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The Implications of Tacit & Explicit Knowledge for Technology Transfer: When it goes well & when it goes wrong & what can Digital do to help!

Paige Kane Dr.
PRST,TU Dublin

David Twohig Dr.
Accenture

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Authors
Dr Paige Kane, PRST, TU Dublin
Dr David Twohig, Accenture

Introduction
The pharmaceutical industry is known for the development, production, and delivery of medicines to patients. What is often not necessarily appreciated is the extensive and complex range of product and process knowledge that is created during the lifecycle of these medicines. *Knowledge*, in the context of medicinal products and process development is discussed in many regulatory guidance documents. However, *knowledge management* was not discussed until it made its way into regulatory guidance with the publication of ICH Q10 [1], where Knowledge Management (KM) and Quality Risk Management (QRM) were identified as the two enablers to a Pharmaceutical Quality System (PQS). Although KM is defined in ICH Q10, knowledge, and knowledge types (tacit/explicit) are not.

To explore the challenges and opportunities for effectively managing knowledge, this article will examine a use case where a biopharmaceutical company is introducing an existing product to a new facility. This referred to as Technology Transfer (TT) activity. The example will discuss the challenges of both knowledge availability and flow within the TT process. From there it will explore how organizations may use concepts such as the Pharmaceutical Product Knowledge Lifecycle (PPKL) and DPP (Digital Product Profile) which have the potential to address these challenges.

Key Concepts
The following key concepts set the stage for the use case:

1. Knowledge created in the pharmaceutical product lifecycle may be explicit (documented or codified) and/or tacit (that which is known but not codified, typically thought of as the knowledge in the heads of people).

2. The Pharmaceutical Product Knowledge Lifecycle (PPKL) Model (Figure 1) [2]: Highlights knowledge creation activities along the product lifecycle calling out non-routine elements of knowledge transfer in technology transfer, technical support, and continual improvement. Knowledge must be visible and available across the lifecycle for scientists, operators, and technical services personnel to perform their roles most effectively.

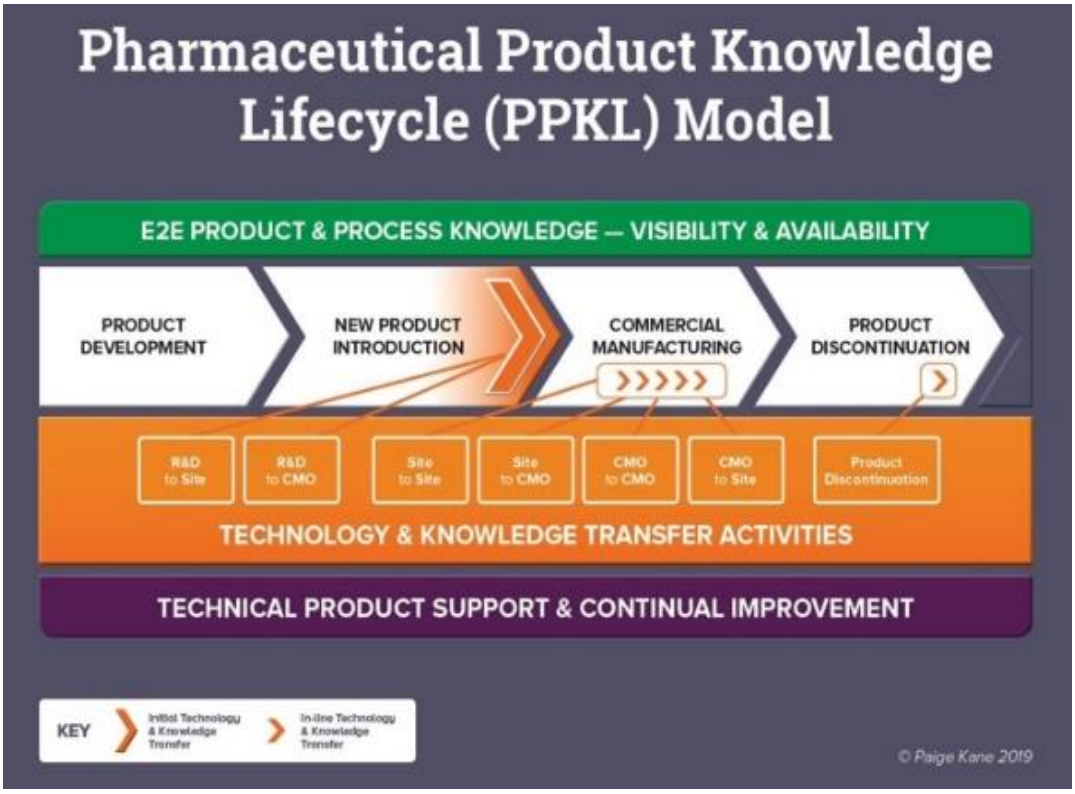

Figure 1 - The Pharmaceutical Product Knowledge Lifecycle (PPKL) Model [2]

3. Technology Transfer Knowledge Challenges: Challenges in Technology Transfer are depicted in Figure 2 below [3]. This diagram was introduced in the opening paper of this journal issue and will be referenced in the example case in the section following.

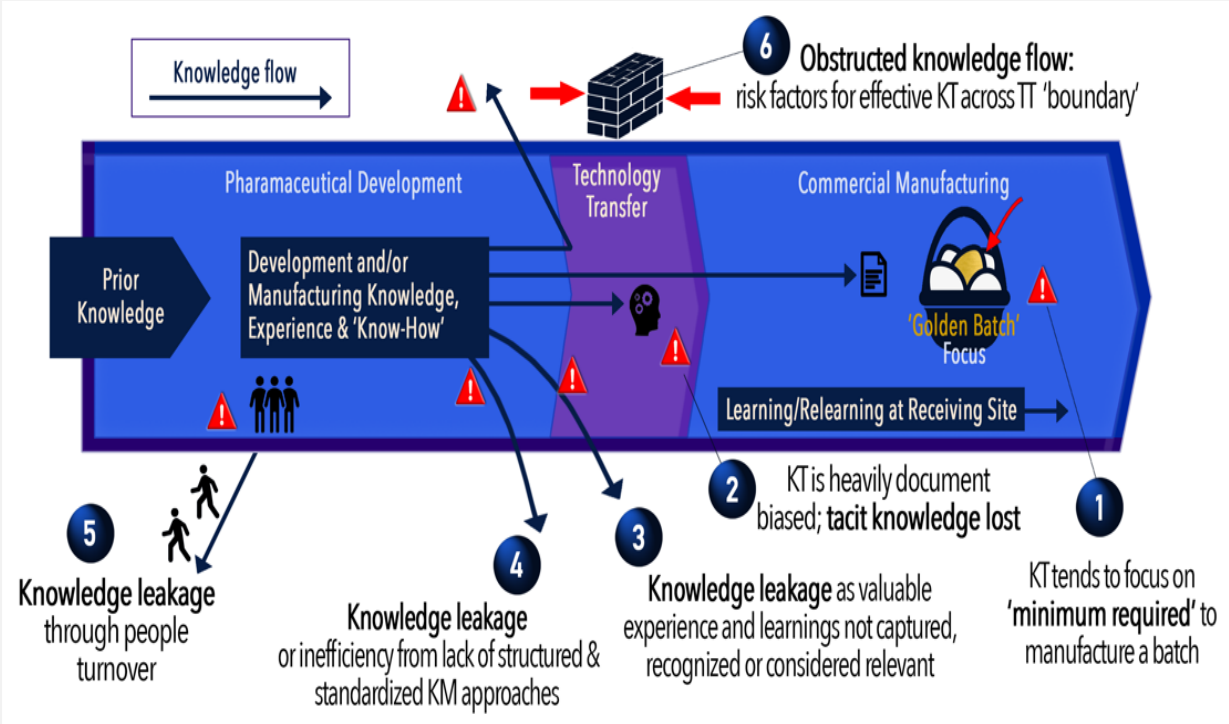

Figure 2- Knowledge transfer challenges during technology transfer [3]*(Lipa)*

4. Digital Product Profile (DPP): The digital product profile represents a business contextualised framework that manages all associated product and process data. It does this by availing of eco-system technologies to define and manage materials, equipment, process design, critical quality attributes, quality control specifications and process parameters to create a single source of truth. This framework also enables organisations to manage target product profiles (TPP), quality target product profiles (QTPP) and established conditions (EC), in addition to enabling the quality by design (QbD) concept. Figure 3 provides a visual representation of what a DPP may encompass.

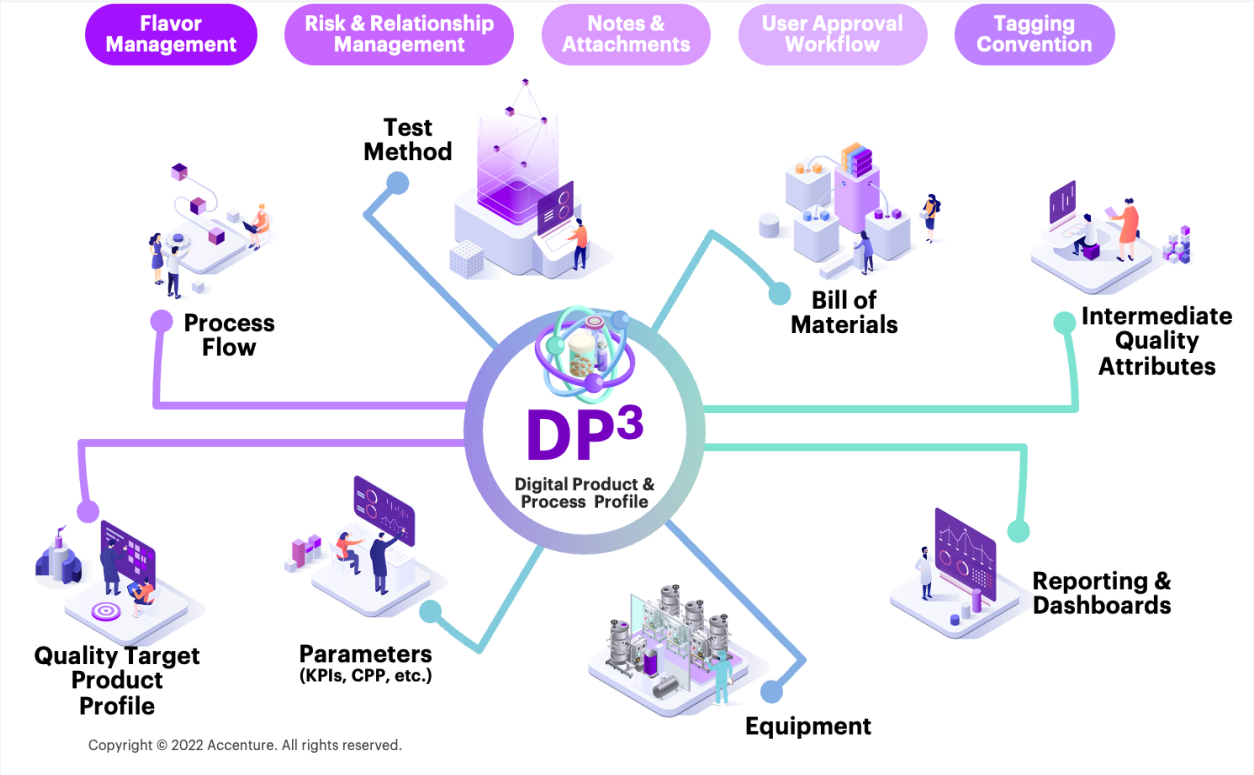

Figure 3 DPP - Digital Product Profile Framework

Leveraging industry standards such as ISA S88 [4] the DPP structures data in a hierarchy consistent with the type of batch processing we see in biopharmaceuticals i.e., process stage, process operation and process action.

By digitising the data model in a "single source of truth", the digital product profile enables innovative concepts such as:

- *Relationship Management:* Where the supporting system can interlock data objects and alert users of their interdependencies. For example, creating a digital interlock between a target product profile → intermediate quality attribute → process parameter.

- *Product and Process Genealogy:* Enables the supporting system to visualise the evolution of the product and process data in an S88 context over a predefined time horizon. (Note: This concept provides end users a consolidated view of all explicit and tacit knowledge through the development and transfer of the product.)
- *Product & Process Intelligence:* The DDP enables analytics to better understand variability within the product and process. Analytics are also key to understanding the difference in how technology transfers are executed across sites.

Knowledge, Knowledge Availability and Knowledge Flow

Linking back to the depiction of the PPKL in Figure 1, knowledge must flow end-to-end along the product's lifecycle as the body of knowledge expands. Lack of visibility or availability of knowledge presents challenges to the development, manufacture, transfer, and improvement of medicinal products. Lipa [3] characterised knowledge transfer challenges which are represented in Figure 2.

- *Tacit knowledge and people:* Defining the boundary between explicit and tacit knowledge can be difficult. Organisations need to be able to record and recall information in an efficient way such that the management of data, information and knowledge is not overburdensome for the people involved. In addition, when people leave the project or company, their tacit knowledge may leave with them. Codifying the intangibles such as people's experience continues to present a challenge (Figure 2, points 2, 3, and 5)
- *Knowledge Silos*: There are many organizational functions that interact with the product along its lifecycle. With disparate processes, systems, and people turnover, knowledge silos may be created. Without a strategy or holistic approach, knowledge may be trapped in silos of people, process, systems, and organizations (Figure 2 points 4 and 6)
- *Interoperability:* The dispersed and disparate nature of the data constrain people's ability to execute holistic risk assessments and solve process deviations. The knowledge landscape has multiple systems and source files which tend to be manual and discrete i.e., paper, excel-based etc… (Figure 2 point 6)

- *Knowledge Management (KM) and Quality Risk Management (QRM):* KM and QRM have been linked as enablers to a Pharmaceutical Quality System in ICH Q10. This linkage is articulated in the *Risk-Knowledge Infinity Cycle* (*RKI Cycle*) [5] discussed in the paper 2 of this journal issue. The RKI is a framework to intentionally and methodically unite risk management and knowledge management, whereas knowledge informs risk to better inform decisions.

In the next section the use case will explore how these issues had significant and real implications for a technology transfer which ultimately impacted the supply of product to market. In order to address these challenges, the use case will also explore how using concepts such as PPKL and DPP can help organizations better manage knowledge.

Day in the life – Technology Transfer Putting Knowledge to Work

Existing State:

One of the most challenging parts of the product lifecycle is when it is being transferred from R&D to manufacturing as a new product (new product introduction technology transfer). Even transferring mature products between existing manufacturing facilities has historically presented significant challenges for organisations.

Typically, at this point in the lifecycle complex product and process data sets are being converged into explicit and tacit knowledge packs. This compilation of data, information and knowledge are disparate in nature i.e., they define and manage materials, equipment, process design, critical quality attributes, quality control specifications, process parameters etc. and while differing in nature they have interdependencies that ultimately impacts the final product.

In this example we meet Paul who is managing the introduction of an existing product to a new manufacturing facility. While the company has manufactured the product for a number of years Paul knows the original introduction of the new product and process was challenging. The failure of the team to properly manage the flow of knowledge into the site resulted in a series of production issues. These impacted the commercialisation schedule and delayed the shipment of product by several weeks.

One of the main production issues was related to variability of yield in the bioreactor processing phase. During the subsequent root cause investigation, it became evident that:

1. The control strategy to manage the supply of air to the bioreactor had previously shown to impact the yield when the flowrate dropped towards but not beyond the lower limit for longer than 30 minutes. While this was noted in the design of experiment report at the time the issue was difficult to re-create consistently and as such subsequent process development activities i.e., changing in materials and equipment determined the risk associated with this issue had diminished.

2. While this issue was documented as part of the lessons learned during process development, the receiving site team were unaware of this information. The tacit knowledge captured in the lessons learned activity was never formalised in a procedure or work instruction and was located in a limited access SharePoint site. In addition, this learning should have been updated in the product risk assessment.

Without a knowledge management strategy, inclusion of lessons was overlooked and not included in the handover pack during this transfer.
In addition, the risk assessment did not identify the flowrate issue as a potential risk. This lack of knowledge transfer had the knock-on effect on the commissioning and qualification strategy i.e., the process qualification scripts were not designed to stress test the lower limits for aeration and their potential impact on production.

In this example we see that key knowledge was created in the development organization, and while the tacit knowledge was captured as a lesson learned activity, it was not stored in a way that was helpful to receiving site.

While it is easy to look back retrospectively on technology transfers, anyone involved will know the challenge associated with managing this level of knowledge under pressurised schedules and how challenging it can be to get the information you need.

Future State:

To ensure this project is set up for success, Paul's product introduction strategy looks to better enable knowledge exchange and visibility. By adopting concepts like the PPKL model (visible and available knowledge across the lifecycle) and a digital product profile, he is seeking to centralise the data sets into a framework which is then supported by robust knowledge management governance.
Re-engineering the issue above using these frameworks and concepts we observe:

1. All design of experiment data sources is attached to the digital product profile. This is enabled via a series of system integrations and data configuration. The digital product profile tracks all associated data and uses the relationship feature to tie interdependent process data together such that end users are easily alerted to knowledge as it is developed.

2. Because all product and process specifications are stored within a single source framework it is readily visible and accessible by the end user. In addition to product and process specifications, tacit knowledge that has been captured via risk assessments, can also be linked into the single source framework. Paul has also compiled links to other materials that captures tacit knowledge such as lessons learned, relevant communities of practice and training videos created using mixed reality technologies.

By getting the team to adopt both the PPKL and DPP concepts (ensuring knowledge is captured, visible and available throughout the product lifecycle), Paul is confident the transfer strategy is set up in such a way as to ensure all knowledge is managed effectively and efficiently such that it makes it simple for users to define and visualise the data.

Conclusion

With the large volume of knowledge created during new product introduction and technology transfer, opportunities exist via knowledge management models and principles to improve the visibility and accessibility of that knowledge. It is evident that digitisation presents both opportunity and challenges for organisations. With new science driving more complex products, processes and ultimately patient treatments, it is imperative that businesses understand how the constraining forces of legacy practices and systems will impact product development and speed to market.

While there are many factors that influence the development of a product and its commercialisation through the supply chain, the management of lifecycle data is going to play an ever-important part. Greater product complexity is already driving significant increases in data volumes and velocity. In order to avoid the trap of being “data rich and information poor” organisations are going to need to evolve their working practices and supporting systems.

Through this article we have examined some of the challenges and an array of models and concepts that we believe can better enable knowledge management:

- Using the concept of knowledge visibility and availability in the PPKL Model, the knowledge created in new product introductions and in-line technology transfers contributes to the body of knowledge. This knowledge should be used for informing risk (linking to the RKI cycle), for continual improvement and for efficiencies in knowledge transfer and on-boarding.

- We observed in the use case how the breakdown of knowledge management led to an incomplete evaluation of risk. This was a failure on a people, process and system level:
    - *People:* The lack of judgement on how best to manage the knowledge. Because the knowledge was not managed effectively, the risk assessment overlooked a key risk. The receiving team then were unaware of this potential issue.
    - *Process:* Over reliance on legacy manual work practices made it difficult to effectively co-ordinate the knowledge transfer package into the site.
    - *System:* In the absence of a digital knowledge management strategy (PPKL) model and platform (digital product profile) it was difficult to define and govern data at a foundational level to enable effective knowledge management.
- By re-engineering the problem through the lens of the PPKL model and DPP framework the team were set up for success:
    - *People:* The availability of all explicit and tacit knowledge via the DPP made it easier for end users to evaluate risk and assess any potential gaps.
    - *Process:* The introduction of the PPKL model ensured the knowledge management strategy was structured and simple to follow.
    - *System:* Supported by a digital backbone via the DPP systemising the knowledge via a single source of truth ensured the data were managed and governed in a structured and secure way.

Going forward, as organisations seek to digitise their product lifecycle, they are in fact setting the foundation for the adoption of new and emerging technologies such as mixed and augmented reality, and, while these technologies certainly hold significant potential, they will only realise their full benefit if organisations get better at structuring and managing their data.

In closing, while it may not be possible to manage knowledge such that organisations will never misplace information or fail to identify risks appropriately, the utilisation of models such as the PPKL and data frameworks such as the DPP can surely help close the gap. With the ever-increasing complexity of new science data sets the industry needs to better manage product lifecycle. The failure to do so has the potential to constrain an organisation's ability to deliver treatments to the market and ultimately to improve patient outcomes.

References

[1] International Conference on Harmonisation, "Pharmaceutical Quality System Q10," *ICH Harmon. Tripart. Guidel.*, no. June 4, 2008.

[2] P. Kane, "A Blueprint for Knowledge Management in the Biopharmaceutical Sector,"

2018.
[3] M. J. Lipa, “Unlocking Knowlege to Benefit the Patient: How Connecting KM and QRM Can Strengthen Sceince and Risk-Based Decision Making,” TU Dublin, 2021.
[4] ANSI/ISA, *ANSI/ISA–88.01–1995: Batch Control, Part 1: Models and Terminology*. 1995.
[5] M. Lipa, P. Kane, and A. Greene, “Advancing competency in managing risk and knowledge: Steps toward operationalisation of the Risk-Knowledge Infinity Cycle (RKI Cycle) - Part 1: Improving effectiveness of Risk-Based Decision Making (RBDM),” *Arrow @ TU Dublin*, pp. 0–12, 2022.