

Knowledge Management in the Pharmaceutical Industry

ICH Q10 PQS Enabler

Explicit and Tacit
Knowledge

Knowledge as an Asset

Product and Process
Knowledge

Share Know-how

Knowledge Worker
Connectivity

Improve QRM

Knowledge Transfer

Operational
Effectiveness

Business Continuity

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GOOD PRACTICE GUIDE:

Knowledge Management in the Pharmaceutical Industry

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Preface

Embracing the ICH Q10 objectives, *achieve product realization, establish and maintain a state of control, and facilitate continual improvement*, can be achieved using the dual enablers, Knowledge Management (KM) and Quality Risk Management (QRM). The pharmaceutical industry has worked hard to adopt QRM throughout their systems and processes. However, companies have been slow in implementing KM, thus missing the Quality and business advantages KM methods and tools have to offer.

This *ISPE Good Practice Guide: Knowledge Management in the Pharmaceutical Industry* provides insights to increase the awareness of what KM is and why it is a critical enabler to an effective Pharmaceutical Quality System (PQS). This Guide also offers a range of practical KM strategies, methods, and tools for personnel to incorporate into their day-to-day activities, increasing the impact and sustainability of KM. The Guide also provides practical approaches to help advance the KM maturity within existing programs.

Using KM alongside a strong QRM program enables organizations to implement ICH Q10 throughout the product lifecycle, providing the opportunity to enhance the effectiveness of their PQS.

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1 Introduction

The development and manufacture of biopharmaceutical products is a highly complex scientific endeavor, and individuals and organizations have always managed knowledge in various ways and to varying degrees of effectiveness. Anecdotally, there are arguably familiar challenges associated with managing knowledge such as:

- Poor filing systems
- Multiple competing databases
- Different Information Technology (IT) systems across different departments and across the product lifecycle
- Challenges in finding Subject Matter Experts (SMEs)
- Difficulty in understanding why certain decisions were made
- Repeated issues and mistakes (not learning lessons)
- Difficulty in finding historical product knowledge
- Incomplete knowledge transfer

Further, the wide availability of personal computerized systems and various electronic databases has made findability of knowledge increasingly complex. As the pace of data accumulation and the associated knowledge generation continues to accelerate, the need to manage knowledge systematically has become increasingly apparent, important, and expected.

1.1 Background

In the pharmaceutical industry, consistency of product quality (composition and performance) within and between lots is critically important for the patient as the ultimate user, and by extension, for all those engaged in its provision. There is now a global general acceptance that the control of product quality must commence during product development and continue up to, and in certain respects beyond, the time of product discontinuation from the market. The Quality Guideline Series from ICH [1] describe foundational principles for the achievement of process understanding and quality throughout the product lifecycle. This is based on the belief that quality cannot be tested into products but rather should be built in by design and demonstrated by the results and conclusions of the development studies undertaken. With new countries joining ICH, the guidelines are approaching a de facto standard, although there remain differences in levels of adoption and regional interpretations.

Within the ICH Quality Guideline Series, the topic of applying prior knowledge, and more broadly Knowledge Management (KM), emerged starting with ICH Q8 [2] Pharmaceutical Development. This has been reinforced in subsequent guidelines. Recommended for adoption in November 2005, ICH Q8 introduced a number of new key concepts including Quality by Design (QbD), Design Space, Quality Target Product Profile (QTPP), and Critical Quality Attributes (CQAs). These concepts are discussed in greater detail in Section 10.1.1.

It is, however, noteworthy that ICH Q8 [2] provides the first reference to the concept of KM in the field of pharmaceutical quality. In ICH Q8, KM is a tool to be used along with Quality Risk Management (QRM) for a more systematic QbD approach to development throughout the lifecycle of the product.

ICH Q9 [3] (also recommended for adoption in November 2005) describes in detail the principles and practices of QRM. While ICH Q9 makes no explicit reference to KM, it makes multiple references to the *knowledge* available for making risk-based decisions, for example:

“The evaluation of the risk to quality should be based on scientific knowledge and ultimately link to the protection of the patient.”

Following ICH Q9, ICH Q10 [4] was adopted in 2008 and specifically identified KM as one of the two enablers of a PQS, stating:

“Use of knowledge management [italics in original] and quality risk management will enable a company to implement ICH Q10 effectively and successfully.”

Furthermore, ICH Q10 [4] connects the successful implementation of an effective PQS, enabled by KM and QRM, to the interest of public health and establishes the connection to innovation and continual improvement as follows:

“ICH Q10 demonstrates industry and regulatory authorities’ support of an effective pharmaceutical quality system to enhance the quality and availability of medicines around the world in the interest of public health. Implementation of ICH Q10 throughout the product lifecycle should facilitate innovation and continual improvement and strengthen the link between pharmaceutical development and manufacturing activities.”

The realization of this desired state has been central to ISPE’s efforts to advancing the state of pharmaceutical quality within the industry [5], and this Guide supports those efforts by demonstrating the value of systematically managing organizational knowledge as part of that journey.

The incorporation of KM in pharmaceutical organizations has been slower than in other industries [6, 7]. Beyond the specific arena of pharmaceutical quality, KM is becoming more widely recognized as a stand-alone discipline that focuses on ways organizations create, manage, and use knowledge. This is not surprising in the current era where business activities are becoming increasingly dominated by **knowledge workers** and the widespread utilization of complex digital systems for storing the ever-growing knowledge generated in different types of enterprises. ISO 30401 Knowledge management systems — Requirements [8] was published in 2018 with the stated objective to:

“...support organizations to develop a management system that effectively promotes and enables value-creation through knowledge.”

Thus, KM can be considered as an important enabler of an effective modern management system and the content of ISO 30401 is worthy of consideration. Appendix 15 provides further comparison between this Guide and ISO 30401, including a map of the contents of each document.

1.2 Purpose

This Guide seeks to embrace and advance KM for the pharmaceutical industry.

The practical principles and methods and tools provided in this Guide are intended to help organizations improve their capabilities in managing knowledge and using that knowledge to support an effective PQS resulting in improved organizational performance, among other benefits. One such practical approach is the Knowledge Management Maturity Assessment Tool (see Appendix 3), which can be used to measure an organization’s KM maturity and identify opportunities for improvement.

The goals of this Guide are to:

- Define and explore the meaning and importance of KM in the context of the pharmaceutical industry

- Discuss the importance of KM to the PQS
- Describe KM principles, key concepts, the general KM process, and foundational KM methods and tools
- Discuss forward looking opportunities for KM
- Share practical pharmaceutical applications and case studies of KM

This Guide is relevant to organizations across the pharmaceutical industry in their pursuit for effective and practical solutions to common KM issues.

1.3 Benefits

It is envisioned that the practices presented in this Guide will result in broad benefits to a variety of stakeholders including patients, organizations involved in the discovery and manufacture of pharmaceutical products, regulatory agencies, and the employees of these organizations as *knowledge workers*. By further socializing and educating on the topic of KM, the understanding and resulting effectiveness of KM methods and tools can be meaningfully improved. The author team of this Guide in turn believes the pharmaceutical industry will be better positioned to realize the important objectives of ICH Q10 [4], ICH Q8 [2], and other regulatory guidances that prescribe the capture and application of knowledge.

1.4 Scope

The scope of this Guide is aligned with the ICH Q10 [4] scope:

“...systems supporting the development and manufacture of pharmaceutical drug substances (i.e., APIs) and drug products, including biotechnology and biological products, throughout the product lifecycle.”

The principles described may also be applied to medical devices, over-the-counter products, personal care, and cosmetics. In addition, to be maximally effective these principles should be applied throughout the product lifecycle from research and development, technology transfer, commercialization, up to and including product discontinuation.

1.5 Key Features

This Guide provides a variety of materials to advance the understanding of KM and its application in pursuit of improved KM effectiveness and maturity to enable the aforementioned goals. This Guide features:

- A description of the importance and associated benefits of effective KM
- Definitions and principles behind KM and supporting concepts
- Frameworks to enhance the understanding and application of KM
- A section on *Getting Started* to foster the first steps for a KM effort
- A maturity model to assess the current-state performance and identify opportunities to improve effectiveness
- A variety of methods and tools, and systematic approaches to improve KM effectiveness
- Advice to relate KM to other industry guidance
- Case studies demonstrating the application of KM

1.6 Structure of the Guide

This Guide is organized as follows:

- Chapters 1 and 2 explain the **Why** behind KM
- Chapters 3 and 4 provide basic information on KM to enhance the understanding of **What** KM is
- Chapter 5 discusses KM Application across the product lifecycle
- Chapter 6 introduces principles for digitally enabled KM
- The appendices provide resources for the **How** and supplemental information
 - Appendices 1 – 7 discuss KM methods and tools
 - Appendices 8 – 13 present KM case studies
 - Appendix 14 contains example KM templates
 - Appendix 15 is a map of this Guide to ISO 30401 [8]

1.7 Key Concepts and Terms

1.7.1 Knowledge Management

ICH Q10 [4] defines Knowledge Management as:

“Knowledge management is a systematic approach to acquiring, analysing, storing and disseminating information related to products, manufacturing processes and components. Sources of knowledge include, but are not limited to prior knowledge (public domain or internally documented); pharmaceutical development studies; technology transfer activities; process validation studies over the product lifecycle; manufacturing experience; innovation; continual improvement; and change management [italics in original] activities.”

The focus of this ICH Q10 [4] definition is on documented knowledge. A more holistic definition comes from APQC¹ [9]:

“The application of a structured process to help information and knowledge flow to the right people at the right time so they can act more efficiently and effectively to find, understand, share, and use knowledge to create value.”

This definition is commonly used by KM practitioners because it embraces the two main aspects of KM: the needs of the knowledge user and the needs of managing knowledge within an organization.

A useful thought model when considering the role of KM in organizations is that of *knowledge* and *knowledge recognition*. Figure 1.1, depicts whether an organization *possesses the knowledge* (i.e., does the knowledge exist) versus *knowledge recognition* (i.e., are we aware it exists). While this may seem relatively simple at an individual level, it is much more complex at an organizational level across many people, functional areas, products, processes, etc.

¹ APQC (American Productivity & Quality Center) is a not for profit organization recognized as a world leader in KM research and benchmarking [10].

Figure 1.1: Knowledge and Knowledge Recognition

Knowledge Recognition	Known	(1) What We Know We Know <i>known-knowns</i>	(2) What We Know We Don't Know <i>known-unknowns</i>
		Concepts we are aware of and understand <i>Facts</i>	Concepts we are aware of but don't understand <i>Questions</i>
	Unknown	(3) What We Don't Know We Know <i>unknown-knowns</i>	(4) What We Don't Know We Don't Know <i>unknown-unknowns</i>
		Concepts we understand but are not aware of <i>Unaware</i>	Concepts we are neither aware of nor understand <i>Exploration</i>
		Known	Unknown
		Knowledge	

- Arguably the most central role of KM begins with ensuring effective management of Box 1 in Figure 1.1, described as **Facts** (inclusive of tacit knowledge). We know what we know and can find this knowledge when and where needed. An example of this is applying prior knowledge at the start of development of a new product.
- Box 2 in Figure 1.1, described as **Questions**, represents instances where we are aware we do not have sufficient knowledge. Experimentation is directed to answer such questions and grow the body of knowledge. Risk management also plays a role in how risks associated with unknowns are managed. As these questions are answered, this knowledge should be managed effectively henceforth, including what did not work or other unanticipated learnings (in Box 1).
- Box 3 in Figure 1.1, described as **Unaware**, represents untapped potential and knowledge loss within an organization, such as when expertise exists in an organization to solve a problem, but the connection is never made, or knowledge is lost due to the departure of key personnel or during transfers between different teams in a product's lifecycle. Tacit KM techniques such as lessons learned, communities of practice, tacit knowledge retention and transfer processes can play a key role in creating dialog that can lead to new insights. This knowledge should be codified and shared as appropriate (and therefore in Box 1). An effective systematic KM program within an organization's PQS is a key administrative tool to help minimize such knowledge loss and maximize knowledge awareness.
- Box 4 in Figure 1.1, described as **Exploration**, represents the opportunity for ongoing learning and knowledge acquisition whether intentional (experimentation or other directed recognition efforts) or unintentional (investigations resulting from process deviations). This new knowledge may lead to new *Questions* and new *Facts* and should be managed appropriately.

1.7.2 Types of Knowledge



Explicit Knowledge: A declarative type of knowledge that can be readily articulated (in words or images), coded, stored, and accessed.



Tacit Knowledge: A context-specific type of knowledge, acquired through personal experience or internalization that resides within people's minds rather than any physical media or information system. Often referred to as *know-how*.

An important theme throughout this Guide is the emphasis on tacit knowledge. Given the regulated and document-centric nature of the pharmaceutical industry, the importance and impact of tacit knowledge is arguably underappreciated. This Guide aims to highlight this, and where appropriate, provide KM methods and tools to better recognize, capture, transfer, and apply tacit knowledge.

Explicit and tacit knowledge are explored further in Section 3.2.

1.7.3 Additional Terms

Principles and additional key concepts for KM are discussed in Chapter 3.

Knowledge Management Methods and Tools: Structured and standardized solutions to facilitate effective knowledge management. Also known as KM *approaches*, *capabilities*, or *practices*.

Knowledge Workers: Workers who *think for a living* and use expertise, education, and experience to solve work problems through the creation, distribution, or application of knowledge. The pharmaceutical industry is considered a knowledge industry and as such, its workforce is comprised of knowledge workers.

Lessons Learned: The concept of **Lessons Learned** is often referred to as **After Action Review**. This Guide treats them as synonymous and will refer to the activity as Lessons Learned.

2 Knowledge Management: A Critical Enabler to the Pharmaceutical Quality System and Operational Effectiveness

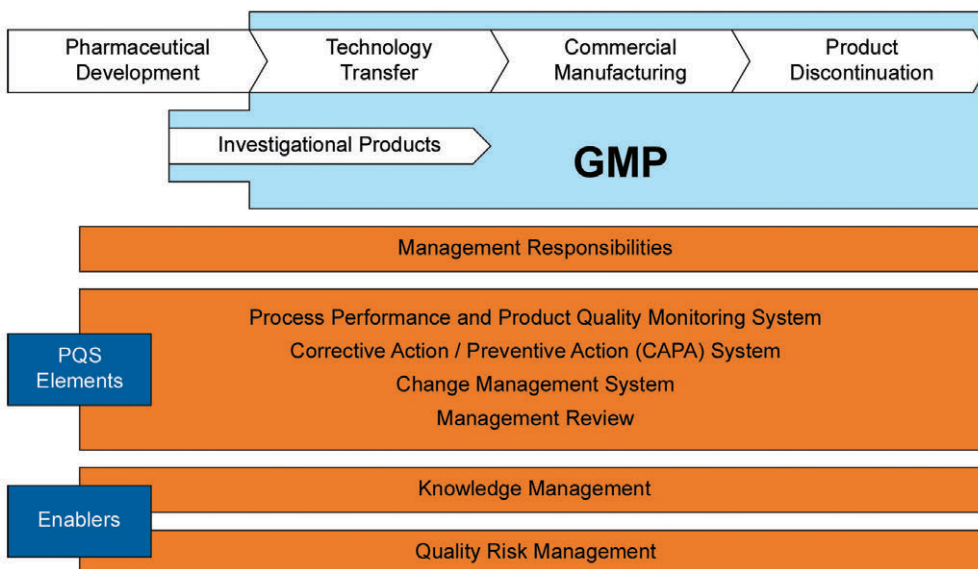
Effective KM is an expectation established in a number of regulatory guidance documents, most notably the ICH series of Quality Guidelines [1]. This chapter explores the importance of KM positioned as an enabler of an effective PQS in ICH Q10 [4]. Further, while the quality system requirements for managing knowledge effectively are of primary concern, there are substantial and compelling benefits of effective KM beyond the quality system, including improved business performance² (see Section 2.2) and employee engagement (discussed in Section 3.5).

2.1 Knowledge Management and the Pharmaceutical Quality System

2.1.1 Introduction

Figure 2.1, adapted from ICH Q10 [4], shows the PQS elements with the key enablers KM and QRM employed throughout the product lifecycle.

Figure 2.1: Diagram of the ICH Q10 Pharmaceutical Quality System Model



ICH Q10 [4] states:

“...knowledge management and quality risk management will enable a company to implement ICH Q10 effectively and successfully,” [thereby facilitating the achievement of the ICH Q10 objectives] “by providing the means for science and risk based decisions related to product quality.”

In this context, appropriately managing knowledge is important. ICH Q10 continues with:

“Product and process knowledge should be managed from development through the commercial life of the product up to and including product discontinuation.”

² For example, increased efficiency, more robust processes, continual improvement.

As shown in Chapter 1, ICH Q10 [4] defines Knowledge Management as:

“...a systematic approach to acquiring, analysing, storing and disseminating information related to products, manufacturing processes and components.”

A wide variety of sources of knowledge are outlined in ICH Q10 (see Section 1.7.1 of this ISPE Guide) that cover the lifecycle of a product and beyond. ICH Q11 [11], adopted in May 2012, includes references to other key sources of knowledge such as those associated with process development activities. It draws particular attention to the importance of considering knowledge transfer during technology transfer activities to internal network sites or externally to contract manufacturing partners. ICH Q11 states:

“The knowledge and process understanding should be shared as needed to perform the manufacturing process and implement the control strategy across sites involved in manufacturing the drug substance.”

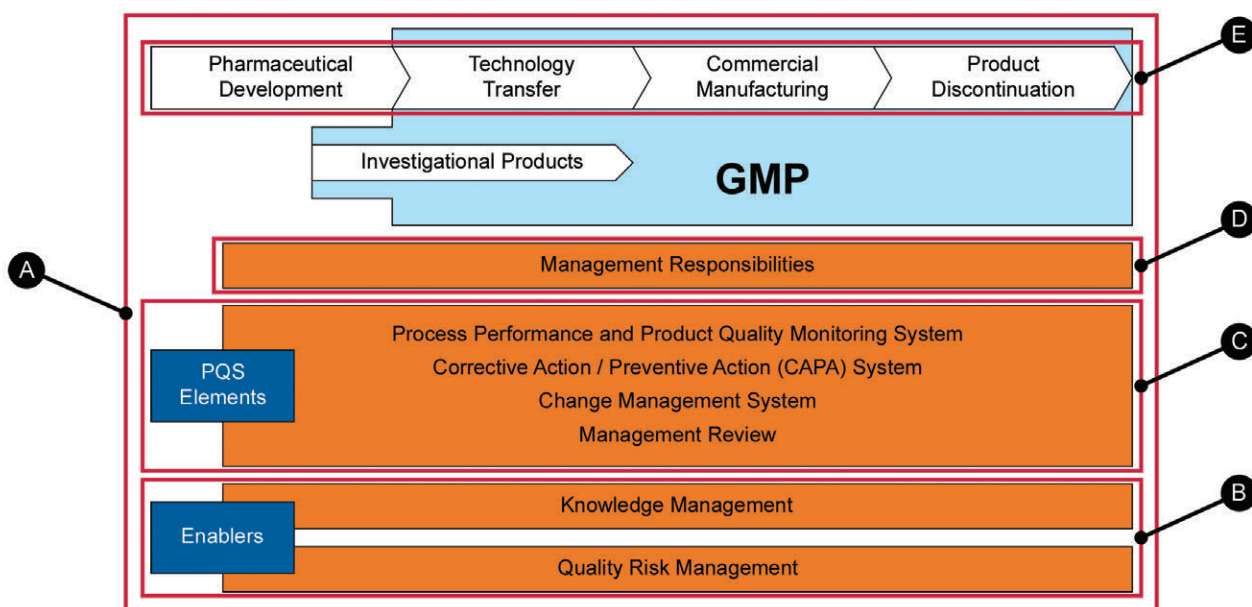
Most recently, ICH Q12 [12], adopted in November 2019, describes the connection between KM and the change management process, stating that:

“An effective change management system includes active knowledge management, in which information from multiple sources is integrated to identify stimuli for changes needed to improve product and/or process robustness.”

ICH Quality Implementation Working Group on Q8, Q9, and Q10 Questions & Answers [13] and ICH Q12 both note that the need to actively manage knowledge does not confer any additional regulatory requirement to implement a formal KM system [12].

A key aspect of this chapter is how to operationalize the management of knowledge central to the overall PQS. An understanding of some of the key concepts of KM, and the systematic processes by which knowledge is managed, is therefore essential for all who work in any capacity across the pharmaceutical product lifecycle. Figure 2.2 provides a visual mapping of the relationship of KM to each component of the PQS as presented in the next several sections of this Guide.

Figure 2.2: Diagram of the ICH Q10 Pharmaceutical Quality System Model (adapted from ICH Q10 [4])



- Ⓐ Section 2.1.2 focuses on how KM enables the overall objectives of an effective PQS
- Ⓑ Section 2.1.3 discusses how KM can be united with QRM to enable more effective, risk-based decision-making in support of a more effective PQS
- Ⓒ Section 2.1.4 highlights how KM enables each of the four major PQS elements
- Ⓓ Section 2.1.5 outlines basic management responsibilities for an effective KM program
- Ⓔ Section 2.1.6 introduces opportunities for KM across the product lifecycle

2.1.2 Knowledge Management in Support of ICH Q10 Objectives

The three objectives of ICH Q10 [4]:

- Achieve product realization
- Establish and maintain a state of control
- Facilitate continual improvement

can be better achieved using KM and QRM. Additionally, the ICH Quality Implementation Working Group on Q8, Q9 and Q10 Questions & Answers [13] clarifies that:

“Knowledge Management is not a new concept. It is always important regardless of the development approach. Q10 highlights knowledge management because it is expected that more complex information generated by appropriate approaches (e.g., QbD, PAT, real-time data generation and control monitoring systems) will need to be better captured, managed and shared during product life-cycle.

“In conjunction with Quality Risk Management, Knowledge Management can facilitate the use of concepts such as prior knowledge (including from other similar products), development of design space, control strategy, technology transfer, and continual improvement across the product life cycle.”

How an organization might use KM to enable these three objectives is the subject of Appendix 4, and specific KM approaches that can help facilitate the three objectives (including the use of prior knowledge, technology transfer, and continual improvement) can be found in Appendix 6. In addition, a KM program should be in place to support and enable the capture and reuse of knowledge to enable the objectives of ICH Q10 [4] and the principles included in ICH Quality Guidelines [1].

2.1.3 Knowledge Management and Quality Risk Management as the Dual Enablers of an Effective Pharmaceutical Quality System

Effectively operating KM requires thoughtful integration with QRM [4]. These dual enablers need to function together so that the evolving knowledge base is readily available as a key input into the quality risk-based decisions that drive actions to maintain a state of control and facilitate continual improvement. Risk and knowledge (when applied) are inversely proportional. That is, increased knowledge leads to decreased uncertainty and therefore decreased risk. This concept is illustrated in Figure 2.3. Over time, as knowledge increases, risk decreases [14].

Figure 2.3: The Risk-Knowledge Infinity Cycle: Decreasing Risk through Increasing Knowledge [14]
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The expectation for applying scientific knowledge, for using experienced people, and for ensuring appropriate expertise is used for risk assessments is repeatedly emphasized in regulatory guidance documents. However, this knowledge must be recognized, available, and applied to be of benefit. Further, the output of the QRM process is in itself knowledge, and how this is captured, assessed, and positioned as prior knowledge is also an important consideration.

While the practice of QRM is systematic in many pharmaceutical organizations, the practice of KM still lags, and QRM and KM are not well integrated [6, 7]. Many companies conduct QRM and KM as discrete disciplines with discrete tools, approaches, and functional responsibilities. To be fully effective, the PQS needs to be configured around the integration of KM and QRM, harnessing the expertise and processes of the respective disciplines.

One pragmatic way this can be achieved in part is by instituting regular cross-functional product-level review meetings as a central part of the PQS. The outcome of such meetings should include a documentary record of the continually evolving knowledge about the product and its associated processes. This evolving knowledge should be in a format that supports effective QRM, change management, and Corrective Action and Preventive Action (CAPA), enabling the ongoing continual improvement of products, processes, and the PQS itself. This topic is further explored in Appendix 5.

The world of pharmaceutical development and manufacture is growing more complex as it moves beyond traditional manufacturing processes. Considering emerging trends such as advanced therapy medicinal products (e.g., cell and gene therapies), the use of big data and Artificial Intelligence (AI), and other trends to follow, an integrated knowledge and quality risk-centered approach will become an essential element in effectively managing product quality on an ongoing basis. An integrated approach will also support the acceleration of product launch timelines as part of routine business, getting breakthrough therapies to patients faster, or in response to a pandemic by enabling more streamlined decisions grounded in strong science, recognition of control strategy risks, and rapid regulatory submissions.

2.1.4 Knowledge Management as an Enabler to the Four Major PQS Elements

KM, or systematically managing knowledge, is an enabler to the four PQS elements described in ICH Q10 [4]:

- *“Process performance and product quality monitoring system;*
- *Corrective action/preventive action [italics in original] (CAPA) system;*
- *Change management system;*
- *Management review of process performance and product quality.”*

Each of these PQS elements requires inputs (data, information, and/or knowledge) and a systematic approach to use these inputs to make decisions related to the process and the product. There are many mechanisms to collect data and information necessary to make decisions. In addition, KM methods and tools (see Appendix 6) can help make such information visible and, in conjunction with QRM tools and processes, capture tacit knowledge that may also facilitate the four PQS elements.

2.1.5 Management Responsibility for Knowledge Management

Management has a responsibility to understand the requirements for effective KM and its role in the PQS. At the most basic level, this responsibility ensures the existence and relevance of KM efforts as a PQS enabler. These responsibilities are presented elsewhere in this Guide, including the need for KM-dedicated roles and ensuring appropriate sponsorship and governance for a KM program. (See Appendix 7.)

2.1.6 Knowledge Management across the Pharmaceutical Product Lifecycle

To effectively manage pharmaceutical product knowledge, it is important to adopt an *End-to-End* (E2E) view of product technical knowledge, that is, across the product lifecycle. This requires evolving the traditional product lifecycle view to a product knowledge lifecycle, which enables integration of product lifecycle and platform knowledge.

Addressing this concept includes an overview of the respective KM tools, KM processes, and KM roles that can be applied to best utilize knowledge across the pharmaceutical product lifecycle. Many organizations have a collection of legacy processes and systems (IT and business) operating across this lifecycle and phases may span multiple internal and external organizations, geographies, and business processes. It can therefore be challenging to holistically identify sources of knowledge and to surface knowledge across the lifecycle. This topic is explored in more detail in Chapter 5.

2.2 Knowledge Management and Operational Effectiveness

While the previous sections in this chapter have highlighted the expectation to manage knowledge as part of an effective PQS, effectively managing knowledge leads to a number of additional benefits with broad business impact. This section briefly introduces some of these benefits, including operational excellence and business continuity.

A key underlying concept is that the pharmaceutical industry is a *knowledge industry*, as characterized by its extensive use of technology and a highly educated and highly skilled workforce. Companies compete on their ability to leverage what they know to invent, develop, and manufacture highly complex products. Further, the employees of the industry are for most part *knowledge workers*, expected to use knowledge in their day-to-day activities rather than complete purely repetitive and transactional tasks.

2.2.1 Knowledge Management Leading to Improved Business Performance

As with the pursuit of operational excellence, KM can improve the efficiency and effectiveness of business operations.

Take for example the pervasive waste and inefficiency in the ability of knowledge workers to find the knowledge they seek to do their jobs. It has been reported that Fortune 500 companies lose roughly \$31.5 billion (26.07 €) a year by failing to share knowledge [15, 16]. An IDC study [17] found:

- “Knowledge workers spend from 15% to 35% of their time searching for information.
- Searchers are successful in finding what they seek 50% of the time or less, according to both Web search engines and our own surveys.”
- “Only 21% of [survey] respondents said they found the information they needed 85% to 100% of the time.

- *40% of corporate users reported that they can not find the information they need to do their jobs on their intranets.”*

These striking figures present a tremendous efficiency opportunity for those who can effectively remove the waste and inefficiency (and likely frustration) in finding knowledge, for which KM can play a central role. When employees have the knowledge they seek when and where they need it, informed decisions can be made in less time.

Another example of the effectiveness of KM is in the power of reflection as a means for efficiency continual improvement. Teams who pause and reflect on how they did their work and build these improvements into future work perform on average 20% better than those who do not [18]. This is the focus of KM approaches such as lessons learned (see Appendix 6), which aim to operationalize such opportunities.

2.2.2 **Transfer and Retention of Knowledge Essential for Business Continuity and Complexity**

A common issue is the need to retain knowledge essential for business continuity, to navigate highly complex products, and/or ensure the sustainability of product quality. Proactive measures are essential to avoid knowledge loss and the ensuing consequences.

In today's pharmaceutical industry environment, for example, increasing numbers of novel therapies are developed in small start-up companies subsequently acquired by larger companies. This is often the point of greatest danger for knowledge loss.

During the start-up period, a typical small company may operate in a very lean manner, with relatively rudimentary Quality and KM systems in place. Once acquired, key founding personnel may depart the new entity and subsequent efforts to retain or recreate the *why* and *what* of the foundational product and process knowledge can become extremely difficult.

The strategic focus is often on the acquisition of the products and not on the knowledge about the products. In the absence of such knowledge, future understanding about the impact of changes on process or product quality can become problematic. The challenge may well be as simple as the start-up employing only fit for purpose processes with no intention, or desire, to consider the long-term commercial viability of the process. Arguably this is especially true for the highly complex therapies emerging in the industry. Research [19] shows that:

“[the] dilemma of knowledge loss [italics in original] is not specific to the biopharmaceutical sector; however, there may be a false sense of security regarding the ability to recreate such knowledge within the sector due to the traditional focus on retention of regulated data, records, and information. However, ‘know-how’ often provides the key necessary to unlock the critical knowledge from within these retained records. Without the ‘know-how’, retained data and information may never progress up the hierarchy to be converted into useful knowledge. Therefore, in the biopharmaceutical sector it is important that knowledge retention strategies should never be mistaken for record retention policies and procedures.” [19]

Another common scenario faced by the industry is the retirement of highly tenured and experienced staff, whom all too often are the singular go to person based on their experience (with product histories, relationships with suppliers, know-how for a specific process, etc.). These employee transitions pose risks to business continuity and can be addressed in a proactive manner.

There are a range of knowledge retention techniques that can be employed via KM tools and processes, including:

- Systematic **Lessons Learned** processes
- Formal reports at milestones that review how key knowledge about the product has evolved, e.g., technology transfer reports or Product Quality Reviews (PQRs)
- Creation of **Communities of Practice**, which review how results are achieved in specific areas

- Content management guidance for knowledge created in functional groups (inclusive of non-GxP technical content and business process content)
- Facilitated knowledge transfer risk assessments and interviews

Although these concepts are straightforward, they have not been widely adopted, as discussed in the 2020 publication "Knowledge Management Implementation: A Survey of the Biopharmaceutical Industry ISPE KM Survey." [6]

3 Knowledge Management Principles and Key Supporting Frameworks

All disciplines have principles and concepts as their foundations. Several of the principles and concepts that form the basis of KM practices include:

- The Data, Information, Knowledge, Wisdom Framework (DIKW)
- Types of Knowledge
- Knowledge Flow
- Four Pillars of KM – People, Process, Technology, and Governance
- Engagement and Enablement of a Knowledge Workforce

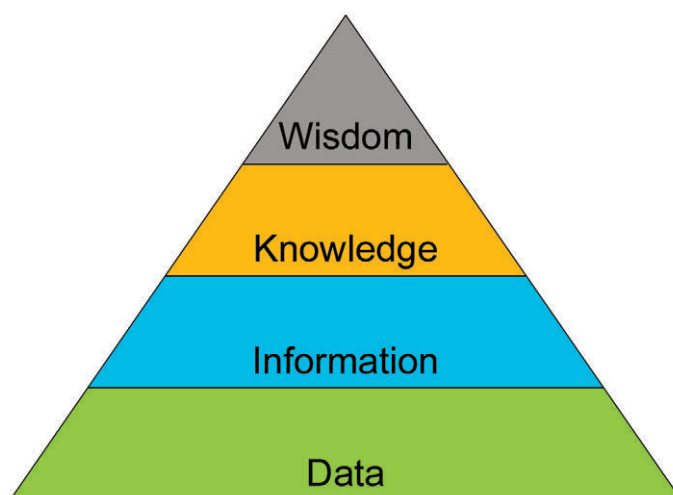
3.1 The Data, Information, Knowledge, Wisdom Framework

A common model used in data science to describe the relationship and hierarchy of data, information, and knowledge is the DIKW Framework [20].

The DIKW hierarchy is considered foundational in many information science curriculums and is commonly represented as a pyramid commencing with the base of data, and progressing up through information, knowledge, to wisdom at the top, as shown in Figure 3.1. While there are variations of this framework in the literature and debate over the exact definitions, the structure presented here highlights these key concepts:

- Data and knowledge are not synonyms
- There is a continuum of events leading from data to true understanding

Figure 3.1: Example DIKW Hierarchy [21]



"In the context of the DIKW hierarchy, the following definitions provide context:

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

- *Information: Information consists of processed data, the processing directed at increasing its usefulness, i.e. data with context*
- *Knowledge: As defined by the Cambridge Dictionary, knowledge can be described as: 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...*
- *Wisdom: Wisdom is the ability to act quickly or practically in any given situation.” [21]*

In addition, knowledge in the context of an organization can be a combination of explicit knowledge (codified knowledge) and tacit knowledge, including an individual's experience and know-how. (Explicit and tacit knowledge are further defined in Section 3.2.) ISO 30401 [8] defines knowledge as:

“Human or organizational asset enabling effective decisions and action in context.”

From an organizational perspective, a useful alternative to the DIKW pyramid replaces wisdom with insights [19] and may be considered more fitting in the current context. Insights may be derived by people with knowledge and experience; however, new technology trends suggest that insights may also be derived by advanced computing or AI models, which identify trends and correlations not previously identified with experience alone. Figure 3.2 illustrates the journey toward insights, showing the relationship between the producers and the consumers of data, information, and knowledge. A strong foundation of good data and accessible information is required to generate knowledge and build insights [21].

Figure 3.2: The Journey to Insights: Relationship between the Producers and Consumers of Data, Information, and Knowledge [21]

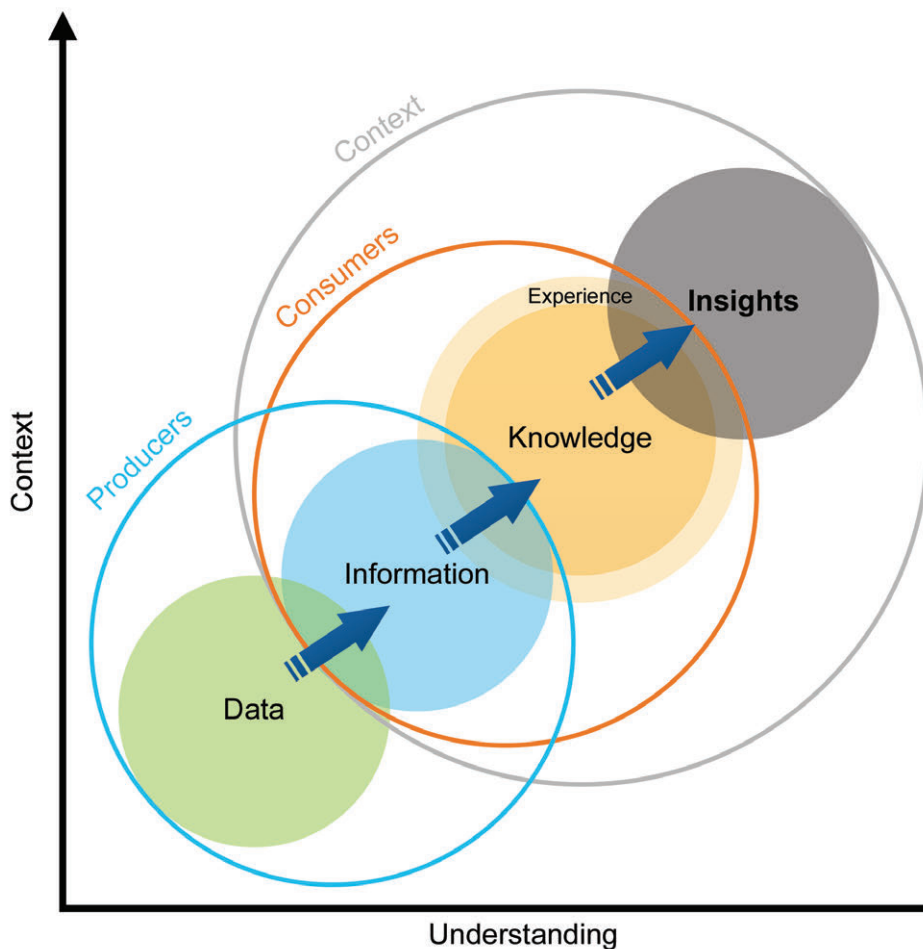


Figure 3.2 shows how data transforms into information by assigning meaning or context to that data. The moment the data is processed, linked, and stored, whether by a machine or a human being (producers), it becomes information. The ability of people to appropriately apply that information translates the information into knowledge. Finally, it is the application and utilization (consumption) of information and knowledge that leads to insight. Context is critical throughout this transformation process from data to information to knowledge toward insight. Chapter 6 discusses future opportunities to harness new technologies in transforming data and information into insights.

3.2 Types of Knowledge

Within the discipline of KM, the terms explicit and tacit knowledge are often used to distinguish between two key categories of knowledge:

Explicit knowledge typically refers to the knowledge that is codified and formally documented within an organization. Some examples are product specifications, Standard Operating Procedures (SOPs), work instructions, analytical methods, batch records, reports, documented presentations, web pages, recordings. Capture of this knowledge is paramount as many of these documents (GMP and non-GMP) form the basis of our technical understanding of pharmaceutical products and processes.

Tacit knowledge refers to the knowledge gained from personal experience, for example, when working in a particular organization. Tacit knowledge is often referred to as *know-how*, that is, knowledge understood or implied without being formally documented. This can happen because it is often very difficult or impossible to articulate and document tacit knowledge. There are additional manifestations of tacit knowledge, including *know-why* and *know-who*, referring to other examples of knowledge often not documented, such as why a certain decision was made, or who to go to for help on a given topic.

Generally, the assumptions and rules observed within a company in determining what should be treated as *tacit* or *explicit* are often not expressly documented but rather are assumptions of individuals based on their experience of what does or does not work well. However, in an organization that adopts a more mature approach to KM, these assumptions and rules regarding capturing, retaining, and sharing both tacit and explicit knowledge are typically stated in a formal KM policy with supporting KM processes and work practices. Applying KM methods and tools such as communities of practice and lessons learned may help convert tacit knowledge to explicit knowledge. (See Appendix 6 to learn more about KM methods and tools.)

3.3 Knowledge Flow

Knowledge flow is a key concept for organizations: knowledge should freely flow across the organization without friction or barriers, available on demand to the person who needs it. Barriers, for example, include lack of access to a repository, inability to find an SME, and no lessons captured from the prior project. The fundamental intent of standard KM tools and methods is to enable knowledge flow across the organization. Knowledge mapping is a standard KM tool used as a diagnostic means to identify barriers to knowledge flow, whether for a business process or in an organization. Further discussion on knowledge mapping is found in Appendix 6.

3.4 The Four Pillars of Knowledge Management – People, Process, Technology, and Governance

KM practitioners are grounded in the concepts of *People, Process, Technology, and Governance*. To ensure sustained effectiveness of a KM effort, each element, or pillar, of *People, Process, Technology, and Governance* must be addressed [22]. These are not unique to KM; rather they are about building robust business capabilities with the necessary roles and behaviors to support their effectiveness.

- **People** – The people of the organization need to understand the importance of treating their knowledge as an asset for themselves and the organization: a culture that values knowledge. This requires the mindsets, behaviors, and skills to utilize KM methods and tools, and to proactively seek, share, and grow organizational knowledge (see Section 3.6). These mindsets and behaviors cannot be distinct from the broader organizational culture but rather woven into it.
- **Process** – Standard KM methods and tools (e.g., lessons learned, communities of practice) exist and should be leveraged to help capture and share knowledge across the organization. These are discussed in Appendix 6.
- **Technology** – Suitable technology solutions should be available to ensure that organizations can capture and share knowledge across the organization. Some examples of technology solutions are:
 - Community of Practice (CoP) enabled by a technology platform
 - Expertise location³ enabled by an IT system
 - Technology solutions leveraged for other KM processes, such as lessons learned, content management, etc.
- **Governance** – Sustained KM effectiveness greatly benefits from a sponsorship and governance structure. Active governance ensures support for and alignment of the KM approach/program identification, implementation, and realization of the KM process and benefits. Active sponsorship makes certain that the organization recognizes the importance of KM and the associated expectations.

Another important element is **Content**. KM focuses on information and knowledge. Content is explicit knowledge typically manifested as documents, web content, etc. Establishing guidance or standard practices for management of content is key to ensuring that explicit knowledge (GxP and non-GxP) is easily located and accessible to those that need it.

3.5 Engagement and Enablement of a Knowledge Workforce

As discussed in Section 2.2, the pharmaceutical industry is a knowledge industry employing knowledge workers. There are a variety of less tangible but very important benefits to be achieved when an organization can enable its knowledge workforce to *do their best* work. There are familiar themes to which KM can uniquely contribute, such as:

- Creating a learning organization, e.g., through lessons learned and communities of practice
- Improving employee engagement, e.g., through communities of practice and stewardship roles
- Reducing time to competency, which is facilitated by almost every KM approach

Furthermore, there is important knowledge held by the workforce, often tacit knowledge that is context specific and acquired through experience, which can result in a variety of outcomes when applied. KM methods and tools are paramount to foster the processes and conditions for these outcomes to flourish. Table 3.1 summarizes several key manifestations (i.e., outcomes) in the application of workforce knowledge.

³ Expertise location is explained in Appendix 6.

Table 3.1: Manifestations of Workforce Knowledge

Category	Description
Performance	<p>Performance should be characterized in terms of both <i>effectiveness</i> and <i>efficiency</i> [23]. Effectiveness can be understood in terms of achieving the goals or task deliverables, while efficiency implies using minimum resources to get the task done.</p> <p>Success criteria include the timeliness of the action, doing it right the first time, reducing variability in the actions to enhance reproducibility. In short, performance is knowledge in action through the application of the knowledge available in the organization and the know-how of the individual.</p>
Insights and Decision-Making	<p>Problem-solving requires knowing when, where, and how to apply knowledge. In today's complex environment, knowledge workers are regularly responsible for solving non-standardized organizational problems using their knowledge and experience. Non-routine problems require <i>extensive thinking</i>, which allow workers to identify and close gaps in knowledge and to learn [24].</p>
Communication and Networking	<p>Knowledge work is increasingly social and the existence of informal personal networks to connect knowledge holders often compensates for shortcomings in more formal organizational arrangements [25]. The level of engagement and activity across these networks can be measured as an indication of the <i>organizational health</i> of this critical knowledge channel.</p> <p>This also highlights another example of important tacit knowledge, <i>know-who</i>, which can enable individuals to accomplish their work by knowing who to go to for help, guidance, historical information, or other knowledge not readily found elsewhere.</p>
Organizational Understanding and Engagement	<p>Knowledge workers make decisions on the basis of their understanding of their organizational culture, values, mission, and vision. This reflects the level of organizational alignment and clarity of purpose.</p> <p>An employee's understanding of the organizational jargon and technical terminology is indispensable for the proper understanding of the organizational culture and dynamics. Awareness of historical failures and organizational threats reflect the maturity and depth of the mental models the knowledge worker draws upon to make decisions. There has been an increasing focus on the role of culture in driving organizational performance in recent years, and a useful resource in this area is the <i>ISPE Cultural Excellence Report</i> (2017) [26].</p>
Mastery of Product and Process	<p>ICH Q8 [2] and Q10 [4] present product and process understanding as the core of KM activities and the outcome of applying scientific approaches across the product lifecycle. Knowledge holders manifest the tacit and explicit knowledge of product and process in different forms.</p> <p>Roles such as product steward, SME, or simply <i>the go to person</i> are evidence of mastership of a certain discipline, often described as the <i>know-why</i>. This can take the form of <i>technical advising</i>, where the knowledge worker is not only capable of doing his/her role but can also teach it to others and explain the technical background. The transferred knowledge through training can take several forms. While training can simply imply self-study, mentors or coaches are often required to transfer the heuristics⁴ they unconsciously use to perform certain tasks in a process [27].</p> <p>Although sharing product and/or process knowledge with coworkers may be limited by factors such as personality traits or level of trust, the ability to pass technical knowledge to others through formal or informal training can be seen as manifestations of deep knowledge [28]. Such knowledge transfers include training successors, sharing accumulated knowledge from prior roles, and other forms of coaching.</p> <p>Finally, <i>know-where</i> is another important manifestation of knowledge, where workers know where to locate and access missing pieces of information across the product lifecycle.</p>

⁴ "A heuristic is a mental shortcut that allows an individual to make a decision, pass judgment, or solve a problem quickly and with minimal mental effort." [30]

3.6 Attributes of an Organizational Culture Supportive of Knowledge Management

The culture of an organization is based on its values and beliefs, which translate through the leadership to inform the mindsets and behaviors of the employees. There are documented examples of attributes supportive of an organizational learning and KM culture [8, 29], which include traits such as openness, transparency, trust, collaboration, empowerment, and the willingness to share knowledge.

Linking these traits to concepts in this Guide, illustrative mindsets and behaviors that support KM include that the organization – both as individuals and a collective:

- Manages knowledge as an asset, through how knowledge is captured and made available for future use, including the use of standard KM methods and tools (and expecting such of others)
- Proactively seeks knowledge, such as prior knowledge, lessons from past projects, or the help of experts (inside or outside the organization) to solve problems
- Proactively shares knowledge, such as expertise and experience, solutions to problems, best practices and lessons learned
- Pursues learning and continual improvement through intentional reflection to identify lessons, and ensures these lessons are implemented and shared broadly
- Recognizes opportunities to grow the knowledge of the organization, and ensures knowledge is thoughtfully captured (e.g., learning during a technology transfer that informs the control strategy)

These mindsets and behaviors are most successful when they are not distinct, but rather integrated with the broader cultural mindsets and behaviors of the organization in support of the its mission and objectives.

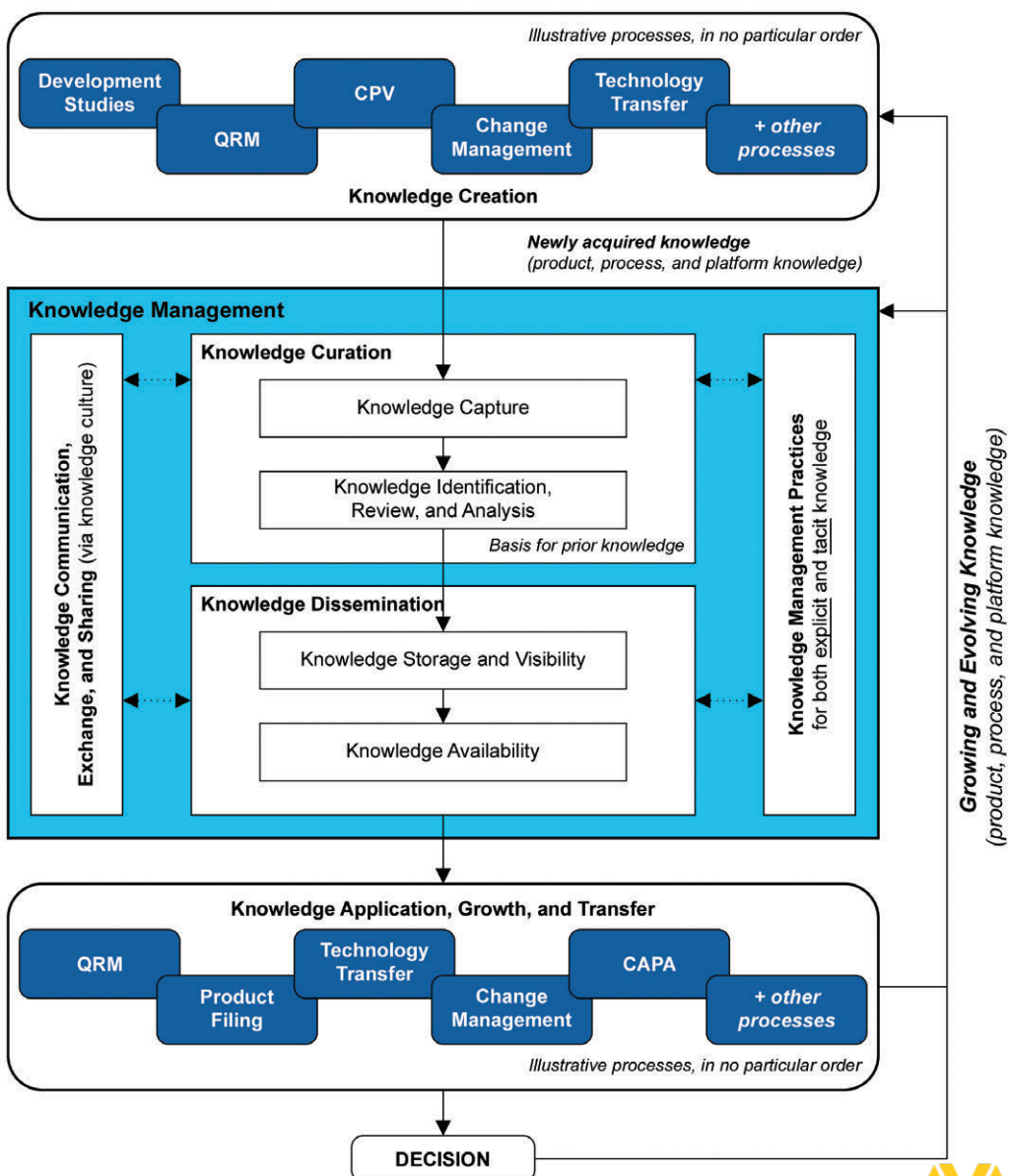
4 General Knowledge Management Process

The overarching goal of KM is to ensure that the right knowledge is available to the right person at the right time to enable an optimal outcome (e.g., timely and informed decision-making).

4.1 Knowledge Management Process Model

A Knowledge Management Process Model is depicted in Figure 4.1 outlining the typical steps involved in KM. This model encompasses the definition of KM provided by ICH Q10 [4], and enhances it with additional context, details, and mapping of interactions within the model. This process model is intentionally similar to the familiar ICH Q9 QRM process flow [3] to aid in understanding and to relate KM to the dual PQS enabler QRM.

Figure 4.1: Knowledge Management Process Model (Adapted from Lipa, O'Donnell, and Greene 2020, 4 [31])
Used with permission. © 2020 Lipa & O'Donnell. All rights reserved.



A key feature of the model is its position relative to the core business processes of a pharmaceutical organization. Note the starting point to KM lies in the business processes themselves that create, consume, and grow the knowledge of the organization. KM should not be seen as a distinct activity but rather embedded in the flow of these important processes – a subprocess so to speak – where knowledge created is treated as an asset by being intentionally captured and reviewed as appropriate. Subsequently, when knowledge is required for a process, for example to inform risk-based decision-making, this knowledge asset⁵ should be visible and available to flow on demand to whom, when, and to where it is needed through embedded KM processes.

The subsequent sections in this chapter provide detail about each element within the model.

4.2 Knowledge Creation and Curation

The goal of knowledge creation and curation is to ensure knowledge is methodically captured through a variety of context-appropriate means and that this knowledge is well inventoried and characterized. Curation is defined as:

“The action or process of selecting, organizing, and looking after the items in a collection” [32]

This term implies proactive care and oversight of an organization's knowledge assets. Said differently, this step is about ensuring *the organization knows what it knows* (see Box 1 in Figure 1.1).

4.2.1 Knowledge Creation

Knowledge is created continuously in a pharmaceutical organization. This includes the day-to-day experiences that grow personnel expertise, the analysis of experimental and in-process data, and the new insights and learnings generated by lessons learned and interactions with colleagues to name just a few. Much of this knowledge is created during execution of specific business processes (e.g., process monitoring or a risk assessment evaluating a proposed process change) and must flow into a KM system to be managed. In addition, several KM methods and tools directly foster the creation of new tacit and explicit knowledge, such as the interactions between colleagues asking for help solving a problem in a CoP, lessons created during lessons learned, and competency building through tacit knowledge transfer techniques.

4.2.2 Knowledge Capture

Knowledge capture is capturing or recording knowledge in a consistent and suitable manner to be used both for its intended purpose and for potential future use as *prior knowledge* [13]. Furthermore, standardizing knowledge capture allows knowledge to be found later when needed.

Considerations for knowledge capture include:

- Is the knowledge capture activity defined in the business process?
- Is there a well-defined place for the knowledge to be captured?
- Is it clear what should be captured, and in what format?
- Have employees been trained on expectations and system use?
- Is there suitable governance in place to ensure the standard process is followed so that shadow or other unsanctioned locations are not used? In the case of an IT repository, is there alignment with the IT roadmap such that new tools released by IT do not cause competition and confusion?

⁵ “The term ‘knowledge assets’ refers to the accumulated intellectual resources of an organization. It is the knowledge possessed by an organization and its workforce in the form of information, ideas, learning, understanding, memory, insights, cognitive and technical skills, and capabilities.” [33]

- Are there metrics available to monitor use?

Not all knowledge can be written down (nor should be, considering effort and knowledge relevance over time). As such, sometimes capture is about knowing where to go to get the knowledge, for example, by having a well-defined list of SMEs to contact for important topics.

4.2.3 Knowledge Identification, Review, and Analysis

Knowledge identification, review, and analysis is about ensuring captured knowledge is well-characterized, is approved or otherwise sanctioned for use as appropriate, and has been analyzed or assessed to generate new insights.

Considerations for knowledge identification, review, and analysis include:

- Are there clear and consistent instructions stating how to describe knowledge (e.g., file naming conventions)?
- Is there a common language in the form of a taxonomy (to cover both explicit knowledge and tacit knowledge, such as types of expertise)?
- Are there processes in place for knowledge review and approval as appropriate, whether for formal use in a GMP process, or for sanctioning lessons learned for future use?
- Are record-retention processes enacted?
- Is there consistency across projects, teams, departments in how knowledge is identified, reviewed, and analyzed?
- Is there a knowledge steward or other person responsible for a given repository of knowledge to ensure compliance with standards and to engage for help?
- Are there opportunities for analytics, e.g., to see trends in lessons learned?⁶
- Are there proactive processes in place to mitigate future risks, such as determining SMEs who possess unique, critical knowledge that may pose a risk to business continuity if they left?

4.3 Knowledge Dissemination and Application

Knowledge needs to be methodically distributed to the right person at the right time so that it can be applied to achieve an optimal outcome. In other words, this step is about ensuring *the organization can find what it knows and who knows*.

4.3.1 Knowledge Storage and Visibility

Knowledge storage and visibility involves ensuring knowledge is available when and where it is needed, starting with how it is stored and made visible to the organization on a push and/or pull basis. Having standards for knowledge capture and curation greatly support this activity, as the places where knowledge is stored have been defined.

Considerations for knowledge storage and visibility include:

- Do employees know where to go to find different types of knowledge? Are these sources well defined and consistent? Is there a finite and well-defined list of places to go? Can a newcomer figure it out? Is it part of new employee orientation?

⁶ This is an opportunity for emerging technologies, such as AI, to mine and recognize trends. See Chapter 6 for more on future-facing considerations.

- Is there a taxonomy or other tagging standardization process that enables people to find content reliably and efficiently, and from different contexts?
- Is there a comprehensive search function or other means that helps people search for knowledge across multiple sources efficiently? Is the search feature equipped with semantic capabilities, synonyms, and other practices to reduce the natural variability of how content is described?
- Can people easily find lessons learned and other tacit knowledge, such as experts? Do people know where to go on important topics such as platform technologies?
- Are communities of practice available and well publicized to support problem-solving, best-practice sharing, and capability building?
- Is it understood on a role basis what knowledge is required, and role-based access evaluated?
- Is finding explicit knowledge intuitive and more process-based than people-based?
- Is there a single source of authoritative knowledge, as opposed to each department having their own copies of the same document, repetitive communities, etc.?

4.3.2 Knowledge Availability

Knowledge availability consists of making certain knowledge is obtainable when and where it is needed, without depending on restrictive access models or on who you know. This is the “last mile” of all the steps to capture, curate, and store knowledge.

Considerations for knowledge availability include:

- Does the business process specify where to find certain knowledge?
- Do roles automatically have all of the necessary permissions to access the knowledge they need?
- Is the access model biased toward open access, rather than the typical narrow and restrictive mindset of *who needs to know*?
- Can a person reasonably find out what their organization knows about a given topic, or be able to quickly find out who knows it or how to get it?
- Is knowledge visible and accessible across organizational boundaries?
- Are there notifications when a new community question is asked?
- Is there a knowledge *push* where appropriate (e.g., a newly captured lesson pushed to people who should know about it)?

If there are gaps in knowledge availability, why is this? Gaps look like time wasted searching for knowledge, revealing a difficulty in finding prior knowledge, repeated issues due to lessons not learned, difficulty in finding experts, etc. When these occur, a simple analysis (e.g., 5 Whys⁷ or other root cause analysis) can be helpful to trace back to the problem for it to be addressed.

⁷ “The 5 Whys typically refers to the practice of asking, five times, why the failure has occurred in order to get to the root cause/causes of the problem.” [34]

4.3.3 Knowledge Application, Transfer, and Growth

Knowledge application, transfer, reuse, and growth are where the knowledge assets – having been captured, reviewed, stored, and made available – generate value. Effective KM can ensure these knowledge assets are found when needed, and can be reused in the future as prior knowledge. Further, given the difficulty in finding knowledge as cited previously, wasted time and rework can be avoided, which also translates to savings.

These knowledge assets can be used to:

- Inform risk-based decision-making as an input to QRM
- Support effective post-approval change management
- Ensure a right-first-time technology transfer
- Improve process robustness
- Foster continual improvement across the business through application of lessons
- Reduce the burden of problem-solving by engaging the broader community and their experiences

Importantly, there is also a feedback loop included for the growth and evolution of knowledge back into business processes and the collective knowledge of the organization.

It is important to realize the prior steps in this process are in large part going on irrespective of a formal KM program. For example, when it comes to content management, every team is capturing and storing knowledge. The problem is they are doing this *in their own way because they do not know any other way, introducing a large degree of subjectivity and variability, thus creating waste and inefficiency* (and unintentionally building knowledge silos). **The steps prior in this process are not additive work but rather are about committing to standard processes** to remove and prevent waste and variability from the work of individuals and teams across the organization.

4.4 Knowledge Management Practices

Structured, standardized practices (i.e., methods and tools) are needed to ensure efficient flow, transfer, and retention of essential knowledge, enable the efficient use (and reuse) of knowledge, and other outcomes to create value for patients, pharmaceutical organizations, and regulators. The goal is to integrate KM methods and tools into the flow of daily work in order to continually improve knowledge flow and reuse. This is achieved by operationalizing the activities of knowledge creation and capture through knowledge dissemination and application. Aligning with other industries, a best practice is to integrate KM into core business processes. For the pharmaceutical industry, this includes all processes that deal with technical product knowledge, including:

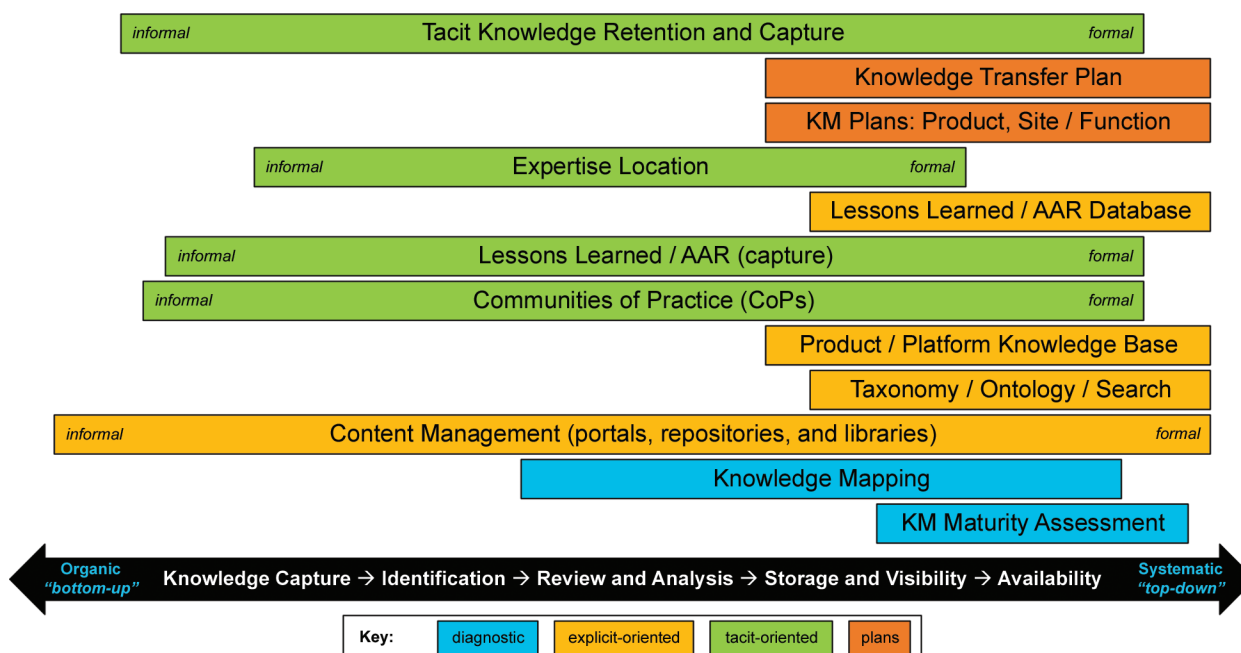
- New product introductions
- Technology transfers
- Process changes
- Investigations
- Regulatory audits

Each of these activities is heavily dependent on both explicit and tacit knowledge. Importantly, these methods and tools should not be deployed without:

- Understanding the set of leading practice enablers to help ensure sustained success, including KM sponsorship/ management engagement (see Appendix 7)
- A written KM strategy that defines the KM problem, desired outcomes, and the methods and tools selected

APQC [10] is recognized for their KM benchmarking and collection of best practices across multiple industries. APQC's benchmarking identified that common knowledge transfer approaches can be grouped as either systematic or organic approaches to knowledge transfer [35]. Figure 4.2, adapted from APQC's model, categorizes examples of KM methods and tools common (but not unique) to the pharmaceutical industry, including the characterization of the methods and tools to focus mostly on tacit or explicit knowledge. The methods and tools depicted in Figure 4.2 are based on commonly used methods and tools and is not an exhaustive listing.

Figure 4.2: Pharmaceutical Systematic and Organic Knowledge Management Methods and Tools
(Adapted from APQC [35])



Systematic KM methods and tools are formalized, structured approaches to identify both explicit and tacit knowledge, and tend to be more *top-down* in the organization (i.e., intentionally deployed by a senior sponsoring organization intended for broad use). Examples include an enterprise-wide content management system or communities of practice applicable to all of manufacturing.

Organic approaches tend to be more informal, often localized approaches (i.e., *bottom-up*) where a person or a group often tries to connect personnel to specific sources of knowledge in a more ad hoc, unstructured manner. Examples include creating new department-specific SharePoint sites or a small group designing a lessons learned program for their own use.

Appendix 6 provides guidance, identifies potential areas of application and impact within the pharmaceutical industry, and describes additional resources for the following methods and tools:

- Knowledge Mapping

- CoPs
- Lessons Learned
- Expertise Location
- Storage and Search: Content Management, Taxonomy, and Ontology

Methods and tools should build KM core principles into the applicable business process, and should focus on both tacit and explicit sources of knowledge. Thoughtful choices are required in deploying these methods and tools. For example, once a decision is made to deploy communities of practice, what will be the list of communities and scope of each? For lessons learned, in which business process will reflections be embedded (to capture lessons), and which processes will routinely seek lessons? Additionally, the specific list of methods and tools and where they are deployed (e.g., to what processes and teams) will evolve over time.

4.5 Knowledge Communication, Exchange, and Sharing

Knowledge communication, exchange, and sharing represent the interaction of the organization (the knowledge workers) with the knowledge assets and KM methods and tools. This encompasses the mindsets and behaviors of a culture that manages knowledge as an asset, proactively seeks and shares knowledge, pursues learning and continual improvement, and recognizes the opportunity to grow the body of knowledge. This is outlined in Section 3.6.

The overarching goal is to seek, share, reuse, and apply the best knowledge available in the organization to benefit the PQS and operational effectiveness. This starts with linking KM behaviors to the cultural aspirations of the organization. For example, an organization that aspires *to make problems visible and solve them at root cause* could establish related KM behaviors to make expertise visible and engage CoPs for help with difficult problems. This would encourage the organization to ask communities for help and to provide timely responses to those that seek support. It might also mean starting new work with a search of lessons from prior projects. These types of behaviors could be reinforced in individual performance objectives as well, akin to obligatory safety, quality, and financial objectives, similarly linking rewards and recognition to desired behaviors and corresponding outcomes.

Everyone should be trained in the basics of what KM is and why KM is important to the organization to build basic fluency in the appropriate methods and tools. Ideally this is part of the onboarding package for all employees.

4.6 Enablers for an Effective Knowledge Management Strategy

Establishing an effective KM strategy requires a change from current business practices and ways of working for most organizations. The implementation of a culture embracing KM is an advantage to all aspects of the pharmaceutical industry.

KM requires basic frameworks to ensure ongoing effectiveness in the face of competing priorities. Structures to consider when developing and deploying an effective KM strategy include:

- Sponsorship to communicate the importance of the KM effort, and to legitimize the need for people to change their work habits
- Governance to ensure appropriate direction, risk management, decision-making, and accountability for KM efforts
- Clearly defined roles to ensure the right support is in place to execute KM-related tasks

- KM strategy linkage to the organization's/team's objectives, to relate KM to the broader priorities (and not KM for the sake of KM)
- Organizational Change Management (OCM) to facilitate colleague engagement and ensure people understand the reasons to focus on KM and successfully adopt more effective ways of working

These enablers to an effective KM program/initiative are presented in further detail in Appendix 7.

5 Knowledge Management Application across the Pharmaceutical Product Lifecycle

This section expands the discussion in Chapter 2 on the importance of adopting an E2E view of product technical knowledge across the product lifecycle. It is critical for the knowledge generated across the pharmaceutical product lifecycle (Figure 5.1) to be visible and available to those that need it to ensure the effectiveness of a PQS and achieve the goals of ICH Q10 [4].

Figure 5.1: Pharmaceutical Product Lifecycle per ICH Q10 (Adapted from ICH Q10 [4])



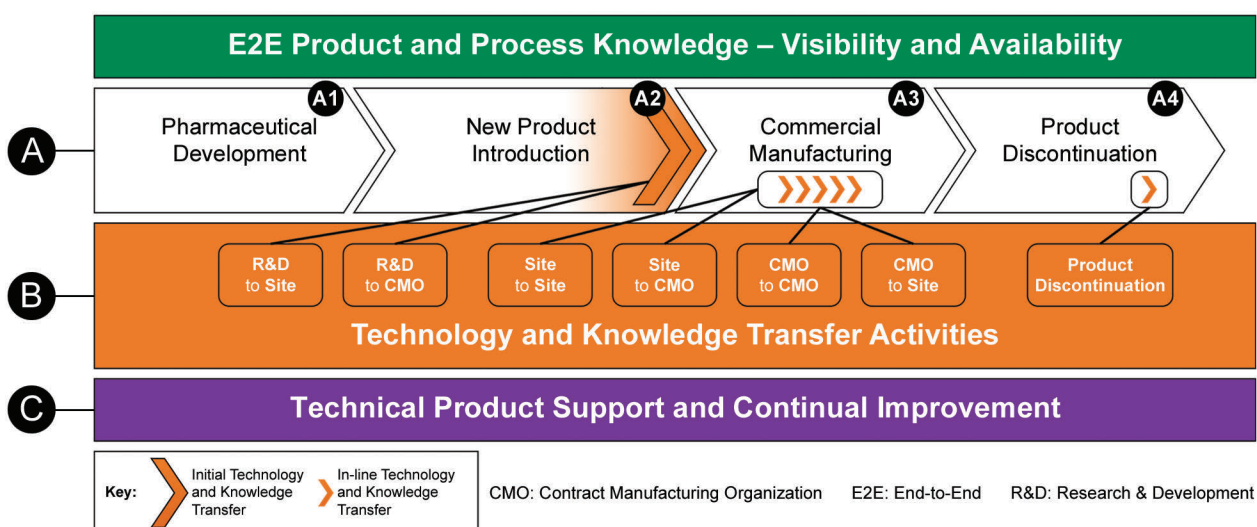
The visualization of the lifecycle model in this chapter is offered to encourage those responsible for the development, manufacture, and distribution of medicines to think differently about the knowledge (tacit and explicit) created during the lifecycle of a product.

5.1 The Pharmaceutical Product Knowledge Lifecycle

An enhanced view of the pharmaceutical product lifecycle is found in the Pharmaceutical Product Knowledge Lifecycle (PPKL) Model as depicted in Figure 5.2.

Figure 5.2: The Pharmaceutical Product Knowledge Lifecycle (PPKL) Model [36]

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The PPKL model represents lifecycle activities in the context of knowledge creation and knowledge flow. The model addresses the nonlinear nature of technology transfer along with the rich knowledge created during technical product support and continual improvement activities. The model illustrates the following [36]:

- A vision for E2E product and process knowledge asset visibility, transparency, and availability is shown in order to enable the flow of critical knowledge across the product lifecycle.

- New Product Introduction (NPI) replaces the ICH Q10 [4] depiction of the Technology Transfer phase (as technology transfer may not be a one time activity for a product).
- Technology Transfer is depicted as an activity that may occur multiple times across the product lifecycle and renames this multiple phase lifecycle as Technology and Knowledge Transfer, highlighting the critical knowledge transfer element of technology transfer.
- Technical Product Support and Continual Improvement activities are visible as an E2E activity across the product lifecycle.

This PPKL model is a helpful reminder to illustrate the continuum of knowledge creation, application, and transfer throughout the product lifecycle rather than at fixed and finite points. Data and knowledge are created for a product every time a batch is manufactured. In addition to routine manufacturing, there are periods of significant knowledge creation that drive a need for ensuring knowledge availability and use.

The balance of this chapter highlights the phases of the pharmaceutical product lifecycle (shown in Figure 5.2) including what knowledge is required for the phase and what knowledge is created by the phase. Corresponding KM methods and tools are identified for key activities in each phase.

5.2 Pharmaceutical Knowledge Creation and Use across the Product Lifecycle

Note: This is labeled A in Figure 5.2.

The *ISPE PQLI® Guide: Part 1 – Product Realization using Quality by Design (QbD)* [37] highlights basic expectations for KM, stating that:

“An important outcome of the science- and risk-based approach is managing the totality of data, information, and knowledge produced, covering variables not only which are important, but also those which are not.”

The *ISPE PQLI® Guide: Part 1 – Product Realization using Quality by Design (QbD)* [37] reinforces the concept that development and continual improvement are ongoing processes that produce new knowledge that needs to be managed. Additionally, the Guide recognizes knowledge summarized in written reports (and associated electronic storage), expert systems for storing and retrieving knowledge, e-laboratory notebooks, and product stewardship roles as examples of KM methods and tools. The Guide also acknowledges that:

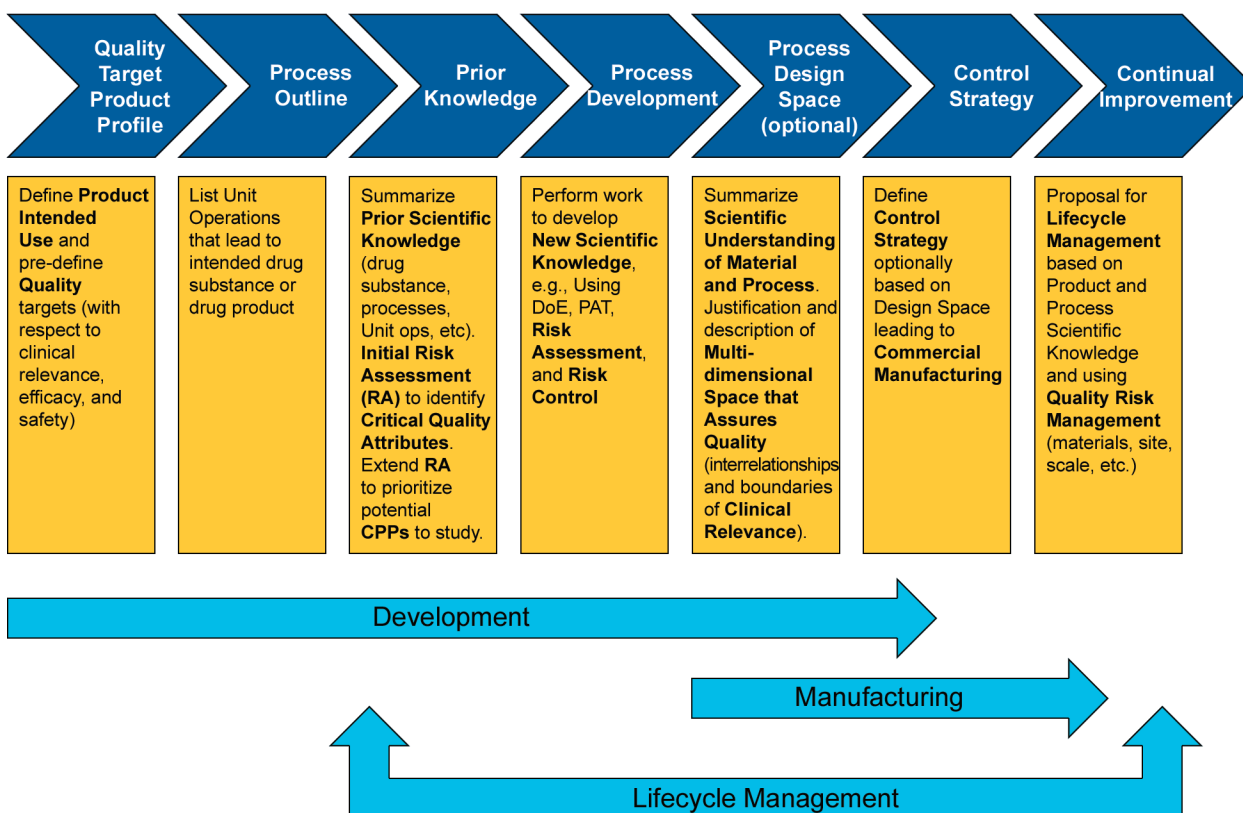
“Managing knowledge across the R&D and manufacturing boundaries and throughout the product lifecycle is a complex subject that is evolving throughout the use of new business processes and technology”.

This highlights the dependence not only on technology to manage knowledge, but also processes and roles.

5.2.1 Lifecycle Phase: Pharmaceutical Product Development

The key activities associated with the Pharmaceutical Product Development phase (labeled A1 in Figure 5.2) are the research and development efforts intended to sufficiently define the product and process (including process parameters and quality attributes) for reliable commercial manufacture. Figure 3.1 in the *ISPE PQLI® Guide: Part 1 – Product Realization using Quality by Design (QbD)* [37], reproduced here as Figure 5.3, provides a helpful visual of the sequence of activities (represented by the chevrons) and knowledge application and build for a QbD application (represented by the rectangles).

Figure 5.3: Conceptual Application of QbD through a Product's Lifecycle [37]



Note: Figure 5.3 depicts product/process development and continual improvement in a linear model, however, some may be parallel activities and are typically iterative.

The Pharmaceutical Product Development phase typically begins with the application of prior knowledge (e.g., platform technologies used in previous products) and risk assessments to determine the areas of study for the new product. This is followed by development activities capturing new knowledge to better understand and characterize the product and process, with ongoing risk assessment and risk control in place. This ultimately leads to decisions about how to ensure quality by using the best process, and how that process will be controlled. Often, early in product development only a small fraction of knowledge is relevant to the final product and process and as such, it can be difficult to ensure appropriate rigor in how knowledge is managed. Determining an appropriate milestone⁸ in the product development process to implement structured KM methods and tools is a good practice.

Notable for this phase is that the timeline may span many years and many development sites, which are becoming increasingly external. There are numerous people involved, and likely some personnel turnover will happen prior to completion of development activities. There may be interruptions to development based on clinical data or business priorities that cause the development to slow down, accelerate, pause, or stop entirely. Furthermore, there is the often-overlooked opportunity to learn from *what didn't work* to avoid repeating issues and to accelerate problem-solving. There is other rich tacit knowledge created during product development that is not always captured, including the rationale behind decisions and ideas to improve yield, cycle time, and quality.

Table 5.1 in Section 5.2.6 describes how KM can benefit this phase along with example KM methods and tools one might employ.

⁸ Appropriate milestones are determined by the organization. It is a balance of when to start collecting everything in a more structured fashion. If it is early in the product development process, there is more work but more knowledge is obtained. If structured KM methods are implemented later, everything is more relevant but early knowledge may have been missed.

5.2.2 Lifecycle Phase: New Product Introduction/Technology Transfer

Note: This is labeled A2 in Figure 5.2.

The *ISPE Good Practice Guide: Technology Transfer (Third Edition)* [38] positions technology transfer as an activity highly dependent on effective KM, as described in ICH Q10 [4]:

"The goal of technology transfer activities is to transfer product and process knowledge between development and manufacturing, and within or between manufacturing sites to achieve product realisation. This knowledge forms the basis for the manufacturing process, control strategy, [italicized in original] process validation approach and ongoing continual improvement."

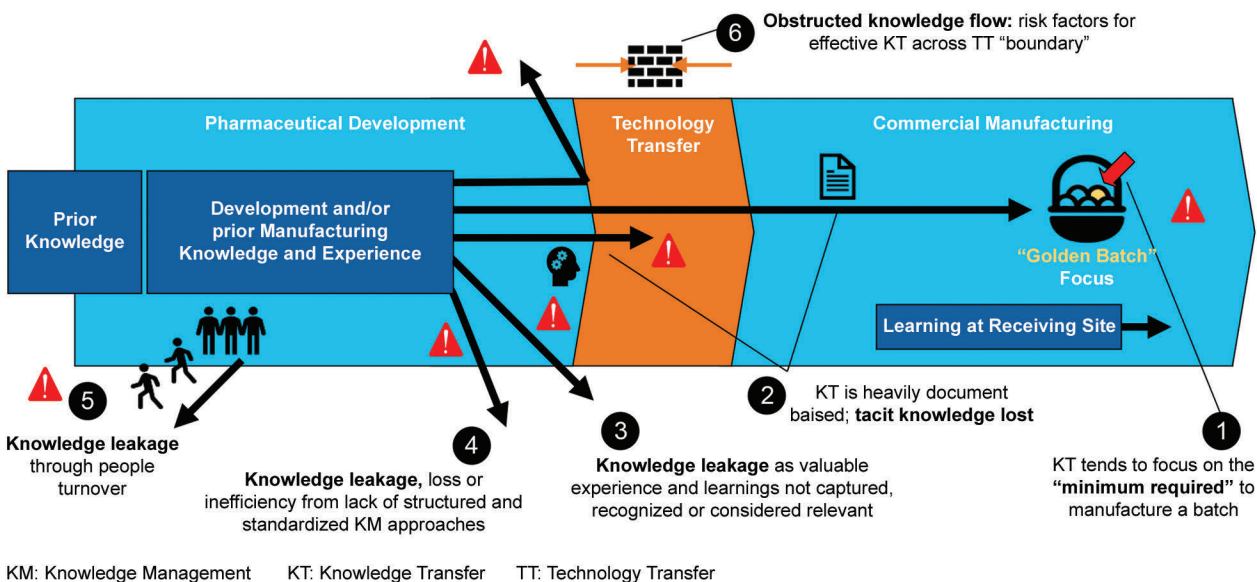
In fact, a key rationale for the third edition of the *ISPE Good Practice Guide: Technology Transfer (Third Edition)* is based on the need to improve KM, as follows:

"Recognition that knowledge management is a critical component of effective technology transfer and that companies have employed various practices and technologies to identify and manage knowledge throughout the development and manufacturing lifecycle including technology transfer."

The mindset for technology transfer should arguably be technology *and* knowledge transfer, as is the case in other industries. However, there are many challenges associated with knowledge transfer during technology transfer, as illustrated in Figure 5.4. Recent findings suggest explicit knowledge transfer is *marginally effective* and tacit knowledge transfer is *somewhat ineffective* [39], clearly indicating an opportunity for improvement.

Figure 5.4: Challenges Associated with Knowledge Transfer during Technology Transfer [39]

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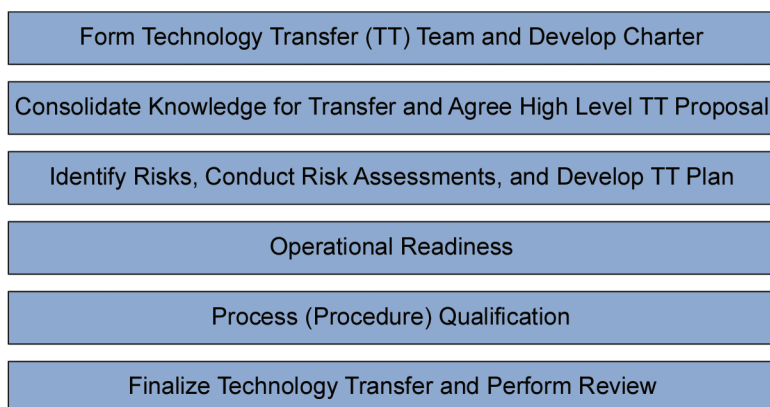


Recent guidance, starting with the third edition of the *ISPE Good Practice Guide: Technology Transfer (Third Edition)* [38], have more expressly stated the expectations for KM and have introduced the concept of tacit knowledge, described generally as knowledge from experience (not written down), nuance, and hands-on information. *ISPE Good Practice Guide: Technology Transfer (Third Edition)* Section 3.6.3, *Lessons Learned* (under *Finalize Transfer and Perform Review*) lists a number of examples of tacit knowledge including historical knowledge, informal knowledge, and interventions. The *ISPE Good Practice Guide: Technology Transfer (Third Edition)* further reinforces the need to transfer tacit knowledge throughout, and acknowledges that GxP systems may be insufficient for capturing/transferring tacit knowledge (with engineering knowledge specifically cited).

The *ISPE Good Practice Guide: Technology Transfer (Third Edition)* [38] also has a section on *Effective Knowledge Transfer* (Section 2.2.4, part of *Technology Transfer – Planning Considerations and Success Criteria*) where scientific, regulatory, operational, business, and cultural aspects are listed.

Chapter 3 of the *ISPE Good Practice Guide: Technology Transfer (Third Edition)* [38], Technology Transfer Project Phases, outlines the high-level steps and sequence of a technology transfer, depicted in Figure 5.5.

Figure 5.5: Phases of Technology Transfer [38]



KM is a consistent consideration for every step in this process:

- Ensuring that both the sending and receiving units are familiar with tools and techniques to support effective knowledge transfer
- Consolidating knowledge (including tacit knowledge) for the transfer package
- Ensuring appropriate knowledge is available for risk assessments and operational readiness
- Capturing new knowledge during qualification
- Evaluating knowledge transfer effectiveness during project review

A detailed review of Chapter 3 of the *ISPE Good Practice Guide: Technology Transfer (Third Edition)* [38], coupled with the application of the principles, methods, tools, and enablers outlined in this *KM Guide*, can help improve knowledge transfer effectiveness and technology transfer outcomes, including cost, schedule, right-first-time activities, process robustness, and receiving-site capability building.

Appendix 8, Knowledge Management Enabling Technology Transfer: A Case Study in this Guide, describes a holistic knowledge transfer framework proposed to standardize knowledge transfer processes along with techniques to improve the transfer of tacit knowledge.

Table 5.1 in Section 5.2.6 includes a description of how KM can benefit technology transfer along with corresponding KM methods and tools.

5.2.3 Lifecycle Phase: Commercial Manufacturing (Inclusive of Continual Improvement)

Product Development, NPI, and the respective Technology Transfers are easily perceived as knowledge intensive activities. However, knowledge is also routinely created during the Commercial Manufacturing phase (labeled A3 in Figure 5.2), and the organization continues to learn and build knowledge about the product both through ongoing commercial manufacturing and a variety of technology transfer activities (labeled B in Figure 5.2). In addition to this, learnings may arise as a result of planned and unplanned activities (labeled C in Figure 5.2) such as:

- Implementing new plant floor or laboratory IT systems
- Learnings from deviation/investigation resolution, product customer complaints, and PQRs
- Continuous Process Verification (CPV) activities
- Lifecycle management, including post-approval change management
- Additional studies for process improvement and optimization

The product knowledge created over the lifecycle of the product typically resides in an array of different business process systems, IT repositories, personal computers, and/or as tacit knowledge possessed by SMEs. Lack of a proactive plan to capture and manage knowledge (both GMP and non-GMP) may contribute to the *knowledge island* or *knowledge silo* issues that have been identified in the industry [40]. Business processes and systems should be designed with knowledge-flow interoperability from product development through to product discontinuation, to ensure the knowledge is available in the future and can be leveraged for new platforms and continual improvement activities.

Effective KM provides a means to manage the knowledge gained over the course of commercial manufacture in a methodical manner and provide access to the knowledge within the organization to support change management, problem-solving, and other activities.

Table 5.1 in Section 5.2.6 contains a description of how KM can benefit commercial manufacturing along with corresponding KM methods and tools.

ICH Q12 (Lifecycle Management) Considerations

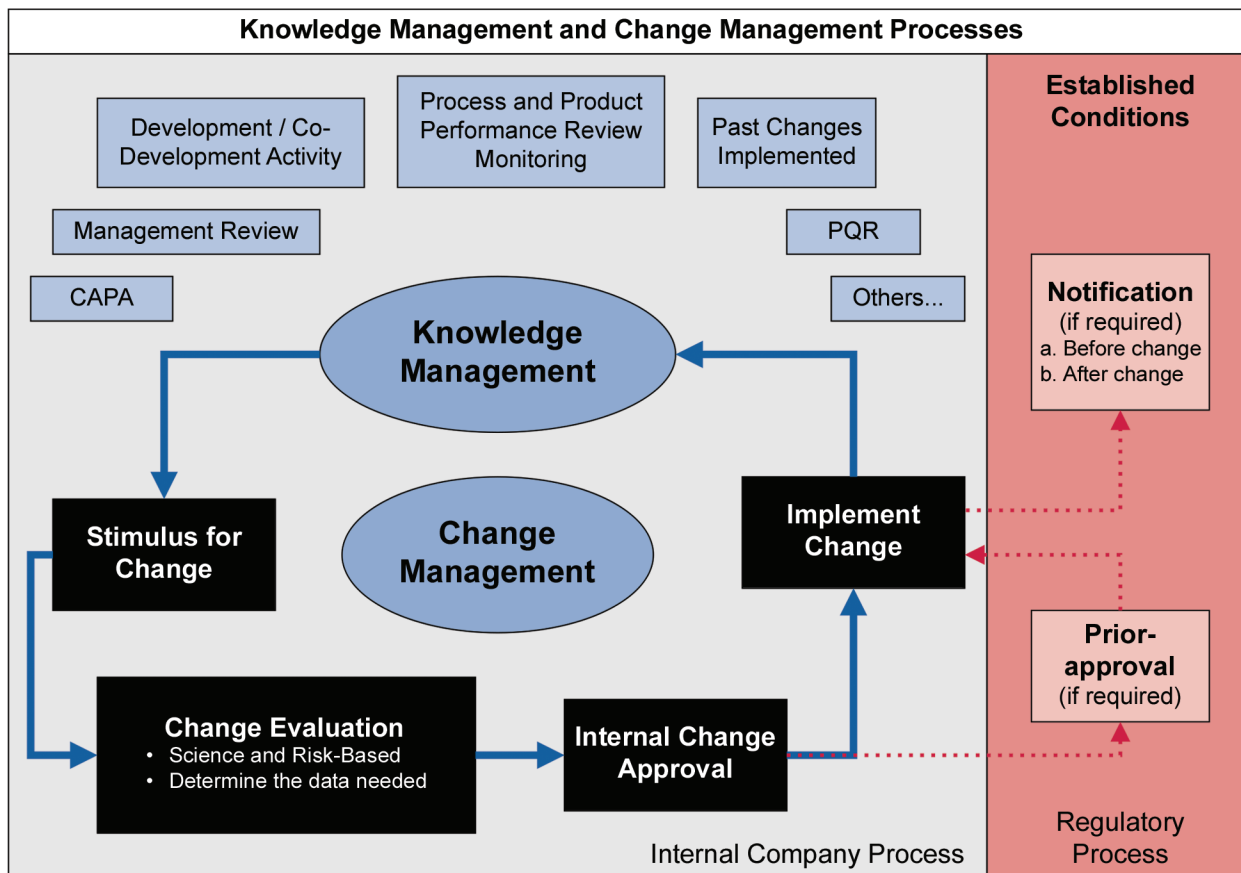
For the lifecycle of authorized products, ICH Q12 Section 6 (Pharmaceutical Quality System (PQS) and Change Management) [12] provides further operational guidance for the Commercial Manufacturing lifecycle phase without being excessively prescriptive. In particular it states that:

“An effective PQS as described in ICH Q10 and in compliance with regional GMP requirements where the application is filed, 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 Q12 [12] also provides a very helpful diagram of the connection between KM and change management (see Figure 5.6) for Established Conditions (ECs), showing KM as a systematic ongoing process of review of various data sources including:

- CAPA
- Management review
- PQR
- Product complaints

Figure 5.6: Connection Between Knowledge Management and Change Management Process (Q12) [12]



CAPA: Corrective and Preventive Action PQR: Product Quality Review

The outcome of this may be a stimulus for change that drives ultimately a process change via change control. This is processed through internal approval and, if it relates to one of the ECs, through a regulatory process that may include a disposition decision by a regulatory SME.

In essence, throughout the product lifecycle, the management of knowledge occurs in a systematic iterative manner as one important driver for a change management process that interfaces with a regulatory review and disposition process. ICH Q12 [12] is silent on how such a process might be carried out. Considering the ICH Q10 [4] requirement for management review and recognizing the centrality of KM in the PQS, one approach is to create a council of cross-functional management responsible for periodically conducting this knowledge review and acting on the conclusions.

Further details about the role of KM to support change management are found in *ISPE PQLI® Guide: Part 3 – Change Management System as a Key Element of a Pharmaceutical Quality System* [41], where KM is cited as an enabler to the change management system. In addition, Section 3.3.2 of that Guide recommends that for an effective review of a change:

"Data and knowledge gathered from implementation of the change should be shared with the development function and other locations, as appropriate, to ensure that all learning can be applied in products under development or to similar products manufactured at the same or other locations."

The *ISPE PQLI® Guide: Part 3 – Change Management System as a Key Element of a Pharmaceutical Quality System* [41] reinforces the importance of knowledge visibility and availability across the product lifecycle.

5.2.4 Lifecycle Phase: Product Discontinuation

The last lifecycle stage as noted in ICH Q10 [4] and the PPKL model is product discontinuation. This is the final transfer of product knowledge to an archive facility or location when the product is scheduled to be discontinued; in essence it is the final knowledge transfer activity. It is important to proactively plan for not only the explicit knowledge that needs to be transferred and stewarded, but also capturing a listing of SMEs for the respective technology platforms. KM considerations for product discontinuation are:

- Where will the technical product knowledge be stored for the remainder of the records retention period? This is particularly important in the event of a manufacturing site closure.
- What is the associated process or technical platform knowledge that is important to capture?
- Will lessons learned from the product/processes be captured, and are those lessons available?
- Is there a list of SMEs?

Table 5.1 in Section 5.2.6 includes a description of how KM can benefit product discontinuation along with KM methods and tools to employ.

5.2.5 Additional Considerations from the PPKL

Taking into account a holistic view of the PPKL over a traditional product lifecycle depiction (see ICH Q10 Annex 2 [4]), there are two additional considerations:

- **Knowledge Visibility and Availability across the Product Lifecycle** (represented in Figure 5.2 as the bar above the lifecycle elements): A vision for E2E product and process knowledge visibility, transparency, and availability is presented to represent the knowledge flow across the product lifecycle – not only to the next lifecycle step but forward and backward as well. The *ISPE PQLI® Guide: Part 3 – Change Management System as a Key Element of a Pharmaceutical Quality System* [41] highlights this need to share knowledge back with the development organization and with other sites to ensure the knowledge is reinvested in the product lifecycle. To enable visibility of lifecycle knowledge, a strategic approach to holistically managing knowledge is recommended. This may be accomplished by developing strategic plans describing the way KM will be deployed at the product level and at a manufacturing site/functional level (e.g., corporate or above site Science & Technology). These non-GMP documents inform program management rather than GMP decisions. Outlines for site KM plans and product KM plans are found in Appendix 14.
- **Technical Product Support & Continual Improvement** (represented in Figure 5.2 by the bottom bar): During activities that require support from the manufacturing technology function, additional knowledge is generated. These activities could be proactive such as driving planned process/equipment improvements, or reactive when supporting investigations. Regardless of how the activities are initiated, new knowledge is generated by providing technical support for non-routine activities and should be captured.

5.2.6 KM Tools and Approaches to help make Product Knowledge Visible and Accessible across the Lifecycle

Table 5.1 provides an illustrative summary of KM methods and tools for use across the product lifecycle phases. Table 5.2 provides a high-level mapping to where more information on each KM method or tool is in this Guide.

Table 5.1: Knowledge Management Methods and Tools across the Product Lifecycle Phases [42]
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			KM Methods & Tools																	
			Planning & Requirements Definition					Mostly Explicit-based				Mostly Tacit-based					Enabling elements			
			KM Maturity Assessment	Knowledge Mapping	Product KM Plan	Knowledge Transfer Plan	Site / Functional Area KM Plan	Content Management	Taxonomy & Search	Platform Knowledge Base	Product Knowledge Base	Communities of Practice	After Action Review / Lessons Learned	Expertise Location	Decision Rationale Capture	Tacit Knowledge Retention & Transfer Practices	KM Roles	KM Training	Knowledge-valuing Culture	Sponsorship, Governance, Metrics & Other enablers
Lifecycle Phase	Areas of emphasis where knowledge is required	How Knowledge Management can provide benefit...																		
	Note 1: Illustrative concepts, not an exhaustive listing Note 2: References below to knowledge refer to <u>both</u> explicit and tacit knowledge Note 3: Additional concepts or complexity may be introduced when multiple entities are involved																			
Product Development	• Application of prior knowledge for risk assessments to determine areas of study • Development work to capture new knowledge • Ongoing risk assessment and risk control	Common KM elements for <i>Product Development</i> phase	X	X													X	X	X	X
		Access to prior knowledge (platform technologies, other products, expertise in the company (individuals and CoEs), external scientific literature, prior learnings and lessons, et al.)																		
		Capture of new knowledge during early development work (both what worked and what didn't)			X		X	X	X	X	X	X	X		X					
		The record of product development, including scientific knowledge and supporting design choices and other decision rationale			X	X		X	X	X	X		X		X	X				
New Product Introduction / Technology Transfer	• Application of knowledge for risk assessments • Comprehensive knowledge transfer • Opportunity to learn more about the product/ process • Supporting the goal to ensure a right-first time transfer, robust process and capable receiving site	Common KM elements for <i>Technology Transfer</i> phase		X													X	X	X	X
		Access to comprehensive product and process knowledge, including development and manufacturing history, including key decisions, learnings from failures, changes, etc.			X	X	X	X	X	X	X	X	X	X	X	X				
		Access to subject matter experts/personnel with process experience				X		X			X		X		X					
		Capture of new learnings including increased knowledge and understanding of product/ process, lessons learned, etc.			X	X	X	X		X	X	X	X		X	X				

Table 5.1: Knowledge Management Methods and Tools across the Product Lifecycle Phases [42] (continued)
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			KM Methods & Tools																		
			Planning & Requirements Definition				Mostly Explicit-based				Mostly Tacit-based				Enabling elements						
Lifecycle Phase	Areas of emphasis where knowledge is required	How Knowledge Management can provide benefit...	KM Maturity Assessment	Knowledge Mapping	Product KM Plan	Knowledge Transfer Plan	Site / Functional Area KM Plan	Content Management	Taxonomy & Search	Platform Knowledge Base	Product Knowledge Base	Communities of Practice	After Action Review / Lessons Learned	Expertise Location	Decision Rationale Capture	Tacit Knowledge Retention & Transfer Practices	KM Roles	KM Training	Knowledge-valuing Culture	Sponsorship, Governance, Metrics & Other enablers	
	Note 1: Illustrative concepts, not an exhaustive listing Note 2: References below to knowledge refer to <u>both</u> explicit and tacit knowledge Note 3: Additional concepts or complexity may be introduced when multiple entities are involved																				
Commercial Manufacturing / Continual Improvement	<ul style="list-style-type: none">Ongoing knowledge build through accumulated manufacturing experienceLifecycle management, including planned and unplanned changesSeek to minimize disruptions to product availability by rapid problem solving and solving problems at root cause	Common KM elements for <i>Commercial Manufacturing</i> phase	X	X														X	X	X	X
		Capture of new learnings including increased knowledge and understanding of product/process, lessons learned, etc.			X		X	X	X	X	X	X	X		X	X					
		Knowledge visibility and availability across the full product lifecycle (including development) to ensure broad access to knowledge to support process monitoring, continual improvement, change management, investigations, et al.			X		X	X	X	X	X	X	X	X	X	X	X				
		Support for problem solving and sharing of best practices and improvements across the supply chain and back to development organization			X		X	X	X	X	X	X	X	X	X	X					
Product Discontinuation	<ul style="list-style-type: none">Knowledge transfer for archival and future access on demandHarvesting learnings to inform 'prior knowledge'	Common KM elements for <i>Product Discontinuation</i> phase		X														X		X	X
		Capture of knowledge in a complete and structured manner to allow for future access (e.g., stability, complaints, etc.)			X			X	X		X		X	X	X	X					
		Capture of learnings including insights for platform knowledge and other potential 'prior knowledge'				X				X		X	X	X	X	X					