EBOOK

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Digital Tech Transfer in the Pharmaceutical Industry

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Executive Summary

The pharmaceutical industry can move slowly, especially when it comes to adopting innovative technologies. There are important legal and ethical reasons for them to advance with caution including strict regulations about drug development as well as the need for exact documentation of processes to achieve results.

Pharmaceutical, biotechnology and contract development and manufacturing (CDMO) companies need to securely optimize data and knowledge flow through their extended value chain networks to accelerate product realization.

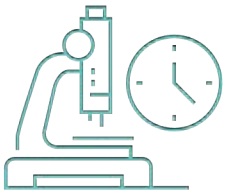
Technology transfer, or tech transfer, refers to the ability of the pharma or biotech innovator to share Chemistry and Manufacturing Controls (CMC) knowledge and analytical methods of a drug product with a recipient site such as a CDMO (contract development and manufacturing organization). or a downstream manufacturing unit within the same company - regarding the manufacturing process from discovery & development to commercial production.

Today this is a largely manual and extremely time-intensive process that primarily utilizes paper or paper on glass (electronic) documents that disrupt a continuous flow of reusable digital data. It can be long, laborious, and sometimes complicated, process. However, it is necessary at every stage of pharmaceutical manufacturing.

Rockwell Automation's digital technology transfer solution utilizes natural language processing and machine learning to extract and parse digital data from existing documents to establish a continuous product and process information flow – with robust change control from discovery, clinical and commercial development through internal or external manufacturing. This enables secure and seamless technology transfer and scale-up, unlocking significant timeline, cost and profitability improvements.

Trends Impacting the Pharmaceutical Industry

A major focus in the pharmaceutical industry is time to patient. Three trends increasing the need to get products to market faster include:



Push to reduce time from discovery through commercial manufacturing phases for new drugs.

Transformational new approaches will need to be leveraged to reduce current timelines by the 1-3 years necessary to achieve true end to information and knowledge transfer across multiple functional domains. On average, 88% of the drugs that enter a clinical trial do not result in an approved medicine, resulting in a tremendous amount of incurred time and expense that ultimately cannot be recouped. Traditionally, pharmaceutical companies were able to manage this risk because the patient populations were large, and a successful new novel drug launch would justify the investments across the portfolio.

Personalized medicine and therapeutics.

Advanced Therapy Medicinal Products (ATMP), including cell and gene therapy (CGT), that are formulated for a particular patient based on their genetic makeup or other biomarker information and will transform the ability to treat medical conditions, however these will also require much smaller batch sizes than the higher-volume, small-molecule or traditional biologic drugs. These novel new approaches utilize advanced manufacturing modalities add additional complexity to the tech transfer process. This is fundamentally changing the way drug companies think about tech transfer and manufacturing; challenging them to operate very differently. Due to the smaller patient populations, long expensive development and tech transfer cycles will be prohibitive to conduct.

Relationship between societal need and time to market.

Nowhere has this been more evident in the pharmaceutical response to the Covid-19 pandemic. The entire process including development, clinical trials, regulatory approval, and large-scale manufacturing was highly accelerated due to the number of lives being lost and the human efforts and perseverance to bring vaccines to market quickly. Future pandemics will require even faster time to market as expectations to quickly respond become more aggressive. Traditional human labor driven tech transfer effort will not scale for vaccines or for commercial drug products.

The Cost of Inefficient Tech Transfer

Bringing lifesaving therapies to patients faster is the goal of the industry. With that in mind, it's important for organizations to think of the drawbacks of inefficient tech transfer.

Extra Costs

Current tech transfer approaches also require a significant level of human capital, estimated at up to 20-30 resources per receiving site who are primarily focused on tech transfer.

Incomplete Knowledge Transfer

Since traditional tech transfer is largely a manual process involving countless documents, semi-structured, and unstructured data, incomplete knowledge transfer is a problem that often plagues the receiving organizations.

Reduced Revenue

One of the other negative impacts of the human centric approach to tech transfer and the extra time required is the impact on patent life and exclusivity. Depending on the market and governing regulatory agency, with the clock ticking immediately after approval, any delays in the ability to scale up manufacturing operations due to an extended tech transfer process will reduce the amount of time the company can market the drug before loss of patent protection and exclusivity. A delay of 6-months could potentially be worth hundreds of millions in lost revenue.

Data Integrity Impacts

Manual implementation of tech transfer can lead to inefficacies due to lack of resources and errors caused by the physical transcription of data into a system. Firstly, manual tech transfer is a strain on resources due to the human element of having to enter data. Humans are prone to error and manual tech transfer can lead to mis-entering of data.

For example, if there is an error in data entered and it flows into a machine or equipment that produces a product, there can be an impact on the integrity or quality of that product. Automated processes are more routine and consistent. An error made in an automated process would be present across the board and therefore more likely to be caught. These processes can then be adjusted, rerun and corrected.

Industry Factors Creating Challenges for Tech Transfer

In a conservative, risk averse, and highly regulated industry, like the pharmaceutical industry, with famously long product development cycles, innovators and manufacturers face mounting tech transfer challenges as the size and complexity of the value chain network continues to grow:

While it is generally acknowledged that much of drug discovery processes conducted by scientists in a lab is complicated work, the complexity of being able to scale up for clinical trials materials manufacturing and commercial manufacturing cannot be overlooked. There are many challenges with the traditional approach to tech transfer in either case.

Volume of Information. One of the most significant challenges is the large volume of knowledge that must be shared across multiple siloed organizations. The accumulation of data and documentation is substantial. For example, the Covid vaccine has 50,000 process steps from manufacturing mRNA to bulk drug substance. Also needed are Technology Transfer Plans, Analytical Methods, Assays, Sampling and Testing Methods, Manufacturing Batch Records, Critical Process Parameters, Bill of Process, Bill of Material, and more. All of this must be communicated between organizations and physically be transcribed into the appropriate systems, ultimately affecting data integrity.

Multiple Data Management Systems. This includes electronic lab notebooks, laboratory information management systems, product, quality, and regulatory management systems that are siloed and don't necessarily talk to one another.

The Human Element. There are manual processes for technology transfer that are time consuming and don't scale. Ultimately, under the traditional model of tech transfer, the challenges above have heavily relied on human capital to bridge the gap. Brute force with a large, expensive workforce has been the primary method of accomplishing this.

Plus, typos can occur, and values misread during transcription – all leading to costly mistakes and loss of data integrity. However, by leveraging current technologies there is a more sophisticated approach that can provide many positive benefits.

Non-linear scaling. Certain key process and critical process parameters (KPPs and CPPs) established in a laboratory environment and other production areas need to be adjusted to achieve consistent critical quality attributes (CQAs) at scale.

Unstructured Data. Traditionally, the shared data is unstructured, which means that the ability to use, leverage or repurpose the data in other necessary ways is very limited without a significant level of manual data entry. One example is the drug recipe, which includes more than simply the ingredients. The primary data domains include information about the Product, Packaging, Process and specifies raw materials, packaging, process phases, equipment, inspection plans, etc. However, when this data is initially captured, it is not managed in a format that allows for it to be read by other systems such as ERP, MES, batch systems, or quality management systems. There is also insufficient digitization from paper on glass scans that don't make all data elements extractable and reusable.

Consistency. Safety, Quality, Efficacy: Drug manufacturers are heavily focused on safety, quality, and efficacy due to regulatory mandates and requirements to ensure patient safety. The key to achieving this is by driving consistency throughout the process can be challenging when trying to replicate processes and results on different equipment and in different facilities while maintaining market specific regulatory compliance. Another related element is the challenge of replicating conditions across facilities to maintain consistency and meet steep compliance mandates on product quality and efficacy.

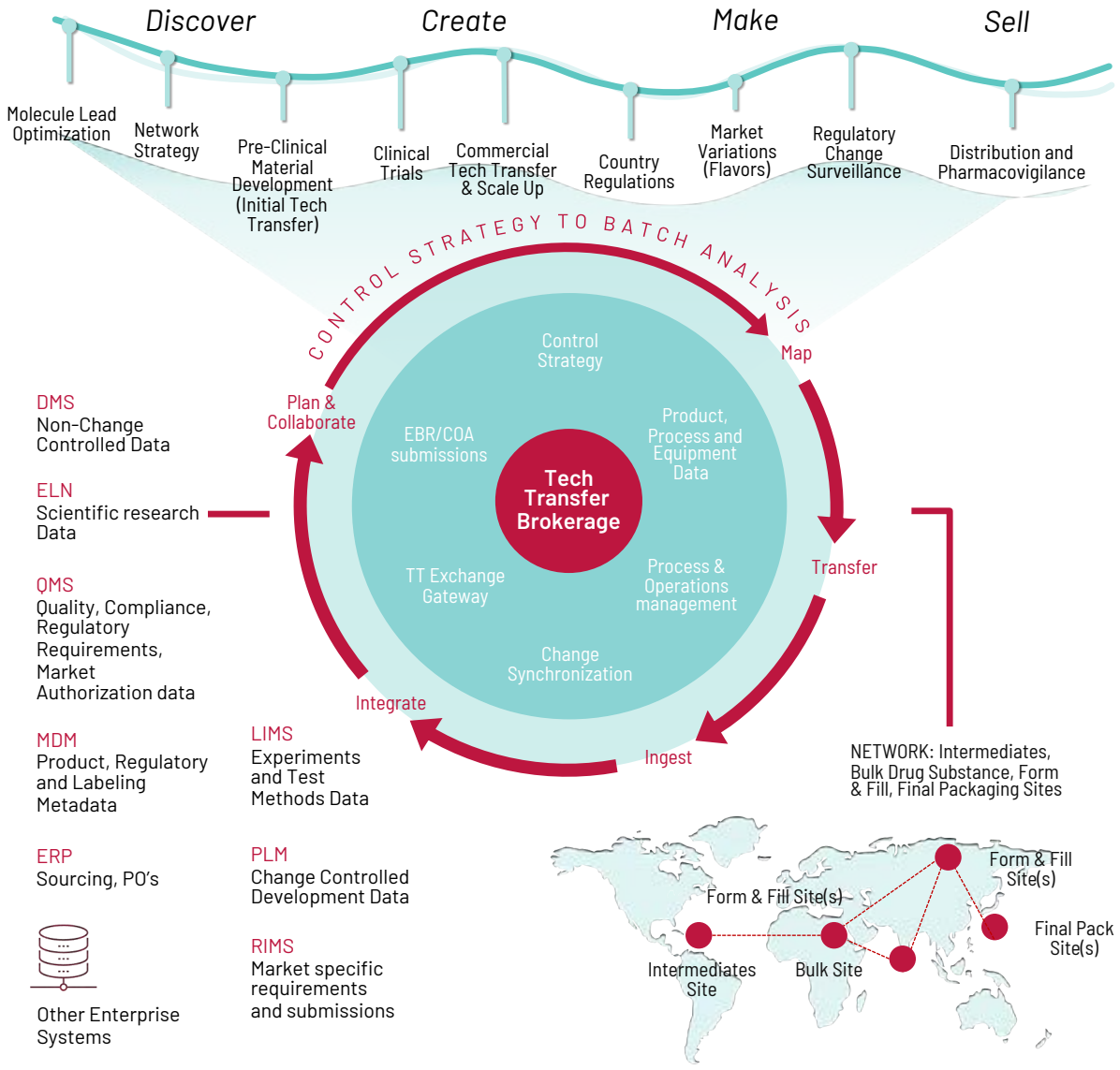
Disparate People and Systems. This large volume of information must also be shared amongst the various teams of scientists, chemists, process development engineers, – along with those in supply chain, manufacturing, quality, regulatory, and engineering. There is also documentation that must be shared between network partners including the CDMO's that will be manufacturing the drug. Generally, these teams are not working in integrated systems that allows for the easy flow and sharing of information. General recipes that were developed in a lab may need to be modified to run on equipment specific to the manufacturing facility. The complete site level drug substance and drug product recipe includes much more than the raw materials and process models; it has details on the API drug master files, packaging information, cleaning processes, and equipment process parameters. There may be different manufacturing facilities for different markets, each requiring a site-specific recipe. These variations can be challenging and complex to manage and are generally not shared between sites. It is common among many organizations to utilize multiple data management systems, including LIMS (Laboratory Information Management Systems), ELN (Electronic Lab Notebooks), PLM (Product Lifecycle Management), and others that are silos of information and do not natively interface with each other. Yet, there is a need to maintain, share and reuse information with stakeholders across extended, global value chains.

Ultimately, this all means there is not a single source of the truth from which to operate, which requires extra time and creates opportunities for mistakes to be made.

Tech Transfer and the Digital Thread

When data is transferred to manufacturing operations, they typically need to reverse engineer the information to feed the enterprise resource planning (ERP) or manufacturing execution system (MES) that operate on well-defined and structured digital data.

When we looked at that challenge with our clients, we thought there had to be a better way to leverage that data — digital or not — and convert it to a consistent format that can enable a continuous digital thread.



Different Pathways

There are two possibilities for how these challenges can be solved.

Fully Integrated PLM (Product Lifecycle Management) Solution

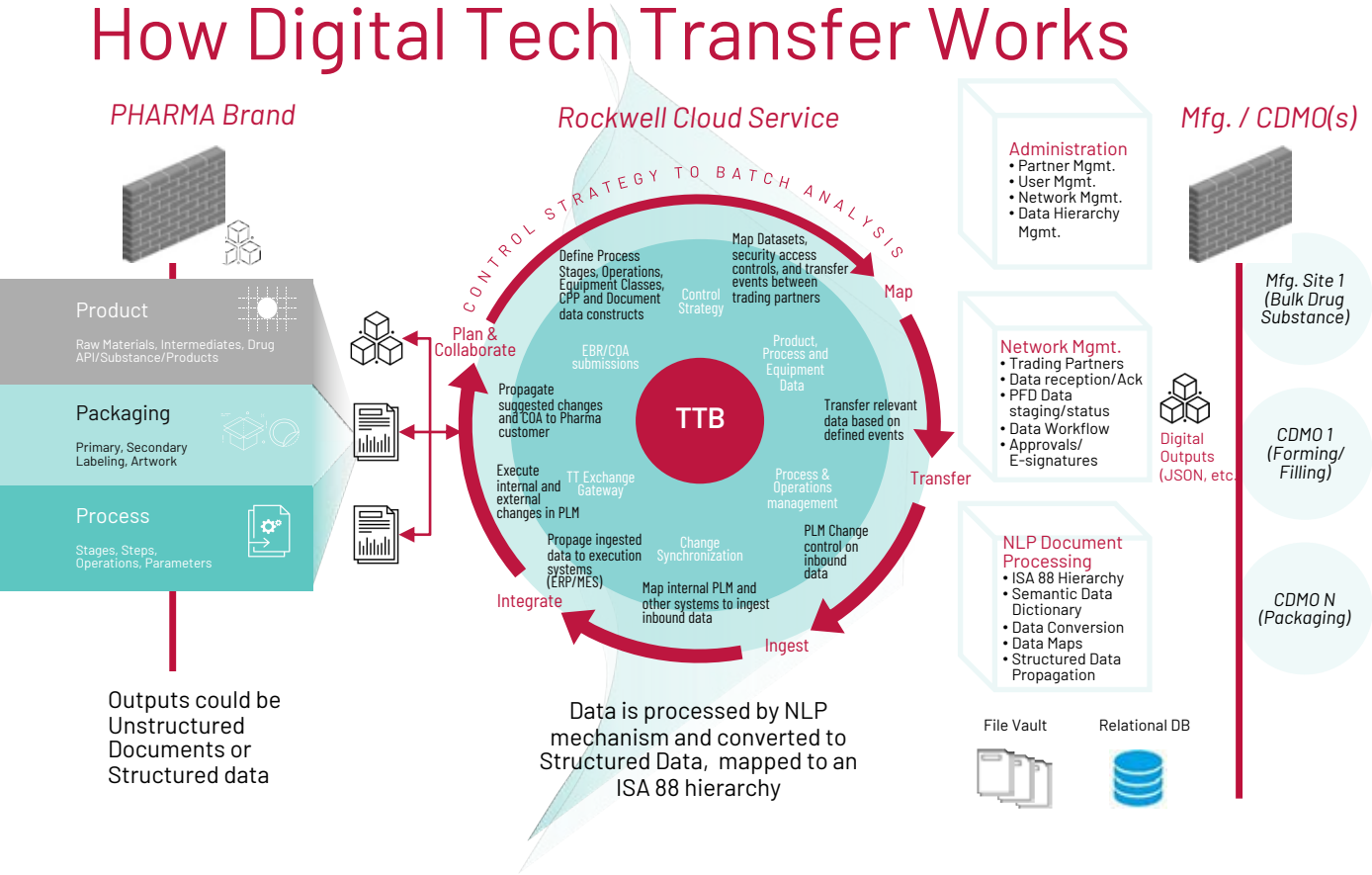
While an end-to-end, fully native digital approach that fully connects the enterprise with reusable digital product, process, and packaging data would be the preferred approach, this requires significant cultural change, potentially significant investments, and can take years for full rollout and cross-functional adoption.

Tech Transfer Cloud

This "leverage what you have" approach is more agile and utilizes a secure cloud-based infrastructure that establishes a digital data structure with accessibility to all collaborating organizations. This solution can be implemented without nearly the same level of capital investment and organizational change management required for a complete PLM system.

The system provides audit trail and traceability that can be used in regulatory filings. Digital Tech Transfer can also incorporate data from downstream manufacturing systems, such that electronic batch records (EBR's) and other records generated during production can be integrated back to retrospective Continued Process Verification (CPV) analytics processes.

How Digital Tech Transfer Works



The use case is as follows: A pharma innovator creates tech transfer documents detailing materials, manufacturing processes, testing, and quality requirements among other critical information to produce safe and efficacious drug products. Those documents are almost always delivered to manufacturing organizations in a "flat" format: usually in .PDF files or Word documents. Traditionally, those documents (once approved) would be copied and passed along several times until being translated into ISA 88-compliant recipe formats and delivered to a manufacturing plant, where it is implemented (with significant modification for variations and site-specific adjustments).

Using the digital tech transfer tool, documents are passed through several semantic natural language processing algorithms, marking sections both by keyword and meaning, and creating a fully digitized, disambiguated, searchable version of the documents. Tables are parsed, charts and graphs are preserved and tagged, and pages of text are organized by phase, stage, operation, sequence, and content into a cohesive digital format. Because of the nature of machine learning, all processed content of tech transfer documentation makes the algorithm smarter and more capable of parsing the next set of documentation more accurately. At this point, a uniform, fully compliant ISA 88 digital data package can be automatically generated. The original documents are preserved for traceability alongside the generated digital data in a "package," which can be propagated and reused effortlessly. Pharma brand intellectual property is secure in a database fully protected with access permissions at different levels customized by the owners of the IP.

Benefits to Digital Tech Transfer

- Reduced overall cost of internal and external transfers to manufacturing
- Increased labor efficiency of development, manufacturing, quality, and regulatory resources
- Improved speed to clinical trials and market authorizations (variations or flavors)
- Faster, more efficient process validation
- Reduced latency of facility, line and equipment provisioning and start-up
- Improved batch quality and reduced scrap and waste
- Faster regulatory submission and approvals
- Improved closed loop quality by design from development to manufacturing and regulatory
- Improved traceability into batch genealogy

How to Get Started

Organizations must first collect their tech transfer templates. This includes identifying templates for use authoring tech transfer files. An organization needs to understand what templates they have used over time and what variables are in them. There needs to be a clear understanding of how data elements in those templates map to the ISA 88 structure. This will help in implementation when you convert to a digital structure.

The digital transformation journey in life sciences requires a good deal of strategy and investment. Fortunately, life science enterprises don't have to start from scratch in charting that journey.

More and more companies are beginning to leverage the Pharma 4.0 framework and the benefits of digital technology transfer solutions to drive transformation toward reduced overall costs and increased efficiency of the entire pharmaceutical value chain.

The Future

Future capabilities look to add a brand-specific database of manufacturing partners and their capabilities, instantly matching the necessary processes in each innovation to plants that are already under contract with the pharma innovator, or even matching external partners when necessary. Pharma innovators will be able to grow and manage their network of contract development and manufacturing resources right in the tool and execute both internal and external capability-oriented facility fit analysis.

In the not-so-distant future we see AI preparing and negotiating much of this business-to-business commerce of intellectual property automatically. It could intelligently apply changes for the site-specific resources, constraints, and other requirements of a given location and optimize recipes based on continuous data feedback from the completed batches.

The future is exciting, but you can adopt the digital transfer tool now; leverage existing paper on glass document to start the journey towards leverageable and reusable digital data, and be on the forefront of network optimization, automation, facility fit analysis, pre tech transfer recipe editing and optimization, and machine learning as development progresses. The digital transfer tool will run in the background if needed, quietly digitizing your documents with daily-decreasing necessary supervision.

Employing this new Digital Transfer solution can help you digitize, secure, and introduce future-proofing technology today without disrupting (and even accelerating) current tech transfer workflows!

About Kalypso

Kalypso, a Rockwell Automation Business, helps clients fundamentally change the way they discover, create, make and sell products by powering innovation and autonomous operations with a digital value chain. From product ideation to production to the end customer, Kalypso provides professional services in strategy and change management, data science and artificial intelligence, enterprise technology, and managed services. Kalypsonians bring deep expertise in discrete, hybrid and process industries and serve clients around the world.

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