Partnership Leads to Improved Supply Chain Quality Control

Waters partners with Fikst Product Development to troubleshoot unknown manufacturing problems using physical and chemical characterization of materials, leading to a revised quality assurance protocol

TECHNOLOGY: ACQUITY APC System, ACQUITY UPLC System, Xevo G2-XS QTof Mass Spectrometer, Discovery TGA

PRODUCT DESIGN AT FIKST PRODUCT DEVELOPMENT

From product conception to manufacturing support, Fikst's goal is to accelerate and streamline the product design experience. Founded in 2005, the company's 20 employees serve clients in the biomedical, microfluidics, energy, technology and consumer product fields.

Extraordinary customer service is this consulting firm's foundation. The name *"Fikst"* means *"Well done"* in Danish. But it's more than a name; it's the cornerstone of Fikst's dedication to its clients.

Located in Boston, Massachusetts, Fikst serves multiple customers with both short-term and long-term needs, whether it's new product development, engineering, product evaluation, and/or manufacturing support. Fikst's close relationship with its clients means that the firm is continuously involved at many business stages.

Doug Sabin, Fikst Principal, explains: *"We have long-term relationships with our clients. If our clients are successful, we're successful. We want them to grow and succeed, and eventually reinvest in new products that we can help develop."*

This case study explains how that dedication to customer service lead to a supply chain troubleshooting project with unexpected, yet very effective results.

Sage Science Polystyrene Cassette.

WORKING WITH WATERS

Fikst and Waters embarked on a joint troubleshooting project to identify the source of a manufacturing defect and find a solution to improve Sage Science's quality control of the raw materials and suppliers.

Waters brought the technical expertise, as well as a wide range of cutting-edge technologies. As with its relationships with its own customers, Fikst found a like-minded partner in Waters.

Sabin explains: *"Waters understood the project and the ramifications. It was very helpful to have a partner who understood both the business issues and the testing methods."*

The experience lead Sabin to believe working with Waters made all the difference in finding the right solution. As a result, Sabin says: *"Any chance I get to work with Waters, I would do it."*

Doug Sabin, Principal, Fikst.

MANAGING QUALITY CONTROL OF RAW MATERIALS AND SUPPLIERS

It's the call no product developer wants to get – defects discovered by customers in the field lead to the discovery that something in the manufacturing process has gone awry. But where do you start when you're looking for an unknown problem?

That was the situation facing Sage Science, one of Fikst's long-time clients and a developer of novel lab instruments targeted for use by larger instrumentation companies. Sage develops and sells polystyrene cassettes for DNA prep work. Their customers use those cassettes to load samples, which are processed while being measured using fluorescence technology.

But recently Sage found several batches of cassettes were defective, which was undetected by their quality control process at the time. Unexpected contamination introduced at some stage was causing autofluorescence in the cassettes, leading to false readings that rendered the results useless.

While the cost of the cassettes themselves was relatively small, the samples were far more valuable – each one worth as much as several thousand dollars. Much was at stake, as these types of product failures can cause revenue losses, cost increases and long-term damage to the company's reputation.

Sage turned to Fikst for help. It's a business relationship that's lasted more than 10 years, and Fikst was closely involved in the company's first product development stages – as well as many others since then. Fikst originally helped Sage set up contacts with manufacturers in Asia to produce the polystyrene cassettes. Fikst engineers were also involved in explaining the raw material specifications, formulation, manufacturing procedures, and other key technicalities to the vendor.

So Fikst had a vested interest in finding a solution – and fast.

> "We needed to be proactive. As product designers, we have select vendors. We need our vendors to perform well, and we need to help them perform well."
>
> DOUG SABIN
> *Fikst Principal*

Initially, Fikst engineers suspected the problem was contamination or additives somewhere in the raw materials or the manufacturing process.

The journey to find the problem lead to a serendipitous meeting with scientists from Waters.

FINDING AN UNKNOWN

As any scientist knows, finding the unknown isn't easy. Fikst and Waters agreed on an approach, which Sabin light-heartedly describes as *"throwing all the technologies at the problem."*

Fikst and Waters personnel started with the hypothesis that the fluorescent material had been introduced at some stage during the manufacturing process. There were two likely scenarios:

- Polystyrene comes in different formulations and from a variety of grades, including formulations that contain optical brighteners to enhance the aesthetic qualities of the final products. The supplier could have used the wrong grade for the application in question.
- It is also possible that waste material from manufacturing processes was reground and added to the feedstock for the cassette manufacturing process. Again, that regrinding could contain optical brighteners from a different original process, or an optical brightener could have been added to reduce the yellowing appearance that reground material can possess.

Waters personnel came up with a materials analysis strategy to identify the source of the autofluorescence. The plan was to determine if the samples were different and if their physical problems could be addressed by understanding the manufacturing process (elasticity, color, hardness, brittleness, etc.).

But the larger goal was to find the problem and locate its introduction, so the team could adjust its concentration or eliminate it entirely.

GROWING NEED FOR MATERIALS ANALYSIS

Waters tapped into its extensive expertise on materials analysis, which measures the various physical properties of a substance. Waters is the leading manufacturer in the materials analysis market, and the company sells thermal analysis and rheometry products through its TA Instruments division (1).

These techniques are in high demand. Materials analysis covers a diverse class of instruments used in many industries. Microcalorimeters are generally used in the pharmaceutical, food, and environmental industries, while thermal analysis and rheology is applied more in materials characterization. Understanding how a material behaves under heat or external force helps a manufacturer in determination of end-use for the material.

Waters focused on four techniques to find the source of Sage's autofluorescence problem:

Thermogravimetric Analysis (TGA) measures changes in physical and chemical properties of materials measured as a function of increasing temperature or of time.

TGA can provide information about physical phenomena, such as phase changes like vaporization, sublimation, absorption, and desorption. Likewise, TGA can provide information about chemical phenomena including chemisorptions, desolvation, decomposition, and solid-gas reactions.

Fourier Transform Infrared Spectroscopy (FTIR) is used to obtain an infrared spectrum of absorption or emission of a solid, liquid, or gas. An FTIR spectrometer simultaneously collects high spectral resolution data over a wide spectral range. The spectra can provide bulk chemical composition information, some structural information and, in some cases, minor compositional differences between samples.

Gel Permeation Chromatography (GPC) provides information on polymer molecular weight distributions and structural information. It can also detect low molecular weight additives and contaminants in polymers.

Liquid chromatography coupled with mass spectrometry (LC-MS) provides separation of complex samples as well as detection and identification of components at trace levels. With LC-MS, it is possible to analyze low molecular weight polymers directly and to look at extracts of polymer-based materials to detect and identify low molecular weight oligomers, by-products of polymerization, additives, and contaminants.

THE APPROACH

The Waters team approached the troubleshooting project by using these techniques to compare two cassettes – one without the defect and one with the problematic autofluorescence.

Starting with TGA and TGA/MS instrumentation, they found:

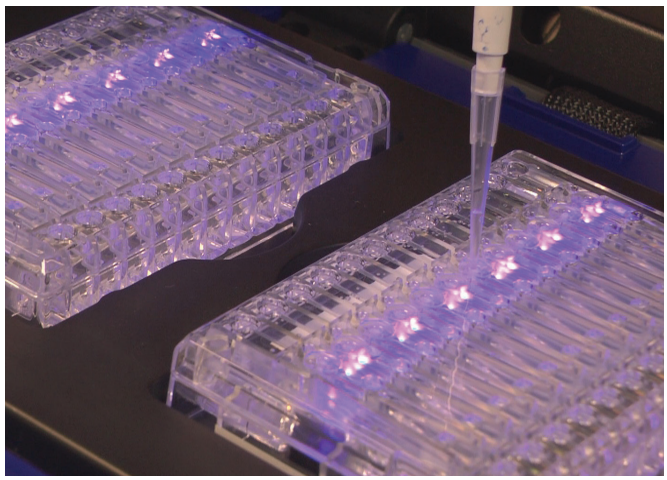
- The defective sample was less thermally stable than the good sample.
- Thermal degradation of polystyrene was more rapid in the bad sample.

But the team needed more direct evidence to find the source of the autofluorescence.

Continuing with their strategy, the team turned to FTIR spectroscopy, which found the defective sample showed the presence of some aliphatic fatty acid esters. Such compounds are often used as mold release agents.

That finding narrowed down the original hypothesis – the differences in stability may be related to blending of regrind material into resin formulation used for the manufacture of the cassettes.

Working on this theory, Waters turned to chromatographic techniques to seek confirmation of differences in composition of the defective sample and to identify a chemical source of fluorescence.



Autofluorescence in polystyrene cassettes.

Waters scientists continued their analysis with size-based separations of polymers to profile molecular weight distributions. This approach enabled a comparison of the polymer used in the cassettes as well as potential degradation or differences in the resins. It also separates the bulk polymer from lower molecular weight compounds, helping detect small molecule candidates for causing the potential fluorescence.

The team employed the Waters® ACQUITY™ Advanced Polymer Chromatography™ (APC™) System, which incorporates Waters' hybrid particle technology and engineered UPLC™ technology to enable very fast, high-resolution separations on small particle columns. In this case, the technology is particularly useful as the higher resolution achieved, helped detect small molecule contaminants.

The results showed a significant difference between the good tray and bad tray data. But more sensitivity was needed, so the team turned to LC-MS to detect and identify components at trace levels.

For the LC/MS analysis, the team used the ACQUITY UPLC System coupled to a Xevo G2-XS QTof Mass Spectrometer. The ACQUITY UPLC provides rapid, high resolution separation of complex samples, and the Xevo G2-XS QTof provides high resolution, accurate mass spectra – allowing for sensitive detection of separated components and structural elucidation of compounds.

The LC-MS results showed the presence of fluorescing compounds in the processed samples at levels greater than in the raw, unprocessed resin. This suggests that the raw material (resin) was not likely the source of the fluorescing compounds and indicates that the contamination resulted from the production process.

The team determined that the most likely cause of the autofluorescence was either lubricants added by mistake or regrind material added back into the vessel.

WORKING WITH SUPPLIERS

Detecting the likely source of the contamination, however, was only the first goal. Fikst turned to the much larger problem – working with the supplier to investigate activities at the manufacturing site.

Fikst used the results from the troubleshooting project to work with the vendor on concerns about consistency in the manufacturing processes. It wasn't completely straightforward, as this supplier was in Asia and there was a significant language barrier.

Sabin explains: *"It's very difficult to communicate about highly technical issues. I wanted to use the samples here to identify the specific process, so we wouldn't have the problem in future cassettes."*

With the materials analysis results in hand, Fikst was able to focus investigation on activities at the manufacturing site, specifically:

- Was regrind material being used on occasion?
- If so, was an optical brightener added to that regrind material?
- Are additives required to facilitate manufacturing (mold release) due to use of regrind?

It worked. All subsequent batches of cassettes have not had any autofluorescence issues.

Perhaps most importantly, Fikst and Sage were able to develop new quality control testing procedures to detect any problems before the cassettes were sold.

"This project definitely lead to a higher quality product for Sage, enabling them to maintain and increase sales"

DOUG SABIN
Fikst Principal

MEETING THE CHALLENGES OF MODERN SUPPLY CHAIN MANAGEMENT

The situation facing Fikst and Sage is one that's familiar to manufacturers across all industries. The usual causes of product failures are supply chain management issues or in-house quality issues. While global supply chains have helped companies like Sage stay competitive, they also risk outsourcing product reliability.

And the potential costs are much greater than the price of manufacturing or loss of sales revenue. Supply chain issues affect security and end-users' confidence in product quality. Long-term damage to a company's reputation can make the difference between a company's success and bankruptcy.

A growing interest in materials analysis is spurred by these concerns. The 2017 total market for materials analysis is $2.5 billion. Top-Down Analytics (TDA) Research projects that the market will grow to $2.6 billion, an increase of 3.9%, in 2018. Part of that growth is due to the wide array of industries making use of the instruments included in the materials analysis segment.[1]

Many manufacturers are discovering the value in materials analysis and the expertise of industry leaders like Waters. The wide range of available technologies coupled with an open-minded partnership – like the one between Fikst and Waters – can help companies solve similar real-world problems.

Sabin considers the results of the troubleshooting project with Waters to be a success, and not just because of the improved quality control procedures now in place at Sage. The joint project was important for Fikst's business strategy too.

Sabin explains: *"We recommend those vendors. If they aren't performing well, it affects our reputation with our clients. The extent to which we can help our customers solve problems is going to strengthen our relationship and make us valuable as partners."*

References

1. "2018 Outlook: Analytical Instruments Industry." *Top-Down Analytics (TDA) Research* [2018].

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