

Achieving Visibility in a Pharmaceutical Supply Chain



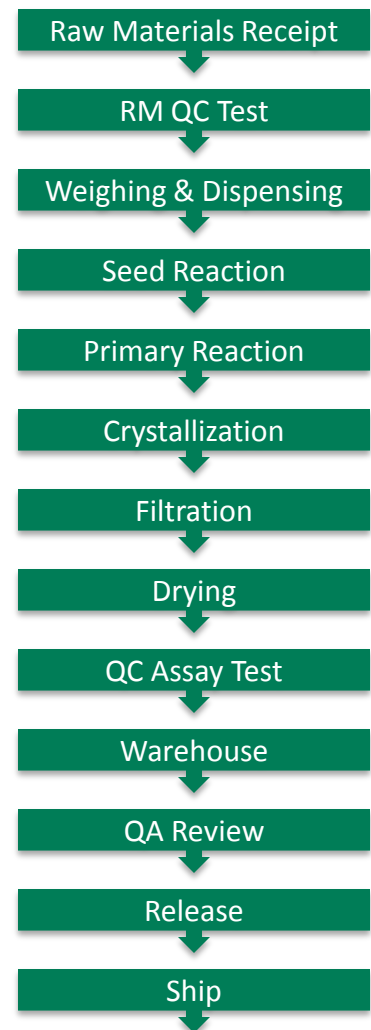
By TC Baker, Vice President, Industry Solutions, WAM Systems

“In my consulting work with customers I often hear Supply Chain Directors complain of a lack of visibility. Despite the proliferation of systems like ERP, MES, LIMS, TMS, WMS, CRM and others, it’s still hard for many to have visibility into fairly basic things like: Do I have enough tested raw materials? What orders are at risk of being late? Will we release enough batches this month to meet the corporate plan? Can I afford to make some clinical or qualification batches next week without disrupting commercial orders?”

What is it about a pharmaceutical supply chain that makes it so hard to answer questions like raw materials testing, order fulfillment and batch production? It is hard and dangerous to generalize but consider a process model that flows like the sequence shown to the right.

Any APICS certified industrial engineer or six-sigma black belt with a stopwatch can measure how long each of the above steps takes and create a spreadsheet for estimating the cycle time for a given product. In fact, a few senior executives claim that "our business is simple; we don't need any sophisticated software to model it". Where it starts to get complicated is the addition of the dreaded details.

First, the above processes are rarely all managed under one roof. At a minimum, production operations, QC/Lab, and QA/ Compliance all have their own organizational silos and management chains. As much as new management tries to morph into matrices and lattices and other ways of encouraging intradepartmental cooperation and communication, at the end of the day, each is accountable for their own area's performance and therefore wants to be in control of their own resources. This leads to islands of decision-making and a fragmentation of the internal supply chain. It gets more challenging when certain functions are outsourced, when the process spans multiple plant sites and world regions.



This used to be referred to as 'black holes' in the supply chain, i.e., material flows through manufacturing where it remains reasonably visible to the local production supervisor or scheduler until it goes to the QC/Lab where from an operations perspective, it disappears into a black hole. A QC/Lab supervisor, also sympathetic to the visibility thing, once pointed out that while the production folks may not know when a sample will come back from the lab, it almost always will come back so it is not fair to call it a black hole (things do not normally come back out of a black hole). So adjust the description to refer to this as "blackness".

It is a blind spot in the material flow to a production person. But in the spirit of fairness, the same blackness goes in the other directions. The QC/Lab gets paged to take a dryer sample at 4:00 am and has to get someone out of bed to do it, and they had no visibility that request was coming (hopefully there is a Starbucks on the way to the plant). So it all depends on job function and which spreadsheet is being referenced.

Second, what about making more than one product and sharing resources at different levels? Imagine that different products have different recipes with the possibility of different combinations of equipment being qualified to produce the same validated finished good. Now there is a resource contention issue and a possible sequencing problem. The need exists to account for clean-in-place (CIP), sterilize-in-place (SIP) for the basic between-batch transitions as well as considering the potential to optimize for campaigning of like-processes together, e.g. maybe some recipes need the reactor to be set up with a heater jacket, etc.

Perhaps different validated batch sizes can be used depending on the demand levels. If the demand is volatile (and it usually is), the potential exists for moving bottlenecks in the plant. Being able to measure the process for a single set of conditions sounded

straightforward. When starting to layer in more possible variations, it gets harder to have predictability without a good simulation engine that understands finite capacity, sequence dependencies, resource consumption, etc. Having more choices or degrees of freedom is good from an operational flexibility perspective, as long as it is possible to manage the complexity.

Waging War Against Complexity

Because there seems to be enough complexity to go around, many big pharma companies design their plants to be 'focused factories', i.e. build a plant, or a building on a campus and dedicate it to making one and only one thing. This follows logically from the way clinical product used to be developed. If a researcher succeeds to the point of filing an initial new drug discovery form (IND) with the regulatory board (FDA) for moving a new chemical entity in clinical trial, the management has committed to spending roughly \$500 million and up to 15 years to commercialize a product and bring it to market.

In that context, the time and cost to construct a building and put some reactors in it seems like a pittance. But recognize that dedicating equipment to a specific purpose in order to simplify operations and make it easier to manage is like sacrificing supply chain agility on the altar of simplification. In doing so, artificial constraints are imposed for the sake of simplification. As an aside, most process development guys are also excellent brew masters and make outstanding stout, ale, lagers, or just about any style or flavor of beer imaginable. So if diversity is the spice of life then the ability to manage diversity and complexity is a key ingredient in supply chain agility.

The old timelines are contracting and big pharma is being forced to innovate faster. Instead of building dedicated pilot plants, researchers are being told to borrow time on the commercial production assets. Between the time-to-market opportunity cost, patent expiration window, and the increasingly significant working capital cost considerations, pharmaceutical companies are being driven towards operational excellence and better supply chain planning practices.

This represents a challenge for the design engineers. A host of old and new technologies are available to attack the challenges of new product introduction, recipe design and scale-up from lab to production settings, and even the broader context of product lifecycle management. While really good at configuring equipment trains and managing recipe data, the limiting issue that all of these tools face is their 'push' view of the supply chain. In the recipe or design tool users can visualize how many batches of gagaprin-euphoriton-X could be made using a certain batch train configuration.

What users cannot visualize is what the cycle time and total monthly production might be for a given product mix if some of the reactors are shared, i.e., under changing demand scenarios, effective capacity varies and these tools don't help users see that. As innovation cycles get compressed, as supply chains get leaner, there is a heightened need for enterprise collaboration, especially between production planners and new product introduction.

Design for Change

Extending the tangential discussion on process design and new product introduction, by the time a NCE is being scaled up for commercial production, there are decisions to be made about how to validate the production process. An emerging theme is the greening of the supply chain and designing for sustainability. On the subject of degrees of freedom in the supply

chain, design engineers should also consider the lifecycle of the products they are introducing and think about what size batches they will need and what combinations of equipment will be required to support clinical material supply, pre-launch inventory build, commercial under-patent production, post-patent competition with generics, and product decline/cannibalization. This means collaboration with supply chain planning during design. Due to the high cost of change once validation is complete, it is so much easier to validate a few more options during initial design. This adds a few degrees of freedom to the manufacturing operation in exchange for a negligible upfront cost during validation.

Switching on the Lights

Getting back to the original questions regarding visibility, what are the requirements? How is the right kind of visibility created to project the timing of future batch releases given the variability of the supply chain? A simulation engine is required which understands the capabilities of the equipment and the validated processes and where they can be run. But to see the whole process, visibility is needed into the QC/Lab and QC/Compliance areas since these can be a big contributor to material idle time (aka 'muda' in lean-speak). Again in the spirit of fairness, it is not that the lab folks are evil or anti-supply chain, it's because the approach to management historically has fragmented the material flow governance.



How is visibility to the lab possible? From a systems perspective, there are laboratory information management systems (LIMS) that provide a range of functionality from basic electronic note keeping to expediting the review process to sophisticated integration with lab equipment to automated tracking, testing, and sample handling. But what do these systems know about the production schedule? About batch release due dates? About that brand manager from corporate that keeps calling daily? Sadly, back to that silo fragmentation issue, the answer is: not much. LIMS systems were designed just for the needs of the lab. They expedite the compliance review process and can cut paper work and lab cycle time, but they do not know much about finite capacity planning or scheduling.

What about MES (Manufacturing Execution Systems)? They are designed to model the manufacturing process in excruciating detail, support electronic batch records, facilitate validated compliance with regulations like CFR 21 part 11, integrate with electronically capable equipment like digital scales, flow meters, PLCs, SCADA and the like. Is it possible to use an MES to essentially model the lab? In short, yes, and in some medical device manufacturing processes, people have done just that. However in processes that are making or formulating and dosing API's the LIMS packages provide specialized capabilities for integration with chromatography and process equipment that make their requirements unique. Nevertheless, an installed MES is a great data source for understanding where in the manufacturing train a given batch or lot number resides at a given moment. Yet the MES view of the supply chain world is a 'work order' and usually has no connection to a forecast, customer order, or any kind of corporate plan.

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Approaching the IT department and saying "I need a tool for matching supply and demand, projecting inventories, planning raw material requirements" will probably yield an explanation like "Corporate IT bought a global license for SAP Oracle JDE PeopleSoft and are in the midst of rolling it out, a legion of consultants is scheduled to visit in the year 2013". Or, "Yes we know your functional requirements and they will be met in the next release (also coming out in the year 2013)". Unfortunately, if the corporate IT group has the business by the jugular there is not much that can be done. The best advice is to make like a hummingbird and fly under the radar, flit around to local management and see if dispensation is possible to do something on a more local basis.

Event Simulation

There are a host of best-of-breed solutions on the market that can model a pharmaceutical process from a supply chain planning and scheduling perspective. Many of them are extensible and configurable enough to cover the range of events from raw material procurement through production to shipping and distribution. There are a couple of ways of modeling the fact that the lab and compliance areas are a required step in the material flow, either explicitly as an activity that can be separately manipulated, or implicitly with leadtime.

There are pros and cons to each. Depending on the capabilities of the tool, one of the cons of explicitly modeling the lab activities is possibility of creating busy work for the scheduler(s) to keep the timing of those activities aligned with production activities as things move around. Scheduling is about managing change and avoiding the trap of managing too much detail too far into the future because at some point it's like building a sand castle when the tide is coming in.

Implicitly modeling the lab events is a good starting point because a) it's probably better than anything done so far and incremental improvement is low risk, b) the lab cycle time data is probably approximate at best, and c) this sets up an environment for incremental improvement (kaizen) - monitor the theoretical or plan lead-time through the lab versus actual and revise while learning more about various details. Depending on the data structure options provided by a company's best-of-breed scheduling software provider, this could be handled as part of a bill of materials, routing, bill of resources, formulation, recipe, etc.

What's the Value?

Like most things, it depends. For those struggling with lab cycle time issues, a framework for collaboration between lab requirements and production requirements can help shrink overall make span or cycle time from raw material to finished product release. The finance people can help calculate the value of one day of cycle time recovered from a working capital perspective (usually in six digits), and then there is the time-to-market perspective.

In the absence of good visibility, there is a tendency to over produce some products thereby contributing to excess inventory while under-producing others and thereby contributing to expediting costs. If the connection between demand and supply is very weak, there is the possibility of facing expiration and product obsolescence risk.

Generic producers and contract manufacturers face many of the same pressures of other cost-and-time driven supply chains like in chemicals and high-tech. Banner Pharmacaps, Inc. is a specialty contract manufacturer that is working to shrink cycle time by increasing visibility and alignment between production operations and QC/Lab activities in order to increase throughput. Since a significant portion of their supply chain involves adding value to API's

produced by big pharma companies, they have even more pressure to understand the status of inbound materials from customers so they can have their value-add completed and tested fast and return that enhanced material to the customer.



Benchmarking Surveys

Companies analyzing the potential improvement from increased visibility and control over their supply chain may want to consider engaging in an outside-in review of their workflows, processes and supporting technologies. WAM Systems conducts ongoing benchmarking surveys with process companies throughout the world in an effort to assess the overall maturity of industry supply chain practices. The purpose of the surveys is to help companies compare their supply chain process maturity with that of their industry peers. Each survey includes a telephone interview and confidential summary report.

To participate in these surveys, please visit www.wamsystems.com

About WAM Systems

WAM Systems, Inc. delivers advanced supply chain planning solutions designed for the process industry.

WAM's Picaso™ solution is used throughout the global process industry, providing a broad set of visualization, decision support, and optimization tools that address the unique challenges found in managing complex supply chains.

Picaso solutions address a wide range of business processes including collaborative demand management, inventory and distribution optimization, production planning and scheduling, and procurement planning.

The company and its worldwide partners also provide a full range of consulting, support, training and implementation services.

Headquartered outside of Philadelphia, WAM's customers include Banner Pharmacaps, Pfizer, Basell, Celanese, Eastman, Equistar, Honam, Lanxess, Lyondell and Solvay.



WAM Systems – North America

Corporate Headquarters

600 West Germantown Pike

Suite 230

Plymouth Meeting, PA 19462

Phone +1.800.358.8305

Fax 484.530.4854

Email info@wamsystems.com

Web www.wamsystems.com

WAM Systems – South America

Av Nações Unidas, 12551

9th and 17th floors

CEP 04578-903 - São Paulo

SP - Brazil

Phone +55.11.3443.7732

WAM Systems - Asia

80 Raffles Place

Level 35 UOB Plaza 1

Singapore 048624

Phone +65.6248.4772

WAM Systems – Europe

Gustav-Stresemann-Ring 1

65189 Wiesbaden

Germany

Phone +49 (0)611.97774.410

Email eu@wamsystems.com