



The State of PAT in the Pharmaceutical Industry

In a Pavilion Technologies survey, major manufacturers share details and insights regarding their PAT initiatives.

In the fall of 2004, Pavilion Technologies (Austin, Texas) conducted a survey of leading pharmaceutical companies about their approaches to FDA's process analytical technology (PAT) initiative. In conducting the survey, Pavilion wanted to assess how and to what degree the pharmaceutical industry was taking advantage of the opportunities presented by PAT.

Pavilion, a firm specializing in solutions in the field of advanced process control (APC), works with leading pharmaceutical companies to demonstrate PAT benefits through the use of multivariable data analysis, software online analyzers, and multivariable predictive control. It uses what it calls the ValueFirst customer relationship methodology to identify the economic value of each PAT initiative and guarantee results based on the performance benchmark.

Pavilion received feedback from 18 pharmaceutical manufacturers, 12 in the U.S. and six in Europe. They included: Abbott Laboratories, Amgen, AstraZeneca (Europe), Bayer (U.S. and Europe Operations), Bristol-Myers Squibb, Eli Lilly (U.S. and Europe Operations), GlaxoSmithKline (Europe), Johnson & Johnson (Europe), Merck, Perrigo, Pfizer, Schering-Plough, Teva Pharmaceuticals, Watson Pharmaceuticals and Wyeth (US and Europe). The interviews were conducted with individuals directly involved in their companies' PAT applications and strategies.

Respondents were, for the most part, positive about PAT and its potential to effect change. "The FDA has recognized that the regulatory environment has been restrictive to bringing innovative technologies for analysis and for process control," said one principal scientist. "This is a very positive attempt to get rid of those restrictions. So, it is essentially a golden opportunity to change the entire way we develop drugs."

The extent of initiatives

The survey confirmed that most companies already have a defined PAT strategy.

- Most interviewees described a corporate PAT initiative and have established steering committees.
- All European interviewees described a corporate PAT initiative and have established steering committees.

“Most companies are already well into what they want to do with PAT and how they are going to use it,” said one VP of quality operations. That doesn’t mean, however, that the manufacturers have PAT all figured out. “The bottom line is that PAT provides more data, and that data has to be converted into knowledge, and then the knowledge has to be used to reduce variability,” the same VP said. “So the real challenge is what to do with all the data.”

Participants diverged in their perceptions of how broadly PAT is defined. Some see PAT as primarily an initiative to provide quality data during the manufacturing process through on-line, rather than laboratory, analysis — a somewhat limited view of PAT. Others understand PAT in a broader context of scientific principles: process understanding, risk-based approach, integrated systems approach and real-time release (RTR).

“The ability to make that measurement is one thing, but the ability to react to that measurement, to do something about it if you see a problem developing, is the key to what this is all about,” said one firm’s head of process technology. “So predictive systems, modeling systems, and then of course the decision-making algorithms are very important.”

Investing in PAT

Many of the companies had specific budgets in place to address PAT needs in the near future. Interviewees were asked to break down their PAT spending plans according to various tools: multivariable data analysis, software online analyzers (e.g., Pavilion’s trademarked “soft sensors”), predictive process control, and performance management and monitoring.

- Eleven of the 18 companies surveyed are investing in all of the PAT tools identified above;
- Fourteen companies are investigating multivariable data analysis;
- Fifteen companies are investigating Software Online Analyzers;
- Fourteen are investigating Predictive Process Control.

The European community expressed a bias towards multivariable data analysis — all six said they were investing in the approach, as compared to 67% of the U.S. companies. Conversely, U.S.-based manufacturers appear to favor the use of software online analyzers for in-line and predictive measurements over multivariable data analysis.

Whatever the investment, some survey respondents clearly see the potential for significant returns. “We have an existing plant for making [Drug X], for instance, but if there happens to become a rapid sensor that we can put on-line to help us improve that process and squeeze out a couple more percent yield, that would actually increase our profit by millions of dollars,” said a PAT corporate team leader.

Reaping the benefits

Participants had mixed opinions about which firms — large or small, U.S. or European — would get the most immediate benefit, financial or otherwise, from the PAT movement.

“PAT is going to have a big impact for the smaller pharmaceutical companies that are very flexible and can make changes very quickly,” said one regulatory affairs consultant. “I think larger pharmaceutical companies are going to have major difficulties getting up to speed on PAT, and it is going to take them a long time — just because of the bureaucracy and the inflexibility of those businesses. . . Small pharmaceutical and biotech companies are going to have a major advantage here and be able to quickly recoup the cost savings, the efficiencies and such with PAT.”

“Pioneer early adapters will take to it pretty well, and will see that it is a very good thing, a very positive thing,” said another regulatory affairs contact. “Certainly those companies that have European affiliations, where it is more widely spread, will take to it more easily.”

While the survey was heavy on data, it also generated many open-ended responses from interviewees on both sides of the Atlantic. What follows are more of the insights shared. For more information on the survey, please contact the Pavilion representatives listed at the bottom of this page.

The U.S. perspective:

“I do not think that everybody understands clearly what PAT is, and what the benefits could be for the industry. . . It is taking time to identify an area, a single area, where we could apply some of those technologies and see results.” — QA Director

“What a company like us would be looking for is basically experience. Have they beta tested this? Have they alpha tested this somewhere? We do not want to be the first ones to use it. We want to see prototypes. We want to see how the process has been developed somewhere in order to go large-scale with it.” — Senior Validation Engineer

“What we could benefit from is some facilitation at the manufacturing site level to basically embrace and apply PAT to their everyday way of doing business, as opposed to another added thing from headquarters that is being added as a burden.” — PAT Representative for Regulatory Affairs

“Since we are so heavily regulated, it is tough to find our way and to change the many years of thinking. . . I think it will help us in a way that we can understand our processes better.” — Scientific Project Manager

The European perspective:

“I think the main influence is going to come from the FDA, because that is the largest market for ourselves and other pharmaceutical companies. I think most companies are moving towards PAT as a way of monitoring processes. . . But in the long term, it is going to influence the way in which we clear drugs as well. So obviously that is going to have a big impact, and it will reduce the amount of end product testing that is done and increase the amount of in-process testing.” — Senior Scientist

“One of the things I have definitely seen here is the value of using PAT for continuous process validation. Just in terms of what is normal in the industry at the moment, or what is typical in the industry, the requirement typically is to run three batches to meet the PQ requirements. . . With PAT, you can have continuous validation, not just checking three batches on a ‘why not’ arrangement. . . The technology is there, but I do not think it is in place.” — Senior Analytical Scientist

“I think that the holy grail for this is continuous validation of the process.” — Senior Analytical Scientist

“The golden carrot being put out is that, if you can demonstrate that your process is under control, and that your critical process parameters are correlated at a surrogate or direct correlation to your product quality attributes, then you can do parametric release — you can get rid of or reduce your end product testing. So that is a carrot that is being put forward to the industry to introduce PAT.” —Principal Scientist

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