LIMS) are in place and integrated to the ERP to manage the production and laboratory operations in a paperless manner for greater efficiency and right first time controls. These systems ensure point of use checks of data to better ensure correct data, instruction, sequence of activities and to make the records available for faster review and approval. Now we have more accurate information available with which to improve the relevant business functions and then by finally connecting the shop floor and lab equipment into the factory systems we can reduce even further the process times and eliminate large amounts of human efforts to further boost quality and performance metrics. Figure 3 shows that once all such platforms are setup then we have reached an effective basis for Industry 3.0. From here we can now start to add and pilot cool and interesting Pharma 4.0 ideas such as to get closer to process with human interface devices, IoT sensors for control and tracking, PAT applications for advanced process control, robotics / automation to speed things up and to apply data analysis tools for insights to become wiser about our production and supply chain operations - at this time we can consider we are now really on the road to the factory of the future!

So now we are ready for Pharma 4.0, what does it look like?

Pharma 4.0 is today not a dream, there are now working examples in commercial pharmaceutical production that adopt many of these new concepts and technologies at production facilities which are qualified and validated according to the guidelines as established by ISPE's GAMP5, (ISPE). The image in Figure 4 shows a real case study for new human-system integration using an Augmented Reality (AR) operator headset. The AR device is worn by the Operator and provides the strong controls and data capture of the MES at the same time being really useful for users who must work with their hands alongside the physical process.

Figure 4: Augmented Reality operator headset for equipment Line Changeover

Figure 4 shows the perspective of using the system from the operator eye view and how the system guides through a graphical visual aid that is overlaid 'on reality' through the headset to show physically on the equipment that the operator must install a specific change part. The description of the part and important settings and parameters that are required are displayed and integrated from the Electronic Batch Record (EBR) managed by the MES. Once the step is actually completed then the operator uses a gesture control to authorize the step is competed and the relevant records are automatically updated in the EBR. The next step is then displayed according to the correct sequence and overall completion status of the tasks at hand. Such use of human interfaces has already been shown to result in faster and more controlled processes, in the real life study then a 13% increase in the effective run time of the equipment was gained from a higher performance line change-over process.

In the shorter term, Pharma 4.0 concepts using AR and other techniques such as voice command integration will bring electronic systems even closer to humans who are still involved with the operations, at the same time then further automation and robotics will reduce the manual tasks to only those critical for decision making and management of the overall

production and quality processes. Later as more information becomes integrated and available and complex decisions are automated using AI then we can start to really envisage and discuss how factories of the future will operate with an exceptionally high degree of autonomy and independence.

In summary, then as we start the Pharma 4.0 journey we do not yet know the final destinations that we will travel to, but it is certain to be highly exciting as we can already see from initial pilots and the possibilities of modern IT solutions in other industries and sectors. This is clearly an excellent time to be working in the industry as pharma becomes more responsive and open to change than ever before. As we have discussed then this fantastic future will not be possible if we continue to attempt to record, manage and extract information from data that is today locked away on paper records. It is now apparent that the end of the use of paper for critical data is fast approaching, as the data integrity expectations for regulators increases, the product demands for more flexible manufacturing such as QbD, personalized medicine, smaller batch sizes and continuous manufacturing grows. With the constant fast moving prevalence of technology in the consumer world then we have to ask ourselves, 'if it is on paper, is it data?!

The sun is still rising on Pharma 4.0, will Asia be there first?

In the past then the pharma industry in Asia has lagged behind other industries in terms of technology capability, expertise and adoption. This is starting to impact the achievable productivity and quality regulation levels that can be attained but the region is starting to realise that it can be a leader in this new pharma area. Many companies in China, Japan, Singapore and Korea are already advanced in their digitization initiatives and across Asia even in less developed countries there is a greater awareness of the need to modernise using information technology than ever before.
It is time for Asian pharma to do what the region's other manufacturing industries have excelled at for many decades; utilise the latest global technology and methods and drive forward to world beating levels of performance!

Thank you for taking the time to read our article. The Werum IT Solutions' team and I are always available to discuss with you on your ideas for Pharma 4.0 and to explain any questions you may have. We greatly look forward to working together to developing the factories of the future! – David Margetts, Managing Director, Werum IT Solutions (Asia).

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About the Author

David Margetts is the Managing Director of Werum IT Solutions' hub for Asia and is responsible for key markets in the Asia-Pacific region. Through his experience over 15 years, as an entrepreneur, business manager and principle consultant for companies providing IT solutions, engineering and GxP consulting services to the Pharmaceutical and Biotech industry he brings a breadth and deep practical knowledge of the requirements of our clients. He is a trusted advisor in the rapidly changing environments of regulation, compliance and technology and previously worked in Engineering and Validation roles for Industrial Technology Systems and AstraZeneca PLC in the UK and more recently as the founder and Managing Director of Factorytalk. David is an ISPE certified trainer for Computer Validation and has been deeply involved in 100's of consulting assignments and manufacturing IT projects across Asia, US and Europe for top 30 leading multinational companies and local Asian clients.

About Werum IT Solutions Asia

Werum IT Solutions is the internationally leading supplier of manufacturing execution systems (MES) and manufacturing IT solutions for the pharmaceutical and biopharmaceutical industries. Its out-of-the-box PAS-X software product is run by the majority of the world's top 30 pharmaceutical and biotech companies but also by many mid-sized manufacturers.
Werum's manufacturing IT solutions help pharma manufacturers to increase efficiency, improve productivity, and meet regulatory requirements. The range of projects includes global MES programs with multi-site rollouts all over the world as well as single-site solutions in India and other Asian countries.
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Werum is part of Medipak Systems, the Pharma Systems business area of the international technology group Körber. The Business Areas companies, Dividella, Fargo Automation, Mediseal, Rondo, Seidenader Maschinenbau, Systec & Services, Traxeed and Werum IT Solutions, are global leading providers of high-quality solutions for the manufacturing and packaging process of pharmaceutical products. As a Medipak Systems company, Werum provides integrated IT solutions for all phases of pharmaceutical and biopharmaceutical production – including process development, commercial production, and packaging as well as track & trace serialization. Körber unites worldwide almost 11,500 professionals in industry-leading companies, achieving annual earnings of more than 2.3 billion Euros.
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