Harnessing the Real Capacity Potential of Pharma Manufacturing with SmartFactory Rx® Smart Scheduling

White Paper

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Introduction

Production planning optimization has become a critical driver for pharmaceutical manufacturers to gain operational excellence. When starting their journey toward advanced digital manufacturing capabilities, manufacturers first look at return on investment (ROI) on their technology. This is not an easy question to quantify and analyze.

Pharma manufacturing is a highly complex environment. High product variability, facility layout and process route complexity, product requirements, and other challenges like debottlenecking and standardization needs are only part of the complexity drivers. Based on several aspects of their internal and external environments, pharma industries can be classified in four major categories, as shown in Figure 1. The impact of ever-increasing environment needs is often an exponential growth in variability and complexity that results in rising fulfilment costs and poor utilization of human and equipment resources.

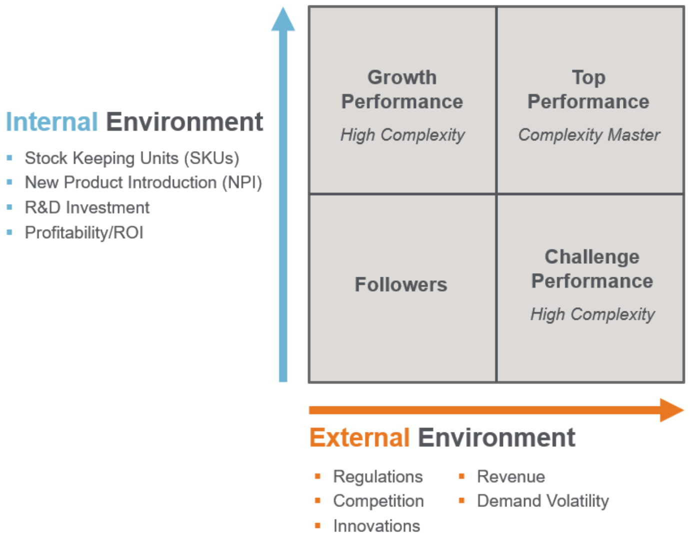

Figure 1. Complexity level for production planning

Several operational advantages exist when implementing simplistic empirical rule-based scheduling systems, including improved visibility, enhanced data sharing, and better process and planner efficiency. The real ROI, however, lies in the production facility’s main key performance indicators (KPIs), such as increased throughput and production capacity, cost savings, meeting demand, shorter cycle times, enhanced equipment and human resource utilization, and more.

To effectively meet these KPIs in this complex manufacturing environment, an advanced simulation and optimization engine is essential to solve the resulting optimization decision-making problems. The significance of advanced simulation and optimization capabilities to solve scheduling, planning, and other production challenges is becoming increasingly important and almost inevitable, especially in this era of digital transformation. These technologies allow pharma manufacturers to efficiently set their goals and get quantified results in a few minutes. Efficient facilities with successful capacity maximization and bottleneck alleviation can be achieved when implementing technologies like short-term scheduling, tactical production planning, and strategic capacity management into daily operations.

Simulation and Optimization-based Tools: Purpose and Value

To highlight the value of implementing these technologies, this paper discusses the impact of advanced optimization and simulation on pharma manufacturing production planning challenges. We compare some typical "gold standard" methods used in the industry with our advanced simulation and optimization-based tool, SmartFactory Rx (SFRx) Smart Scheduling. We show with actual scenario runs how SFRx Smart Scheduling offers an ideal optimization-based tool that can easily create optimal production plans that fully take advantage of the production capacity of pharma manufacturing sites. The results show that SFRx Smart Scheduling optimizes the use of major assets and other resources to satisfy clinical and R&D production targets, and it can result in considerable KPI improvements—an average of **30%** (even more than 50% in some cases).

Production Planning in Pharma: An Overview

The Association for Supply Chain Management defines *planning* as "the process of setting goals for the organization and choosing various ways to use the organization's resources to achieve those goals." *Schedule* is defined as "a timetable for planned occurrences." Without effective production planning, manufacturing facilities are unable to schedule their production processes to meet their goals, which limits the entire production output. Late or missed orders, unhappy customers, high production costs, lower revenue, and lost business are some of the potential outcomes.

Within pharma manufacturing facilities, enterprise resource planning (ERP) systems, Excel spreadsheets, and simplistic rule-based scheduling algorithms are some of the most common or traditional approaches for management and planning. These methods provide mainly visualization, data sharing, and slow, static, and simplistic plans. To respond to changes in customer demand, react to conditions in a complex production environment, and maximize capacity usage, pharma manufacturers must use production plans derived by optimization-based tools.

Furthermore, in pharma manufacturing facilities, production planning results in a complex, optimization decision-making problem that consists of thousands of constraints and decision variables. In short, a representative planning problem considers:

- **A planning time horizon** divided into time periods of specified length
- **Products** with **demands** in terms of **orders (or campaigns)** with known **priorities**, **quantities**, **earliest start dates**, **due-dates**, and **drop-dead dates** along the planning horizon of interest
- **Production routes**: each product follows a known **multi-step production process** where each **step corresponds** to a given major unit operation
- **Time-links** between consecutive steps of the production routes (for example, some steps need to take place in the same or consecutive period—that is, with acceptable waiting times between steps)
- **Equipment and human resources** with known:
    - **availability** per time period for each equipment and human resource
    - **predictive maintenance** periods for equipment resources
- **Bill of materials**
- **Priority-dependent** costs for inventories and backlogs, as well as unsatisfied demands

The **drop-dead date** for an order is the last possible date on which the order must complete (that is, the order production after this date is not acceptable). In the pharma industry, drop-dead dates typically reflect material expiration dates, related factory operations, contractual agreements with clients, development plans, and so forth. In general, two order satisfaction policies exist for orders with drop-dead dates: Full order Satisfaction (FoS) and Partial order Satisfaction (PoS). In FoS, manufacturers must complete the full order before the drop-dead date; otherwise, the order isn't produced at all. This is an all-or-nothing, hit-or-miss binary policy. In contrast, with the PoS policy, manufacturers aim to complete as much of the order as possible before its drop-dead date, allowing for partial satisfaction of the order. This is a *better-something-than-nothing* policy.

Typical Planning Approaches

Pharma companies and scheduling/planning systems providers usually use a simplistic approach. For our comparison we use a typical empirical production planning approach that creates a production plan by following a production sequence rule. This rule prioritizes product orders according to earliest due-date → highest priority → largest size. This means that orders with earlier due-dates will be produced before orders with later due dates. Also, if two orders have the same due-date, then the order of higher priority of the two is prioritized. Now, if two orders have the same due-date and priority, then the largest-size order must be produced first. Based on the drop-dead date policy employed, we consider two different versions of this traditional rule-based production planning approach: H-FoS for the FoS policy and H-PoS for the PoS policy (H=hit-or-miss).

The SFRx Smart Scheduling Advanced Planning Approach

We have developed and used a discrete-time pharma manufacturing capacity model. For each time period on the overall planning horizon, the model considers all the features described previously and provides optimal decisions with respect to:

- Campaign building to **satisfy product orders**
- **Asset utilization** or allocating campaign production steps to equipment resources
- **Human resource utilization** or allocating campaign production steps to human resources
- **Material utilization** according to the bill of materials
- **Inventories** for final products
- **Backlogs** for final products
- **Unsatisfied** demand/orders

As shown in Figure 2, the main KPIs for this pharma planning problem are meeting the demand for products in time according to order priorities (that is, minimizing backlog), minimizing the total inventory for final products, and minimizing unsatisfied demand for orders missed.

Figure 2. KPIs for the pharma manufacturing planning problem

Case Study: Traditional Rule-Based vs Optimized SFRx Smart Scheduling Production Plans

To demonstrate the benefits and competitive advantage that SFRx Smart Scheduling offers pharma manufacturing facilities, we compare SFRx Smart Scheduling with the traditional rule-based production approaches described previously.

The production planning problem of this case study considers:

- **Single shift** mode for a “five days a week” pharma manufacturing facility
- **5 weeks planning horizon** divided in weekly time periods
- **7 pharmaceutical products** (A–G) following an **8-step production route** shown in Figure 3.
    - D and F are R&D products, and the rest are clinical products. Clinical products are of higher priority than R&D products
    - Product priority is as follows: Highest (A, E), High (B, C, G), Medium (D), and Low (F)
- **Orders for 19 products** shown in Figure 4 with different drop-dead dates
- **11 equipment resources**: one equipment per unit operation, except for granulation, tablet pressing, and coating for which two available equipment resources are available for each
    - Each unit operation processing step involves a setup and a run stage. The durations of these stages depend on the unit operation.
    - Setup and run stages of a unit operation processing step must take place in the same time period.
- **Time-links**: a processing step in a production route must take place in the same or next time period from the time that the previous step completes
- **Bill of materials** to produce each product
- Given **priority-dependent costs** for inventories and backlogs and unsatisfied demands
- Two types of products: clinical and R&D (or development)

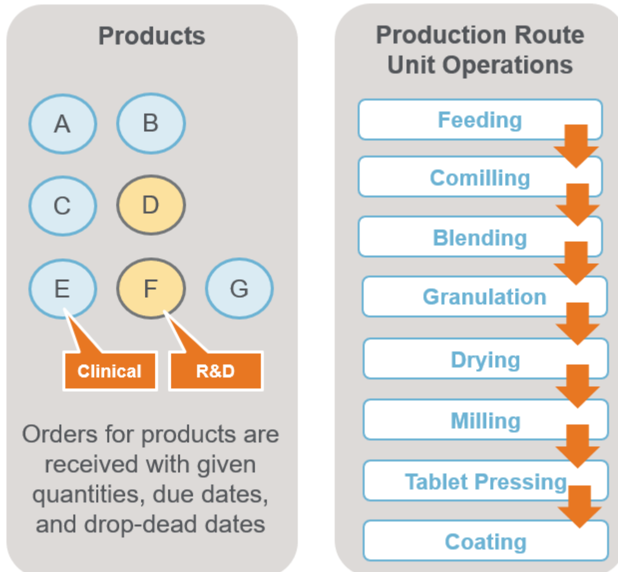

Figure 3. Product types and the production route used as a sequence of unit operation steps

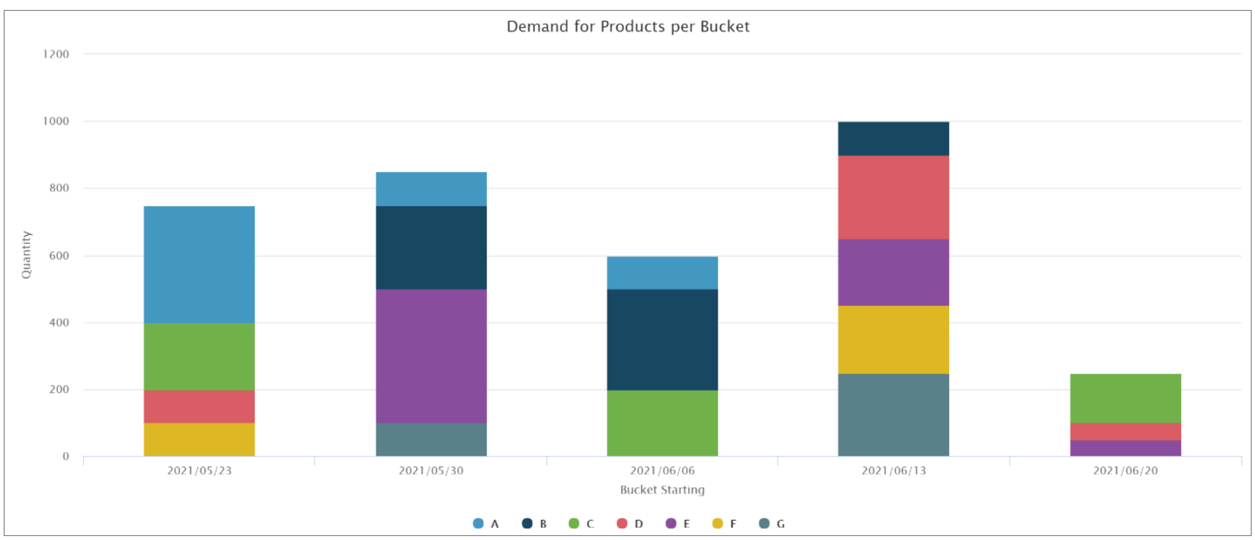

Figure 4. Demands for products: size and due time period per product order

Case Study: Results & Comparative Analysis

In the Applied Materials OP infrastructure, the user can easily build models, run scenarios, and obtain production plans in just a few minutes. For this case study, we created the following three scenarios:

- **H-FoS**: production plans based on a traditional rule under a full order satisfaction policy
- **H-PoS**: production plans based on a traditional rule under a partial order satisfaction policy

- **SFRx Smart Scheduling**: production plans created by the optimization-based SFRx Smart Scheduling tool

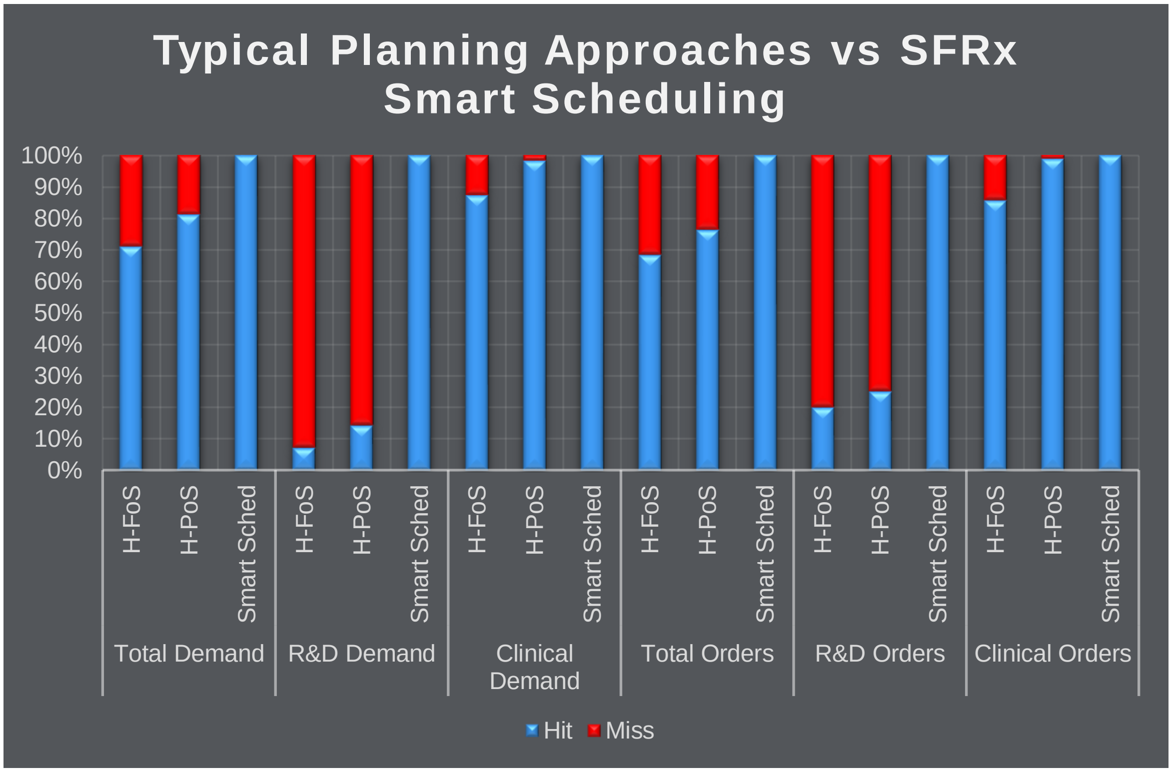

Figure 5. Comparative results: typical planning approaches vs SFRx Smart Scheduling

Not surprisingly, the results shown in Figure 5 clearly demonstrate that empirical, traditional production planning approaches fail to efficiently exploit the production capacity of the pharma manufacturing facility. Note that about **a quarter to a third of the total demand is missed when creating production plans based on these planning approaches**. This considerable percent of unsatisfied demand results in lost revenue, unreliable customer satisfaction and relations, and potential lost market share and competitive advantage in the global pharma market.

Additionally, typical production planning approaches notoriously struggle to accommodate the production of R&D orders in the overall production plan that includes high-priority clinical orders, as Figure 6 shows. About **90%** of the total R&D demand is missed by creating production plans based on traditional rule-based planning approaches. This means that R&D production is extremely limited, which certainly has a negative effect on the enhancement or discovery cycle times of pharmaceutical products, which is critical for any pharma manufacturer who wants a future or place in today's competitive global market.

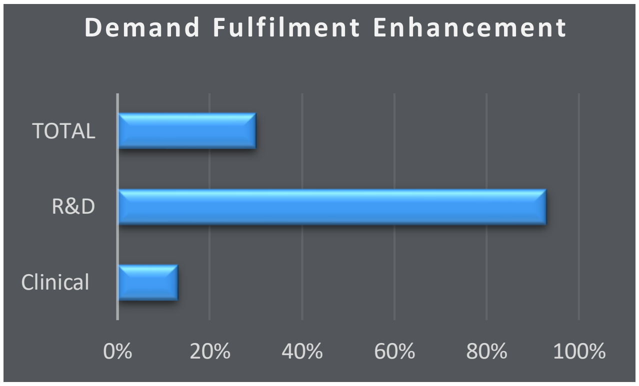

Figure 6. By how much can SFRx Smart Scheduling accelerate demand fulfilment?

Table 1. Comparative results: main highlights per comparison category

Demand fulfilled

Scenario	Clinical	R&D	TOTAL
H-FoS	87%	7%	70%
H-PoS	98%	14%	80%
SFRx Smart Scheduling	**100%**	**100%**	**100%**

Order fulfilled

Scenario	Clinical	R&D	TOTAL
H-FoS	86%	20%	68%
H-PoS	99%	25%	76%
SFRx Smart Scheduling	**100%**	**100%**	**100%**

SFRx Smart Scheduling is an ideal smart optimization-based tool that can easily create optimal production plans that completely exploit the production capacity of pharma manufacturing facilities (see Figure 6). SFRx Smart Scheduling optimizes the use of major assets, materials, and human resources to satisfy clinical and R&D production targets. In this case study, observe that the SFRx Smart Scheduling production plan completely satisfies the total demand for both clinical and R&D products. All clinical orders are met, resulting in full revenue creation in the present. Also, all R&D orders are completed, resulting in shorter enhancement or discovery cycle times of pharmaceutical products.

The total cost for the production plan derived by SFRx Smart Scheduling is **59%**, less than that of the H-FoS plan and **28%** less than that of the H-PoS plan. This means that on average SFRx Smart Scheduling reduces the total cost by about **43%**.

More importantly, SFRx Smart Scheduling can create optimal production plans **in just a few seconds**, while nowadays the process of creating production plans is very cumbersome and can take hours to days. The reason relates with using multiple spreadsheets from different stakeholders and the cadence of meetings in which decisions are taken sequentially without a holistic view of the overall production planning problem. In this respect, SFRx Smart Scheduling can not only provide optimal production plans very quickly but also **make the production plan generation process much more efficient and transparent**.

To address the qualitative aspects of the production planning problem through SFRx Smart Scheduling, manufacturers can run and experiment among different scenario settings and run several “what-if” scenarios to create a production plan that captures all the requirements. SFRx Smart Scheduling is a great tool for quickly creating several scenarios that can then be shared and discussed in internal meetings with the stakeholders responsible for approving production plans.

What-if-scenario: increase production capacity to avoid missing any demand in the H-FoS scenario

To further highlight the value of optimal production plans, we made a capacity analysis and executed scenario runs under the traditional rule-based H-FoS approach. We discovered that if we add an additional blender, granulator, coater, and table presser equipment, then the H-FoS approach meets most of the demand. However, acquiring new equipment assets can be extremely expensive, is not practical, and often (not unexpectedly) is not even a choice. SFRx Smart Scheduling uses available capacity efficiently, reducing any need for capacity expansion or plant retrofitting. This capacity benefit equates with major cost savings for the pharma industry. In fact, the SFRx Smart Scheduling plan demonstrates that **capacity expansion is NOT even needed to satisfy total demand**.

Case Study: SFRx Smart Scheduling Representative Results

With SFRx Smart Scheduling, users have easy access to all the key decisions and production plan metrics of the created production plan through an interactive user interface, which enables users to easily view:

- The optimal production, inventories, and backlog levels per product and time period (see Figure 7)
- The overall and daily utilization profiles for unit operations and equipment (see Figure 8)
- The detailed production schedule (see Figure 9). In the Gantt chart tooltip, users can see all relevant information with regards to the equipment and associated campaign step in the order that it takes place (for example, order due date, order size, unit operation, step type, start and end times of that step, etc.)

SFRx Smart Scheduling also reports the usage of materials and human resources. All this information displays in the form of graphs or Gantt charts, and users can download it in various formats (xls, csv, png, etc.). In SFRx Smart Scheduling, users can configure all visual analytics and can easily create advanced analytics, dashboards, and other interface components according to the needs of clients. It also offers different role-based access to SFRx Smart Scheduling.

Figure 7. Results for SFRx Smart Scheduling: profile examples for (1) production, (2) inventories, and (3) backlogs

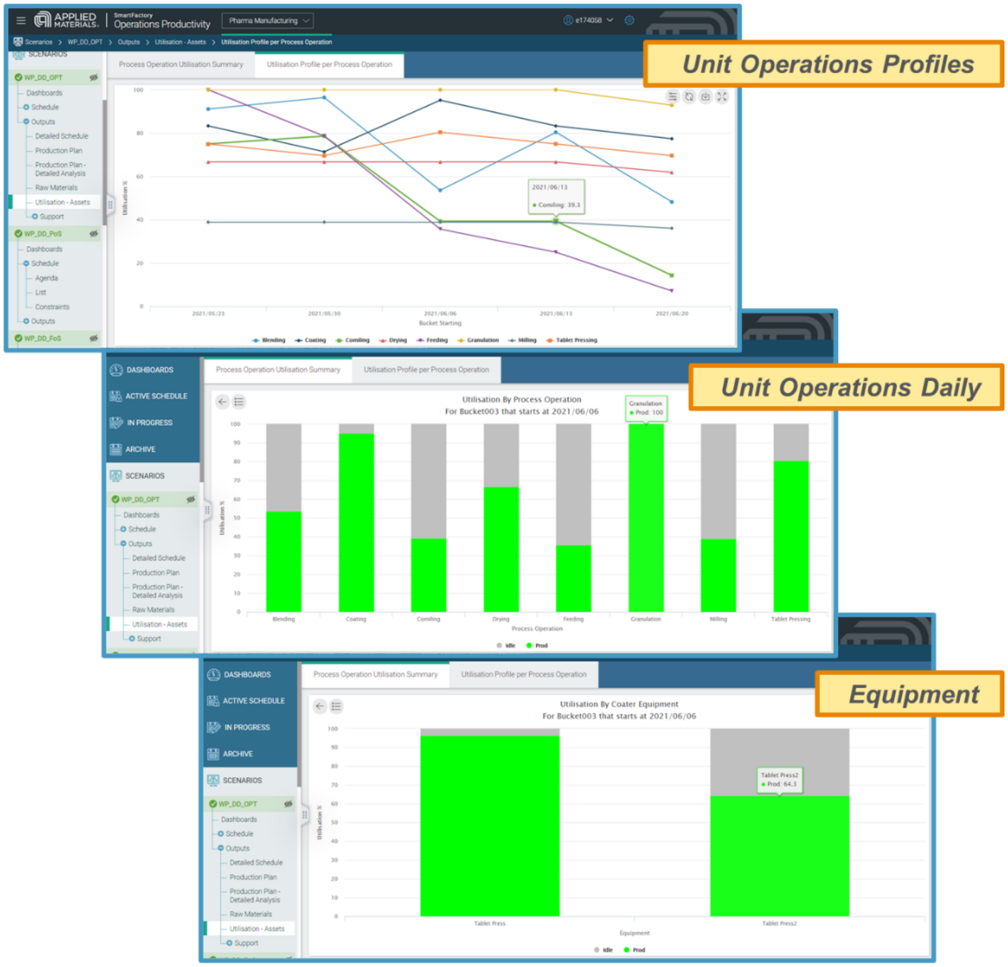

Figure 8. Results for SFRx Smart Scheduling: utilization profile examples for (1) unit operations for the whole planning horizon, (2) daily unit operations, and (3) daily equipment usage

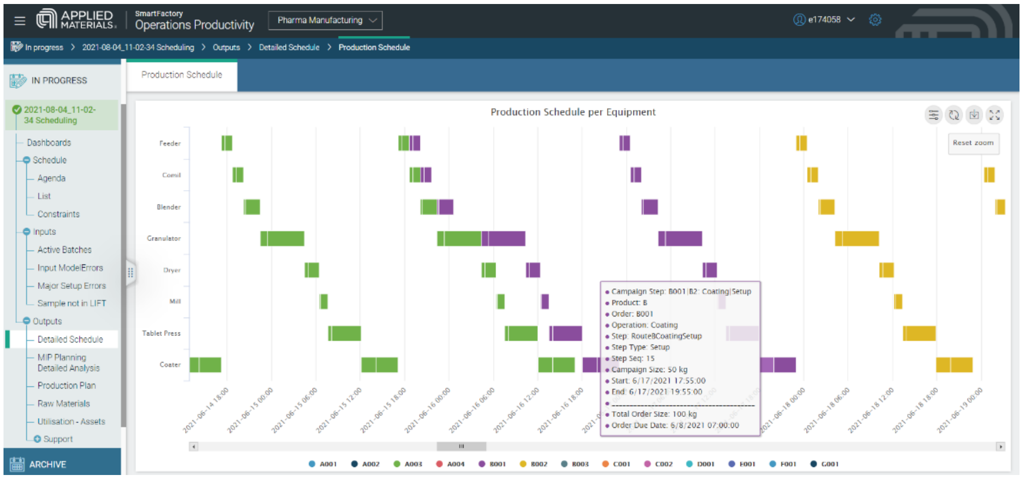

Figure 9. Detailed scheduling: an example production schedule from SFRx Smart Scheduling

The Future of Pharma Manufacturing: A Digital World Ahead

Digital transformation in the pharmaceutical industry is crucial for improving product quality, cost-effectiveness, greater transparency, production efficiency, and new drug development. A stable, integrated platform is needed to meet these challenges. Applied Materials has developed a sophisticated infrastructure with five main software components, illustrated in Figure 10. SFRx Smart Scheduling, built specifically for the pharma industry, can easily connect to existing data information systems, and it follows all the relevant industrial standards. Figure 11 highlights the five pillars of the SFRx bundle and includes a short description of features and advantages.

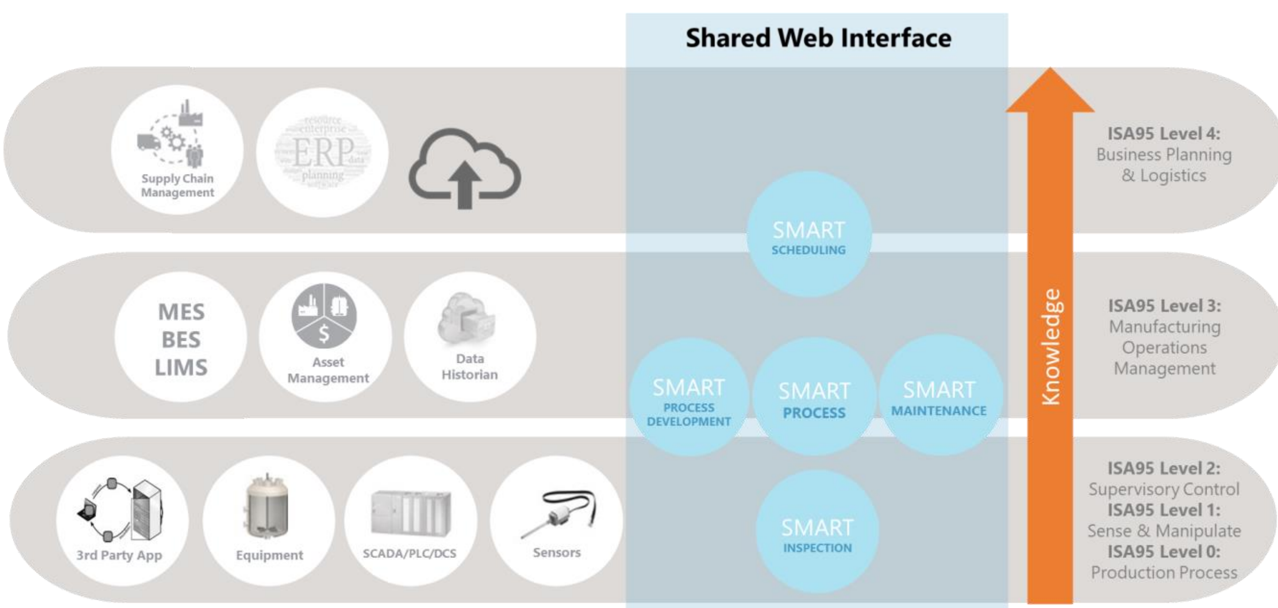

Figure 10. SFRx components suite

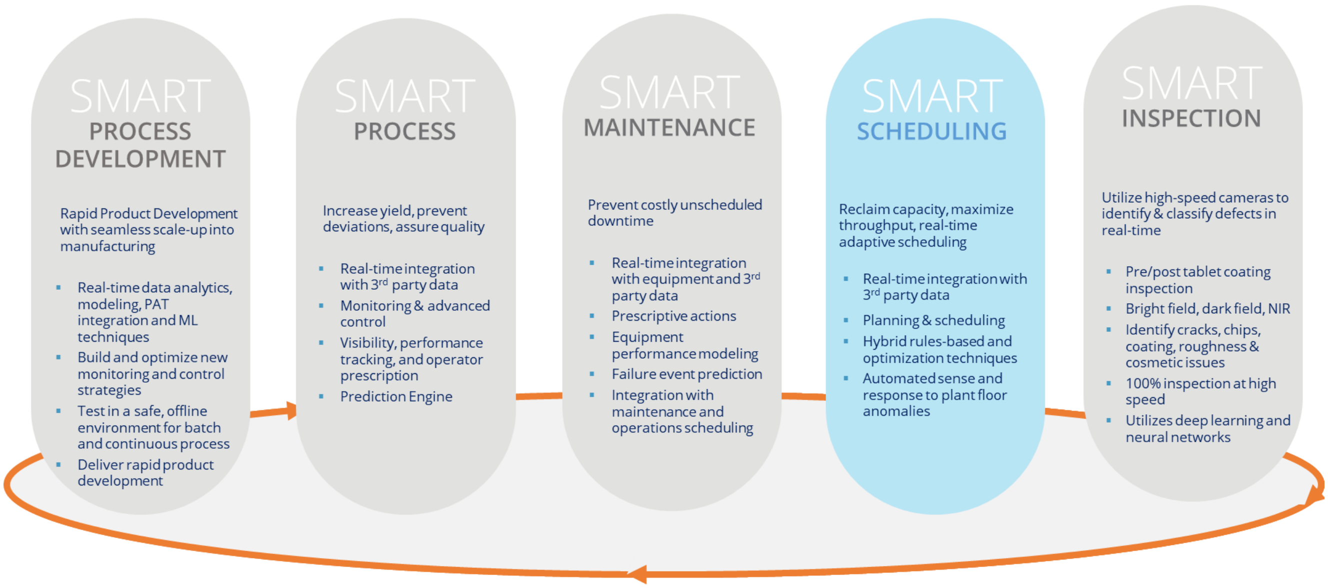

Figure 11. SFRx main pillars

The Future of Pharma Supply Chain: Enterprise-Wide Integration

Pharma industries are highly regulated and deploy numerous quality control (QC) activities across the whole manufacturing process and chain. As illustrated in Figure 12, large pharma companies have their own dedicated QC labs that perform all major QC for raw materials, intermediate products, and finished products for the main pharma manufacturing sites. In most cases the QC labs become one of the main bottlenecks in the process.

Although QC labs and pharma manufacturing facilities are highly interdependent, production plans for these sites are created separately, causing large whole-system inefficiencies and loss of competitive advantage. SFRx Smart Scheduling has already been successfully deployed in a large QC lab of a major pharma company. One of our targets in SFRx Smart Scheduling is to integrate these two systems and simultaneously optimize pharma manufacturing and QC lab operations to provide coordinated and optimal production plans for the whole pharma manufacturing chain of the future.

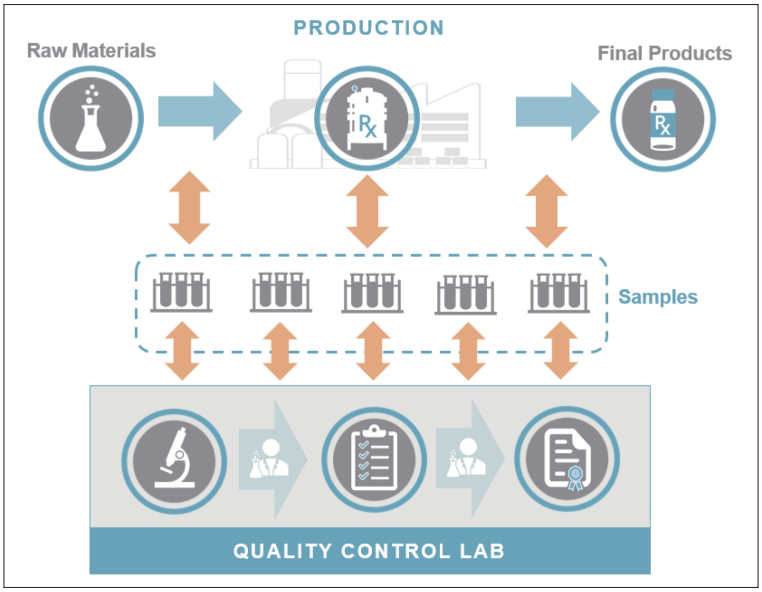

Figure 12. Pharma manufacturing supply chain integrated with quality control labs

Summary

This white paper illustrates how the SFRx Smart Scheduling tool generates—in just a few seconds—optimal production plans for pharma manufacturing. This decision-making and support tool relies on advanced optimization and integrates with a comprehensive platform that includes other interconnected software components that take advantage of the digital transformation occurring in the pharma industry today.

As this case study shows, SFRx Smart Scheduling production plans efficiently use available capacity and satisfy all clinical and R&D production targets, creating higher revenue in the present and favoring much shorter development cycle times for the future. In the SFRx Smart Scheduling plan, total costs are reduced by about **43%**, compared to traditional rule-based approaches.

SFRx Smart Scheduling effectively uses the whole capacity potential of the pharma manufacturing industry. It is a user-friendly tool that modern pharma companies could rely on for increasing their (1) competitive advantage, (2) reliability to customers, (3) overall manufacturing chain efficiency, (4) material and resource utilization, and (5) revenue.

Currently, the pharma industry is undergoing a digital transformation and Applied Materials advanced software solutions are ready to play a key role in bringing major quality and productivity benefits to this industrial sector.

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