

Cost of Ownership Comparison: HPLC to TOC for Cleaning Validation

introduction

In accordance with industry best practices for the lifecycle approach to process validation, improving quality through process understanding is the cornerstone from which operational efficiencies emerge. Justifying any capital expense is an important first step to implementing the technologies that drive these efficiencies and typically hinges on determining the Return on Investment (ROI).

The ROI is defined as the benefit to an investor resulting from some resource. The ROI can be measured by either increased profits, decreased cost, increased productivity, or even reduced risk to the business. When considering a shift from High Performance Liquid Chromatography (HPLC) to Total Organic Carbon (TOC) analysis for Cleaning Validation (CV), all of these metrics contribute to the ROI.

While these metrics support the use of TOC analysis for CV, they can be subjective and, therefore, hard to quantify. One assessment that is easier to quantify for ROI is a cost of ownership comparison. Thus, this application note compares instrument cost, annual maintenance cost, and annual operating cost for HPLC and TOC analysis to demonstrate savings generated by deploying TOC analysis for CV.

comparison assumptions

When comparing HPLC and TOC analysis, several parameters must be fixed to establish true equivalency. To start, the throughput for both HPLC and TOC instruments is fixed at 2,500 samples per year with triplicate repetitions of each sample. This equates to a total of 7,500 measurements over the course of a 2,000-hour work year. Both the HPLC and TOC instruments require an operator to run the samples. It is a valid point of differentiation that HPLC operation and data analysis are inherently more complex than TOC analysis and, therefore, demand a more skilled operator at a higher

compensation. For the sake of this comparison, however, labor cost is held equal.

instrument cost

Relative capital cost investment for TOC and HPLC instruments is shown in **Table 1**.

Table 1: Comparison of relative capital cost of TOC and HPLC instruments

Sievers* M9 TOC	HPLC
M9 Lab Instrument	Integrated HPLC Instrument
Autosampler	HPLC Software
DataPro2 Software	
MSRP: 99%	MSRP: 100%

For this comparison, the most economically comparable HPLC instrument has an integrated configuration. The instrument consists of a 4-channel degasser, quaternary valve, pump, high capacity autosampler, column oven, and UV detector. This HPLC instrument is specifically designed for high throughput Quality Control labs. The relative cost listed for a TOC instrument is for the Sievers M9 Laboratory TOC Analyzer with a Sievers Autosampler. In addition to the instrument hardware, the pricing also includes the necessary software to operate both instruments.

maintenance cost

The manufacturer of the HPLC instrument provides a list of recommended annual preventative maintenance items on its website¹ and prices for those items on its webstore². Due to different recommendations for maintenance components based on the years of service for the HPLC, items in **Table 2** are annualized to arrive at a true representation of the annual maintenance cost.

Table 2: Comparison of annual preventative maintenance parts and pricing for TOC and HPLC instruments²

Sievers M9 TOC	HPLC
Maintenance Kit includes:	Suction Filter Assembly
Acid (2x)	Plunger Seal (2x)
Oxidizer (x4)	Plunger Holder Assembly (2x)
UV Lamp (x2)	Diaphragm (2 pack)
Pump Head (x2)	Inlet Check Valve (2x)
Resin Bed	Outlet Check Valve (2x)
	Air Filter Side
	Air Filter Front
	LPV Rotor
	LPV Stator
	HPV Rotor
	HPV Stator
	Detector Air Filter
	Metering Pump Seal
	Needle
	Needle Seal
	100 uL Sample Loop
	Flow Cell Gasket
	UV Lamp
Total 75%	Total 100%

For both the TOC and HPLC instruments, only annual service part prices are compared. If a service engineer performs the maintenance, additional labor expenses are incurred but are not included in the current analysis. It is a valid point of differentiation that HPLC service costs are more expensive than TOC as they are inherently more complex and therefore more time consuming to perform all the necessary preventative maintenance.

operating cost

The primary annual cost driver for any analytical instrument is the operating cost. This includes consumables, reagents, and labor- with labor being the largest expense. For TOC analysis, the total sample run

time for 7,500 measurements is 500 hours in normal mode of operation. For HPLC analysis it becomes more complex, as method times vary greatly depending on the analyte chemistry, matrix, column, reagents, and pressure. A conservative estimate on the sample run time for HPLC is five minutes per sample repetition making the total sample run time for 7,500 measurements 625 hours. Considering an equal instrument operator cost, this amounts to an annual savings of 20% on labor alone, as shown in **Table 3**.

Table 3: Comparison of operator cost for TOC and HPLC for a 7,500 measurement per year workload

Sievers M9 TOC		HPLC	
Time	500 hours	Time	625 hours
Total	80%	Total	100%

Similar to labor cost, the HPLC consumable cost is also a complex calculation. For this comparison, a standard 4.6mm x 100mm C18 column is used³. Reagents for the method are set as 50/50 water and methanol mix. As mentioned previously, if a 5-minute method is assumed with a 1 mL/min mobile phase flow rate and 7,500 repetitions annually, the amount of HPLC grade methanol and water consumed in a year can be calculated. Pricing for the reagents is obtained from an industry leading reagent provider and quoted in the largest volume possible to minimize price per liter⁴. **Table 4** highlights the annual consumable cost for TOC and HPLC.

Table 4: Comparison of annual consumables cost for TOC and HPLC instruments

Sievers M9 TOC	HPLC
Vials	Vials ²
	Column ³
	HPLC Grade Water ⁴
	HPLC Grade Methanol ⁴
Total 81%	Total 100%

discussion

The calculated difference between the two analytical methods' cost of ownership, when combining maintenance, labor, and consumable cost, highlights the benefits of using TOC for CV (**Figure 1**).

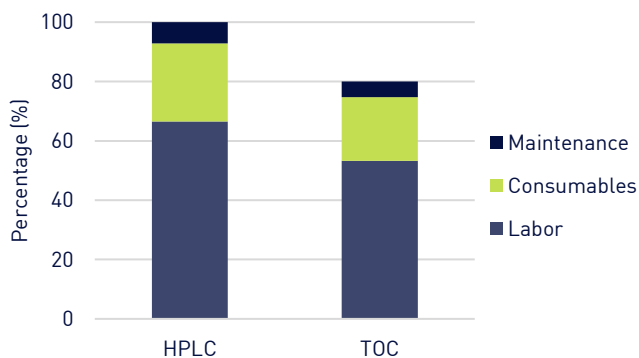


Figure 1: Comparison of annual cost of ownership of HPLC and Sievers M9 TOC Analyzer for CV

In summary, **Table 5** highlights the easily quantifiable differences between using a single TOC instrument compared to an HPLC instrument for CV. **Figure 2** shows the breakdown of where savings are achieved in the cost of ownership.

Table 5: Total annual cost of ownership savings using TOC instead of HPLC for CV

Sievers M9 Annual Cost of Ownership Savings	
Instrument Cost Savings	1%
Maintenance Cost Savings	25%
Operating Consumables Cost Savings	19%
Operating Labor Cost Savings	20%
Total Cost of Ownership Savings	12%

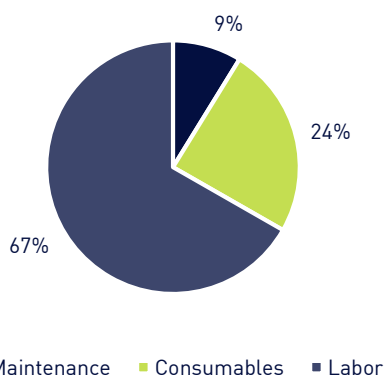


Figure 2: Total cost of ownership savings using TOC instead of HPLC for CV

What these figures fail to capture is the increase in production efficiency gained by quicker release times

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for equipment and better use of laboratory facilities and personnel. These additional efficiencies are specific to individual manufacturers and can lead to significant increases in revenue.

conclusion

This application note makes conservative and favorable assumptions about the cost of operating an HPLC instrument for CV compared to a TOC analyzer. Even in this example, with favorable assumptions for HPLC cost, the Sievers M9 TOC Analyzer has a lower cost of ownership across the board. In this example with a workload of 7,500 measurements, the Sievers M9 Lab TOC Analyzer has a payback period of less than three years based on cost savings alone compared to HPLC. If used to capacity, the Sievers M9 TOC instrument payback occurs during the first year based on cost savings alone compared to HPLC.

These savings, in conjunction with increased productivity, lower labor cost, and better risk management through process understanding, render TOC analysis the preferred method for CV by regulatory bodies as well as industry leaders. As demonstrated in this comparison, the Sievers M9 Lab TOC Analyzer is more cost effective to purchase, maintain, and operate than HPLC for cleaning validation.

References

1. Shimadzu Liquid Chromatography LC Consumables Catalog. 2017 Catalog. Retrieved November 19, 2017, from <https://www.ssi.shimadzu.com/products/literature/hplc/SSI-LC-10-2017.pdf>
2. Shimadzu Scientific US Webstore. Retrieved November 19, 2017, from <https://store.shimadzu.com/>
3. ShodexHPLC Webstore. Retrieved November 19, 2017, from <https://www.shodexhplc.com/product/shodex-c18-4c/>
4. Sigma-Aldrich Webstore. Retrieved November 19, 2017, from <http://www.sigmaaldrich.com/catalog/product/sigald/34860?lang=en®ion=US>