Exploring Pathways from Data to Knowledge to Insights in the Pharmaceutical Industry: 'Introducing the Pharmaceutical Knowledge Ecosystem'

Melanie J. Adams
Technological University Dublin, melanieadamsphd@gmail.com

Paige E. Kane
Technological University Dublin, paige.e.kane@gmail.com

Anne Greene (editor)
Technological University Dublin, anne.greene@tudublin.ie

Martin Lipa
Technological University Dublin, d18127069@mytudublin.ie

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'Introducing the Pharmaceutical Knowledge Ecosystem'

Authors
Melanie J. Adams, Pharmaceutical Regulatory Science Team (PRST), Technological University Dublin
Paige E. Kane, PRST, Technological University Dublin
Anne Greene, Director, PRST, Technological University Dublin
Martin J. Lipa, PRST, Technological University Dublin

Abstract
The ecosystem of how the pharmaceutical industry acquires data, transforms these data into tangible knowledge, and derives valuable insights throughout the process, is highly complex. Data, information, knowledge, and the resulting insights, are necessary to support decision-making, manage risk, problem solve, ensure product realisation, enable continual improvement, and enhance operational effectiveness. Building on the fundamental concepts established in the well-known Data Information Knowledge Wisdom (DIKW) hierarchy, this paper reviews the basic concepts involved in the DIKW pathway and begins to relate these concepts to both established capabilities (e.g., PAT), existing requirements (e.g., data integrity), and emerging trends in the industry (e.g., industry 4.0). This paper introduces additional research studies which the Pharmaceutical Regulatory Science Team (PRST) is considering, regarding how one might apply systems thinking concepts to develop a framework which will enable key stakeholders (Industry, Regulatory and Academia) to better relate the many elements of this ecosystem. The paper concludes by identifying preliminary foundational principles which could form the basis of such a framework, coined by the authors as '*The pharmaceutical knowledge ecosystem',* and makes the case for further exploration of this concept.

Introduction
In general, Knowledge Management (KM) is the process of improving business performance by increasing efficiency, building more robust processes, facilitating continual improvement, and creating an engaged knowledge workforce. In the pharmaceutical sector, such knowledge could be pharmacovigilance data, or product and process information. KM is a multidisciplinary and cross functional approach, designed to achieve target metrics and other company objectives. It includes dimensions of people, process, content, and technology (BPOG, 2017).

A long-standing framework in the discipline of information science is the Data, Information, Knowledge, Wisdom (DIKW) hierarchy shown in Figure 1 (Rowley, 2007).

Figure 1 - DIKW Hierarchy

This framework provides a simple visual how data, information, knowledge, and wisdom are related. In context of the DIKW, hierarchy is used to aid the articulation of knowledge. Its development is often credited to Ackoff, as described by Rowley. The following definitions of the terms are useful to consider (Rowley, 2007):

- **Data**: Symbols that represent the properties of objects and events.

- **Information**: Processed data, such that the processing results in increasing the data's usefulness e.g., data with context.

- **Knowledge**: As defined by the Cambridge dictionary (Cambridge University Press, 2011), *'awareness, understanding or information that has been obtained by experience or study, and that is either in a person's mind or possessed by people. However, in the content of an organisation, knowledge can be a combination of context (explicit knowledge), information, as well as tacit knowledge'*

- **Wisdom**: Wisdom is the ability to increase effectiveness. Wisdom adds value, which requires the mental function that we call judgement.

While the DIKW hierarchy is helpful, it is not necessarily pragmatic in application in the current pharmaceutical technology environment. Kane, as part of her PhD research, proposed an alternative to the above DIKW hierarchy, replacing *wisdom* with *insights*, shown below in Figure 2 (Kane, 2018).

Figure 2 - Data-Information-Knowledge-Insights (as adapted by Kane)

Wisdom is widely agreed to be a "uniquely human" characteristic, whereas *insights* take account of current technological advances where data transformation can lead to *insights*. While *insights* may be derived by people with knowledge and experience, they may also be derived from computing or machine learning models that identify trends and correlations previously not possible to see with experience alone.

This paper explores Data, Information, Knowledge, and Insights, and how these required elements in the pharmaceutical development and manufacturing sector can be utilised to develop, continually improve, transfer, monitor and sustain pharmaceutical products.

Thought Models for connecting data to understanding

While it is useful to replace *wisdom* with *insights* in the DIKW hierarchy, on reflection, the successive goal is to achieve *understanding*. Whereas insights could be regarded as discrete, understanding represents a holistic comprehension – a state of mastery for a given domain or topic. This state of mastery could manifest, for example, as a mechanistic understanding of a complex chemical reaction or as an accurate predictive model for the relationship between process parameters and their impact on final product quality attributes. In each case, there is a progression from being naïve to developing understanding (i.e., a state of mastery) based on accumulated data, information, knowledge, and insights as depicted in Figure 3 below (Lipa, 2020).

Figure 3 - Data-Information-Knowledge-Insight & Understanding (as adapted by Lipa)

Having mastered this progression of data to information to knowledge to *insights and understanding* – it presents the opportunity that one will be able to make informed and effective decisions, based on accumulated evidence, as provided by the underlying structure.

Another model that depicts this concept is published in the Pharmaceutical Manufacturing Technology Centre (PMTC), Data Analytics Good Practice Guide (PMTC, 2020) as shown below in Figure 4.
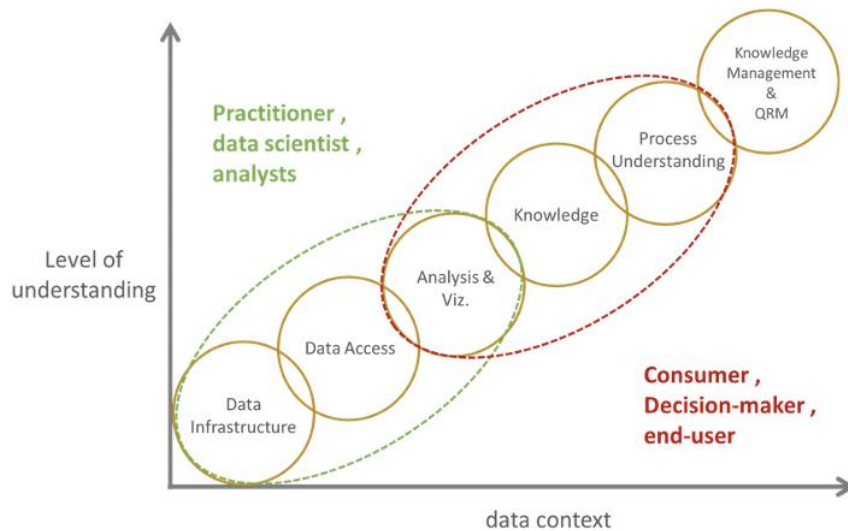
Figure 4 - PMTC model for data to understanding

The PMTC model includes several features:
- The progression from *data infrastructure* through *data access* to *data visualisation* (through the green dotted ovals), and ultimately linking to *process understanding* (through the red dotted ovals), then ultimately applied through *knowledge management* and *QRM*.
- Also, on this diagram the x-axis represents the concept of data context, and that there is a positive correlation between data context and the level of understanding: As you increase context (e.g., through data analysis), you can increase understanding.
- In addition, on this diagram you see the transitioning from _producer_s of data (the practitioners, scientists and analysts) to _users _or _consumers_ (the decision-makers and end-users). The producers on the left of the diagram involved with generating the data and its preliminarily analysis and the consumers more to the right of the diagram, involved with consuming the data to create knowledge and understanding, and ultimately apply to make decisions.

KM and QRM as the foundation of the PQS
In 2008, ICH Q10 described effective Pharmaceutical Quality System (PQS) (ICH, 2008). The three objectives of the PQS defined in ICH Q10 are:

- *Achieve product realisation*
- *Establish and maintain a state of control*
- *Facilitate continual improvement.*

ICH Q10 identified Knowledge Management (KM) and Quality Risk Management (QRM) as the two enablers of an effective Pharmaceutical Quality System as depicted on the ICH Q10 PQS process model shown below in Figure 5. (ICH, 2008)
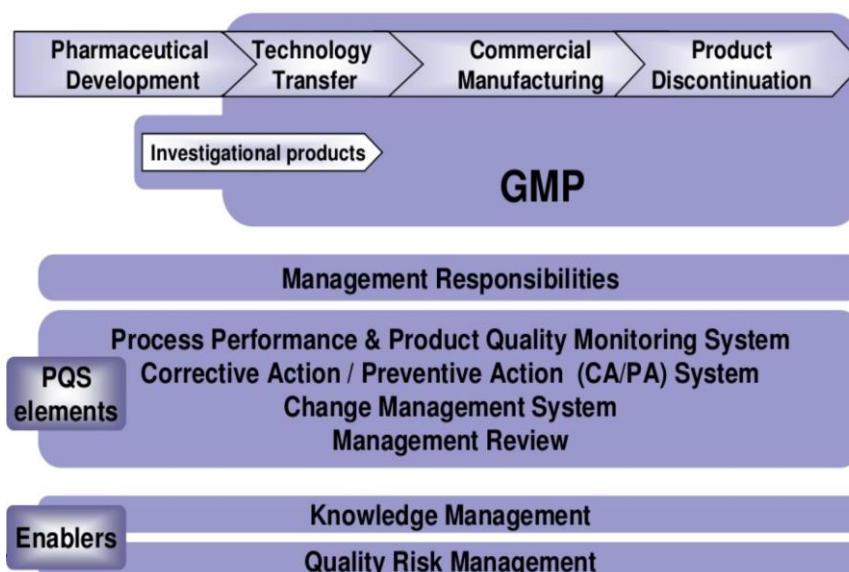
Figure 5 - PQS as defined by ICH Q10

ICH Q9 presented the **_QRM process flow model_** (shown below in Figure 6) outlining **_how_** to manage risk to the patient, based on the best scientific knowledge, thus enabling effective decision making.
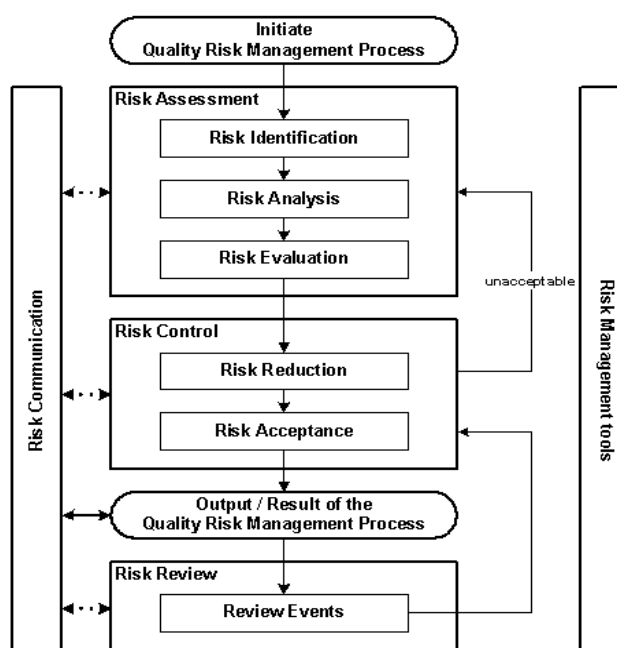

Figure 6 - QRM process model as defined in ICH Q9

While the ICH Q9 process flow model is well known – perhaps iconic – what was lacking was a **_KM process flow model_** to outline **_how_** to ensure best scientific knowledge is available to support PQS realisation and effective decision-making. A contributing factor may be that risk management has been around for more than 70 years as management science, while KM only surfaced in the last 20 years or so, thus the level of guidance on risk management from other industries far exceeds the guidance on knowledge management. Lipa, as part of his PhD

research, proposed a **_KM process flow model_** shown below in Figure 7, to enhance the practical understanding of KM as the complimentary PQS enabler to QRM (Lipa, 2021a).
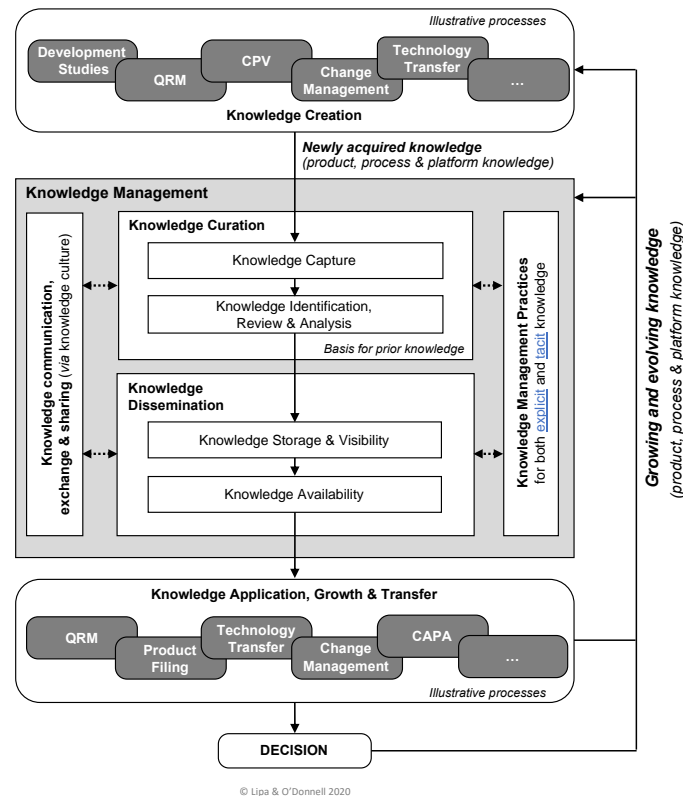

Figure 7 - Knowledge Management Process Model

While this KM process flow diagram is explained in detail in Lipa *et al*. 2020, what is important for this paper is to understand that it incorporates the elements of the definition of KM proposed in ICH Q10[1] and further enhances it by:

- Highlighting the need for **knowledge to flow *and* to subsequently be *applied***
- Featuring the need for **KM practices** to facilitate the management of **both explicit and tacit[2]** knowledge
- Providing channels for **knowledge communication, exchange and sharing,** which is how the organisation interacts with the knowledge base that exists (both explicit and tacit), supported by a **_knowledge culture_**
- Identifying the basis of **_prior knowledge_** by depicting specific steps which must occur for knowledge to be available, with appropriate context, for future application (e.g., knowledge capture, identification, review, and analysis).

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[1] A systematic approach to acquiring, analysing, storing, and disseminating information related to products, manufacturing processes and components

[2] Explicit knowledge is defined as codified knowledge, typically documents, whereas tacit knowledge is knowledge in the heads of people, often referred to as "know how"

Linking Data, Knowledge and Risk

The PMTC Good Practice Guide for Data Analytics indicates that:

> *"Data becomes knowledge through the vehicle of data analytics. Knowledge is a critical milestone that can be integrated and built upon to develop process understanding. Value is realised through such understanding."*

Reflecting on this and returning to the simple hierarchy of data, information, knowledge, insight and understanding, the authors propose that this framework is foundational to many processes and activities common in the pharmaceutical industry. In considering development studies, QRM, continuous process verification (CPV), change management, technology transfer and more – each of these processes and activities generate data and information, which presents the opportunity to create knowledge, insights and understanding by progression "up" the framework. This concept is shown by insertion of the hierarchy in the KM Process flow diagram in Figure 8 below.
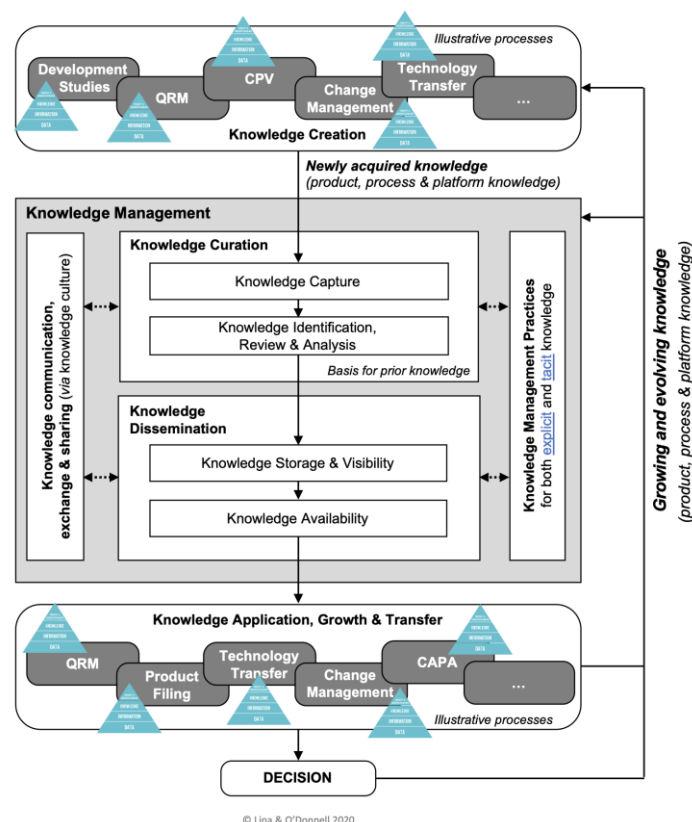

Figure 8 - Data inputs to Knowledge Management Process Model

However, to effectively do this, we need to vertically integrate the hierarchy by having processes and steps in place to be able to progress "upwards" in the hierarchy, from data through information to knowledge, thus ultimately reaching insights and understanding. This does not happen by chance: one needs a strategy to achieve this integration. Work on developing such a strategy is on-going and will be published in subsequent articles by the authors.

Returning to the PQS and ICH Q10 which identified Knowledge Management (KM) and Quality Risk Management (QRM) as the two enablers of an effective Pharmaceutical Quality System, both KM and QRM require data and information and knowledge (both tacit and explicit) as inputs. Between 2008 to 2020, the two enablers were in the main treated separately, until Lipa (Lipa, 2021a) in his PhD research linked them in the *Risk-Knowledge Infinity* (*RKI*) *Cycle*. The *RKI Cycle* highlighted the key activities of the interaction between QRM and KM, as shown in Figure 9 below. (Lipa et al., 2020)
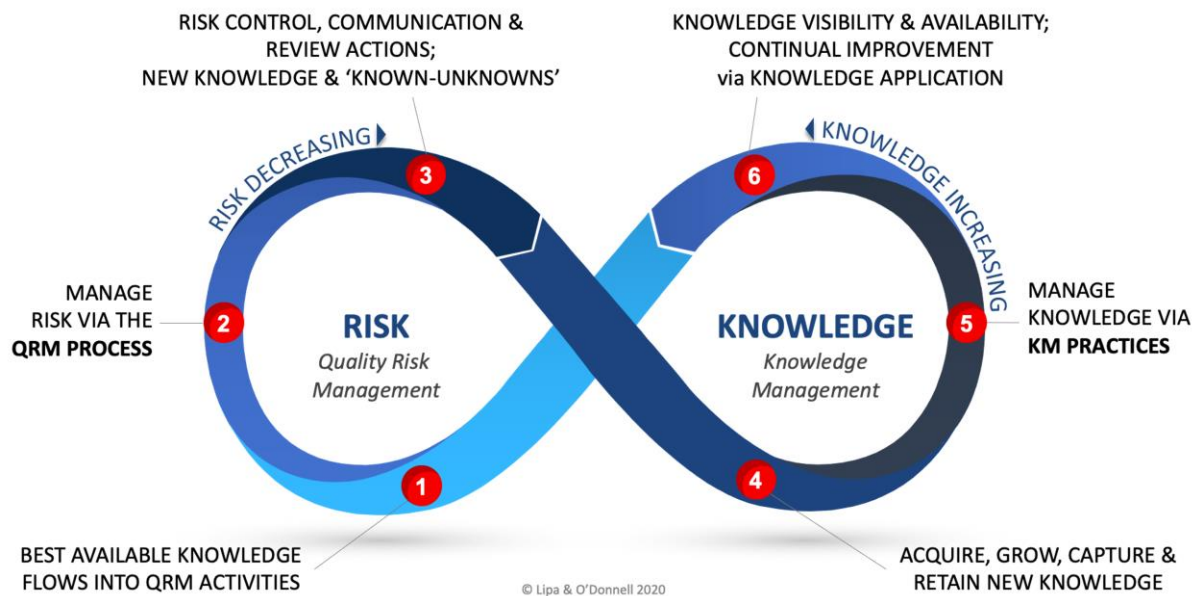

Figure 9 - Risk-Knowledge Infinity Cycle as applied to ICH Q10

An important underlying principle is that risk and knowledge are inversely proportional, that is, increased knowledge leads to decreased uncertainty and therefore decreased risk (ISPE, 2021). Given this realisation, the *RKI Cycle* proposed a continuous pathway for knowledge (both tacit and explicit) to inform risk (nodes 6 and 1). Furthermore, knowledge is recognised as an output from QRM, and can be managed through effective KM (nodes 3 and 4). Both QRM (node 2) and KM (node 5) are enabled via their respective processes where suitable methods and tools are utilised to decrease risk by using increasing knowledge as it emerges.

The key features of the RKI cycle are that:

- **Knowledge is both an input to and an output** of risk management
- **Knowledge has an inverse relationship with risk**: the more knowledge one has, the less uncertainty and therefore, the less risk
- The **Concept of flow**: knowledge flows to inform risk, and risk informs new knowledge (and gaps in knowledge)
- The cycle is **continuous & perpetual**.

All the interrelated concepts in play as discussed in this paper are depicted in the word cloud below (Figure 10):

Figure 10 - Interrelated concepts presented in this paper

There are various disciplines involved which are largely disconnected in practice currently, therefore, it is useful to consider them through the lens of Systems Thinking[3], and see the opportunity for them to work together for the benefit of the patient. Indeed, one can envision the relationship between knowledge and risk as an ecosystem informing each other. (Senge et al., 1999; The MITRE Corporation, 2010)

For example, it is clear that over time in the pharmaceutical life cycle, the aim is to grow knowledge and to minimise risk, thus, considering specifically node 4 on the RKI cycle, (*acquire, grow, capture and retain new knowledge*), one could envisage the DIK(IU)[4] hierarchy integrated here as shown below in Figure 11 (Lipa, 2021b).
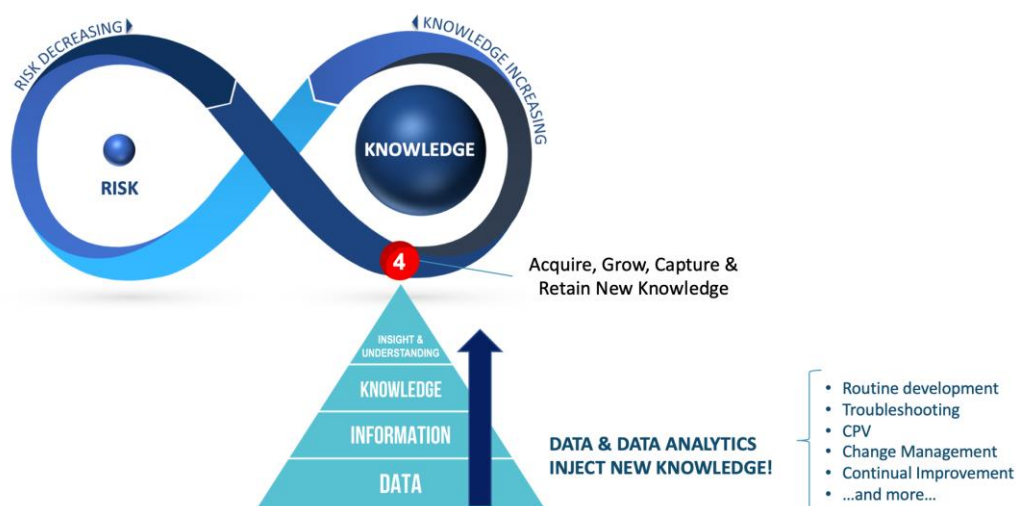

Figure 11 - DIK(IU) as a means to acquire, grow, capture and retain new knowledge

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[3] https://www.mitre.org/publications/systems-engineering-guide/enterprise-engineering/comprehensive-viewpoint/systems-thinking

[4] Data, information, knowledge, insights/understanding

Then returning to ICH Q10 and the PQS, this leads the two enablers of QRM and KM not just be united with each other, but more holistically – as a system – with data, information, knowledge, insights and optimally understanding – in a re-envisioned model of the PQS as shown Figure 12 (Lipa, 2021b).
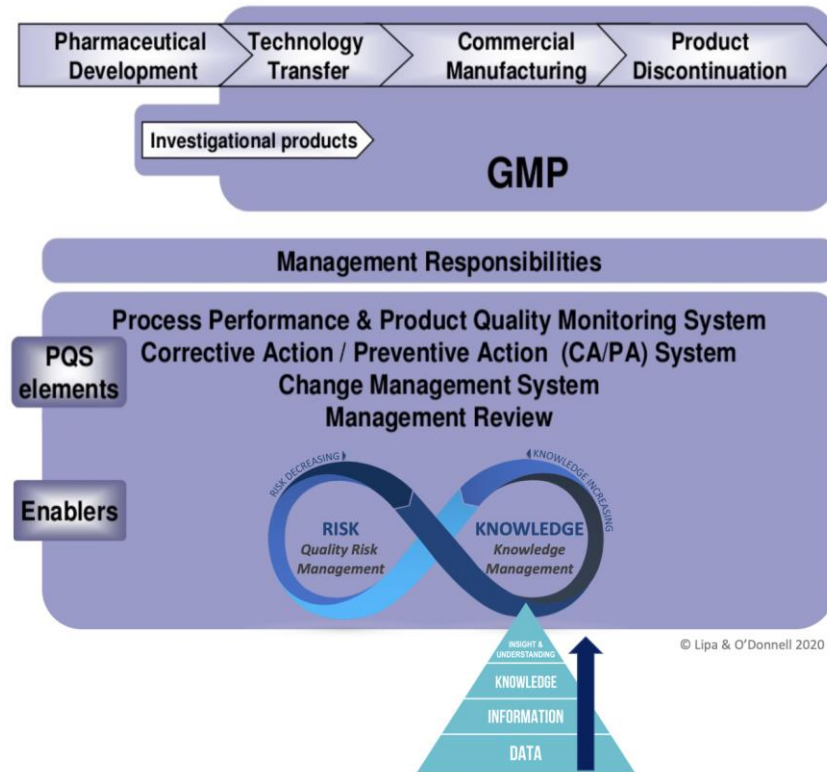

Figure 12 - DIK(IU) as a means to grow knowledge, inform risk and improve PQS

The Pharmaceutical Knowledge Ecosystem

In 2019 a further ICH guidance was published, ICH Q12, Technical and regulatory considerations for pharmaceutical product lifecycle management (ICH, 2019). In it the following was observed:

> *"An effective PQS as described in ICH Q10 and in compliance with regional GMP requirements where the application is filled, is necessary across the entire supply chain and product lifecycle to support use of the tools described in this guideline. It includes appropriate change management, enabled **by knowledge management**, and management review."* (ICH, 2019)

As discussed, researchers believe that **Data Management** and **Knowledge Management** are adjacencies – and part of the ecosystem. Today they are largely looked at independently – but should be examined as part of a systems approach so they are co-optimized. When this occurs the ability to capture, store and provide visibility of product knowledge is critical to enable effective development and manufacture of medicinal product. This ability to capture, store and provide visibility of product knowledge referred to as the 'Pharmaceutical

Knowledge Ecosystem', by the authors, is essential to support continual improvement and post approval change management across the pharmaceutical product lifecycle.

Closing thoughts on transforming data into knowledge and insights

Before COVID 19 there was a measured rise of a geographically dispersed and increasingly mobile workforce which created new barriers to collaboration. Today's transformation into remote ways of working has led to traditional ways of collaborating, such as working with colleagues that sit nearby, no longer reflecting the day-to-day experiences of today's knowledge workers. This, along with the availability of increasingly complex and increasing volumes of data means organisations need to improve their capability to manage data, transition it into valuable information and knowledge that can be readily applied.

Today's pharmaceutical operations are informed by an interconnected network of process control systems, laboratory information systems, data and document management systems, and enterprise management systems. These networks are processing, acting upon, and highlighting information in a dynamic, immediate, and continuous manner. Scanning these ecosystems for important signals, escalations, anomalies, and inconsistencies demands new approaches and the application of new insights.

System and network design creates new layers of control and communication, requiring a System of Systems (SoS) approach to assuring that the correct data flows and that data analytics inform the appropriate and desired insights. The DIKW hierarchy and the RKI cycle are not, in realty, pedestrian pathways. Rather they are superhighways of information that must be rapidly interpreted into knowledge. Detecting trends or patterns, emergences, inter-relationships and new insights (which are essential tools of systems thinking) and 'seeing the big picture', all require access to the relevant information. KM can assure that the right information flows to the right decision-makers, which is critical to the maintenance of system, to process understanding, and to critical systems thinking (Mulholland & Greene, 2020).

Disclaimer
The views expressed in this article are those of the authors and not necessarily those of MSD.

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