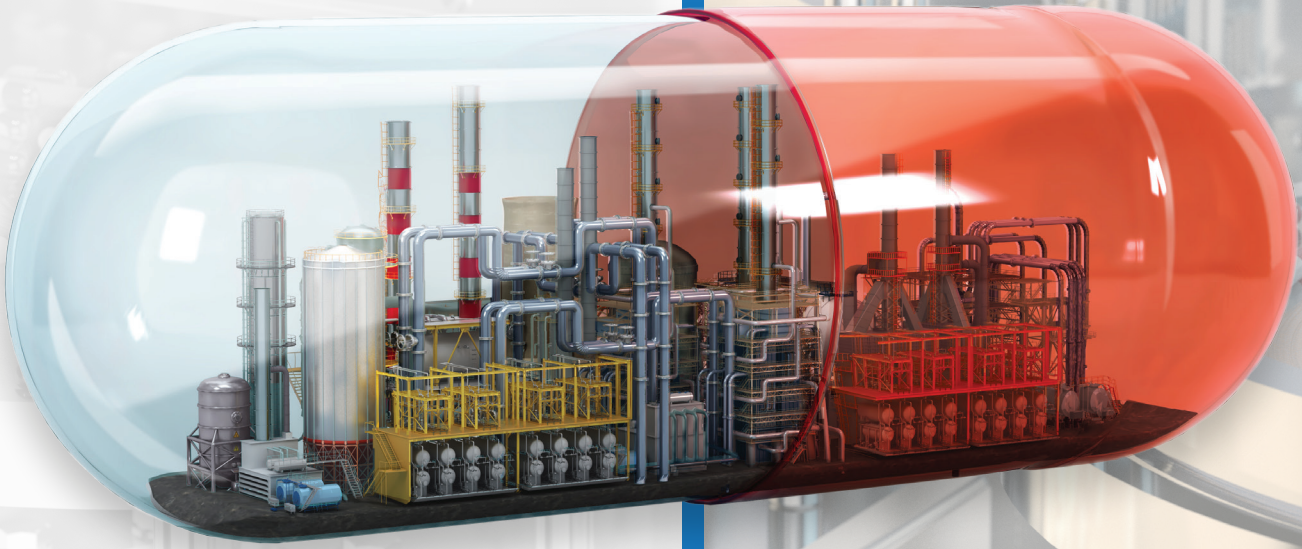
Accelerate Market Growth with New Advances in Process Analytical Technology (PAT)

An AspenTech® solution brief for the pharmaceutical industry



aspentech | Solution Brief

Executive Summary

Pharmaceutical companies, CDMOs and CMOs continue to grapple with the tension between meeting the growing demand for increasingly diverse pharmaceutical products and the escalating challenges in ensuring supply, especially during periods of disruption such as the COVID-19 pandemic and the nitrosamine impurity crisis. Modern process analytical technologies (PAT) help alleviate this challenge by enabling reliable product quality, higher yields and greater throughput, ensuring consistent delivery of more saleable product.

In addition, digitalization advances such as extensive connectivity, increased and elastic computing power and advanced analytics have all continued to strengthen the accessibility and power of PAT to accelerate market growth.

Aspen Technology fast-tracks the returns possible from PAT by bringing the latest advances to the forefront. One aspect is unparalleled capabilities for connectivity, data aggregation and modeling to enable real-time product quality assurance and assessment. Another is built-in tools to digitally map and automatically search the process operating envelope, delivering the ability to quickly learn from past operations and tune the process for optimal quality, yield and throughput—all while maintaining compliance with current Good Manufacturing Practices (cGMP).

Modern PAT is focused on closing the loop to continuously improve production, both in design and operation. This is the key to succeeding with PAT where previous approaches may have fallen short. In this it directly supports the FDA's vision for Advanced Manufacturing.[1] The high degree of flexibility in AspenTech's PAT solution to tackle a wide variety of data from lab to pilot to production makes the technology equally compelling across all types of pharmaceutical manufacturing, for innovator and generic small molecule and biopharmaceutical therapeutics (including peptides, monoclonal antibodies and other large molecule modalities) and across the entire product lifecycle. It supports production from the active pharmaceutical ingredient (API) to the finished pharmaceutical product (FPP). Pharma companies, CDMOs and CMOs can start with right-sized deployments that readily scale in scope and business value.

The Product Lifecycle:

IND | Investigational New Drug **NDA** | New Drug Application **BLA** | Biologics License Application **ANDA** | Abbreviated New Drug Application

AspenTech's transformative PAT solution ensures product quality and process efficiency across the entire product lifecycle.

Typical Business Benefits

- **Increased quality assurance.** A major pharmaceutical company prevented $500K USD worth of waste in one rescued batch alone.
- **Reduced batch cycle time.** A pharma company gained $800K USD per month in revenue with increased operational efficiency, enabling four additional batches per month.
- **Reduced labor costs and reporting errors.** Automated reporting dramatically reduces labor costs and lowers the probability of errors in reporting.
- **Reduced process variability.** Minimizing drift and eliminating guesswork increased production by 1-2% for multiple manufacturers, with millions of dollars in additional revenue gained per year.
- **Direct online measurement of product quality and continuous verification of process health.** This enables ongoing verification that the process is in control, enabling enhanced confidence for customers and auditors alike.

Many Applications. One Solution.

Digitalization advances such as more extensive connectivity, increased and elastic computing power and advanced analytics have all continued to strengthen the accessibility and power of PAT. The deployment and value of PAT continues to grow, as this quote by a former FDA director states: "PAT is experiencing a renaissance due in great part to the advancement of continuous manufacturing and Pharma 4.0 efforts for automation and digitization." The primary benefits provided by PAT are to empower more reliable product quality, higher yields and greater throughput (reduced batch cycle time), thereby consistently delivering an increased supply of saleable product. Below is a list of examples where PAT has been successfully applied to drive these benefits.

Batch Manufacturing

- Key benefits: tighter quality control, higher yield, greater throughput
- Capability:
  - Model the range of past batch operations and use results to optimize the standard batch recipe for ideal quality, maximum yield and minimum batch cycle time.
  - Constantly predict end-of-batch outcomes and provide real-time alerts on a batch that is drifting off course; combined with diagnostic information, take quick corrective action to recover quality, yield and/or batch cycle time.

Ingredients Blending

- Key benefits: tighter quality control, greater throughput
- Capability:
  - Directly measure the composition of blended materials.
  - Monitor continuous blending to provide 100% inspection for quality assurance. This capability enables the process to be run at higher throughput without losing confidence in the quality achieved.
  - For batch blending, directly measure when the materials are perfectly blended to achieve optimal blend uniformity. Avoid quality degradation from over blending and end the batch in the minimum possible time (reduced batch cycle time).
  - For either batch or continuous processes, digitally map and automatically search the process operating envelope to quickly learn from past operations and tune the process for optimal quality and throughput.

Reaction Processes

- Key benefits: tighter quality control, higher yield

- Capability:
  - Directly measure reaction products and determine the optimal reaction end point to balance maximizing the yield of desired product with keeping undesired byproducts below limits.

- Digitally map and automatically search the batch operating envelope to determine the optimal batch recipe for maximized quality and yield and minimum batch cycle time.

Drying Processes

- Key benefits: tighter quality control, greater

throughput, increased energy efficiency

- Capability:
  - Directly measure the residual solvent level to determine the drying end point accurately. End the batch in the minimum possible time and ensure ideal product quality batch after batch.
  - Digitally map and automatically search the batch drying operating envelope to determine the best batch recipe for the optimal balance of residual solvent level, batch cycle time and energy use.

Fermentation Processes

- Key benefits: tighter quality control, higher yield, greater throughput
- Capability:
  - Directly measure the evolution of key metabolites.
  - Digitally map and automatically search the fermentation operating envelope to optimize process parameters (addition of nutrients, temperature profile, pH, dissolved oxygen, etc.) to maximize yield of the biological API, minimize batch cycle time and keep undesired byproducts below limits.

Real-time Release Testing (RTRT)

- Key benefits: 100% assurance of quality — a key enabler for continuous manufacturing. Minimize delays in shipping, and reduce product inventory and associated costs.
- Capability:
  - Directly measure FPP quality in real-time.
  - Achieve at or close to 100% product inspection, enabling real-time release with confidence.
  - Reduce the cost and logistics of product inventory by eliminating the wait time for laboratory testing.

As these examples demonstrate, no matter how your pharmaceutical product is produced AspenTech's PAT solution augments the capacity to deliver a reliable supply of saleable product by optimizing product quality, yield and throughput. In addition, online PAT implementations constantly monitor the health of the production process and provide early alerts with diagnostics that inform timely corrective action.

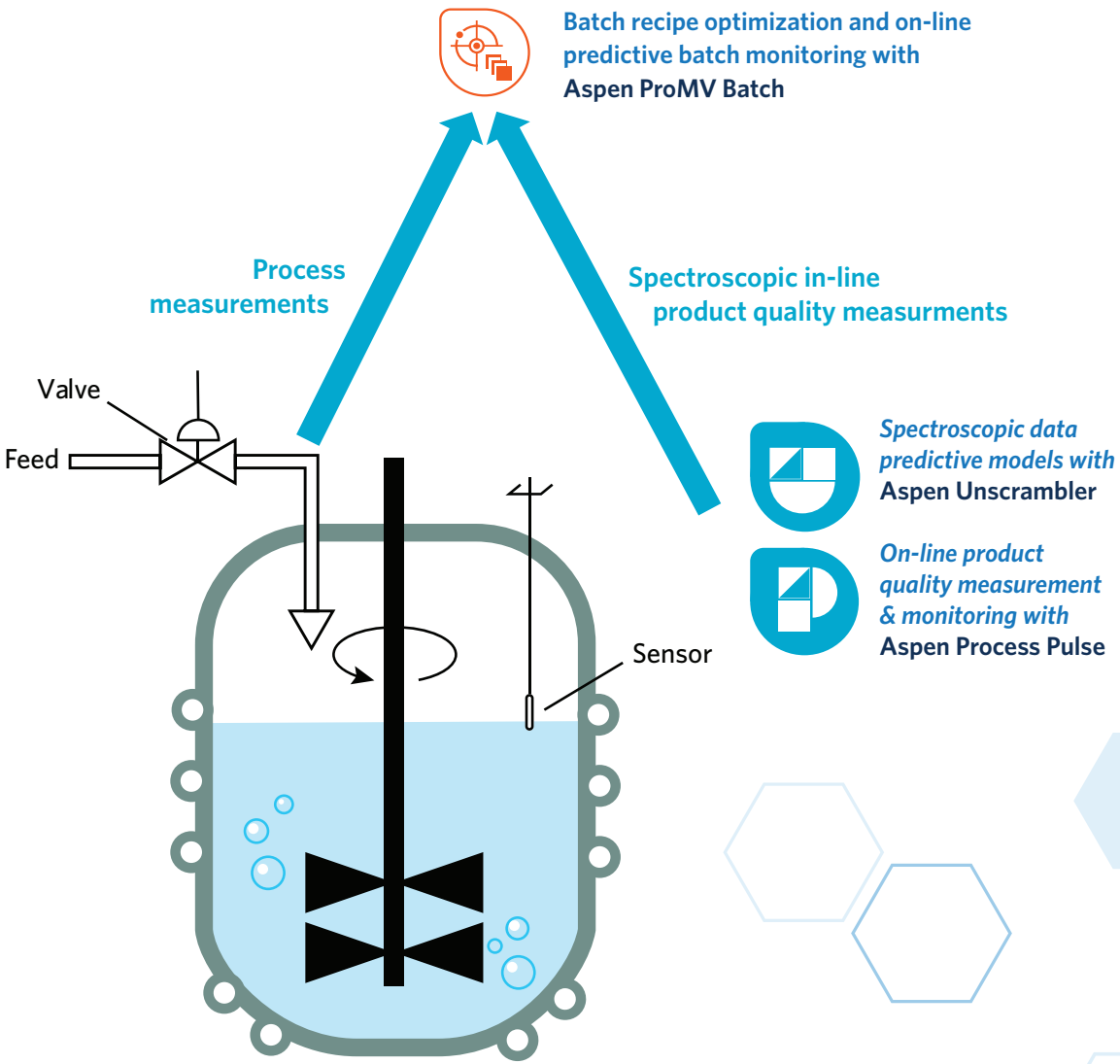
The Key Components of AspenTech's Modern PAT Solution

The figure on the next page of a batch reactor shows an example of how the key components of AspenTech's PAT solution work together to ensure product quality and optimized process performance.

- **Ensure product quality in real-time with Aspen Unscrambler™ and Aspen Process Pulse™**. The available information from traditional process sensors (flow, pressure, etc.) is augmented with real-time product quality measurements and monitoring through the combination of Aspen Unscrambler and Process Pulse. Typically, this is through online spectroscopic instruments such as NIR and Raman. The benefit of the Aspen Unscrambler models deployed online in Process Pulse is unrivaled direct visibility into product quality and yield. Practical outcomes include more accurate batch end-point determination, batch-to-batch quality and yield trend analysis, and real-time release testing for every batch.

- **Optimize process health and performance with Aspen ProMV®.** Aspen ProMV Batch synthesizes the resulting combination of process and product data from many historical batches, creating predictive models and then automatically searches them to discover batch recipes that optimize quality, yield and cycle time. This automates a workflow that would be very challenging if not impossible to achieve with traditional approaches that manually explore the design space captured by the model. Next, these models can be deployed online to predictively monitor whether the evolving batch operation is progressing to optimal quality, yield and cycle time or is drifting off course. Early warning and diagnostics capabilities enable informed and timely intervention as needed by operations personnel.

The enhanced visibility, optimization and control of quality, yield and batch cycle time that this powerhouse toolset delivers greatly improves a pharma facility's ability to produce targeted quantities of finished product reliably and with high quality.

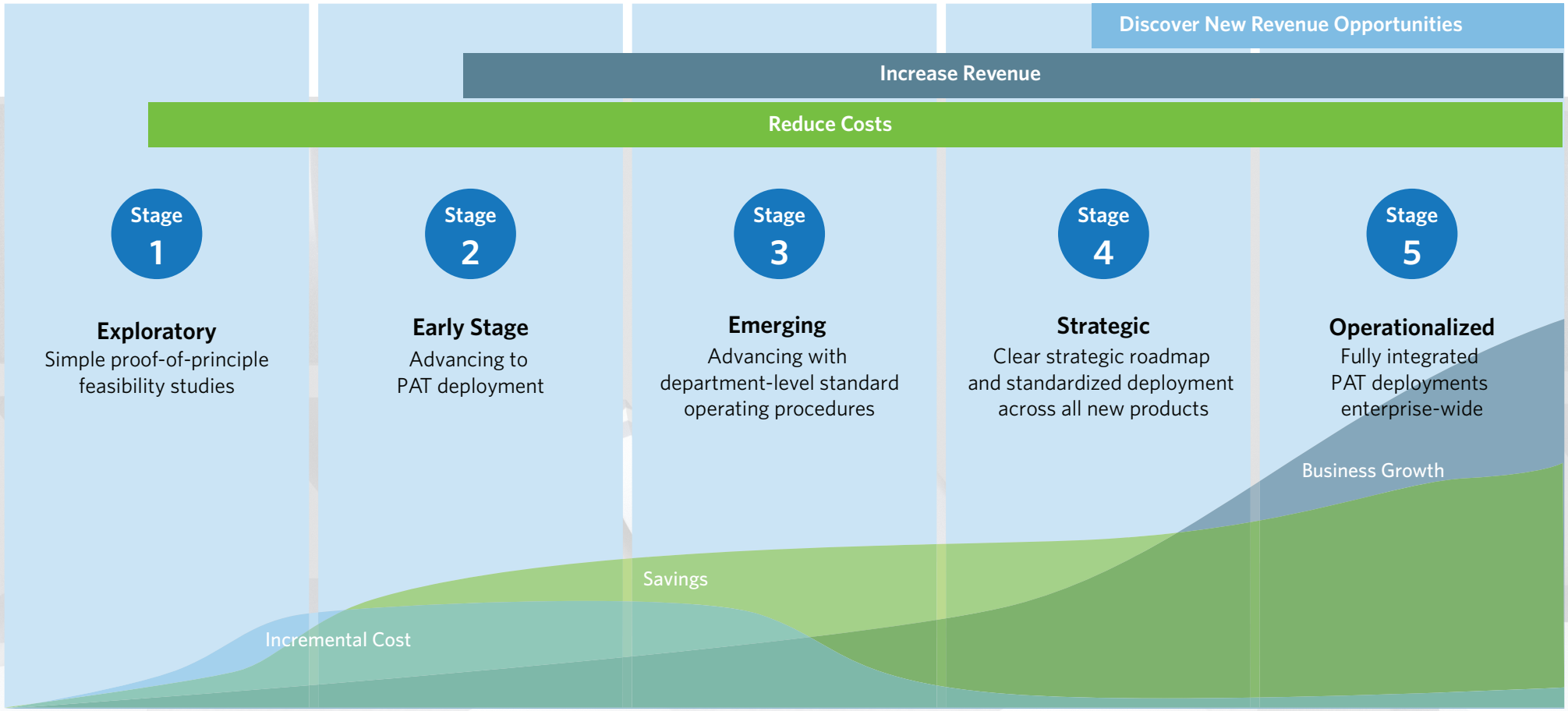


Aspen Unscrambler and Aspen Process Pulse ensure product quality.
Aspen ProMV ensures optimized process performance.

Scale the Benefits Over Time

The typical journey to a fully operationalized deployment of AspenTech's PAT solution follows the five stages outlined below, with payback typically realized in months, even for the first application.

Business Value By Maturity Level



Market Leaders Using Modern PAT Solutions See a Bright Future

Market leaders like Bayer, Pfizer, Lonza and APC have embraced PAT and are bullish on this powerful technology's achievable benefits and exciting future.

What Market Leaders are Saying

"PAT is all about process knowledge. In the end it will open up undreamed-of possibilities for process optimization and cost reduction."

Andreas Litzka
Operations assistant
APR/CPV/PAT

"The expectation is in-line, in-process controls will be the primary option for new commercial products launched on advanced manufacturing platforms."

Andy Palm
Principal Scientist

"PAT and advanced data analysis are indispensable tools to enhance understanding and control of manufacturing processes."

Dr. Hans-Peter Nirmaier
Senior Manager PAT

"PAT will be pivotal in supporting the maintenance of the well understood, optimal and reproducible bioprocesses of the future."

Stephen Craven BE, PhD
Biologics Functional Lead

Accelerate Growth with AspenTech as Your Strategic Partner

No process infrastructure or technology ecosystem is the same when it comes to implementing PAT. That is why AspenTech's advanced PAT solution is flexible, scalable and easy to integrate with the processes, control systems, analytical instruments and data historians you already have in place.

AspenTech has a comprehensive solution that supports:

- **Addressing your most pressing production challenges and opportunities,** whether they include achieving more reliable product quality, higher yields and/or greater throughput. The net result is to maximize your production of high-quality saleable product.

- **Democratizing information access and strengthening data-driven decision-making** across all types of roles, including operators, engineers, subject matter experts, quality assurance, research & development and management. This technology empowers your team to take informed, timely and optimized action every time.

- **Empowering your PAT journey from the exploratory stages to scaling enteprise-wide** as part of standard practice so that these benefits are realized everywhere.

AspenTech's ongoing innovations in PAT can start delivering actionable and impactful results in days or weeks and can typically be fully implemented in months, depending on the complexity of the required solution. Realizing the full value of PAT and accelerating its impact requires applying the right technologies to your process infrastructure in a compliant manner to achieve more reliable product quality, higher yields and greater throughput, and to encourage innovation in product development.

AspenTech offers an advanced and comprehensive solution that leverages and adds value on top of your existing technology investments. We can support your entire PAT journey as your strategic partner with our in-house domain expertise, starting with a right-sized solution.

aspentech | Technology That Loves Complexity

About Aspen Tech

Aspen Technology (AspenTech) is a leading software supplier for optimizing asset performance. Our products thrive in complex, industrial environments where it is critical to optimize the asset design, operation and maintenance lifecycle. AspenTech uniquely combines decades of process modeling expertise with machine learning. Our purpose-built software platform automates knowledge work and builds sustainable competitive advantage by delivering high returns over the entire asset lifecycle. As a result, companies in capital-intensive industries can maximize uptime and push the limits of performance, running their assets safer, greener, longer and faster.

Visit AspenTech.com to find out more.