Roadmap for the adoption of PAT and digital twin technologies in the European Pharmaceutical Industry: Barriers and Opportunities

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Introduction

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The term Industry 4.0 refers to the fourth industrial revolution which brings together rapidly evolving digital technologies such as the internet of things (IoT), artificial intelligence (AI), robotics, and advanced computing to dramatically change the landscape of manufacturing. The adoption of digital technologies in any manufacturing industry is a crucial element in improving the manufacturing processes, which leads to a reduction of costs, improved efficiency and productivity and greater flexibility in adapting to changes.

The pharmaceutical industry has been more hesitant and slower to adopt digital technologies than other industries due to the complexities and expertise required in the development and manufacturing processes. However, with the growing demand for traditional and new drugs, there is a clear need for digitalisation in the pharmaceutical industry.

Digitalisation can be implemented in many areas of the pharmaceutical industry, including clinical trials, drug development, manufacturing, and supply chain management. In clinical trials, electronic data capture systems and wearable devices are being used to track patient data in real-time, which can help improve the efficiency and accuracy of the trials. In drug development, artificial intelligence and machine learning are being used to analyse large datasets and identify potential new compounds, which can accelerate the discovery and development of new drugs. Digital technologies are also being used in manufacturing to optimize the design and operation of pharmaceutical manufacturing facilities, including the use of data analytics to improve efficiency and reduce waste. In the supply chain, blockchain technology is being used to track the movement of drugs and ensure their authenticity, which can improve the visibility and efficiency of the pharmaceutical supply chain.

This review is mostly based on the digital technologies for drug development and manufacturing, implemented in the Industry 4.0 framework which continue to evolve,

The pharma industry is facing a multitude of industry-specific and global trends. But a few major trends point to an industry tailwind; one of them is the advancement of digital and analytics tools.

Source: ***Mc Kinsey & Company 2022***[1]

such as artificial intelligence and advanced computing. These are beginning to challenge the traditional approaches, practices, and business models for the manufacturing of pharmaceuticals. Pharmaceutical businesses are anticipated to spend more than $4.5 billion on digital transformation by 2030[2] . The application of digital technologies to the pharmaceutical industries has the potential to significantly increase the agility, efficiency and flexibility, as well as the sustainability of the drug manufacturing processes, and the quality of the medicines produced.

The future of pharmaceutical manufacturing will be shaped by the effective deployment of digital technologies, encompassing data collection and the attainment of digital maturity, as envisioned in Industry 4.0. The potential benefits of this transformation require a comprehensive vision and a deep understanding of the regulatory, technical, and logistical challenges that must be overcome. Industry 4.0 applied to the pharmaceutical industry will in the future contribute toward an intelligent automation technology and may support augmented manufacturing, such as a personalised medicines, additive manufacturing, localized 3D printing of treatments, etc[3] ,[4] . In the pharmaceutical industry, digitalisation and data analytics can help reduce the high amounts of downtime to which pharmaceutical plants are prone[5] . Machine-to-machine communication and machine-learning artificial intelligence enable seamless procedures, automatic corrective actions, and predictive maintenance via the Internet of Things[6].

Contract Development and Manufacturing Organizations (CDMOs) face a unique challenge in their digitalisation efforts. To successfully digitalise CDMOs, it is crucial to prioritize and maintain a constant focus upon the main aspects of Good Manufacturing Practice (GMP) and maintain a constant focus on it. Collaboration with evolving stakeholders is also essential during the digitalisation process of CDMOs.

Digitalisation and automation are now ensuring that companies minimise errors in the future, resulting in the decrease of financial and reputation damage[7]. To avoid data-transfer concerns between units, some pharmaceutical organizations have introduced digital sensors and robotics and invested in high-availability computing technology. This has resulted in a completely automated production line that makes it much easier to maintain cleanroom procedures, to capture and manage electronic batch records, and analysis of process performance (using root-cause analysis) to find and implement changes[8].

Overall, the pharmaceutical industry is making significant investments in digital technologies, and these technologies have the potential to revolutionize the way drugs are developed, manufactured, and distributed. In this report, we take a look at the current status of digitalisation of the industry in Europe, at the many opportunities that lie ahead, and consider how some of the barriers to digitalisation can be addressed.

State of the art and digitalization of pharmaceuticals industries, with emphasis on green pharmaceuticals

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2.1

Trends driving pharmaceutical industry digitalization

Digitalisation in the pharmaceutical industry involves the use of digital technologies across all levels of pharmaceutical operations. This aims to revolutionize the industry by harnessing vast amounts of data from various sources to support objectives such as research and development, clinical development, drug manufacturing, supply chain management, patient engagement, quality assurance and control, and product safety monitoring. Despite its transformative potential, the pharma industry has been slower than other sectors to adopt digital tools such as cloud storage, Artificial Intelligence (AI), Machine Learning (ML), blockchain, and remote communication technologies, and to make associated changes in workplace culture and strategic priorities. However, the COVID-19 pandemic has been a catalyst to accelerate the pace of digitalisation in the industry.

Indeed, the pandemic shone a spotlight on the need for access to safe, qualitative, and effective pharmaceutical treatments. In the face of time to market (TTM) of new drugs of typically between 10-14 years, the COVID-19 crisis highlighted once again the need to significantly decrease these timelines to enable earlier patient treatment. If the aggressive COVID19 vaccine timelines should be transferred to other essential new drugs, process development needs to be reconsidered. Together with other major challenges related to the limited financial capabilities of public healthcare systems, environment and sustainability aspects, and increasing competition, better process understanding to **develop, and manufacture pharmaceuticals and biopharmaceuticals in less time and more cost effectively** is required. Acceleration of the development process, higher process yields, and lower failure rates during scale-up represent the key drivers to reduce costs. In the case of the biopharmaceuticals industry, reproducing large biomolecules reliably at an industrial scale requires manufacturing capabilities of previously unknown sophistication, and many manufacturers, overwhelmed by the high complexity of their operations and products, suffer from **significant unknown process variability**.

The COVID-19 pandemic also brought to the fore the requirement for sustainable supply chains and consumption patterns, as well as the need to strike a sustainable balance to avoid undue impact of pharmaceutical residues on the environment. Indeed, as highlighted by the pandemic, our health and well-being strongly depend on a healthy environment [9].

Taking all of the above into consideration, digitalisation can be a significant enabler for the green transition of the pharmaceutical industry and in particular helping the industry to optimize and streamline its processes, leading to more efficient use of resources and reduced waste generation.

Digitalization: an opportunity for streamlining business, R&D, manufacturing processes and quality control

According to McKinsey & Company experts, advancements in cloud and mobile technology, sensors, and business intelligence will bring about a new wave of automation in the pharmaceutical industry, leading to streamlined, automated workflows and increased transparency[10] This will drive efficiency, responsiveness, and agility in a wide range of processes, from the back office to R&D and commercial. Clinical-trial management will see dramatic changes with advanced automation, including targeted online recruitment and remote-monitoring technology, enabling trials to take place in "real world" settings, reducing the burden on patients.

To succeed in the digital age, pharmaceutical compa-nies will need to implement advanced technologies to streamline their operations. These companies possess vast amounts of data that are often compartmentalized in various technical and organizational silos[10]. Some have already started to link and analyse these data sets to enhance their pipelines, products, and strategies.

However, there is still significant untapped potential to leverage both internal and external data sources to generate even more value through data analytics[10].

According to the experts, in research and development, digital tools such as advanced modelling and simulation techniques will be commonly used to test molecules and accelerate product development[10]. Access to advanced process control strategies based on advan-ced measurements, simulation and modelling will enable scientifically sound fast process development based on enhanced process understanding, that will in turn accelerate drug development and reduce Time To Market (and enable earlier patient treatment), as well as obtain repeatable batch production (reducing product variability) with maximum yields, reduce Cost of Goods (COGs), reduce environmental impact (footprint), while increasing agility to respond to market demand and novel infections, such as COVID-19.

Key barriers and mitigation actions

While digitalisation presents many opportunities, it also poses significant challenges, as discussed in the SWOT analysis discussed later in this report. These include concerns around data privacy and security, regulatory compliance, and the need for skilled talent to manage digital technologies.

One of the key challenges is the regulatory hurdle. The pharmaceutical industry is heavily regulated, and the adoption of new digital technologies may be slowed down by the need to comply with complex regulatory requirements. Ensuring the quality and security of data is also critical in the pharmaceutical industry, and concerns about this can slow down the adoption of digital technologies. The industry may also face a shortage of skilled workers with the expertise needed to design, implement, and maintain digital technologies. There may be within the pharmaceutical industry some stakeholder resistance to adopting new digital technologies, which can slow the pace of digitalisation. Finally, the expense of implementing new digital technologies may be a challenge for the pharmaceutical industry, which is under pressure to reduce costs. Some of the costs associated with digitalisation include:

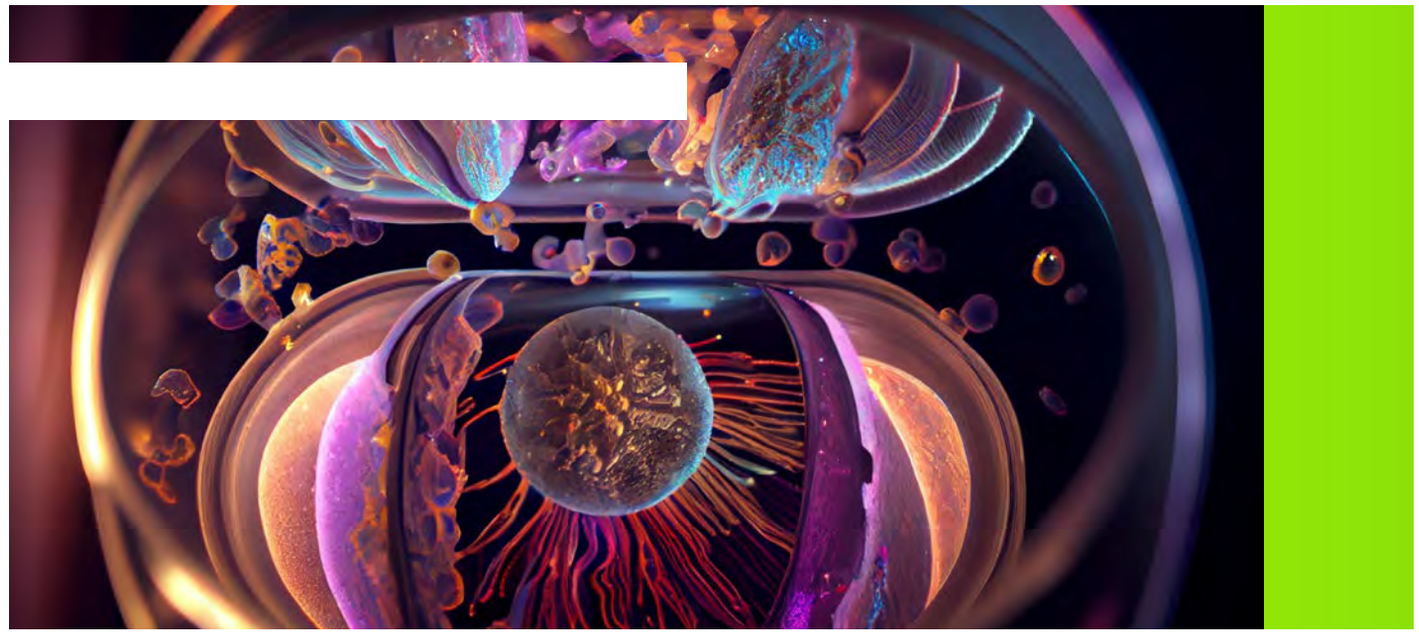
- Purchasing and implementing new digital technologies- costs can vary depending on the complexity and scale of the project.
- Ensuring that staff have the skills and expertise to effectively use new digital technologies- including the costs of training and professional development.
- Integrating new digital technologies with existing systems and processes- can be complex and costly, particularly if significant changes to those systems are required.
- Maintaining and updating digital technologies- including the costs of software upgrades, hardware repairs, and technical support.

Next, we consider the main **risks perceived** to be posed by digitalisation for pharmaceutical companies. One of the significant risks is the threat to **cybersecurity**. The pharmaceutical industry is a valuable target for cyber-attacks due to the sensitive nature of the data and products it handles. As a result, companies need to be aware of the risks and have robust cybersecurity measures in place to safeguard their data and products. Another risk posed by digitalisation is **breach of data privacy.** The use of digital technologies can raise privacy concerns, particularly if personal data is collected and shared. Companies must ensure they comply with relevant privacy regulations and have adequate safeguards in place to protect personal data. In order to mitigate, data security and privacy risks, SOC (System and Organization Controls) compliance is an important factor. SOC compliance refers to a set of standards and guidelines that companies can use to assess and improve the security and controls of their information systems. Companies may need to invest in additional security controls and processes to ensure that their systems are compliant with SOC standards, and they may also need to undergo regular audits to demonstrate compliance.

The use of digital technologies can also raise intellectual property concerns. Companies must ensure they have appropriate safeguards in place to protect their intellectual property, particularly if proprietary information is shared or exposed. Finally, relying on digital technologies can create **dependency risks.** If digital technologies fail or become unavailable, this can disrupt the entire pharmaceutical manufacturing process. Companies need to have contingency plans in place to ensure that they can continue to operate in the event of a technology failure.

In summary, digitalisation in the pharmaceutical industry carries a number of risks, however with awareness of these risks companies can take appropriate measures against them. These measures can include investing in cybersecurity and data privacy measures, protecting intellectual property, and developing contingency plans to ensure business continuity in the event of technological failure.

Application of PAT in the pharmaceutical industry and data capturing methods



In 2004, the Food and Drug Administration (FDA) published its "Guidance for Industry PAT- A Framework for Innovative Pharmaceutical Development, Manufacturing and Quality Assurance"[11] . This defines PAT as 'a system for designing, analysing, and controlling manufacturing through timely measurements (i.e., during processing) of critical quality and performance attributes of raw and in-process materials and processes, with the goal of ensuring final product quality.' In reality, PAT is much broader, including a wide range of ideas, approaches, and tools including 'Multivariate Tools, Process Analysers, Process Control Tools, Continuous Improvement and Knowledge Management Tools.'

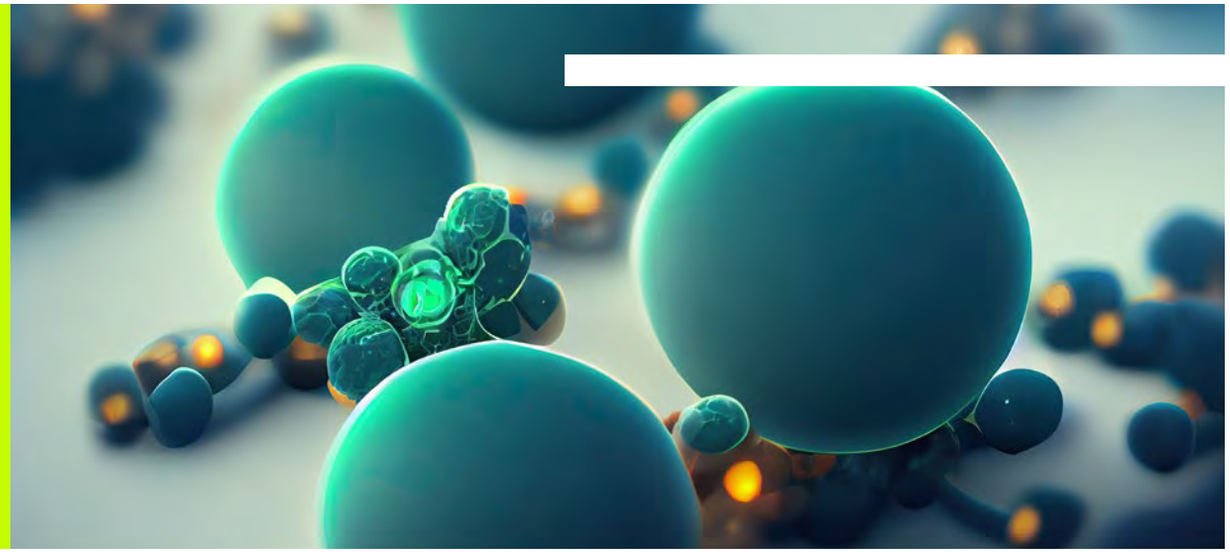
Although the term PAT itself is relatively new in circulation, the underlying fundamental concepts are over 100 years old and have been used extensively across a wide spectrum of industrial sectors. The pharmaceutical industry had been slow to adopt and fully use PAT technologies until about the time the FDA guidance was published. At the root of the conservative approach of the pharmaceutical industry lies its reliance on validated unit operations and quality control to test the final product, rather than continuous monitoring and real-time release testing. Despite this slow adoption, pharmaceutical manufacturing is inching towards implementing more efficient and sustainable processes, including continuous manufacturing and PAT.

Technological advances and risks

In 2002, the United States Food and Drug Administration (FDA) launched an initiative to encourage innovation in pharmaceutical manufacturing technology and quality system approaches. The resulting concept of Quality by Design (QbD) aimed to promote a more systematic and science-based approach to pharmaceutical development and manufacturing, with an emphasis on product quality and patient safety. This transition has created opportunities to integrate real-time process analytics into manufacturing processes[12].

The fundamental principle of QbD is that product quality should be designed into the process, as opposed to tested in stages and corrected afterwards. Achieving this requires a pragmatic and scientific approach that considers both the product and process, but allows the development of efficient, real-time quality control strategies. In this way, it is possible to achieve a predefined quality objective; that is, delivering products that consistently meet or exceed the required quality standards. A key enabler is Process Analytical Technology (PAT), as it provides a systematic structure for measuring product quality in real-time, facilitating process understanding and ultimately controlling the process to ensure product quality. PAT uses a range of spectral (multivariate)- based on photonics analysers located at multiple points within a continuous process- and univariate data sources together with prediction engines to make real-time product quality predictions to achieve a holistic, QbD quality system.

Regulatory agencies strongly advocate this transition. In 2003, the European Medicines Agency (EMA) formed a PAT team that issued guidelines on process PAT, QbD, and real-time release testing[13] . The 2004 PAT framework established by the FDA placed significant emphasis on transitioning from quality testing conducted after the drug product's production to integrating quality assurance into the entire production process through "continuous real time quality assurance"[14]. The International Conference on Harmonization (ICH) Q8, Q9, Q10[15] , and Q11[16] documents reinforced the FDA and EMA guidance, and have been implemented in the USA, European Union, and Japan since 2009. The FDA and ICH documents provided strategic guidance on developing an approach to identify and manage risks that may impact critical quality attributes, rather than being prescriptive. Within this new framework, PAT plays a crucial role in understanding and managing risk throughout a pharmaceutical product's lifecycle.



As opposed to using batch-based systems, the future of many processes within complex manufacturing industries lies in **continuous processing** which is characterised by connected operations, during which each unit immediately feeds the following one without any interruption[17]. The implementation of a continuous manufacturing strategy requires the adoption of the holistic, quality-centric QbD approach to product development and process design for transitioning from batch to continuous processing. As opposed to the traditional Quality by Testing (QbT) approach, which involves testing the material being processed after every manufacturing stage to ensure that the critical quality attributes (CQAs) are in line with specifications (involving lengthy stoppages of production to collect samples for offline testing in analytical laboratories which make it impossible to implement a continuous manufacturing process), QbD is a **responsive system**, featuring the real-time monitoring of product CQAs and adjustment of critical process parameters (CPPs). This allows plant operators to obtain consistent and quality compliant products while reducing the likelihood of rework or rejects.

The consortium behind the Horizon Europe ETERNAL project[18] is working on extending the QbD paradigm to incorporate, in addition to product quality, '**green-by-design**' principles. These will ensure that greener synthesis routes can be designed and once established (and validated), in the manufacturing stage, the process can be controlled in real-time to also ensure the process stays within 'green' limits, while at the same time ensuring product quality. In the novel 'green-by-design' approach, environmental impact Key Performance Indicators are merged with the process control parameters and digital twin technology used for a comprehensive optimization, optimizing not only the process but also the impact in a common framework.

In short, PAT adoption has the ability to increase process understanding, accelerate the drug development process, lower failure rates, improve product quality and safety, process yield and resource efficiency through in a green-by-design approach, ultimately resulting in sustainable competitiveness.

Data capturing, processing and management

Emerging technologies, a dynamic regulatory landscape, and new scientific challenges continue to expand the applicability and utility of PAT in pharmaceutical manufacturing, and bioprocessing. The use of real-time, in-process analytics plays a vital role in ensuring the quality of the product and enabling corrections to be made during the manufacturing process. Tremendous progress has been made in the implementation of inline monitoring in chemical drug manufacturing and real-time monitoring has been implemented for quality control in dissolution, crystallization, drying, and other unit operations.

Data capture methods for PAT implementation typically involve the use of various sensors and analytical techniques to monitor and measure critical process parameters and quality attributes in real-time. Spectroscopic methods involve the use of infrared, Raman, near-infrared, or UV/Vis spectroscopy to measure chemical and physical properties of materials in real-time. Indeed, focused-beam reflectance, infrared, near-infrared, and Raman spectroscopies are attractive as in-process analytics because they rapidly and **non-destructively** provide chemical and physical properties information[7]. Other techniques include high-performance liquid chromatography (HPLC) and gas chromatography (GC), which are commonly used to measure the purity, identity, and quantity of active ingredients and impurities in pharmaceutical products. Mass spectrometry is a powerful tool for identifying and quantifying compounds in complex mixtures and is used extensively in pharmaceutical analysis. Microscopy techniques such as confocal laser scanning microscopy (CLSM) and transmission electron microscopy (TEM) can be used to analyse particle size, shape, and distribution in real-time. Differential scanning calorimetry (DSC) and isothermal calorimetry (ITC) are used to measure thermal properties of materials and can provide information on phase transitions and stability. Acoustic spectroscopy techniques such as acoustic chemometrics and acoustic wave spectroscopy are used to measure particle size, shape, and concentration in real-time.

These data capture methods can be combined with advanced data analysis and modelling techniques to develop soft sensors and real-time process control strategies that enable more efficient and reliable pharmaceutical manufacturing processes. New data fusion approaches whereby optical spectroscopic methods can be combined with other spectroscopic or non-spectroscopic sensors to measure a large variety of attributes[19,20] allow improved measurability and accuracy to be achieved as a result of using data from multiple sensors compared to a single sensor[21,22] . With the combination of multiple, potentially multivariate, spectroscopic sensors, the complexity of data increases, and advanced data analysis becomes necessary to extract information from the multivariate data regarding critical quality attributes or process parameters. Although the analysis of chemical data is commonly referred to as chemometrics, this term typically encompasses only basic analysis from multiple data sources, the application of data fusion methodologies to chemical data can improve classification and prediction[23].

The combination of sensors and data analysis for attribute estimation is often referred to as soft sensing. A **soft sensor** is a software-based system that uses mathematical models and algorithms to estimate process variables or product quality attributes in real-time. Soft sensors use data from various sources, such as physical sensors, chemical sensors, and other process variables, to create a virtual sensor that can provide measurements of process parameters or quality attributes that are otherwise difficult or impossible to measure directly. Soft sensors are used to monitor and control critical processes in real-time[24] and are particularly useful in situations where physical sensors cannot be installed due to limitations such as cost, space, or environmental conditions. Soft sensors are also valuable for providing process insights and enabling proactive decision-making to improve product quality and process efficiency.

The ultimate goal in PAT and the QbD concept can be seen as **model predictive control**. Hereby not only the current state of a process is monitored and controlled, but also the future trajectory under the assumption of constant process conditions is monitored. Based on the model predictive control actions, “out-of-specification” (OOS) events during an operation can be avoided and corrected before they occur, thereby avoiding batch rejection.

Methodology for the design of a PAT system

The design of a PAT system requires a stepwise procedure involving the selection of critical process variables, followed by the selection and placement of suitable monitoring and analysis equipment, and finally, the coupling of the monitoring and analysis tools to a control system to ensure that the selected critical process variables can be controlled, such that the process is kept within its design space [Assessment / 274].

An overview of a methodology for the design of a PAT system consisting of a workflow with nine steps is shown in Figure 1.

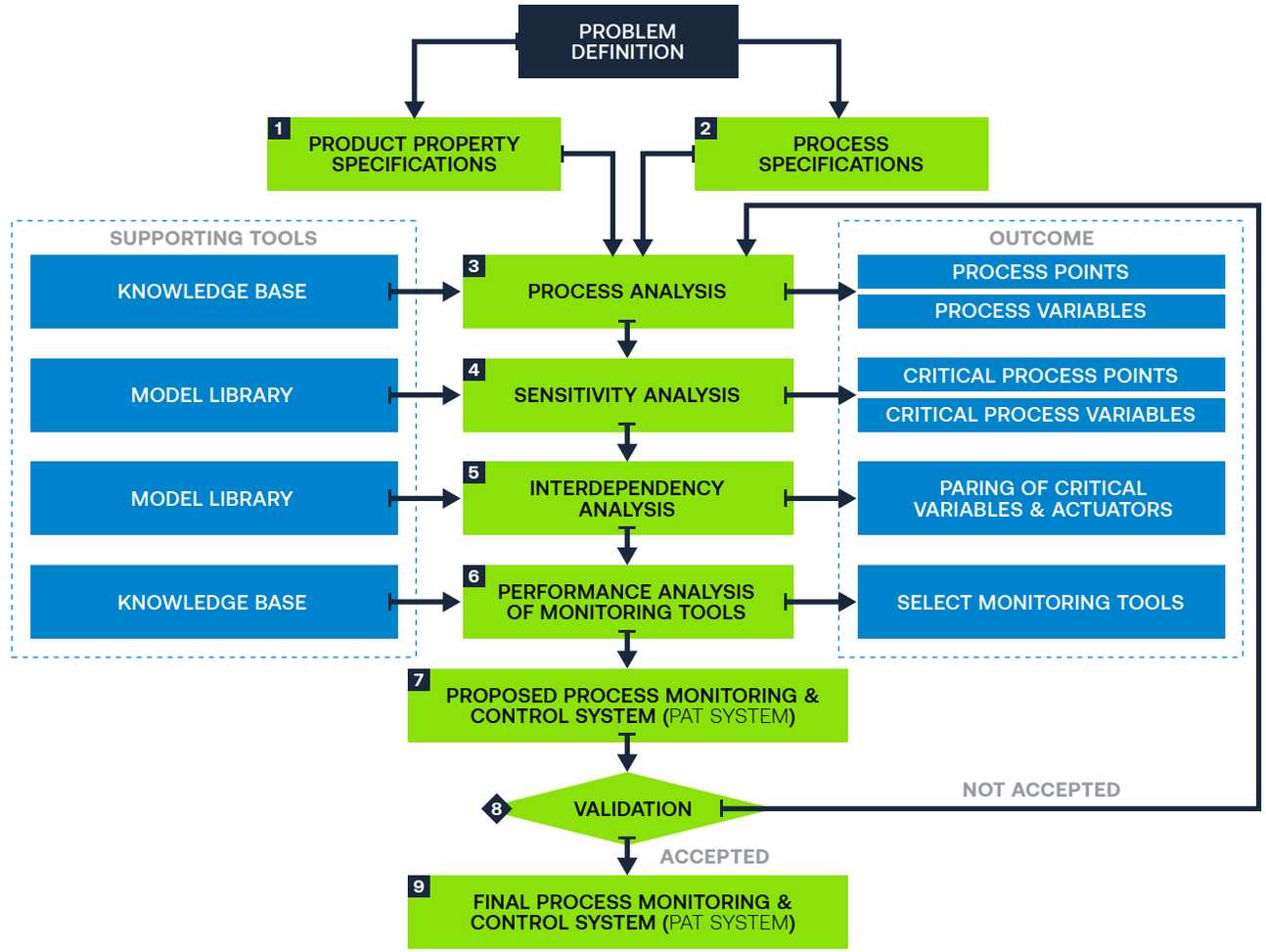


Figure 1: Overview of the nine-step methodology for PAT system design (extracted form [Assessment])

The **first step** (product property specifications) is focused on product properties specifications that are desired to be achieved by the final product in the considered production process.

During **step 2** (process specifications), crucial information related to the process such as the raw materials composition, and the equipment used in the production process are provided.

The information provided through the previous two steps along with the consultation of the knowledge base act as input data for the **step 3** (process analysis) of the methodology, in which a list of process points and the corresponding process variables is generated.

The identification of the critical process points where monitoring and analysis devices need to be placed and the corresponding critical process variables that need to be monitored and controlled in order to achieve the desired end product quality takes place through **step 4** (*sensitivity analysis*).

During **step 5** (*interdependency analysis*), the identification of the appropriate actuators to implement the control system for controlling the critical process variables identified in the previous step is performed.

Step 6 (*performance analysis of monitoring tools*) generates the list of the feasible measurement methods and tools for selected critical process variables.

Based on the outcomes of steps 4–6, a PAT system is finally proposed in **step 7** (*proposed process monitoring and control system*), which consists of a description of the following elements:

- Critical process points,
- Corresponding critical process variables,
- Actuators,
- Monitoring techniques,
- Monitoring tools.

The proposed system is validated in **step 8** (*process monitoring and control validation*), and finally **step 9** identifies the *final PAT system*, after the validation is successful.

Knowledge base and model library are essential sources of information needed for a successful design of a PAT system. The knowledge base provides the necessary information during the design of the PAT system while the model library generates additional or missing data needed for design and analysis [Assessment].

The knowledge base consists of two main parts [275,314]. The first part gathers the process knowledge (type of processes, corresponding process points, process variables, and actuators), while the second part contains the information on measurement methods and tools (type of variables, available monitoring techniques, and tools with specifications such as accuracy, precision, operating range, response time, resolution, sensitivity, drift, cost, etc.). On the other hand, the model library contains a set of mathematical models for different types of unit processes, sensors or controllers.

Different data sources can be gathered in a PAT system:

- **Real-Time Data**: Real-time data is collected during the process. Two types of real-time data can be found, multivariate or complex data and univariate or simple data. Typically, multivariate data are obtained from PAT instruments, such as Near Infrared devices, Raman instruments, or particle size equipment. This type of data can be obtained measuring the product in-line, on-line or at-line. On the other hand, simple data include process data that are typically used to monitor the process unit operation, such as temperature, pressure, or speed, among others.

- **Off-Line Data**: Quality control assays are performed to verify the characteristics of the raw materials employed in the process upon arrival. This information is usually available in the company's LIMS (laboratory information management system) and has a great impact on the process and final product quality. In addition, samples are taken during the batch runs for process and quality control purposes. Usually, the analysis of these samples measured off-line takes minutes, hours or even days. Therefore, this information is relevant to align the sample results with the real-time data obtained previously. The gathering and accuracy of this data, takes a crucial role when it comes to build up process knowledge and especially when creating new mathematical predictive models for the PAT monitoring tools.

- **Metadata**: The identification of the different data gathered can be considered as another level of data. Recollected data must be tagged with batch numbers, DoE run identifications, or sample IDs, to be able to contextualise the data afterwards.

The goal of a PAT system is to integrate all PAT data (real-time data, off-line data and metadata) to a single data platform.

Artificial Intelligence application

In the following section, firstly an overview is given of the basic concepts and definitions related to digital twins and how they are built; secondly, consideration is given to the specific context of the pharmaceutical industry and some examples and uses of digital twins in this sector.

As described in Barriga et. al (2022)[25] , digital twins have recently been identified as a key technology in Industry 4.0[26] ,[27] and the European Union is financing a number of projects in different fields, such as SPIRE (SPIRE is a contractual Public-Private Partnership dedicated to innovation in resource and energy efficiency enabled by the process industries) industries and biomedical applications, among others. Fornasiero et. al (2021)[28] conducted a survey on the degree of implementation of Artificial Intelligence and Big Data systems in the "process industries" in Europe. Cyber-Physical Systems were found to be important, especially for predictive maintenance solutions and tools[29]. It has been seen that digital twin applications are providing solutions to leverage process monitoring data, and that investment is being made by organizations in big data processing and sensor technologies[30]. Furthermore, digital twins make it possible to simulate different conditions to find the optimum configuration, without having to carry out exhaustive physical testing of the system.

Barriga et. al (2022)[25] describe a digital twin as being a virtual representation that serves as the real-time digital counterpart of a physical object or process. For further references see:[31],[32],[33]. Digital twins can be the result of continuous improvement in the development of product design and engineering activities. It can be said that the digital twin of a physical object is dependent on the 'digital thread', the lowest level design and specification for a digital twin, to maintain accuracy.

Outline of baseline concepts: modelling and digital twin theory

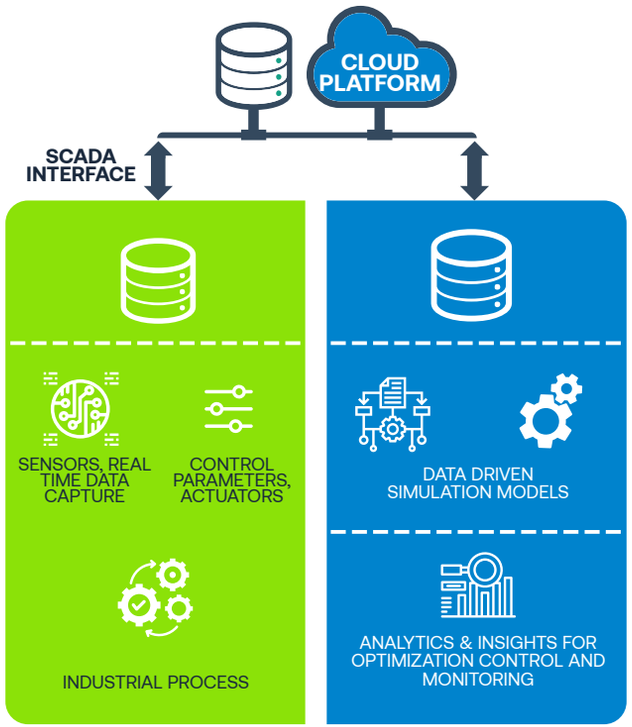


Figure 2: Schematic representation of physical process and digital twin

The basic concept of a **digital twin** refers to obtaining an exact (or the most exact possible) simulation of a physical (in the current context, an industrial) process. It has an initial configuration (e.g. flow rate 'set points', levels of different components, temperature, pressure, ...), some control variables/sensors (e.g. temp. flow rate, pressure) and some variables that measure the result of the process KPI (Key Performance Indicator) variables (e.g. energy consumption, purity of liquid after filtering through the membrane, volume of liquid processed per hour, etc.).

The process simulation (digital twin) can be run "offline" for example, to act as a decision support system to find an optimal configuration which minimises energy consumption while maximising liquid flow and quality. The simulation of the process could also be executed "online" in synchronisation with the physical process to "control and monitor" in real time. This is more difficult to implement and requires synchronisation with the PLC controller.

Figure 2 shows an overall depiction of the digital twin concept in the context of an industrial process, with the physical system on the left, the data driven simulator on the right, and the SCADA/Cloud interface in the centre. Hence, **digital twins are virtual representations of physical assets, processes, or systems that can be used to optimize the design, operation, and maintenance of those assets**.

Typical technologies from the Artificial Intelligence field for process modelling simulation are neural networks, support vector machines, rule induction, multi-agent systems, and techniques from traditional statistics such as Monte Carlo simulation. Also, in data exploration non supervised techniques are used such as clustering (k-Means, DBscan,...), principal components analysis, and visualization with multi-dimensional overlay, among others. A key aspect prior to developing a simulation model is the data exploration phase, in which key factors and variables and their interrelation are identified.

Integration in pharmaceutical processes

Digital twining is a new and exciting technology that is beginning to gain traction in the pharmaceutical industry. The idea behind a digital twin is to create a virtual model of a physical system, such as a manufacturing facility or a drug molecule, that can be used to optimize the performance of the system. In the pharmaceutical industry, digital twins can be used in several key areas to improve efficiency and reduce costs.

As described in Barriga et. al (2022)[18] digital twins are becoming increasingly integrated in pharmaceutical and biopharmaceutical manufacturing systems[34], with example applications such as real-time system monitoring and control using Process Analytical Technology (PAT). Digital twins require an IT infrastructure which includes continuous data acquisition from equipment and from KPIs related to intermediate and final products . The digital twin can be integrated as the 'back-end' for decision support systems.

The integration of a digital twin in a pharmaceutical industrial process requires close collaboration between the process experts, the data science experts, and the IT support team.

In the pharmaceutical industry, digital twins can be used to optimize the design and operation of manufacturing facilities, supply chains, and other critical processes. They can also be used to simulate the performance of new drugs and predict their potential side effects. One of the most promising areas for the use of digital twins is in manufacturing. By creating a virtual model of a manufacturing facility, companies can optimize the layout of equipment and the flow of materials to reduce waste and increase efficiency.

The following are some recent publications in which IRIS has collaborated, of the deployment of machine learning and digital twins applied to installations and processes in the pharmaceutical industry. Barriga et al (2023)[36] explores the sensor data from historical batches as a preliminary step to building the digital twin for the pharmaceutical product drying process. Barriga et. al (2022)[25] is the companion paper to Barriga et al (2023)[36], in which the digital twin is described for simulating the drying machine in order to optimize the energy consumption by identifying the optimum end point for the process. In Nettleton et al (2022)[37], a predictive maintenance decision support system was built by applying machine learning algorithms to historical maintenance data of a water for injection production plant. The predictive models were able to suggest the most likely components (mainly valves, sensors, vessels) to fail in a given future time window, thus indicating to the maintenance teams preventive actions regarding those components, including a prioritisation/ranking.

As an example of the steps required prior to building a digital twin, Figure 3 illustrates the data capture and pre-processing pipeline used in the Barriga et al (2023) drying process optimization model. The data often requires a first step of reformatting, and then descriptive variables are ranked with respect to the process KPIs, with the top ranked chosen for use in the digital twin.

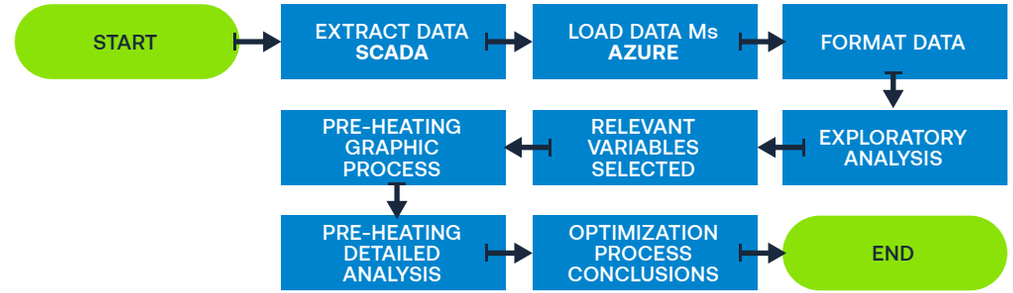
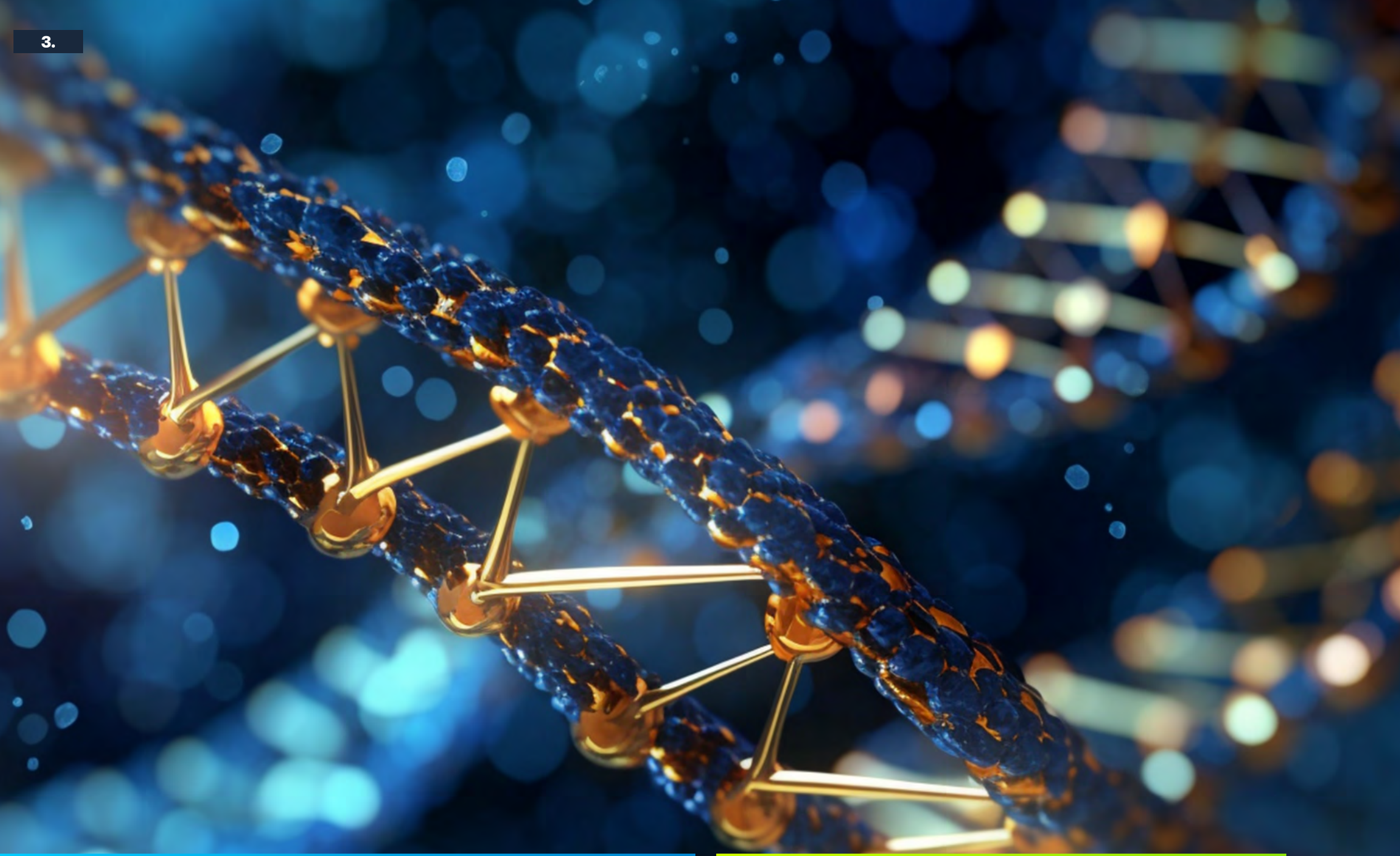


Figure 3: Data capture and pre-processing pipeline for building a digital twin for a pharmaceutical drying process[38]

Digital twins can also be used to simulate the performance of new drugs, helping to reduce the time and cost of drug development. In addition to manufacturing and drug development, digital twins can also be used to optimize the logistics of transporting and storing pharmaceutical products. By predicting potential delays and disruptions in the supply chain, companies can reduce the risk of product shortages and improve delivery times. Finally, digital twins can be used to optimize the design and conduct of clinical trials. By simulating the likely outcomes of different treatment regimens, researchers can design more effective and efficient trials, reducing the time and cost of bringing new drugs to market.

Overall, the use of digital twins in the pharmaceutical industry is still in its early stages, but it has the potential to revolutionize the way drugs are developed, manufactured, and distributed. As companies continue to adopt this technology, we can expect to see significant improvements in efficiency, cost-effectiveness, and patient outcomes.



SWOT analysis

SWOT analysis

SWOT analysis is a useful tool for identifying and analysing both internal and external factors affecting an organization's ability to achieve its objectives. By mapping out an objective and examining the associated strengths, weaknesses, opportunities, and threats, an analysis can be performed to determine how to leverage strengths, address weaknesses, capitalize on opportunities, and mitigate threats. From this analysis, an action plan can be developed.

The pharmaceutical industry can use SWOT analysis to understand how digitalisation could impact individual businesses and the industry as a whole. This analysis can inform the development of strategies to optimize digitalisation efforts.

Based on a literature review performed by the digital team in the ETERNAL project[18], in relation to current adaption of PAT and digital technologies in the pharmaceutical industry, and an assessment of the associated strengths, weaknesses, opportunities, and threats, a high-level analysis has been performed to determine how to leverage strengths, address weaknesses, capitalize on opportunities, and mitigate threats. From this analysis, an initial action plan has been developed.

Table 1 provides a summary of the SWOT, with a focus on digitalisation of pharmaceutical processing and green pharmaceuticals. Each section of the SWOT is discussed in more detail below.

Strengths

- Improved Efficiency: streamlining processes within pharmaceutical processing, for improved efficiency and cost savings.
- Automated Quality Control: use of digital technologies to automate quality control checks, reducing the likelihood of human error and improving product quality.
- Real-Time Data Analytics: collection and analysis of real-time data for identifying trends and patterns in manufacturing processes, enabling proactive identification and resolution of issues.
- Environmental Sustainability: twinning of a green pharmaceuticals focus on minimizing the environmental impact of pharmaceutical manufacturing with digitalisation to enable more efficient use of resources and reducing waste.
- Improved Collaboration: Digitalisation to facilitate collaboration and information-sharing among stakeholders in the pharmaceutical processing chain: CMOs, manufacturers, distributors, and regulators.

Opportunities

- Process Optimization: Digitalisation to optimize manufacturing processes (increase process efficiencies, reduce energy consumption and waste generation) and improve sustainability outcomes.
- Predictive Maintenance: for reducing downtime and improving efficiency by identifying potential issues before they occur.
- Advanced Analytics: machine learning and artificial intelligence for identifying patterns and insights in manufacturing data that may not be visible through traditional methods.
- Remote Monitoring: of manufacturing processes, allowing for greater flexibility and real-time oversight.
- Improved Regulatory Compliance: Digitalisation can help improve regulatory compliance by enabling real-time monitoring of key parameters, reducing the risk of non-compliance and potential fines.
- Sustainable Supply Chain: real-time monitoring and analysis of environmental impact across the entire value chain towards a more sustainable pharmaceutical supply chain.

Weaknesses

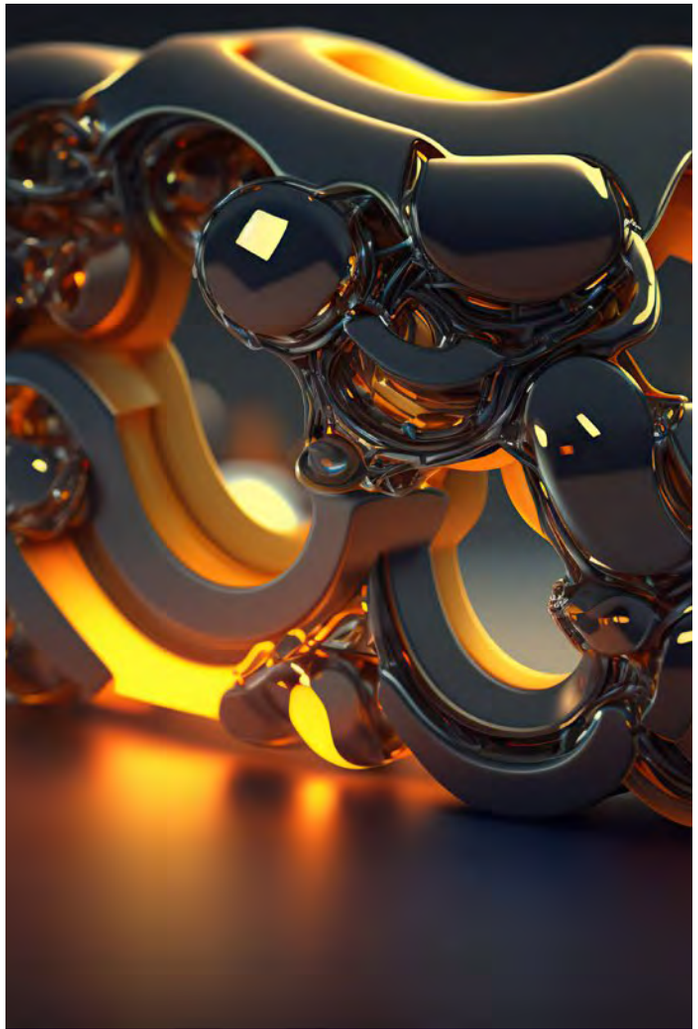
- Implementation Challenges: implementation of digital technologies can be complex, requiring significant investments in infrastructure, training, and cultural change.
- Data Privacy and Security: collection and storage of large amounts of sensitive data can pose significant privacy and security risks (must be addressed to ensure trust and compliance).
- Resistance to Change: Resistance to change among stakeholders can pose a challenge to the digitalisation of pharmaceutical processing (especially for those accustomed to traditional methods of manufacturing and quality control).

Threats

- Cybersecurity Risks: including data breaches and ransomware attacks.
- Regulatory Challenges: digitalisation of pharmaceutical processing may face regulatory challenges, particularly in terms of data privacy and security, which could slow down innovation and adoption.
- Technical Challenges: integration of digital technologies into existing manufacturing processes can be technically challenging, particularly for legacy systems.
- Skills and employee readiness: digitalization may pose challenges for current skills levels of employees.

Table 1: - SWOT analysis of the digitalization of the pharmaceutical industry

Strengths



Digitalisation holds the potential to **streamline various processes** in the pharmaceutical industry, resulting in improved efficiency and cost savings. Automation of routine tasks, more efficient manufacturing processes, and improved supply chain management can lead to faster drug development, better control of manufacturing processes, and reduced errors. Digitalisation can also optimize resource utilization, leading to reduced waste and cost savings. Remote monitoring and maintenance of equipment can minimize the risk of equipment downtime, and digitalisation can lead to increased competitiveness and improved profitability.

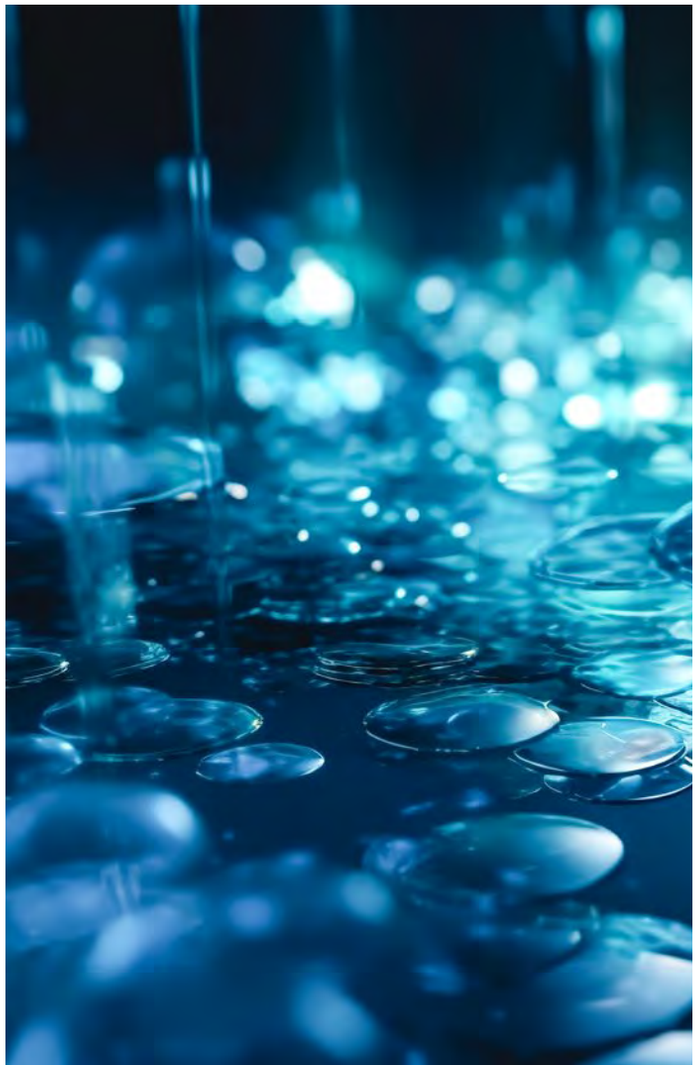
The use of sensors and digital tools for real-time monitoring and continuous monitoring of product quality is a key aspect of the aforementioned Process Analytical Technology (PAT) and Quality by Design (QbD) approaches in pharmaceutical manufacturing. As was discussed in Chapter 2.2, PAT and QbD aim to ensure product quality by monitoring and controlling critical process parameters throughout the manufacturing process. By implementing automated quality control checks with digital technologies, pharmaceutical companies can achieve the goals of PAT and QbD, leading to more consistent and high-quality products while reducing the risk of human error. The use of data analytics tools can also help with the design of experiments and process optimization, which are important components of QabD.

The collection and analysis of real-time data is a crucial aspect of digitalisation in pharmaceutical processing, which is central to QbD and PAT approaches. Automated quality control checks can be implemented through the use of sensors, machine learning algorithms, and other digital tools to monitor various parameters, such as temperature, pressure, and pH levels, throughout the manufacturing process. By collecting data from various sensors and devices, pharmaceutical companies can gain insights into the performance of equipment, the quality of raw materials, and the effectiveness of production processes. Real-time monitoring can help identify deviations from established norms and alert operators to potential quality issues before they become more significant problems. This proactive approach to issue identification and resolution can help minimize downtime and reduce the likelihood of product defects, ultimately improving product quality and reducing costs associated with rework or product recalls. Digital technologies can also enable continuous monitoring of product quality, as opposed to the traditional approach of batch sampling and testing. In addition, real-time data analysis can provide pharmaceutical companies with greater visibility into their manufacturing processes, enabling them to optimize production, reduce waste, and improve efficiency. Data analytics tools can help identify potential quality issues before they occur, enabling companies to take preventative action and avoid costly product recalls or delays. Overall, the use of digital technologies in quality control checks can help pharmaceutical companies improve product quality, reduce waste, and increase operational efficiency, ultimately leading to better regulatory compliance and customer satisfaction.

In addition to optimizing manufacturing processes and reducing waste, a 'Green-by-Design' approach can also be applied in the pharmaceutical industry to achieve greater sustainability. This approach involves incorporating sustainability principles into the design of pharmaceutical products and manufacturing processes, from the outset. By doing so, companies can reduce their environmental impact and improve the overall sustainability of their operations. Digital technologies can play a critical role in implementing a 'Green-by-Design' approach by enabling the analysis of large amounts of data on environmental impact and identifying areas for improvement. For example, digital tools can help identify opportunities to use renewable energy sources, reduce water consumption, and minimize the use of hazardous materials. By taking a proactive approach to sustainability and incorporating a 'Green-by-Design' approach, the pharmaceutical industry can help protect the environment, meet the growing demand for environmentally friendly products, and contribute to a more sustainable future.

Digitalisation can enable the **creation of a connected ecosystem for the pharmaceutical processing chain**, allowing stakeholders to share information in real-time and collaborate more effectively. This can help to streamline processes, reduce costs, and improve overall efficiency. For example, digitalisation can enable manufacturers to share information with distributors on production schedules, inventory levels, and quality control checks. This can enable distributors to plan their inventory more effectively and ensure that they have sufficient stock to meet demand. Similarly, digitalisation can enable manufacturers to share information with regulators on production processes and quality control measures, helping to ensure compliance with regulatory requirements. By fostering greater collaboration and information-sharing, digitalisation can help to create a more transparent and efficient pharmaceutical processing chain, benefitting all stakeholders involved.

Weaknesses



The implementation of digital technologies in the pharmaceutical industry can be a complex and lengthy process, and the pharmaceutical industry has been slower to adopt digital technologies than some other industries due in part to the **complexity of the regulatory environment and the criticality of ensuring patient safety**.

Digitalisation typically involves significant investments in infrastructure, such as upgrading IT systems and implementing data management systems, as well as providing training for employees to use new technologies effectively. It is estimated that the adoption of full-scale digital solutions can require heavy investment— around $50 million to $100 million per year for two to three years[39]. A key challenge in implementing digital technologies in the pharmaceutical industry is ensuring compliance with regulatory requirements. Digital technologies may require additional validation and qualification processes to ensure that they are fit for purpose and comply with regulations. This can add complexity and cost to the implementation process, but it is necessary to ensure patient safety and regulatory compliance. Furthermore, the pharmaceutical industry operates in a highly competitive landscape, which can make it challenging for companies to make the necessary investments in digitalisation. However, the potential benefits of increased efficiency, reduced costs, and improved product quality can make these investments worthwhile in the long run.

Pharmaceutical manufacturing involves the collection and storage of a vast amount of sensitive data, ranging from patient information to manufacturing and quality control data. As the industry moves towards digitalisation, the amount of data collected and stored is only increasing, leading to significant privacy and security risks. Pharmaceutical companies are responsible for protecting this sensitive data and ensuring that it is not misused or accessed by unauthorized individuals. Failure to do so can result in significant reputational damage, legal consequences, and regulatory fines. To address these risks, pharmaceutical manufacturers must implement robust data privacy and security protocols, such as the implementation of secure data storage and transfer systems, encryption, access controls, and regular security assessments and audits. Regulatory compliance requirements, such as the General Data Protection Regulation (GDPR) in the European Union, must be fully understood and followed. Companies require a clear policy framework outlining the approach to data privacy and security, and employees should be adequately trained in data privacy and security protocols.

The pharmaceutical industry has traditionally relied on established, time-tested methods of manufacturing and quality control, which can **create resistance to change among stakeholders when new technologies are introduced**. This resistance can stem from a lack of familiarity with digital technologies or a perception that they may be unreliable or unnecessary. Additionally, there may be concerns about the impact of digitalisation on the workforce, including fears of job displacement or the need for significant retraining. Overcoming resistance to change requires a combination of clear communication, education, and training. Stakeholders at every level of the organization need to understand the benefits of digitalisation and how it can help improve efficiency, reduce waste, and ultimately contribute to a more sustainable pharmaceutical industry. This includes not only frontline workers but also managers and executives, who can play a critical role in driving cultural change and promoting the adoption of new technologies.

Opportunities: breaking barriers greener horizons in the pharma processes

Digitalisation has been shown to play a significant role in optimising manufacturing processes in various industries. In the pharmaceutical sector, **digitalisation can help drive the sustainability agenda by enabling a more efficient use of energy and resources while reducing waste generation**. By implementing digital technologies such as PAT, which involves real-time monitoring of key process parameters, manufacturers can better understand their manufacturing processes and identify areas for improvement. This data can be used to optimise and adjust the manufacturing process to reduce energy consumption, minimise waste generation and improve overall efficiency and lead to more sustainable production processes that reduce environmental impact. PAT technologies can also improve the quality and consistency of pharmaceutical products, reducing the need for rework and ultimately reducing waste. By ensuring that the manufacturing process is operating within optimal parameters, PAT can minimize the need for overproduction, reducing excess waste and energy consumption. Moreover, **digitalisation can help identify the root causes of inefficiencies in manufacturing processes,** leading to more targeted interventions and ultimately reducing environmental impact. For instance, **digital twins and simulation technologies** can help simulate different scenarios and predict the impact of different process changes on energy consumption, resource utilisation and waste generation, enabling manufacturers to make informed decisions.

Digitalisation can **transform maintenance practices** within pharmaceutical manufacturing plants. Predictive maintenance has emerged as a critical application of digitalisation that can help reduce downtime and improve efficiency by identifying potential issues before they occur. With predictive maintenance, manufacturers can continuously monitor equipment using sensors, machine learning algorithms, and other digital tools to detect signs of wear and tear, corrosion, or other factors that could lead to breakdowns. By analysing the data generated by these tools, manufacturers can develop predictive maintenance plans that enable them to take **proactive steps to address potential issues**, such as replacing parts or adjusting equipment settings. This approach can not only help reduce downtime and improve efficiency but can also prevent equipment failures that could result in environmental hazards or other risks to product quality and patient safety. Additionally, by reducing equipment downtime, predictive maintenance can help reduce energy consumption and waste generation, improving the sustainability of the manufacturing process.

The use of **advanced analytics,** such as machine learning (ML) and artificial intelligence (AI), has revolutionized the manufacturing industry by enabling deeper insights and identifying patterns in data that would be difficult or impossible to uncover using traditional methods. In the pharmaceutical industry, digitalisation is enabling the collection of vast amounts of data at every stage of the manufacturing process. ML and AI can then be used to analyse this data to identify patterns that may indicate inefficiencies, quality issues, or potential improvements, such as identifying subtle correlations between raw material properties and final product quality, predicting equipment failures before they occur, and optimizing manufacturing parameters for improved efficiency and quality. Advanced analytics can provide pharmaceutical manufacturers with a deeper understanding of their manufacturing processes, identify areas for improvement,

and ultimately increase efficiency and reduce costs. Additionally, the use of advanced analytics and digital twin technology to improve manufacturing processes, can reduce the need for resource-intensive trial and error, leading to cost savings.

ML and AI can also greatly aid the **transition of the industry to the circular economy** by enabling the analysis of environmental impacts and resource usage, allowing for a more efficient and sustainable use of resources. This can include the identification of opportunities for recycling or repurposing waste materials, and the reduction of energy consumption and carbon emissions. For example, ML algorithms can analyse manufacturing data to identify areas where energy consumption can be reduced without compromising product quality. Additionally, digital technologies can facilitate the use of renewable energy sources, such as solar or wind power, in pharmaceutical manufacturing. Digitalisation can also help reduce the use of hazardous chemicals in pharmaceutical manufacturing by enabling real-time monitoring of environmental impacts across the entire value chain.

Traditionally, manufacturing processes required personnel to be physically present on the factory floor to monitor operations and make adjustments as necessary. This required a significant amount of time and resources, as well as increasing the risk of errors or accidents. The use of digital technologies such as sensors, IoT devices, and real-time analytics, manufacturers can now **remotely monitor and control their production processes** from anywhere. This allows for greater flexibility in scheduling and resource allocation, as well as reducing the need for on-site personnel. Remote monitoring also enables real-time oversight of processes, allowing manufacturers to detect and address issues as they arise, rather than after the fact. This can lead to increased efficiency, reduced downtime, and improved product quality. Additionally, remote monitoring can reduce the environmental impact of manufacturing by enabling optimization of resource usage and reducing energy consumption.

Regulatory compliance is a critical aspect of the pharmaceutical industry, and non-compliance can lead to significant financial and reputational damage. Digitalisation can play a vital role in improving regulatory compliance by enabling real-time monitoring of key parameters throughout the manufacturing process. With the use of PAT analysers for multivariate analysis in real-time for QbD, as well as other monovariate sensors for tracking e.g., temperature, humidity, and pressure, ensuring that critical parameters can be monitored to ensure they remain within the specified range. By monitoring these parameters in real-time, any deviations can be quickly detected, and corrective action can be taken before the problem becomes more severe. This helps to minimize the risk of non-compliance and reduce the likelihood of costly fines. In addition, digitalisation can also facilitate compliance with regulations by providing accurate and timely documentation of all manufacturing processes. Digital records can be easily searched, stored, and retrieved, making it easier for manufacturers to demonstrate compliance during audits or inspections. Digital records can also be automatically timestamped and signed, providing an additional layer of security and auditability. Furthermore, digitalisation can enable better communication and collaboration between regulatory authorities and manufacturers. With real-time monitoring and data sharing, regulators can more easily keep track of the manufacturing processes and ensure that they are compliant with all relevant regulations. Manufacturers can also benefit from improved communication with regulators, receiving timely feedback and guidance on compliance issues. This can ultimately lead to a more collaborative and streamlined approach to regulatory compliance in the pharmaceutical industry.

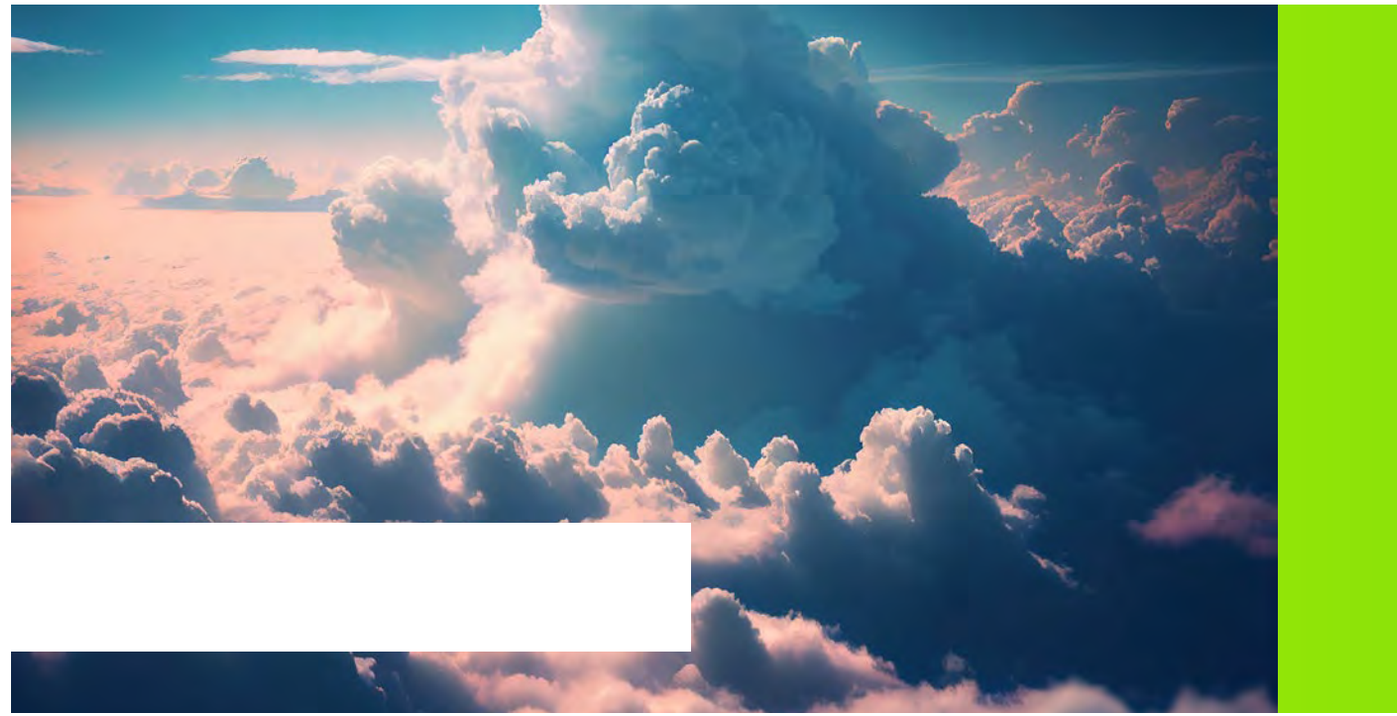
Threats

In the pharmaceutical manufacturing industry, the implementation of digital technologies, such as the use of connected devices and cloud-based storage solutions, has led to the collection and storage of vast amounts of sensitive data, including intellectual property, proprietary formulas, patient data, and confidential business information. While this data is critical to the efficient operation of the industry, it also poses **significant cybersecurity risks that must be addressed to ensure trust, compliance, and business continuity**.

Data breaches and ransomware attacks are two of the most common cybersecurity risks facing the pharmaceutical industry. A data breach can occur when unauthorized users gain access to sensitive data, either through a cyberattack or a physical breach, such as theft or espionage. Ransomware attacks, on the other hand, involve malicious software that encrypts critical data and demands payment in exchange for the decryption key, often resulting in data loss and financial damage.

Given the high stakes involved in the pharmaceutical industry, cybersecurity risks can have significant consequences, including loss of intellectual property, legal and regulatory penalties, reputational damage, and even patient harm if confidential medical information is compromised. As such, it is critical for pharmaceutical manufacturers to take proactive measures to mitigate these risks, such as implementing robust security protocols, conducting regular cybersecurity assessments, and providing ongoing employee training to raise awareness of cybersecurity best practices.

Moreover, the **integration of digital technologies into existing manufacturing processes** can pose a significant challenge, particularly for the pharmaceutical industry which has many legacy systems that were not designed with digitalisation in mind. These legacy systems may not be compatible with newer digital technologies, requiring significant investment in upgrading or replacing equipment and software. Additionally, integrating digital technologies may require changes to existing standard operating procedures (SOPs) and training for employees to adapt to the new systems. One potential solution to this challenge is to start small with pilot projects that focus on specific areas of manufacturing or quality control, gradually scaling up to a more comprehensive digitalisation strategy over time. This approach can help to identify potential issues and develop solutions on a smaller scale, reducing the risk of costly and time-consuming setbacks.



Another potential challenge is the need to ensure that digital technologies are properly validated to **meet regulatory requirements**. This can be a complex and time-consuming process that requires careful planning and execution to ensure that the technology is integrated in a way that does not compromise the safety, efficacy, or quality of the pharmaceutical products being produced. Indeed, regulatory compliance is critical in the pharmaceutical industry, and any digitalisation efforts must comply with strict regulations set by the European Medicines Agency (EMA), as well as those of other agencies such as the FDA. One of the key challenges facing the digitalisation of pharmaceutical processing is ensuring that the necessary regulatory frameworks are in place to support innovation and adoption. This requires a collaborative effort between industry, regulators, and other stakeholders to establish guidelines for data privacy and security that balance the need for innovation with the need to protect patient privacy. Additionally, as the digitalisation of pharmaceutical processing continues to evolve, there may be a need for new regulatory frameworks and guidelines to keep pace with advances in technology. This can be a slow and complex process, and it may require significant investment in research and development, as well as stakeholder engagement and consultation.

The digitalisation of pharmaceutical processing has the potential to significantly transform the industry, but it could also bring about some **disruptions to traditional business models**. One of the most significant impacts could be on the patterns of employment. The adoption of digital technologies may lead to job losses in certain areas of pharmaceutical manufacturing but there may be compensatory new opportunities. For example, as more processes become automated, **the need for manual labour may decrease,** but there may be a **greater emphasis on technical expertise and data analysis**, which will in turn lead to new job opportunities in areas such as data analysis, software development, and cybersecurity.

Conclusions

Conclusions, recommendations (regulatory, decision makers, businesses) and roadmap for digitalisation of pharmaceutical industry towards green pharmaceuticals

While the implementation of digital technologies in the pharmaceutical industry can be complex and challenging, the potential benefits make it a worthwhile endeavour. Companies that successfully navigate this course can gain a competitive advantage in the market and position themselves for sustainable future success. It is important to ensure that any digitalisation efforts **comply with regulatory requirements**, including privacy and data security. To achieve this, close collaboration between industry and regulatory bodies will be essential, as will ongoing investment in research and development to keep pace with advances in technology.

Digitalisation can transform the pharmaceutical industry by bringing about greater efficiency, cost savings, and improved patient outcomes. To successfully adopt digitalisation and digital twin technology, **collaboration between pharmaceutical companies, technology providers, and research institutions is key**. This collaboration can foster innovation and accelerate the adoption of digital technologies. Additionally, **a common framework for digitalisation implementation** can ensure consistency and compatibility across different implementations. Moreover, **investing in R&D** to explore the full potential of digital technology in the pharmaceutical sector can lead to new models for drug development, optimized manufacturing processes, and improved supply chain management. **Addressing regulatory concerns** and **encouraging innovation through funding for start-ups and small and medium-sized enterprises** working on digital technologies can also drive the adoption of digitalisation in the pharmaceutical industry. Finally, **focusing on sustainability** in the adoption of digital technologies can help reduce waste, optimize resource utilization, and minimize the environmental impact of pharmaceutical manufacturing processes. By **fostering a culture of continuous improvement** and staying vigilant about monitoring and evaluating outcomes, the pharmaceutical sector can embrace digitalisation and transform the industry for the better.

Recommendation	Description
Foster collaboration	Encourage collaboration and knowledge sharing between pharmaceutical companies, technology providers, and research institutions to promote innovation and accelerate the adoption of digital technologies.
Develop a common framework	Establish a common framework for the implementation of digital technologies in the pharmaceutical sector, which includes standardized data formats, interoperable software solutions, and shared infrastructure for data storage and analysis. This can help ensure compatibility and consistency across different digital implementations.
Invest in research and development	Invest in research and development to fully explore the potential of digital technologies in the pharmaceutical sector. This can include developing new models for drug development, optimizing manufacturing processes, and improving supply chain management.
Address regulatory concerns	Address regulatory concerns related to digital technologies in the pharmaceutical sector by working closely with regulators to ensure compliance with relevant regulations around data privacy and security.
Encourage innovation	Foster innovation in the sector by providing funding and resources for start-ups and small and medium-sized enterprises (SMEs) working on digital technologies. This can help support the development of new solutions and foster competition in the sector.
Foster a culture of continuous improvement	Promote a culture of continuous improvement in the pharmaceutical sector by regularly monitoring and evaluating the outcomes of digital technology adoption. This can help identify areas for improvement and ensure that the sector continues to evolve and innovate.
Focus on sustainability	Prioritize sustainability in the adoption of digital technologies in the pharmaceutical sector. This can include exploring the use of digital technologies to reduce waste, optimize resource utilization, and minimize the environmental impact of pharmaceutical manufacturing processes.
Plan and execute digital transformation strategies	Working closely with employees to ensure a smooth transition from more traditional processes to digitized one. Investing in training and reskilling programs to help workers adapt to new roles. Exploring new business models and revenue streams that can be enabled by digital technologies.

Table 2: - High-level Recommendations for promoting the adoption of digitalisation in the European Pharmaceutical Industry

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