Panel discussion on...

SUPPLY CHAIN

PANEL ON SUPPLY CHAIN MANAGEMENT (SCM) IN CHEMICAL AND PHARMACEUTICAL INDUSTRIES

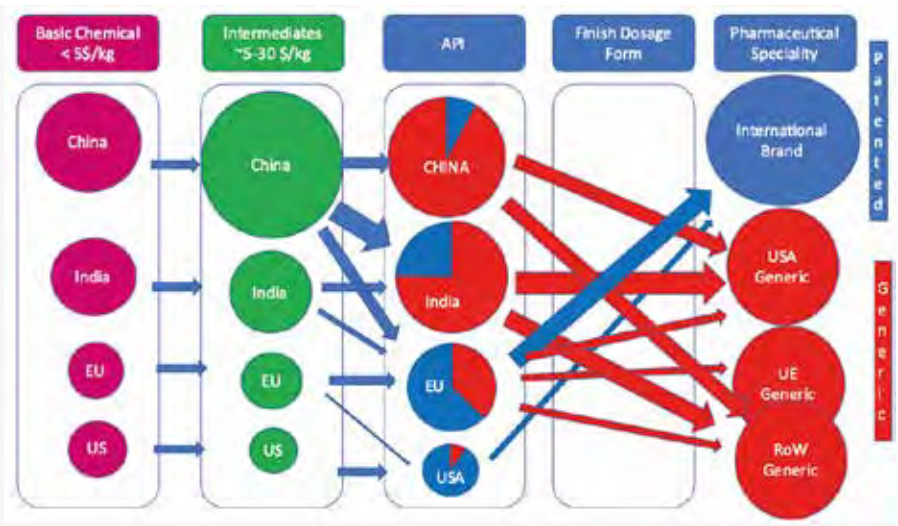
GLOBAL VALUE CHAIN SCHEMATIC DESCRIPTION

A few decades ago, the Western pharmaceutical industry started to outsource the chemical part of its value chain, namely the production of APIs and related intermediates, to local European CDMOs.

Over the past 25 years, due to cost pressures and the development of skills in the Asia-Pacific region (China and India), a large part of the pharmaceutical value chain has been outsourced.

First, the basic intermediates used to produce registered intermediates (GMP) were outsourced to regions with lower costs (lower social costs and wages, as well as less environmental constraints). This was mainly in Asia (India and China). Subsequently, some of these suppliers have successfully integrated into the downstream value chain, offering GMP intermediaries and final APIs. They were largely supported and trained by the big pharmaceutical companies. The latter have increased the intensity of competition among suppliers to obtain lower supply prices.

We propose a schematic qualitative view of the Supply Chain of Pharmaceuticals Figure 1.



Basis chemicals or commodities, like acids, bases, salts, solvents are produced on the locally due to high intercontinental costs of transportation. Upstream there are oil derivates which are globally traded.

Intermediates: China is the largest producer of intermediates for the pharmaceutical market. China supplies largely India as well as EU (and Israel).

Generic APIs

The larger producers of generic APIs are located in India. They receive a large part of the intermediates from China.
China does export generic APIs worldwide but supplies in priority its growing domestic market as well as the other fast-growing markets for low-cost drugs.
EU produces smaller volume / higher price generics for the global market. The APIs production is mainly based on intermediates from China.

Patented APIs (under exclusivity)

The intermediates for patented APIs which are mainly not commercially available, are produced by the API owner or outsourced to CDMO. In both cases the API owner fully controls the supply chain for strategic reason.
EU and US CDMOs are producing the patented APIs (there are few exceptions: First tier CDMOs in India, China or Korea produces under exclusivity for patented APIs).

RESPONSIBILITY OF THE CDMOS / APIS INDUSTRY IN THE MEDICINE SUPPLY

The world of APIs / CDMOs serving the pharmaceutical industry is acutely aware of its role in the continuity of drug supply to the patient. The awareness of its social responsibility towards the patient, beyond its direct customers, reinforces the absolute necessity of a robust supply chain.

In addition to the requirement for impeccable product quality (dictated by GMP rules), we observe that today, the need to deliver products within the agreed time frame reveals

MANAGEMENT

the famous QOTIF (Quality On Time In Full) index is generally chosen as a KPI by the industry to measure this performance.

The CDMO/API industry did not wait for the COVID 19 crisis to strengthen its supply chain. The COVID 19 crisis has just highlighted the absolute necessity to measure, continuously challenge and improve supply chain robustness.

Indeed, in the last half of the decade (2015 - 2019), the CDMO industry has seen a new trend:

- ✓ The pharmaceutical market expanded in volume mainly due the dramatic increase of population having access to medical treatment.
- ✓ In the meantime, the cost difference between western and eastern regions has been reduced due to higher wages and social protection in Asia and due to the improvement of the environmental constraints.
- ✓ China adopted an environment policy which created plan closures. Those have generated sudden and not anticipated disruption in the supply chain at many API suppliers of all regions in the world.
- ✓ The fret cost between EAST and WEST exploded (multiply by 6 in 2-year time!) due to high demand and shortage of containers and ships, which could occur potential delays.

The CDMO Supply Chain Management realizes, when it has not been already the case, that an excellent supply chain risk management system is a key pillar of its operation excellence and becomes a strategic and differentiating strength.

The need to develop a new tool beyond the usual QOTIF has become essential.

For this reason, I have developed "**A Handy Tool for Measuring, Analyzing and Reducing Supply Risk" (1).**

POST COVID 19 CHALLENGES?

Since the pandemic in China has been brought under control, the tension in the supply chain (except for biological products) is returning to a certain normality. Only the transportation of goods remains under stress.

Due to the high demand and the priority given to the production of COVID 19 vaccines, the production of biologics is under great pressure.

PANELISTS

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ANMING LIU
Vice President of Technical Operations at STA Pharmaceutical, a WuXi AppTec company (WuXi STA)

SAURABH GURNURKAR
Executive Director, UQUIFA

JOHANNES KANELLAKOPOULOS
Managing Director and Head of Marketing & Sales, CMT, WeylChem

BUT IS IT THE END OF THE STORY?

As I write this article, we are all very concerned about the situation in India where the expansion of a new variant of COVID 19 seems to be booming and out of control.

What could be the impact on the pharmaceutical industry's supply chain?

India produces a lot of generic APIs for the European Union and North America, and not only! India also produces "Finish Dosage Form" for the North American market (the European pharmaceutical industry has carefully kept most of its FDFs in Europe).

Will India, supported by its own vaccine industry and international solidarity, quickly stop the progression of the pandemic, as we all hope?

NEXT CHALLENGE?

We have seen that the API industry has a sense of social responsibility in delivering medicines to the patient. The most advanced players are taking the next step: limiting their environmental footprint.

After setting up a matrix to measure its footprint, the industry is developing ways of improving it by integrating into its manufacturing processes solvents and reagents made from renewable organic materials, derived from plant-based chemistry. This is a new challenge for quality assurance, R&D and procurement teams.

This is another story which I will not develop here.

Introduction to the **Panel on Supply Chain Management (SCM) in Chemical and Pharmaceutical industries**

With Chimica Oggi we asked a panel of key players in the pharmaceutical industry value chain to explain the role and challenges of the SUPPLY CHAIN. Reading the remarkably interesting testimonials, we realize that supply chain management plays the key role expected for the industry in providing the service the customer expects and, beyond that, in keeping the chain link as strong as possible, allowing patients to have continuous access to medicines.

Improving supply chain reliability begins with defining key performance indicators (KPIs) that assess supply chain risk and continues with action plans for continuous improvement.

In conclusion, I refer to one of our panelist who quoted Peter Drucker: "*if you can't measure you can't improve it*" !

REFERENCES AND NOTES

1. X. Jeanjean, Chimica Oggi – Chemistry Today, 39 (2), 58-61 (2021).

XAVIER JEANJEAN
J2X Consulting, France

Xavier Jeanjean *is owner and president of J2X Consulting. J2X Consulting is a providing support in sales, marketing, sourcing and management to Fine chemical organizations and CDMOs. Xavier Jeanjean is graduate in Organic Chemistry (ESCOM Paris, F) and Process engineering (UTC Compiegne, F) and in strategic management (IFG, Paris) . He spent more than 30 years in sales and marketing executive positions in the fine chemical industry and CDMO's (CU Chemie Uetikon-SEQENS, ISOCHEM, etc...)*

blocks. Also, major quality concerns raised on some Indian supply sites impacted on supplies of intermediates and API arriving in Europe and the US.
SK pharmteco began looking to move key raw material sourcing to company's outside China. We also have in place stringent auditing, business vetting, and contingency planning for catastrophic events and have expanded our own internal audit function to look beyond the typical quality manufacturing attributes. We began looking closely at business continuity as well as SH&E soundness, both within a particular company as well as its surrounding area. This allowed us to align with companies that we felt were in it for the long haul and could sustain all types of regulatory scrutiny.

This response, we believe, has the potential to act as a sustainable differentiator going forward. The ability to not only provide, secure, reliable supply of products when there are challenging environmental factors but also to respond to volatile demand cycles is now something that many customers increasingly place direct tangible value in. There appears a real openness to discuss a premium for such enhanced security and/or actions to place a greater proportion of overall demand with companies that provide this extra guarantee.

We believe that this may become an inflection point for SCM and may accelerate the emerging trend towards the development of true partnerships between suppliers and customers.

ANMING LIU **PhD**
Vice President of Technical Operations at STA Pharmaceutical, a WuXi AppTec company (WuXi STA)

Could you define your major business segments? By which main Key Factors of success are they driven?
WuXi STA is a leading integrated drug substance and drug product CDMO. We focus on partnering with innovators of novel therapeutics of small-molecule, peptide, and oligonucleotide modalities. Our facilities in China, the USA, and soon Europe, support the global launch of new drugs. The key to our success is empowering our partners to reach patients faster through efficient, flexible, and high-quality solutions.

Is Supply Chain Management a Key pillar of the strategical approach of your company? Please explain
Yes, a solid supply chain is an imperative of our global platform. In order to ensure on-time delivery to our partners, we have a business continuity plan. We are constantly evaluating our suppliers and our systems to stay ahead of potential shortages. We monitor the quality of our suppliers and rate them according to risk. We track first, secondary, and even tertiary suppliers according to quality and reliability. As our business continuity plan stipulates, we maintain a minimum stock of essential reagents. Our logistics department is in constant communication with our shipping partners and brokers to estimate lead times to enable on-time delivery between China, the US, and the rest of the world.

Do you consider that the exposure to the risk is the same for all the steps of the value chain? Basic Chemicals, intermediates, API Small molecules and large molecules, Finish Drug Formulation (FDF)
Yes, all the steps of the value chain would face the risk to disruptions like the COVID pandemic in 2020.

Which are the most recent innovations/trends impacting the Supply Chain Management within the chemical and pharmaceutical industries?
Our green chemistry technologies including continuous processing (flow chemistry) and biocatalysis have proven to be resilient technologies bolstering supply chain security. For example with a few of our Continuous processing programs when the cost of reagents or catalyst increased due to supply bottleneck we have found opportunities to reduce the required quantity or an option to use lower-cost alternatives to replace expensive ones, mainly due to a new process window we can access using flow chemistry.

In the case of biocatalysis projects, we had similar constraints with the purchasing of enzymes from suppliers. The enzyme bottlenecks have been an ongoing supply chain concern for which we established internal enzyme evolution capability and increased our fermentation capacity. We now have developed over 20 enzymes and 70 thousand mutations in-house covering 18 reaction types. Our fermentation capacity now includes large-scale 500L and 1,000L fermenters, supporting 50 tons of commercial APIs and intermediates manufacturing annually.

WuXi STA has been implementing these green chemistry technologies for years. The supply chain security advantages realized with the acquired sustainability, including reduced environmental impact and lower raw material risk (access and cost) are just a few of the benefits.

For you, which Key Performance Indicator (KPI) is measuring the Risk of the supply Chain? Do you follow it on a regular basis? Which kind of actions are you implementing to improve it?
Maintaining reliable suppliers is key to the continued success of our business. We develop strong relationships with our suppliers with frequent communications and exchange of information to monitor exogenous situations such as natural disasters and political disruptions. It is important to measure the risk of the supply chain on a regular basis. The evaluation of raw material suppliers is based on several different dimensions (like their geographical location, profile, market dynamics, material risk levels, technical capability, etc.). For raw materials rated as high risk, we will take actions to mitigate the risk by developing second and third suppliers or scout new processes with less reliance on risky components.

How has the COVID pandemic impacted your Supply Chain? Have you experienced raw material breakdowns during 2020? In which step of the supply chain especially (basic chemicals, intermediates, APIs, FDF)?

Right after the COVID-19 outbreak, WuXi STA activated a strong business continuity plan and effective communication to our suppliers and customers to ensure the safety of our operations and continued quality service to our customers. Together we quickly returned to normal operations and in fact, 95% of the raw materials were delivered on time during the lockdown due to effective planning through our multiple basic chemical sourcing strategies. We minimized project delays due to COVID through proactive planning, working overtime, and taking shifts.

Strategically, we have built our capabilities vertically to cover the entire new drug development and manufacturing supply chain including raw material, intermediates, API until final dosage forms to prevent disruptions. Our four centralized facilities in China for both drug substance and drug product in Shanghai, Jinshan, Changzhou, and Wuxi with the same process, equipment, and quality system provided a robust supply to our customers through our multi-site strategy.

Have you adapted your supply chain management strategy? in which way?

Yes, due to the outbreak of the COVID-19 pandemic, we adjusted our mitigation plan to forecast the impact of supply chain shortages by accelerating the development of alternative suppliers and increasing safety stocks of key raw materials, etc. We also qualified internal sites for producing certain key raw materials as a backup supplier. Our four facilities in China are within driving distance of each other, which allows for a great deal of flexibility in storing and sharing raw materials. We follow the same quality system among all sites and increased our stock and inventory visibility across sites to enable flexible and fast reaction to potential supply chain risks.

SAURABH GURNURKAR
Executive Director
UQUIFA

Could you define your major business segments? By which main Key Factors of success are they driven?

The UQUIFA Group is a Barcelona headquartered manufacturer of Active Pharmaceutical Ingredients with cGMP sites in Spain, Mexico and Hungary. We are now increasingly focused on the CDMO sector which contributes to nearly 50% of our sales; in this segment we are providing development services and manufacturing capabilities to the Innovator segment of the global pharma sector. The US, EU and Japan are key markets for us where we sell close to 70% of our products, by value. We are a multi-product business making 40-45 distinct APIs every month across our network of sites and count our global team of 800 plus colleagues as a key factor in our development. The UQUIFA Group also has its Own Portfolio of APIs which has been its traditional business served largely out of a site both in Spain and Mexico. The enhancement of our technology tool-box through the acquisition of Soneas, our Hungarian business in 2018 has broadened our offerings of services and products to the global customer base. In summary, focus on our 3P´s – Products, People and our Plants has been the bedrock of the Group´s evolution in the recent past.

Is Supply Chain Management a Key pillar of the strategical approach of your company? Please explain

Yes, we believe supply chain management is a key driver of customer satisfaction as well operational efficiency. Over the last 5 years, we have consciously tried to mitigate the risks of both supplier as well geographical concentration of our supply chains. The events of last 15 months (COVID, weather related events) have amplified the need to have always near-shore options too for critical raw materials, in addition to the traditional approach of securing solvents. Given that we are focused on the regulated markets of the pharma industry, qualification of new vendors for KSMs/Advanced Intermediates takes time but as a company we have invested resources towards this – vendor selection, supplier audits, documentation support- these are all key in the process of having a diverse and risk-managed supply chain. In our view, it is key to find a balance between driving for efficient costs of procurement and at same time have a stability of supply. Another point is – as a group, we have also adopted Good Distribution Practices (GDP) when it comes to storage, transport and dissemination of our products further down the pharma industry value chain. We believe each of these are important for SCM to become a business differentiator.

Could the SCM become an element of differentiation? Does it create customer Value? how do you monetize it?

We have a strong history of working with our partners to share information including our risk assessment and mitigation plan on raw material suppliers in our supply chain. For some high value, large volume projects we have developed new processes to avoid or reduce quantities of raw materials deemed risky. By sharing our business continuity plan and the progress with our partners, we enhance their confidence in our on-time delivery, thereby improving collaboration for both parties' benefits.

Do you consider that the exposure to the risk is the same for all the steps of the value chain? Basic Chemicals, intermediates, API Small molecules and large molecules, Finish Drug Formulation (FDF)

We are a manufacturer of APIs and in some cases, advanced intermediates. From what we have seen first- hand, over the last 18-24 months, the supply and price volatility has been across both intermediates as well basic chemicals – ostensibly for different reasons. While intermediate supply from Asia has seen impacts due to environment issues driving closure of industrial sites, then COVID related disruptions of supply, now things do appear more stable. However the costs of transport have been fluctuating too which does impact our fully landed costs of procurement. We traditionally have procured basic chemicals /solvents locally- last few months have seen outages due to weather events, alternate applications etc.