Digitization in pharmaceutical manufacturing

White Paper - Dr. Hans-Walter Hoehl, Dr. Jens Scheibner and Norbert Skubch

The digitization topic is omnipresent today. With the COVID-19 pandemic, it has once again gained a significant boost in attention in society - and rightly so.

All companies are working on improving their digital capabilities, but with different focus regarding targets and also with different intensity. What they all have in common is the intensive use of relatively new information technologies. The following deserve special mention here:

- Artificial intelligence (AI), which draws conclusions based on pattern analysis and recognition and thus opens up machine learning and / or deep learning.
- Robotics, sensors in connection with Internet of Things (IoT) technologies, which allow operational processes to be almost completely automated.

  This also includes robotics process automation (RPA) – with this approach, routine, largely manual administration and reporting activities can be automated by software robots (so-called bots).
- As well as combinations of these - this is the case, for example, when sensors provide the data for the AI system in real time, the system draws up instructions for action and in turn forwards them directly to the robots in plants.

In addition, new topics such as digital twins, blockchain-based decentralized trust systems, fog computing or serverless Platform as a service Solution (PaaS) should be mentioned. Whatever the case, the term digitization is very diverse and so are the areas of application in the pharmaceutical production.

In the pharmaceutical industry, there are a large number of operational processes and procedures that can be automated and, due to the high documentation requirements, there is also a huge amount of already available data on which AI models can be built. This applies to manufacturing in the narrower sense, for QC / QA and supply chain management, but also for engineering and site operations, where data from a wide variety of sources and IT systems is used, processed and passed on.

In addition, the industry has well-trained staff. The GMP-compliant and error-free production of pharmaceuticals requires highly qualified pharmacists, chemists, process engineers, chemical technicians and pharmaceutical technicians. This know-how is absolutely necessary in order to successfully transform towards digitized production processes.

Overall, pharmaceutical production is a very grateful and promising field for digitization.

It should also be mentioned that this is no longer about incremental optimization in the sense of a continuous improvement process – the outlined technologies have the potential to be “game changers”. Their use can reduce throughput times from weeks to hours, increase productivity by 50% and more, but also force error rates to zero.

Now we want to deliberately limit our considerations and ask ourselves how we can bring the digitization topic in the pharmaceutical production to success. Here we are guided by 5 principles:

(1) **Don't waste time on detailed long-term planning**

Digitization is content-wise so extensive and its progress is now so dynamic that any forecasts and strategies based on them resemble reading in a crystal ball. Nobody has the complete overview of what is currently emerging in the multitude of disciplines involved.

The path to further specialization is unstoppable, the generalist has long been a thing of the past, which is ultimately also the result of digitization and the associated knowledge explosion in the 21st century.

What good is it to a company if its employees are working on a glossy brochure that systematizes, illustrates and prioritizes the AI areas of action for the next five years? It is out of date as soon as it is available. It is by far more effective and also more efficient to actually experience or pilot technical innovations in order to quickly gain real benefits from them.

This explorative approach - which only appears directionless at first glance - is ultimately a "learning system" itself.

(2) **Rely on short-term projects with proven success**

Following this basic idea, the authors recommend to tackle manageable topics with instruments of digitization and to define corresponding use cases in a functionally precise manner, to limit their scope deliberately, and to be very clear in their economical expectations.

You shouldn't digitize an entire factory right away, and also not the entire supply chain, ideally end-to-end for all products including all CMOs and all suppliers involved. Basically, of course, you will want to develop in this direction, but it is better to move forward step-by-step and gain real experience, otherwise the risk of failure is high.

It should not be about a multi-year program, but preferably about projects with a duration of less than 6 months. The time restriction forces a project team to focus on the essentials – on the value generating content.

A good example in this context is the analysis of master batch records [1] with Natural Language Understanding (NLU) algorithms, on which one of the authors himself contributed. Several thousand records for approx. 400 SKUs of solid forms were scanned and subject to a NLU based text analysis in order to track down the root causes of quality deviations more quickly.

[1] Synonym: master production records, master manufacturing records

Before the pilot, only 25% of the causes were identified manually and analysis was very time-consuming – after the pilot the system can meanwhile correctly deduce more than 75% of the causes using NLU algorithms. This happens almost real-time, since all records are now available electronically. Due to the continuously growing database, the system keeps learning.

This experience can now be used as part of a roll-out for other pharmaceutical forms in other plants. This is how experience becomes a lived strategy.

(3) **Work in digitization projects in an interdisciplinary and open manner**

Far more important in digitization projects than in classical software development projects is an interdisciplinary composition of the project team as well as the intensive cooperation of the team itself – why is that?

Experts from the functional disciplines (e.g., production, quality, supply chain) must understand the pharmaceutical problem and should be able to address it with sufficient accuracy to enable data analysts to find the right abstraction. Data analysts and / or data scientists, in turn, have to gradually create the problem-oriented abstract model and specify the model rules.

This process is iterative, highly dialog-intensive and full of conceptual dead ends that can only be overcome in the mutual critical assessment of reality against the model.

An example illustrates the challenge: the aim was to achieve significantly higher productivity in QC laboratories. The decisive parameters - including characteristics and priorities of the samples, qualifications and experiences of the laboratory employees, performance indicators of the laboratory equipment - were worked out in several weeks of intensive discussion.

And it took additional six weeks to better understand the interdependencies in the sense of a learning system on the basis of a digital twin. As a final result, an increase in laboratory productivity of more than 50% was achieved.

A third central role in a project team should not be left unmentioned: AI systems draw conclusions and learn based on very large amounts of data. High quality requirements have to be placed on this data.

Unfortunately, the IT in companies is not a green field, but a historically grown landscape usually consisting of a large number of heterogeneous and only partially communicating systems that are managed by various internal and external providers.

It is therefore not that easy to get the right data at the right time. This requires a dedicated role, the data acquisition team member.

(4) **Manage data as a resource and pay attention on its quality**

In the literature, we read the keyword data-driven organizations more often. For companies that establish their core business on this idea, such as Facebook or Google, this way of thinking may already apply in full. For many industrial companies however, whose products are real and tangible, even selectively data-driven business models are very often unknown territory.

“The goal of data-driven business models is to create added value by utilizing data. This can be done through the optimization and automation of products, processes or services, a digital transformation of existing business models or the development of completely new business cases.“ [2]

This way of thinking requires next-generation data management that guarantees the correctness, completeness and up-to-dateness of the various data types for a wide variety of applications at all times.

But a well-defined and integrated data architecture is still the exception today. The heterogeneity of the systems as well as the complexity and diversity of the data itself are decisive obstacles. In addition, the necessary investments are considerable and can hardly be justified in direct economic terms.

Such projects are investments in an infrastructure that cannot be justified on their own, but only achieve their economic justification through use by other projects. In this context, a long-term perspective is indeed required, because the transformation into a data-oriented company takes several years.

“If the homework in the field of data quality and data architecture is not done, then in the worst case, AI projects will deliver incorrect results and fail. More than 70 percent of the companies therefore see a big or very big challenge when it comes to data management.“ [3]

In relation with data quality, it is not just about the classic attributes but the keyword “AI bias” has increasingly come to the center of interest – what does that mean?

These are anomalies in machine learning algorithm outcomes resulting from biased assumptions ("biases") being incorporated into the development of the algorithm itself or in the test data for the algorithm.

A well-known example is the recruiting process at Amazon. The project started in 2014 and was designed to automatically evaluate applicants with AI-supported algorithms on the basis of submitted CVs and relieve internal recruiters from the manual assessment of correspondence – unfortunately, it turned out that the system did not evaluate female candidates fairly.

At first glance, one might think that this is not relevant for pharmaceutical production. At this point, however, caution is advisable – human biases from experience can also be found in the mapping of business models. In corresponding AI projects, it is therefore important to pay a lot of attention to the topic of "AI bias" and to use methods and tools that minimize the risk of bias.

2 [at]Blog: Datengetriebene Geschäftsmodelle – Grundlagen für ein neues Zeitalter, M. Tiedemann, 21. Mai 2019
3 Lünendonk-Studie: Künstliche Intelligenz – Studie zu Anwendungsfelder, Herausforderungen und Ziele von KI-Projekten in Großunternehmen und Konzernen, 2019

(5) **Be aware of the specific regulatory environment**

In pharmaceutical production, all GMP-relevant processes or systems have to be validated, and this for good reason. Validation provides documented evidence that a process or system fulfills the previously specified requirements (acceptance criteria) in a reproducible manner in practical use.

AI systems are computer-aided systems and therefore usually also need to be validated. But how do you validate learning systems if you do not fully know their functionality at the time of validation, because the system is learning and will very likely develop functionality that is not yet visible today.

This is a very fundamental challenge that occurs in particular with deep learning-based AI systems. The traditional validation methods (e.g., V-Modell GAMP guideline) fail here and the authorities are currently looking for suitable methods and procedures.

The FDA provides initial guidance on how to tackle the challenge with the action plan “Software as a medical device (SaMD) based on artificial intelligence / machine learning (AI / ML)” issued by the Digital Health Center of Excellence of the Center for Devices and Radiological Health. (January 2021).

In addition, the FDA has announced that it will issue new guidelines on “Computer Software Assurance” in 2021, which will supplement or replace the guidelines on computer software validation.

In order to fully leverage the potential of digitization projects, the goal must be to validate the corresponding systems. If this does not succeed, there will be a parallel use of the non-validated AI system and a still manual, but validated process - a highly unsatisfactory situation.

It is therefore advisable to establish a digital platform with corresponding responsibility on the part of IT and QA in order to document the life cycle of the digital use cases in accordance with GMP.

If the topic has arisen your interest, you would like to discuss some of the addressed topics in more detail or perhaps you are facing one of the following three challenges in the near future ...

- I want to know which topics in pharmaceutical manufacturing are attractive for digital AI solutions
- I want to set up a corresponding project in pharmaceutical manufacturing
- I want to review an ongoing project with regard to data quality and / or validation

... then we look forward to talking to you.

Dr. Hans-Walter Hoehl, Management Consultant
Phone +49 (0) 6123 701 0
Mobile +49 (0) 163 251 2795
hwh@jsc.de

Dr. Jens Scheibner, Management Consultant
Phone +49 (0) 6123 701 0
Mobile +49 (0) 170 661 4254
jes@jsc.de

Norbert Skubch, Director and Chairman of the Supervisory Board
Phone +49 (0) 6123 701 144
Mobile +49 (0) 172 407 5702
nsk@jsc.de

JSC Management- und Technologieberatung AG
Im Pfarracker 24
65346 Eltville am Rhein
Germany

Phone +49 (0) 6123 701 0
Fax +49 (0) 6123 701 170
info@jsc.de
www.jsc.de