Case study | 000866

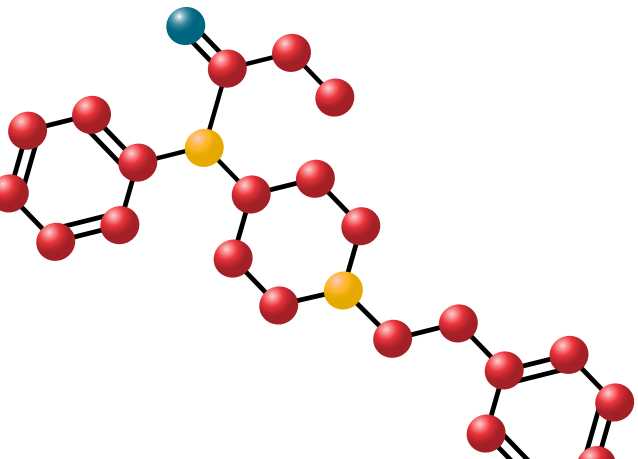
Clinical research and toxicology

# How paper spray mass spectrometry facilitated harm reduction drug checking


## Summary

The Applied Environmental Research Laboratories (AERL) in Vancouver Island University, Canada, conducts pure and applied research in analytical mass spectrometry to measure chemical determinants of environmental and human health. The team desired new technology that would allow them to set up a street-level drug-testing program, HarmCheck, to help check for fentanyls, opioids, and other drugs at a harm reduction site. The results:

- The AERL performed more than 1,700 tests on illicit drugs over an 8-month period during the first waves of COVID-19, to aid reduction in preventable overdose death.
- Fentanyls and a variety of other toxic drugs were successfully detected and quantified in street drug samples, helping to better inform opioid users of risks.
- Unexpected and previously undetected impurities were accurately identified, providing more comprehensive analysis of potential harm.

## Introduction

Since 2013, the number of deaths resulting from illicit opioid overdoses has increased significantly, particularly in North America.[1] Fatalities are often caused by the presence of fentanyl and its analogs in illegally manufactured opioids. The COVID-19 pandemic further worsened the existing opioid crisis,[2] resulting in increased use, both illegal and prescription, as shown in Figure 1. Governments have therefore sought new approaches to reduce death by preventable overdose, including through reducing fentanyl intake.

Drug checking has gained popularity as an effective strategy for harm reduction amongst people who use drugs (PWUD). This method involves PWUD providing samples of their drug so that it can be analyzed for potency and impurities. The composition information is given back to the PWUD, who is then better empowered to make an informed decision on whether to use the drug—thereby reducing risk of harm. However, existing analytical approaches don't allow for detection of trace amounts of harmful fentanyls, so increasingly sensitive methods are needed to obtain accurate composition information and thus maximize the success of drug checking programs.

With significant expertise in analytical instrumentation development and applications, the AERL began to specialize in clinical mass spectrometry (MS) applications to enable point-of-care (POC) analysis with immediate feedback. The AERL team determined

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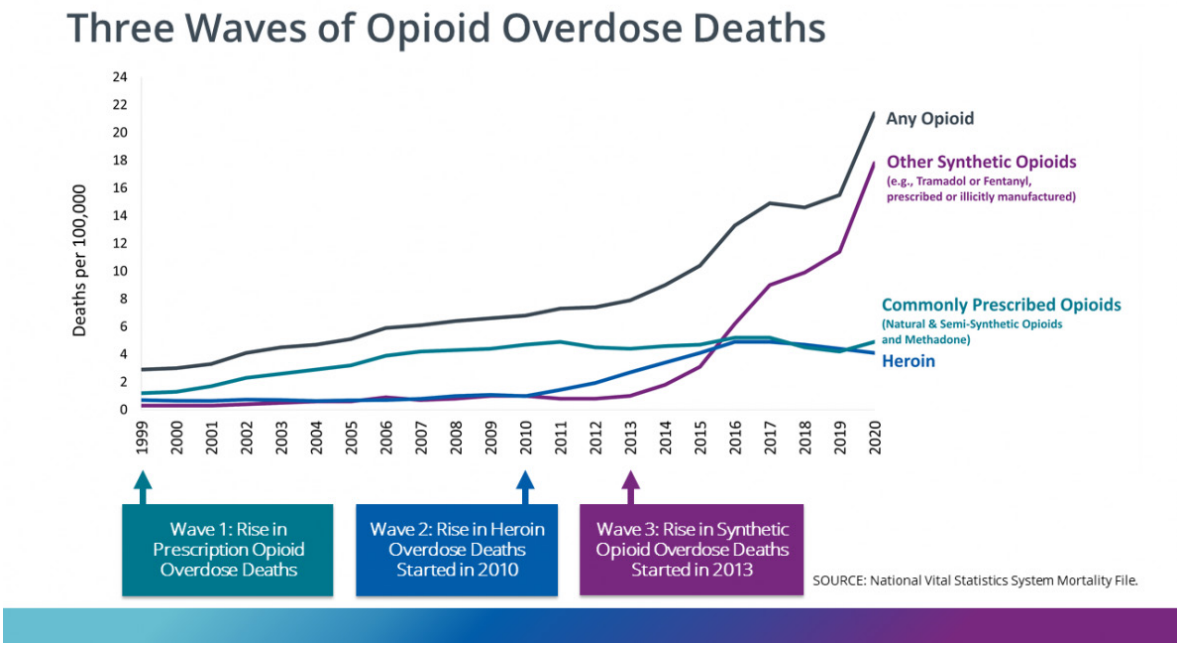
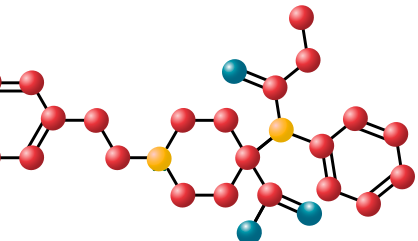



**Figure 1. Three waves of opioid overdose deaths (source: CDC.gov)**

that a sensitive, rapid, and quantitative method could be beneficial to support drug checking and reduce preventable overdoses. To enable the launch of the street-level HarmCheck program and ensure maximum efficiency, the solution would also need to be field-deployable and require minimal training for staff. With these critical factors in mind, the team began to explore options.

## Paper spray mass spectrometry: quantitative, efficient, simple

Drug checking services carried out in clinics or harm reduction centers, such as safe-use sites that offer drug checking, often utilize immunoassay-based test strips. These are easy to use and are sensitive, but only provide qualitative identification of drug class (e.g., fentanyl or an analog). Most harm reduction services providing instrument-based drug checking techniques use Fourier transform infrared spectroscopy (FTIR). Instrument run times for FTIR are typically minutes per sample, but frequently require spectral interpretation and intuition to obtain useful results. FTIR is not very sensitive (3–5% detection limits), and contaminants such as water and common cutting agents (e.g., caffeine) can obscure the results. The semi-quantitative estimates and high detection limits provided by FTIR drug checking mean that PWUD are not fully informed of the risks associated with the drug they intend to use, especially for highly toxic, trace level drugs such as carfentanil, or for new drugs not in the vendor-provided spectral libraries.



Paper spray mass spectrometry (PS-MS) offered an attractive solution to meet the needs of the AERL for an on-site testing program. The technique is a variant of electrospray ionization, generating ions by applying a voltage. In PS-MS, the sample is eluted off a paper substrate directly to the mass spectrometer—requiring minimal sample preparation and eliminating the need for a liquid chromatography (LC) step.

Compared to other clinical methods such as FTIR, PS-MS offers many advantages:

- **Rapid:** Analysis is performed in 1-2 minutes. It has direct sample analysis capability and does not require chromatography-based separation or sample preparation/cleanup.
- **Efficient:** The sampling device is disposable, streamlining processes as a result of reduced labware cleaning requirements and solvent/reagent use.
- **Quantitative:** The technique provides trace level, quantitative results for highly toxic drugs such as carfentanil.
- **Accurate:** The sample is compared against deuterated internal standards for accurate quantification.
- **Ease of use:** Removal of the liquid chromatography (LC) system translates to minimal training and leads to additional cost-savings.
- **Clean:** Each sample is run on a different sample paper, removing the risk of cross-contamination.
- **Adaptable:** As new threats appear in the illicit drug supply, they are readily incorporated into the measurements.

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> —Chris Gill, Co-Director of the AERL

While other methods such as colorimetric tests and Raman spectroscopy are also used for drug checking, they suffer many of the same drawbacks as FTIR. Overall, PS-MS offered the team a cost-effective, fast, and simple analysis option. After careful consideration, the AERL proceeded with investigating PS-MS solutions for the HarmCheck drug-checking program.

## Optimization, collaboration, and ease-of-use—a clear choice

The facility had an existing paper spray mass spectrometry system that was being used for direct analysis of clinical samples, so the team explored applying paper spray technology to high-throughput drug checking. With the existing workflow, the team prepared their own sample papers for PS-MS by cutting up filter paper. While this was cost effective, the papers were challenging to handle and not suitable for repeat analysis. Additionally, a lack of uniformity in the procedure led to reproducibility issues. Investigating their options, the team found a competitor solution that offered a commercially available paper spray mass spectrometry chip. The chips were easier to handle, but samples still needed to be run on an individual basis, which was not compatible with the high throughput testing needs of AERL’s on-site analysis.

Having worked with Thermo Fisher Scientific previously and benefitted from their innovative problem-solving and excellent customer service, the laboratory approached the company to explore a suitable solution. The paper spray consumables designed by the Thermo Fisher Scientific team aligned well with the requirements for this study on the Thermo Scientific™ VeriSpray™ PaperSpray ion source connected with the Thermo Scientific™ TSQ Fortis™ triple quadrupole mass spectrometer. The PaperSpray cartridge plates feature single-use PS-MS sample strips and can be loaded with up to 24 samples.

The VeriSpray PS-MS plate loader magazine can be loaded with 10 cartridge plates at once, so 240 samples can be run unattended (Figure 2). The machine runs the samples sequentially and autonomously, with each taking just 1–2 minutes. This capability makes the system more efficient and provides better throughput than other drug-checking solutions, leading to faster results that help meet the high-throughput requirements of the HarmCheck program. The system also offers barcode traceability for reliable data logging.

Chris Gill, Co-Director of the AERL, explained how the exceptional customer service and bespoke solution accelerated the project. “If it wasn’t for Thermo Fisher developing the custom plate, we wouldn’t be where we are with the HarmCheck program. We received a lot of support from them, particularly in rapidly developing the complex, interlaced scans, and the Thermo Scientific™ TraceFinder™ data analysis workflows. We were invited to work with the R&D teams in advance of the VeriSpray product release and our group had access to a seed instrument, which really helped us to progress quickly. Being able to work with Thermo Fisher’s cutting-edge technology straight from the get-go really catalyzed the project,” he said. “And when we put an instrument in a harm reduction site in downtown Vancouver in 2019, Thermo Fisher sent a team to be on site with us to ensure we had support, should we need it, for early trials.”

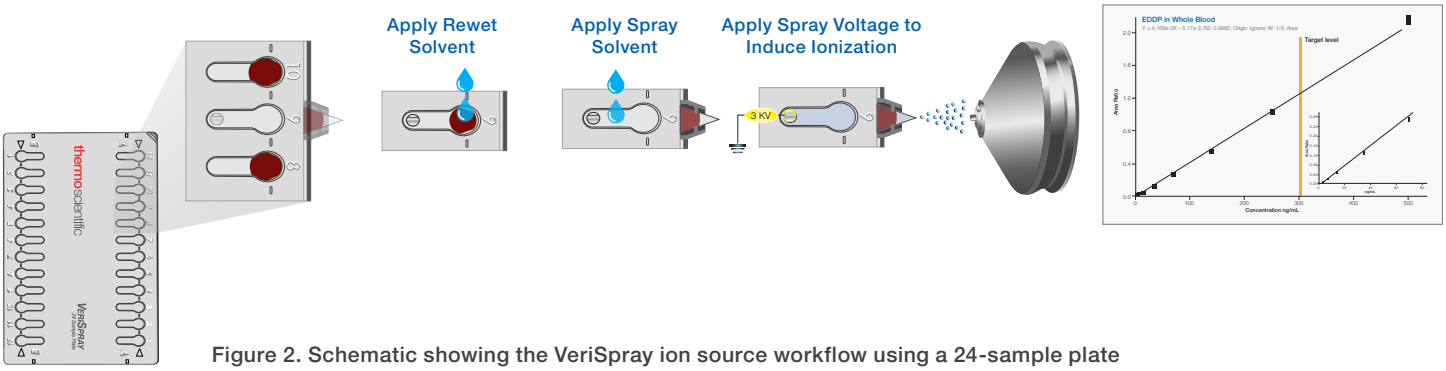



**Figure 2. Schematic showing the VeriSpray ion source workflow using a 24-sample plate**

A significant advantage the team saw over competitor systems was the user-friendly software of the VeriSpray system. Thermo Fisher has a strong reputation for producing equipment with easy-to-use interfaces, which Gill explained was a major influencing factor in his decision to consider a Thermo Fisher solution. The simple interface and output of the TraceFinder software facilitates easier extraction of information, providing a straightforward experience for the user. Using the software allows acquisition, processing, and reporting all to be carried out in a single platform.

## Fast implementation, faster results

The VeriSpray PaperSpray ion source connected with the TSQ Fortis triple quadrupole mass spectrometer offered the perfect solution for launching the HarmCheck program at a safe consumption site—a space designed for PWUD to safely use their pre-obtained drugs with sterile equipment and the support of trained personnel (Figure 3). Gill emphasized how quick the implementation was, as well as the comprehensive support he received for the instrument and the program. “In one month, we’d gone from obtaining the equipment to piloting an operating, quantitative drug screening program that we were able to take to a safe consumption site. The two Thermo Fisher representatives who came to visit the site were deeply impressed by the incredible work we were able to achieve with their system—one representative stayed the entire time!” he explained.


Figure 3. The HarmCheck team at the two-day pilot trial (top) held at Powell Street Getaway, Vancouver (bottom)

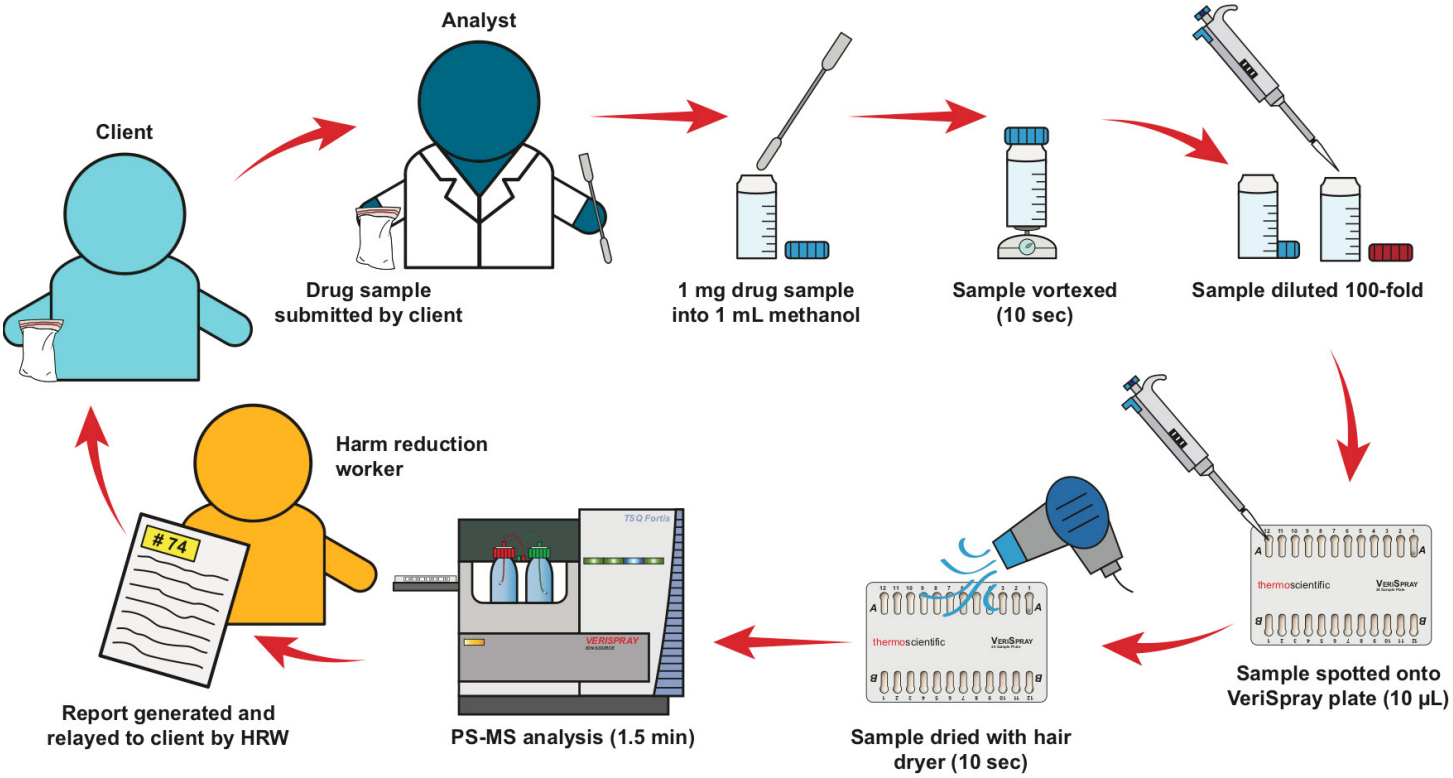
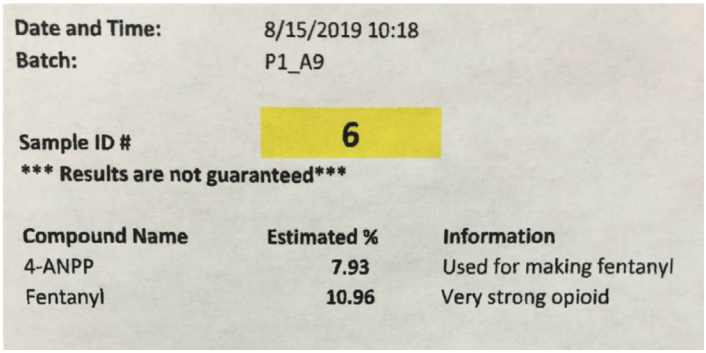



Figure 4. Schematic showing the HarmCheck sample analysis workflow

"Thanks to the new VeriSpray system, we're now able to better monitor the evolving illicit drug situation and further protect PWUD from preventable harm."

—Chris Gill, Co-Director of the AERL

Importantly, the system enables an extremely simple and streamlined workflow for the HarmCheck program (Figure 4). After the sample is run, the strips retract to prevent accidental re-use. TraceFinder software data analysis is embedded in the measurement method, automating the process and providing a printed-out report (Figure 5). The data can then be relayed to the PWUD by the harm reduction worker, with all the required information displayed in an easy-to-understand format.



**Date and Time:** 8/15/2019 10:18
**Batch:** P1_A9

**Sample ID #** 6
***** Results are not guaranteed*****

| Compound Name | Estimated % | Information |
|---|---|---|
| 4-ANPP | 7.93 | Used for making fentanyl |
| Fentanyl | 10.96 | Very strong opioid |

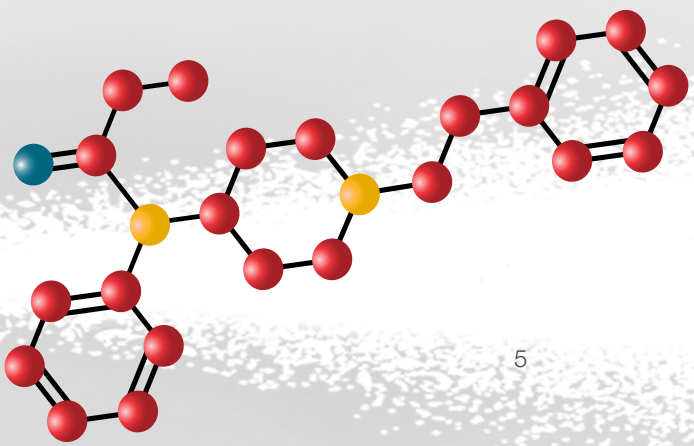
**Figure 5. Printed-out analysis for the HarmCheck program from the PS-MS workflow**

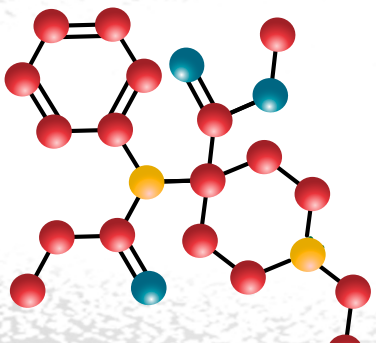
During the first pilot in August 2019, more than 113 street drugs were tested across a 2-day period, facilitated by the high throughput capabilities of the VeriSpray system. Fentanyl was found in 75% of the samples tested, in amounts varying from 0.44% to 38% (although the typical range was 1–4%).[3] With other methods, such as FTIR and Raman spectroscopy, quantities <3–5% would not have been detected—cementing the need for the sensitivity and selectivity of the PS-MS method for effective harm reduction.

In addition to its speed and simplicity, the system is customizable to the needs of the project. Features such as the calibration are easily adjusted, so fentanyl levels as low as 0.01% can be detected, and the system can also be tweaked for analyzing other drugs. For example, MDMA and cocaine tend to be purer, thus requiring different calibration levels, and it is easy to add new analytes to the test panel.

Alongside the contaminants anticipated by PWUD, such as fentanyl, the VeriSpray system identified other compounds that were unexpected. For example, 4-aminophenyl-1-phenethylpiperidine (4-ANPP), the synthetic precursor to fentanyl, was found in many opioid samples. The presence of 4-ANPP indicates poor illicit drug manufacturing and purification processes, further emphasizing the need for careful drug checking to minimize unexpected and potentially harmful contaminant consumption by PWUD. In fact, the team identified that only 5 of the 59 samples (8.5%) expected to contain fentanyl didn't contain any other unexpected adulterants.

The system is also highly adaptable, making it ideal for future drug testing requirements—not only do illicit drug manufacturing processes change, but new illegal drugs are constantly developed and introduced into circulation. These new analytes can easily be added to the test panel over time to keep the team's monitoring processes up to date. "Thanks to the new VeriSpray system, we're now able to better monitor the evolving illicit drug situation and further protect PWUD from preventable harm. There've been a dozen new drugs identified in the tests we've done in Victoria, British Columbia, in the past 4 months, which shows just how crucial it is to understand the composition of circulating drugs so that we're ready for any emerging threats," commented Gill.





## Successfully launching the HarmCheck program

With the new VeriSpray PaperSpray ion source connected with the TSQ Fortis triple quadrupole mass spectrometer, the AERL were able to implement a HarmCheck drug checking program that provides rapid, specific, and quantitative testing of fentanyls and other previously unknown compounds in street drugs. Close collaboration with Thermo Fisher enabled development of a custom paper cartridge that resulted in even faster sample checking and turnaround times for PWUD.

Once a temporary site, the HarmCheck program celebrated its one-year anniversary as a storefront in 2022.[4] Using their PS-MS system in strong collaboration with harm reduction services offered at this site, the team currently analyzes hundreds of client-provided drug samples each week in downtown Victoria, British Columbia. More than 7000 individual drug tests have been performed since October 2021, and the team has the capability to increase testing to meet future demand.

Now the team has established a simple and effective model for drug checking, they are expanding the model to other harm reduction locations around Vancouver Island to help prevent deaths in harder-to-reach rural areas. A drug checking 'mail-in' program has also been implemented, with anonymous results relayed to the client via a web-based platform. The successful program also has potential to be replicated in other provinces, leveraging the PS-MS technology to change lives beyond British Columbia.

## References


1. https://www.cdc.gov/drugoverdose/epidemic/index.html
2. Sun, Y.; Bao, Y.; Kosten, T.; Strang, J.; Shi, J.; Lu, L. Challenges to opioid use disorders during COVID-19. Am J Addict 2020, 29, 174–5.
3. Borden, S.A.; Saatchi, A.; Vandergrift, G.W.; Palaty, J.; Lysyshyn, M.; Gill, C.G. A new quantitative drug checking technology for harm reduction: Pilot study in Vancouver, Canada using paper spray mass spectrometry. Drug Alcohol Rev., 2022, 41, 410-418. https://doi.org/10.1111/dar.13370
4. https://vancouverisland.ctvnews.ca/victoria-drug-checking-facility-marks-one-year-in-community-plans-to-expand-1.5833211


## Resources

- A direct mass spectrometry method for cannabinoid quantitation in urine and oral fluid utilizing reactive paper spray ionization
- A new quantitative drug checking technology for harm reduction: Pilot study in Vancouver, Canada using paper spray mass spectrometry
- BC Government announces support for VIU-developed drug checking technology
- Thermo Scientific VeriSpray PaperSpray ion source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