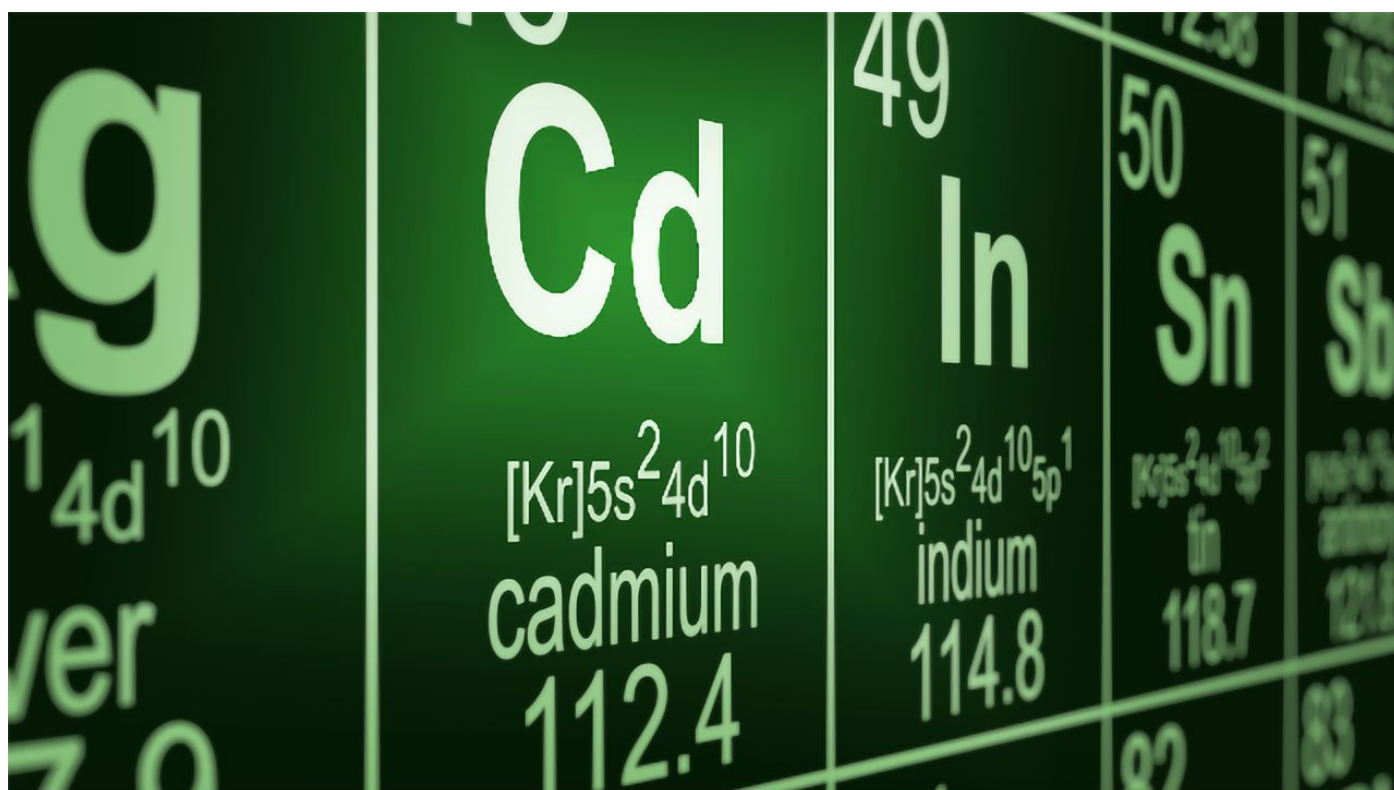


Expanding the Panel of Elemental Contaminants in Cannabis and Hemp Consumer Products by ICP-MS: Do You Know the Cost Difference?

Article

🕒 Published: October 4, 2021



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Imagine you run a cannabis testing lab and have been asked to look at an expanded panel of elemental contaminants because one of your clients just attended a virtual ASTM workshop on measuring heavy metals in cannabis and hemp, which suggested that, as well as the big four heavy metals, there were additional elements being found in many cannabis consumer products¹. You have the capability because you just invested in a brand new inductively coupled plasma-mass spectrometry (ICP-MS)

system that can measure the periodic table in a few minutes. Developing a method is not the problem because you have just hired an experienced lab technician who has been running ICP-MS for the past 5 years in a pharmaceutical contract lab. However, you are concerned that measuring the additional panel of elements will impact your bottom line.

Cannabis testing lab requirements

This could likely be the scenario as more state regulators start to show interest in monitoring additional elemental contaminants to ensure safer consumer products, particularly in cannabis vaping systems, which are notorious for producing aerosols containing metals derived from components inside the device. But how many metals should there be in an expanded list? The majority of the 36 or so states that have legalized medical cannabis require the big four – lead (Pb), cadmium (Cd), arsenic (As) and mercury (Hg) – to be tested. New York State also requires the testing of chromium (Cr), nickel (Ni), copper (Cu), antimony (Sb) and zinc (Zn), while Maryland (and a few other states) adds Cr to the big four².

Moreover, the National Institute of Standards and Technology (NIST) is developing a 13-toxic element hemp certified reference material (CRM) through its CannaQAP Program to include Pb, Cd, As, Hg, beryllium (Be), cobalt (Co), Cr, manganese (Mn), molybdenum (Mo), Ni, selenium (Se), uranium (U), and vanadium (V)³. In addition, if we also include the pharma Class 2A elements, Ni, Co, and V, which are required in all oral, inhalation and transdermal drug products and substances⁴, we end up with a likely panel of 15 elemental contaminants.

To get a better understanding of the cost difference between testing for 4 and 15 elemental contaminants, let us first take a closer look at what it costs to run an ICP-MS system⁵. For the purpose of this evaluation, let us make the assumption that the major operating costs associated with running an ICP-MS are the gases, electricity, and consumable supplies. For comparison purposes, the exercise will be based on a typical cannabis testing laboratory running their instrument for two and half days (20 h) per week and 50 weeks a year (1000 h per year).

Note: This comparison will not include the cost of sample preparation. Clearly there are consumables, vessels, reagents and acids involved with digesting cannabis-based samples, and it would be valid to include them but for this cost exercise, only the cost of running the instrument will be included in the calculations.

These data are based on the cost of gases, electricity, and instrument consumables in the United States in 2021. They have been obtained from a number of publicly available commercial sources, including suppliers of industrial and high-purity gases, independent utilities companies, a number of ICP-MS instrument vendors and sample introduction/consumable suppliers. It is also important to emphasize that these costs might also vary slightly based on a particular vendors' instrument being used with slightly different technology, features and hardware.

Gases

A typical ICP-MS uses a total of approximately 17 L/min (~1000 L/h) of gaseous argon (inc. plasma, nebulizer, auxiliary flows). For this reason, most users install a Dewar vessel containing a liquid supply of argon. Liquid argon tanks come in a variety of different sizes, but a typical Dewar system used for ICP-MS holds about 240 L of liquid gas, which is equivalent to 6300 ft³ (178,000 L) of gaseous argon. (Note: The Dewar vessel can be bought outright but are normally rented.) It costs about \$370 to fill a 240 L Dewar vessel with liquid argon. At a typical argon flow rate 17 L/min total gas flow, a full vessel

would last for almost 175 h. Again, assuming a typical laboratory runs their instrument for 1000 h per year, this translates to 6 fills at approximately \$400 each, which is equivalent to about \$2400 per year.

Note: When liquid argon is stored in a Dewar vessel, there is a natural bleed-off to the atmosphere when the gas reaches a certain pressure. For this reason, a bank of argon cylinders is probably the best option for laboratories that do not use their instruments on a regular basis. A cylinder of argon costs approximately \$120 for 340 ft³ (9630L), so at 17 L/min, a cylinder would last about 10 hours. So, the overall cost of argon would depend on the number of cylinders purchased.

Note: Some ICP-MS instrumentation operates at approximately 30 percent lower argon consumption compared to other instruments. So, this should be taken into consideration if this technology is being used.

Another added expense with ICP-MS is that if it is fitted with collision/reaction cell technology, the cost of the collision or reaction gas will have to be added to the running costs of the instrument. Fortunately, for most applications, the gas flow is usually less than 5 mL/min, but for the collision/reaction interface approach, typical gas flows are 100–150 mL/min. The most common collision/reaction gases used to measure heavy metals in cannabis are hydrogen, and helium. The cost of high-purity helium is on the order of \$450 for a 300 ft³ (8500 L) cylinder, whereas a cylinder of hydrogen is approximately \$320. One cylinder of either gas should be enough to last 1000 h at these kinds of flow rates. So, for this costing exercise, we will assume that the laboratory is running a collision/reaction cell/interface instrument, with an additional expense of \$770 on top of the \$2400 for liquid argon, which translates to a combined total of \$3170.

Electricity

The main power requirements for an ICP-MS are the radio frequency generators. The average cost of electricity in the US is 10.4 c per kW/hour. Based on the voltage, magnitude of the electric current, and the number of lines used, the majority of modern instruments draw about 5 kW total power. This works out to be ~\$520 for an instrument that is run 1000 h per year.

Consumables

The main consumable supplies in ICP-MS are in the plasma torch and the sample introduction components. The major consumable is the torch itself, which consists of two concentric quartz tubes and a sample injector either made of quartz or some ceramic material. In addition, a quartz bonnet normally protects the torch from the RF coil. There are many different demountable torch designs available, but they typically cost about \$600–700 for a complete system. Depending on sample workload and matrices being analyzed, it is normal to go through a torch every 4-6 months. In addition to the torch, other parts that need to be replaced or at least need to have spares include the nebulizer, spray chamber, and sample capillary and pump tubing. When all these items are added together, the annual cost of sample introduction consumables for ICP-MS is on the order of \$3200.

In addition to the plasma torch and sample introduction supplies, ICP-MS requires consumables that are situated inside the mass spectrometer. The first area is the interface region between the plasma and the mass spectrometer, which contains the sampler and skimmer cones. These are traditionally made of nickel, which is recommended for most matrices, or platinum for highly corrosive samples and organic matrices. A set of nickel cones costs \$800–1000, whereas a set of platinum cones costs about \$3000–5000. Two sets of nickel cones and perhaps one set of platinum cones would be required per

year. Other cone materials and tips are available, so whatever is used, just substitute the relevant cost. It is also worth pointing out that unless hydrofluoric acid (HF) is used in the sample digestion, platinum cones may not be required. If that is the case, just substitute an additional set of Ni cones. The other major consumable in ICP-MS is the detector, which has a lifetime of approximately one year, and costs about \$1700. When all these are added together with the torch, the sample introduction components, and the vacuum pump consumables, investing in ICP-MS supplies represents an average annual cost of ~\$10,700.

The approximate annual running cost for an ICP-MS of gases, power, and consumable supplies being operated for 1000 h/year, is shown in Table 1.

Table 1: Typical annual ICP-MS operating costs (\$US) for a laboratory running an instrument 1000 h per Year (20 h per week). Note: ¹ using a liquid argon supply, ² using a collision/reaction cell

Technique	Gases (US\$)	Power (US\$)	Consumable Supplies (US\$)	Total (US\$)
ICP-MS	~3170 ^{1,2}	~520	~10,700	~14,390

Cost per sample

We can take the data given in Table 1 a step further and use these numbers to calculate the operating costs per individual sample, based on the two analytical scenarios of a laboratory determining four analytes per sample and another measuring 15 elements per sample. First let us take a closer look at the difference in analysis time.

Four analytes per sample

Assuming an integration time of two seconds per element, this translates to ten seconds per replicate, including eight seconds actual measurement time plus an overhead time of approximately two seconds for scanning and settling the quadrupole. This equates to 20 seconds per duplicate analysis. When a sample uptake time of 30 seconds, stabilization time of 10 seconds, and a washout time of 30 seconds are factored in, this means a total analysis time of 90 seconds per duplicate.

Note: Use of an intelligent autosampler, with switching valves and rapid sampling capabilities, can reduce sample uptake and washout times by about 50 percent on average, so they need to be factored into the calculation if being used.

Fifteen analytes per sample

Again, assuming an integration time of two seconds per element, this translates to 35 seconds per replicate including 30 seconds actual measurement time plus overhead time of approximately 5 seconds for scanning and settling the quadrupole. This equates to a measurement time of 70 seconds per duplicate. The sample uptake time of 30 seconds, stabilization time of 10 seconds and a washout time of 30 seconds will be exactly the same as for 4 analytes. So, when this is added in, this translates to a total analysis time of 140 seconds per duplicate.

Note: If different measurement times are being used for specific analytes or triplicate analysis per sample is being carried out, the total analysis time needs to be recalculated.

This comparison between 4 elements per sample and 15 elements per sample is shown in Table 2.

Table 2: Difference in analysis times between 4 elements per sample and 15 elements per sample in duplicate

Number of Elements	Integration Time per Element (s)	Total Measurement + Overhead Time Per Duplicate (s)	Sample Uptake + Stabilization + Washout Time (s)	Total Analysis Time in Duplicate (s)
4	2	20	70	90
15	2	70	70	140

It should also be emphasized, that a real-world scenario might also include a recalibration/reslope of the instrument, which is typically done every one-two hours depending on the sample loading and type. So, this would have to be factored into the calculation if a "recal" is being carried out.

From this, the cost per sample can be calculated from the annual operating costs. This calculation is also shown in Table 3 and summarized in Table 4.

Table 3: Difference in cost per sample between 4 elements and 15 elements per sample

<u>Number of Elements</u>	Total Analysis Time (s) per Sample in Duplicate	Number of Samples per Hour (no "recal")	Number of Samples Run per Year (assuming 1000 hours of use)	Annual Operating Costs (\$US)	Cost per Sample (\$US)
4	90	40	40,000	14,390	0.36
15	140	26	26,000	14,390	0.55

Table 4: Operating Costs for a measuring 4 analytes and 15 analytes per sample based on running an instrument for 1000 h per year

Technique	Operating Cost for 4 Elements per Sample (\$US)	Operating Cost for 15 Elements per Sample (\$US)
ICP-MS	0.36	0.55

Final thoughts

It must be emphasized that these figures have been generated for a typical cannabis testing lab workload using the average cost of gases, power, and consumables in the United States. However, if the costs in your region are different, or your analytical scenario, sample loading, measurement/integration times, recalibration frequency, use of a rapid sampling system etc. are different, just plug your numbers into the calculation (a simple spreadsheet would be worth the effort). Even though the final operating costs per sample might be different, the comparative costs should be the same. So, expanding the analyte panel from 4 to 15 elemental contaminants represents a 375 percent increase in the number of analytes, the corresponding increase in cost per sample is only 53 percent.

This is an important point to emphasize because many cannabis testing labs are running “lean operations” and are very concerned that measuring the additional elements might be cost prohibitive. This costing exercise has clearly indicated that this is not the case. It is difficult to know what the final panel of elements will be whenever the FDA eventually has federal oversight of the cannabis industry, but based on the 20-plus years of carrying out a risk analysis of the pharmaceutical industry, regulators eventually ended up with a list of 24 elemental impurities permitted daily exposure limits (PDEs) in drug products and substances by drug delivery method⁴. I am not sure the cannabis industry needs this many, but it definitely should be carrying out a risk assessment of all the potential elemental contaminants during the entire production process. It might not need to be as many as 15, but clearly it should be significantly more than just the big four to ensure the safety of cannabis consumer products.

Further reading

1. **A Recap of ASTM’s Workshop on Measuring Elemental Contaminants in Cannabis and Hemp Consumer Products, Analytical Cannabis, August 5, 2021.**
2. **Measuring Heavy Metal Contaminants in Cannabis and Hemp, Robert J. Thomas, ISBN 9780367417376, CRC Press, Boca Raton, October, 2020.**
3. **NIST CannaQAP Program for Cannabis Laboratory Quality Assurance.**
4. **INTERNATIONAL COUNCIL FOR HARMONISATION OF TECHNICAL REQUIREMENTS FOR PHARMACEUTICALS FOR HUMAN USE Q3D GUIDELINES FOR ELEMENTAL IMPURITIES, 2019.**
5. **Money To Burn: Do you Know What is Costs to Run your Atomic Spectroscopy instrumentation? Robert. J. Thomas, International LabMate, April, 2016.**



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