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Cost and Performance in Analytical LC

Ensuring Operational Excellence

Progress and Innovation in Analytical LC

Analytical Liquid Chromatography:

The Role of Cost, Reliability, and Innovation in Selecting Instruments

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INTRODUCTION

Analytical liquid chromatography (LC) plays a pivotal role in modern laboratories. To better understand end-user preferences, LCGC International *has conducted independent user surveys commissioned by Agilent Technologies every two years since 2012. These surveys have continuously gathered insights from hundreds of respondents on liquid-phase separation techniques and instrumentation. This eBook explores key findings, focusing on the balance between cost and performance, including total ownership costs and instrument longevity. It also highlights the role of reliability, downtime reduction, and customer support for efficient workflows, as well as end-user preference shifts compared to previous surveys as LC technology advances.*

The Balancing Act:

Navigating Cost and Performance in Analytical Liquid Chromatography

It is crucial to consider the total cost of ownership when purchasing a new analytical instrument, beyond the initial price, by factoring in long-term expenses like maintenance, operational costs, and downtime.

INTRODUCTION

When purchasing a new instrument, the inexperienced buyer is likely to pay attention only to the price quoted by the salesperson. They may try to negotiate a discount or additional features for the same price but may not take into account the additional costs that are always associated with using the instrument.

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When calculating the total financial cost of a new instrument, more factors must be taken into account. In addition to the purchase price, aspects of laboratory operation come into play. These include the operating, maintenance, and repair costs, as well as expenses associated with downtime and lost productivity. Other hidden costs can include training, consumables, instrument compatibility, and upgrade options. Each of these can impact the decision of which vendor provides the best value. In the 2024 survey of users of analytical liquid chromatography (LC) instruments, conducted by *LCGC International*, 76% of the respondents cited price versus performance as a priority.

TABLE 1 lists some of the factors that go into the price/performance calculation. Some of the factors, indicated in red, are common to both categories. They impact the price (cost per analysis) and the performance when considering quality, timely data.

To illustrate the concerns that arise in determining the price/performance equation, one can look to a hypothetical laboratory situation. The laboratory needs to replace an analytical LC instrument because it has reached the end of its useful life. The purchaser is required by their organization to get quotes for the instrument from different vendors, and one quote is substantially lower than the other. However, in evaluation, is that really the best deal?

TABLE 1: Factors that impact price and performance to consider in an instrument purchase.

COST	PERFORMANCE
Initial Purchase Price	Accuracy and Precision
Useful life	Precision
Operational Costs	Ease of use
Consumable costs	Flexibility
Support	Minimum training
Compatibility	Versatility
Service Costs	Sample Throughput
Sample Throughput	Reliability
Reliability	

First, it is important to examine initial cost versus long-term costs. What is the expected life of the new instrument? An instrument with a longer usable life may be the better choice. For some labs, a well-functioning, fully depreciated instrument is a financial advantage; in many cases, the longer life is due to a more durable design, which also means less service.

Support, maintenance, reliability, and downtime are all factors that will impact the final cost of the instrument. An instrument that requires more maintenance or is less reliable translates into lost opportunity costs in the laboratory. If the customer support or service is not available easily or rapidly, that again is a lost opportunity cost.

Typically, operational costs like solvents, waste disposal, and consumables are considered lab costs but, in reality, are directly related to the instrument and are a part of the instrument cost equation. A recent survey of LC users showed that 68% of the respondents cited operational costs as a consideration in a new instrument purchase.

Solvents may be the biggest operational cost for an LC instrument. There is a cost associated with solvent purchase as well as disposal. Strategies to optimize solvent usage can go a long way in reducing operational costs. Optimizing the flow rate, using smaller columns, having a more concentrated sample, and using less solvent-intensive preparation techniques will reduce the amount of solvent the lab must purchase and, after analysis, to dispose of as hazardous waste. An ultra-high performance liquid chromatography (UHPLC) system uses many of the strategies such as smaller columns, smaller samples, and lower flow rates. A comparison shows that up to 90% solvent consumption can be saved when switching from HPLC to UHPLC conditions for the same analysis.[1]

If the instrument can run the analyses faster, with less set-up time, fewer consumables, and smaller solvent volumes, then each run will cost less, which is considered savings.

Solvent recycling is also a strategy that can be used, but in analytical LC or liquid chromatography-mass spectrometry (LC-MS) applications, the quality of the recycled solvent is a concern and the systems needed to recycle the solvents may not provide the cost savings desired.

Taking care of the instrument will minimize operational costs, whether due to direct outlay or in downtime. Regular maintenance will prevent catastrophic failures. Properly caring for the columns, including during storage, minimizes replacement costs, and keeping a spare parts inventory reduces the down time while waiting for a spare. A factor that may not be as obvious is using quality consumables (such as columns) to obtain consistent performance and reduce replacement costs.

These are some of the considerations on the cost side, but one should also consider performance. This would include the classic accuracy and precision considerations; however, most instruments now are capable of similar analyses. If the less expensive instrument cannot reach the needed detection limit or multiple analyses are necessary to get results that meet the lab's QC criteria, then it shouldn't be considered savings. Sample throughout, however, does matter. If the instrument can run the analyses faster, with less set-up time, fewer consumables, and smaller solvent volumes, then each run will cost less, which is considered savings.

Training, ease of use, integration into the lab systems, and compatibility of instruments are factors that may not be considered in many calculations but should be. In a simple example, if the analysts need to learn a different software package to run the less expensive instrument, that is not savings.

Finally, there is versatility and flexibility. If the less expensive instrument cannot be upgraded or modified to perform the new analysis the lab is tasked with, that necessitates a new instrument purchase and that would incur a significant cost. When all these factors are considered, the less expensive instrument may not make the most financial sense.

There are a number of ways to address the operational costs. Instrument cross compatibility is a strategy for minimizing operational costs and many laboratories with multiple instruments use this for overall savings and up-time. By nature, LC devices are a series of components and having compatible components from the same vendor means that a component failure on a key analysis might be rapidly dealt with by swapping the offending module. Backwards compatibility and extensive upgrade options will also lower the overall operating costs in the long term.

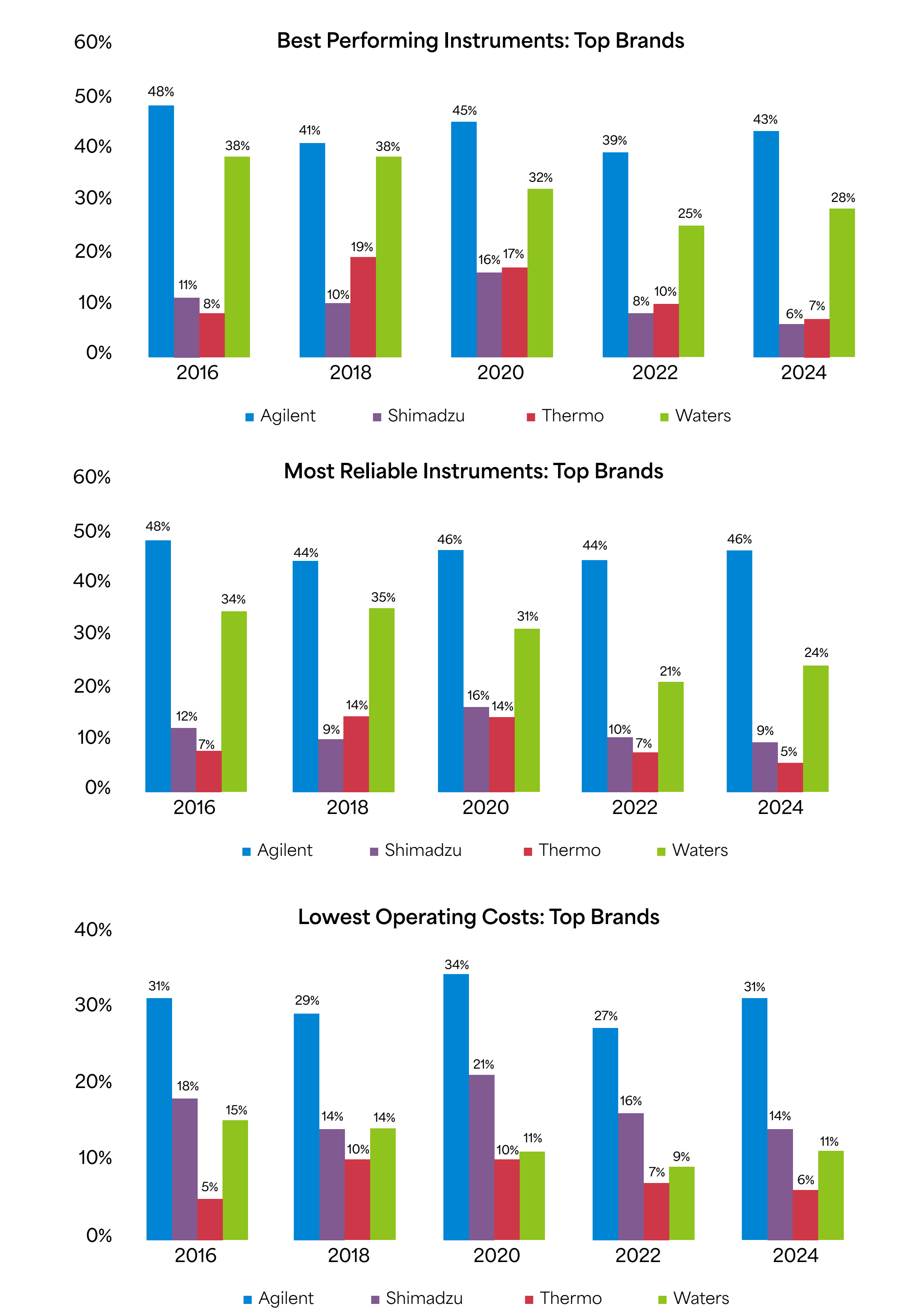
Negotiating favorable contracts with vendors, making bulk purchases, and having instruments under service contract will cut costs for many of these items.

Optimum laboratory layout, reducing power consumption on instruments, and having robust standard operating procedures (SOPs) to minimize false starts also contribute to smaller operating costs. One area that may not be obvious is vendor relations. Negotiating favorable contracts with vendors, making bulk purchases, and having instruments under service contract will cut costs for many of these items.

The survey also asks participants which companies most often meet the above factors: performance, reliability, and lower cost of ownership. Agilent has consistently been the highest rated brand in each of these categories since 2012. The results of the last 5 surveys are shown in the charts in **FIGURE 1**.

It is important to mention that an approach that may be used to reduce the price of an instrument is to purchase second-hand. This is something that is potentially a problem. Purchasing a used instrument from the original vendor, where the instrument has been factory refurbished and has a guarantee, may be cost

FIGURE 1: Year over year comparisons of performance, reliability, and low operating costs for LC instruments. This data was derived from survey results of LC instrument users over the past eight years.



effective. However, purchasing from a third-party instrument broker is an approach that is prone to failure. Secondhand instruments are usually "as is," and one may find that a major component is missing or the software that runs the instrument is unavailable. Worse than that, the original instrument vendor may refuse to put the device on service contract or service it at all. This is an example of false economies.

Conclusion

It is important to consider the total cost of ownership of an instrument over the life of the device and the financial impact on the lab budget. A cost-effective instrument purchase may not be as obvious as the lowest quote. The financial outlay over the life of the instrument is a much better measure of the cost of equipment. When all factors are considered, a more expensive, well-designed instrument—that is purchased from a top-tier vendor with excellent support and a long useful life—is often the least expensive long-term purchase.

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Ensuring Operational Excellence:

The Importance of Reliability, Minimizing Downtime, and Stellar Customer Support

When selecting an LC or LC-MS instrument, reliability, ease of maintenance, and robust customer support often outweigh initial purchase price, ensuring long-term productivity and operational excellence for laboratories.

INTRODUCTION

Chromatographic separations are key to most analyses, including the determination and identification of materials. A recent market report estimated that, by 2030, the market for liquid chromatography (LC) would exceed $8 billion.[1] Although there are other variations in LC such as size exclusion chromatography (SEC), ion exchange chromatography (IEX), and preparative LC, the bulk of the business is in analytical HPLC and UHPLC with either nonspecific detectors such as ultraviolet (UV) or compound specific detectors such as a mass spectrometer (MS).[2]

The liquid chromatography-mass spectrometry (LC-MS) combination is becoming increasingly common in the analytical laboratory. A recent market report predicted that the market could almost triple by 2030 from the 2022 values.[3] With LC being common to LC-MS instruments, such an LC is interfaced to a variant of a single or triple quadrupole MS, or ion trap MS. Each of the variations in the mass spectrometer is designed to provide different data as appropriate for specific problems.

These instruments are the workhorses of the analytical laboratory. Instrument reliability, low downtime, and the ability to connect with the vendor for answers in a very timely manner are critical points in the purchase decision. In many cases, these factors outweigh the purchase price of the instrument.

Most of the installed base of this category of instruments is in industrial settings, including analytical testing, pharmaceutical, life sciences, or environmental analysis laboratories. In these environments, it is key that the user has an operational instrument right off the bat. A non-functional instrument or a poorly functioning instrument costs the laboratory and the company in terms of lost productivity. In a recent survey of users of these analytical LC instruments, 95% of the respondents rated reliability as a key factor when choosing a vendor. FIGURE 1 shows the factors considered most important when choosing a supplier for LC instrumentation according to survey respondents. FIGURE 2 shows a comparison of instrument reliability between the leading brands for analytical LC and LC-MS.

FIGURE 1: Factors important in the selection of LC instruments, illustrating that the reliability of the instrument is key in the purchase decision, based on survey results conducted by LCGC in 2024.

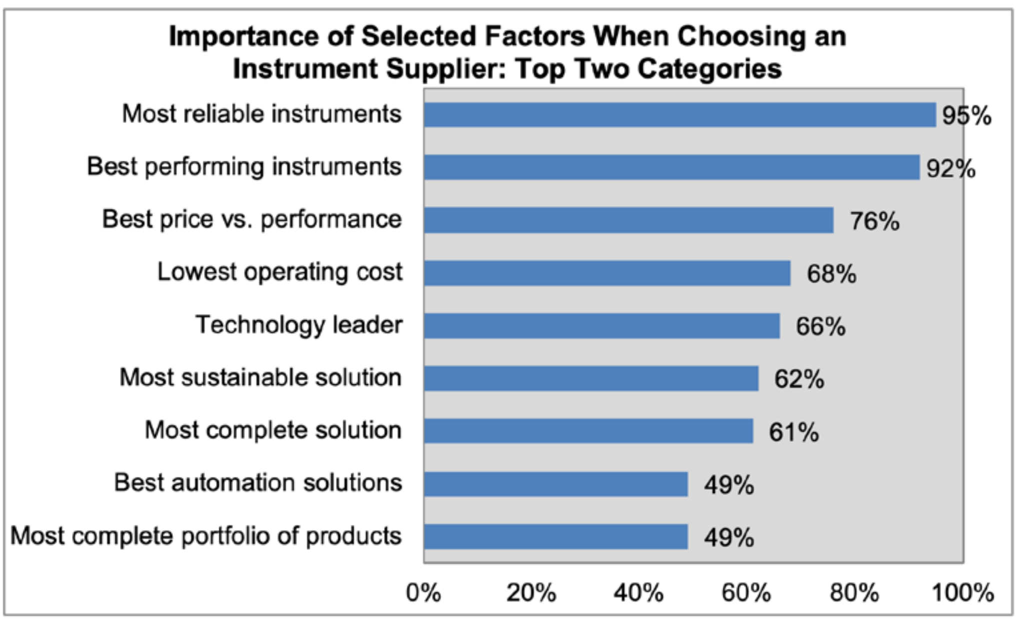
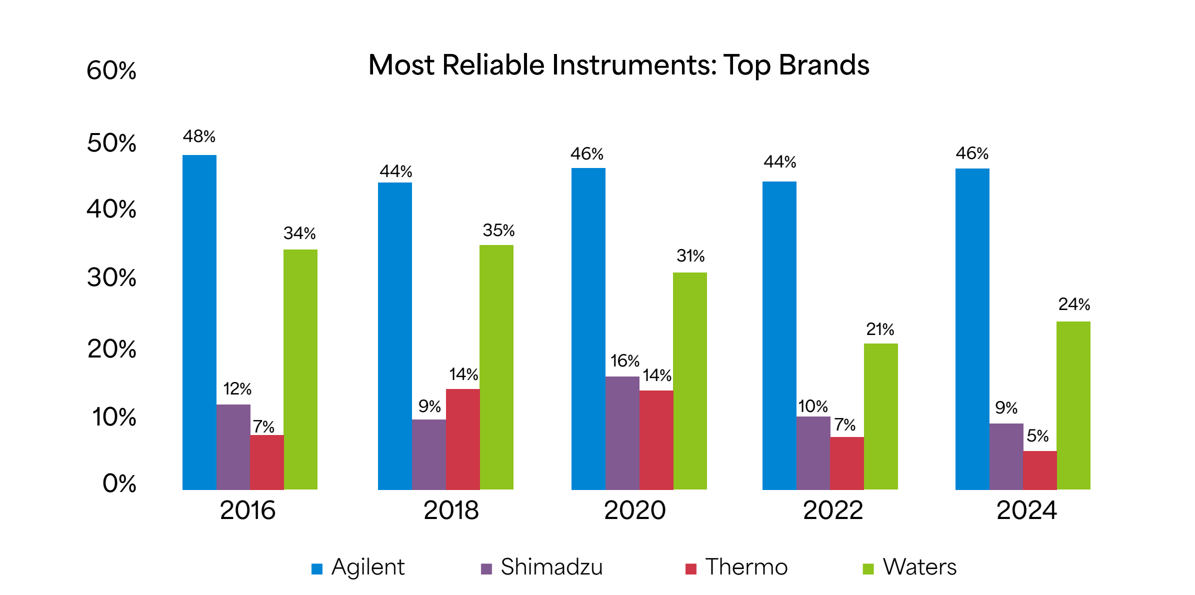


FIGURE 2: Comparison of brands in Analytical LC and LC-MS based on survey results conducted by LCGC over the past eight years.



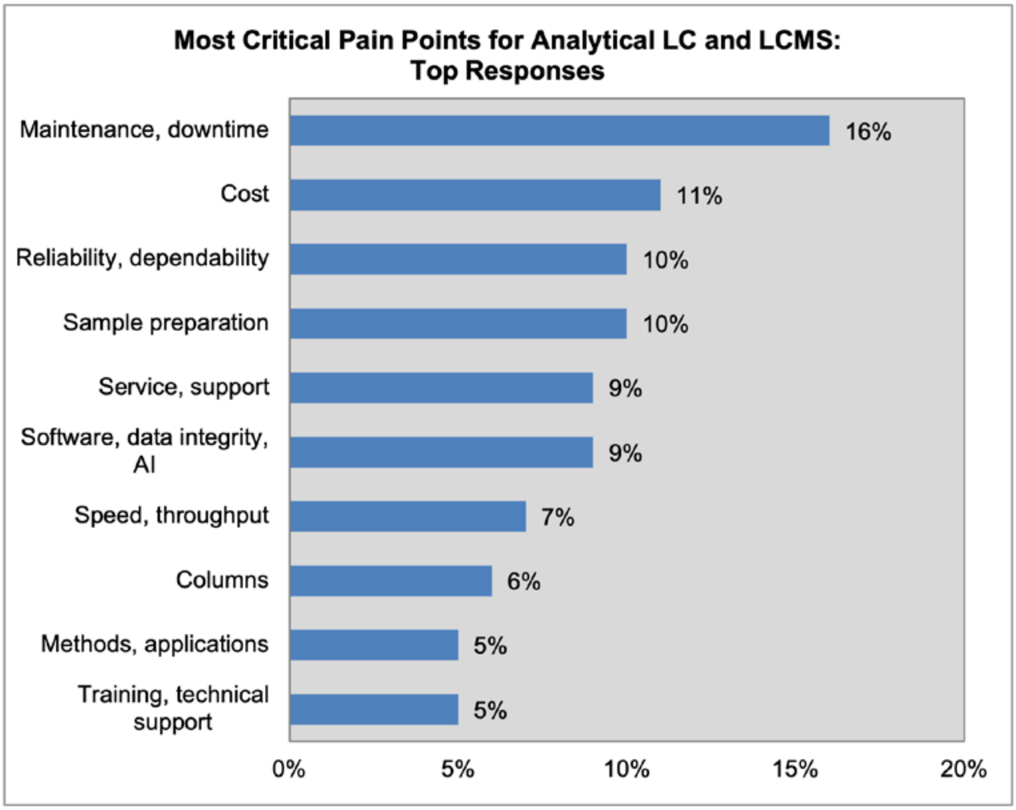
Many of the factors that impact reliability are part of the overall design and manufacturing process. Instrument vendors use a variety of strategies to ensure reliability of their products in the field. Instrument companies adhere to International Organization for Standardization (ISO) principles, which require extensive documentation and change control for all steps in the design and manufacturing process. Robust design specifications that are neither too tight nor too loose can ensure every instrument coming off the assembly line works in the same way. Having narrow specifications on materials—such as seals—means that there is no occurrence of poor material which would otherwise compromise performance. Finally, instruments should be designed to make customer maintenance easy; this includes simple details like how the covers come off.

In the manufacturing process, robust final test procedures are critical to ensure every instrument performs as specified. A well-trained service engineer can install the instrument and field test it, which is the final step in having a device that performs as desired.

In the recent survey, the pain point mentioned most often was maintenance and downtime (**FIGURE 3**). Both of these bottlenecks impact the productivity of a laboratory. Minimizing downtime goes hand in hand with a reliable instrument, and the ability to perform routine maintenance easily is part of this equation.

When an instrument is designed with customer maintenance in mind, it is more likely that a user will perform routine maintenance. This maintenance is key to long-

FIGURE 3: In the 2024 survey conducted by LCGC, 16% of the respondents cite maintenance and downtime as the most critical pain point.



term instrument performance. In the laboratory, a number of strategies exist to encourage this routine maintenance.

The first step is tracking the instrument performance. Running standards or test samples and generating control charts of the results can show long-term degradation. Setting and diligently following a schedule for performance tests and routine maintenance can help prevent errors from occurring which would then result in bad data. Having a standard set of troubleshooting steps that anyone can follow in sequence will help to find the source of the problem more rapidly than a disorganized approach. Instrument vendors that can provide documentation for troubleshooting to their customers are highly valued.

Customer support is the third component of operational excellence. In many cases, this is the area most visible to the average customer and can facilitate easy and fast access to solutions. Can a customer find the information they need on the company website? One of the most frustrating experiences for a customer is having to dig through multiple web pages and guess key words to find the necessary information. Is the customer support organization responsive? Many organizations that extensively use LC run multiple shifts and, when a customer calls in with a question or issue, do they have the option to speak with a real person, or are they forwarded to a voicemail system and told to expect a call back within 24 hours? Although it is employee intensive, help lines that operate 24/7 will demonstrate that an organization is committed to providing quality customer support.

Training a customer also goes a long way in providing customer satisfaction. Training can take a number of forms such as videos associated with the instrument software, on-line courses (whether pre-recorded or live), or, for the most satisfying (and expensive) experience, in-person training at the instrument vendor facility.

Having a supplier that sees the new applications and proactively develops methods is incredibly valuable.

Something that may not be recognized as customer support is applications help. Although many LC instruments are used in routine environments, doing standardized methods in the R&D environment where the more sophisticated instruments are used, discussing problems with a scientist who is the expert in the instrument can significantly shorten the method development timeline. Having a supplier that sees the new applications and proactively develops methods is incredibly valuable.

Finally, the service engineer is crucial, as they represent the company in the eyes of the customer. Typically, the customer discusses problems with the engineer before they arrive on-site, and many customers assume the solution arrives with the engineer. The engineers are expected to understand the instrument and repair the problem.

Conclusion

All the points discussed here are interrelated. Instrument design impacts reliability, maintenance, and service. Reliability impacts productivity, especially minimizing downtime, and performance. Customer support impacts the customer experience, the perception of the instrument usability and reliability, as well as the productivity of the instrument and laboratory. These components add up to operational excellence of the instrument and customer loyalty to a trusted supplier.

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Driving Progress:

The Role of Innovation and Performance in Analytical LC Instruments

Since the introduction of HPLC in the late 1960s, innovations in column technology, hardware, and software—especially UHPLC and LC-MS advancements—have transformed analytical chemistry.

INTRODUCTION

The first high-performance liquid chromatography (HPLC) instrument was introduced in the late 1960s, and this introduction marked a significant advancement in analytical chemistry and separation sciences. Since then, a number of developments have moved the technology forward. In an article published in *Chemical and Engineering News*, the author traced early developments of HPLC, concentrating on the academic achievements published in peer-reviewed journals.[1] However, academics do not produce products and it takes visionary companies to provide products to the market place.

Developments in the technology followed two different paths: developments in instrumentation and development of better, more efficient columns.[2-4] Many companies played a part in these developments and due to the changes and consolidation in the industry since its inception, many of the companies mentioned in these references have been purchased and are now a part of one of the three major analytical liquid chromatography (LC) suppliers: Agilent, Thermo Fisher Scientific, and Waters.[2]

The significant developments made in hardware are shown in **TABLE 1**. These developments are easy to categorize and list by date. However, the real changes that have advanced the separation capabilities have been evolutionary and related to column technology.[1]

Since the introduction of the first HPLC instrument, the market has seen major changes in columns, hardware, and software.

Since the introduction of the first HPLC instrument, the market has seen major changes in columns, hardware, and software. Some of this change has been driven by overall technology improvements in areas such as electronics and computer technology, but most innovations are driven by the industry itself seeking lower detection limits, better compound separation, and enhanced compound identification.

Two technical advancements that have revolutionized the analytical LC area are the introduction of ultra-high performance liquid chromatography (UHPLC) and the major advancements in LC coupled with mass spectrometry (MS), including ultrafast MS and variations in tandem LC-MS.[5] These advances have opened up areas of research that, in the past, would have been nearly inaccessible.

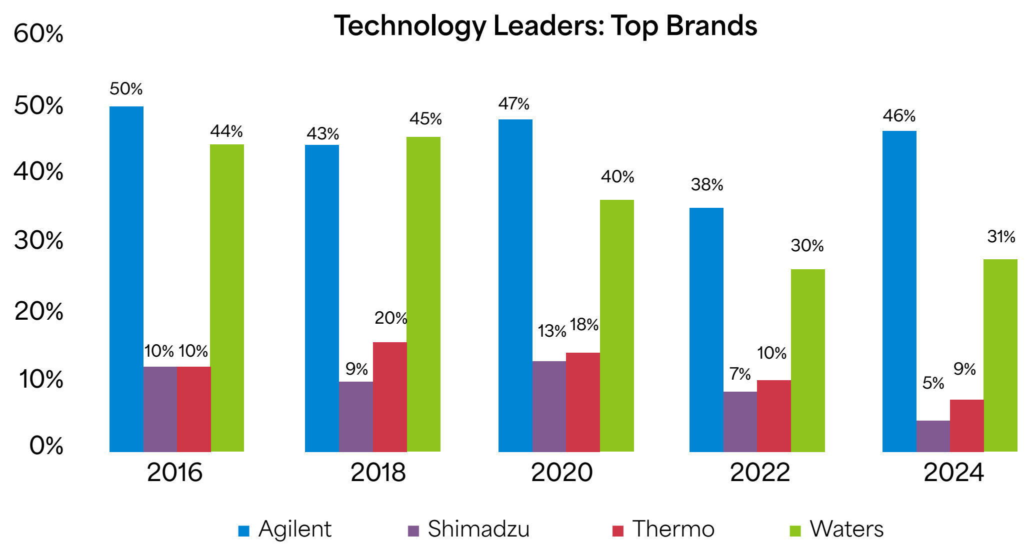
In a recent survey conducted by interviewing analytical LC users, 66% of the respondents said they valued suppliers that were technology leaders (**FIGURE 1**). Agilent and Waters were most often mentioned as the technology leaders, as both companies have been responsible for many of the significant developments in instrumentation (**TABLE 1**).

Perhaps the most significant innovation in recent years derives from advancements in LC-MS metabolomics, a technology that has impacted areas such as epidemiology, pharmacology, toxicology, and disease biology.[6]

TABLE 1: Significant hardware developments in analytical LC and LC-MS. This is not an exhaustive list but meant to illustrate the role that major suppliers have played in the industry's progress.

YEAR	TECHNOLOGY	COMPANY
1967	First commercial integrated HPLC instrument	Picker Nuclear (now Agilent)
1968	6-port injection valves	Valco
1968	First modular LC detectors	Milton Roy
1972	First modular pump designed specifically for HPLC	Waters
1974	First microprocessor-controlled integrator	HP (now Agilent)
1974	First modular autosampler	Micromeritics (now Malvern Panalytical)
1976	First integrated HPLC with digital processor control for automated sample injection, flow control, UV detector recording and reporting	HP (now Agilent)
1976	Introduction of radial compression columns	Waters
1977	First diode array detector (DAD) for HPLC	HP (now Agilent)
1977	Moving belt LC-MS interface	Finnegan (now Thermo)
1978	First refractive index detector for HPLC	Waters
1981	First HPLC-MS instrument	PerkinElmer
1987	Thermospray HPLC/MS interface	Vestec
1989	Electrospray HPLC/MS interface	Sciex
1989	Introduction of ChemStation software	HP (now Agilent)
1990	First modular HPLC system	HP (now Agilent)
1996	First Empower software	Waters
2004	First ACQUITY UPLC system	Waters
2005	First HPLC-Chip/MS system	Agilent
2005	First charged aerosol detector (CAD)	ESA Biosciences (now Thermo)
2007	First HPLC system with RFID technology	Agilent
2010	Introduction of the H-Class UPLC system	Waters
2012	First Intelligent System Emulation Technology (ISET)	Agilent
2014	Agilent 1290 Infinity II Series (UHPLC)	Agilent
2014	Vanquish UHPLC	Thermo
2016	Infinity II Evaporative Light Scattering detector	Agilent
2016	ZipChip Interface for MS	908 Devices
2020	SureSelect XT HS2 RNA system	Agilent

FIGURE 1: In the 2024 survey conducted by LCGC, respondents highly value suppliers who are technology leaders.



The entry of LC-MS into these research areas is enabled by improved performance of the systems in resolution, sensitivity, and sample throughput. These were key metrics cited by respondents as the components of a high-performing instrument, and 92% of the respondents prioritized high performance.

An interesting development, cited in a panel discussion recorded by *LCGC*, is the shift toward easy to use instrumentation, which enables anyone to use the technology correctly.[5] This is in addition to the high-performance criteria and is driven by the need for scientists to accomplish their research without spending valuable time and resources on instrument maintenance.

Over the past 10 years, the most significant advancement has been the introduction of UHPLC. With higher pressure and smaller particle size, there is a significant increase in sample throughput without sacrificing resolution or sensitivity. In fact, the implementation of this approach has improved both the resolution and the sensitivity, accomplishing lower detection limits.

TABLE 2 shows the most important trends in analytical LC and LC-MS according to survey respondents. New methods, more automation, and a further shift to UHPLC were the most cited trends. The shift to UHPLC is, of course, tied to increased speed and throughput. On the data side, improved software, increased data integrity, and better use of artificial intelligence (AI) were also mentioned. It is interesting that AI was ranked as low as it was, because better use of AI has the potential to shorten method development time, optimize the maintenance cycle, and automatically detect anomalies in the data runs.

TABLE 2: The top five trends cited as important in the next five years by survey respondents.

Most Important Trends in Analytical LC and LC-MS for the Next Five Years (N=458)	
CATEGORY	**%**
Methods, applications	14%
Automation	12%
Shift to UHPLC	12%
Speed, throughput	10%
Software, data integrity, AI	8%

Conclusion

Innovation has, since the introduction of the first HPLC system, been the key to growth and increased applications for analytical LC. That being said, research drives developments and developments drive research. By listening to key customers, focusing on emerging areas of research, and enabling the in-house experts to explore the bleeding edge of separation sciences, the technological leaders in analytical LC and LC-MS will maintain their leading positions.

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