Characteristics of wipe sampling methods for antineoplastic drugs in North America: comparison of six providers

https://doi.org/10.1515/pthp-2020-0016
Received November 12, 2020; accepted December 1, 2020; published online December 22, 2020

Abstract

Objectives: Several societies have published guidelines to limit the occupational exposure of workers. Several of these guidelines recommend periodic (once or twice a year) environmental monitoring of specific sites where antineoplastic drugs are prepared and administered. However, most of the guidelines provide no guidance concerning which antineoplastic drugs should be monitored, the preferred sampling sites, appropriate test methods or limits of detection. The aim of this study was to characterize providers that quantify antineoplastic drug measured on surfaces.

Methods: This was a cross-sectional descriptive study. To identify service providers offering environmental monitoring tests, we searched the PubMed database and used the Google search engine. We contacted each service provider by email between June 3rd and June 15th, 2020. We specified the objective of our study and described the information needed and the variables of interest with standardized questions. Additional questions were sent by emails or via teleconferences. No statistical analyses were performed.

Results: We identified six providers offering services to Canadian hospitals, either based in Canada or in the United States. Five of these providers were private companies and one was a public organization. Each service provider was able to measure trace contamination of 3–17 antineoplastic drugs. Five of the providers quantified drugs using ultra performance liquid chromatography coupled with tandem mass spectrometry (UPLC-MSMS), which allowed for lower LODs. The sixth provider offered quantification by immunoassay, which has higher LODs, but offers near real-time results; the surface area to be sampled with this method was also smaller than with UPLC-MSMS. The services offered varied among the service providers. The information about LODs supplied by each provider was often insufficient and the units were not standardized. A cost per drug quantified could not be obtained, because of variability in the scenarios involved (e.g. drug selection to be quantified, number of samples, nondisclosure of ancillary costs). Four of the six service providers were unable to report LOQ values.

Conclusions: Few data are available from Canadian service providers concerning the characteristics of wipe sampling methods for antineoplastic drugs. This study identified six North American providers. Their characteristics were very heterogeneous. Criteria to consider when choosing a provider include the validation of their analytical method, a low limit of detection, the choice of drugs to be quantified and the sites to be sampled, obtaining details about the method and understanding its limits, and price. This should be part of a structured multidisciplinary approach in each center.

Keywords: antineoplastic drugs; environmental surveillance; hazardous drugs; wipe sampling.

Introduction

In 2004, the US National Institute for Occupational Safety and Health (NIOSH) published an alert regarding prevention of occupational exposure to antineoplastic and other antineoplastic drugs in healthcare settings [1]. The definition of antineoplastic drugs used in that alert was based on a definition first proposed by the American Society of Health-System Pharmacists in the 1990s [2] and includes antineoplastics (as “Group 1”).

In 2004, the alert recognized the presence of traces of antineoplastic drugs and recommends that healthcare organizations “conduct environmental sampling and/or biological monitoring when exposure is suspected or symptoms have been noted.”

In response to this alert, several societies have published guidelines to limit the occupational exposure of workers, including the International Society of Oncology Pharmacy...
Practitioners [3], the American Society of Health-System Pharmacists [4], the Canadian Society of Hospital Pharmacists [5], and the Quebec health and safety prevention association [6]. The United States Pharmacopeia has also proposed guidelines for handling antineoplastic drugs in healthcare settings [7]. Several of these guidelines recommend periodic (once or twice a year) environmental monitoring of specific sites where antineoplastic drugs are prepared and administered [8–10]. However, most of the guidelines provide no guidance concerning which antineoplastic drugs should be monitored, the preferred sampling sites, appropriate test methods or limits of detection.

In healthcare facilities, environmental monitoring may be the responsibility of the manager of the occupational health and safety department, the director of the pharmacy department, or another staff member. This designated person may need to choose a service provider with suitable expertise to periodically measure traces of antineoplastic drugs in surface samples. Several research groups have developed analytical methods and performed studies to determine surface contamination with one or more antineoplastic drugs [11–14]. Some of these initiatives have led to the commercialization of environmental monitoring tests [15, 16].

The selection of a service provider may involve a needs analysis, specification of relevant selection criteria, a request for proposals, and a call for tenders. To support such a tendering process, we investigated the availability of wipe sampling services for antineoplastic drugs in North America. The aim of this study was to characterize providers that quantify antineoplastic drug measured on surfaces.

Methods

Study type

This was a cross-sectional descriptive study.

Search strategy

To identify service providers offering environmental monitoring tests, we searched the PubMed database and used the Google search engine. Our search strategy used the following terms: environmental sampling, environmental monitoring, surveillance, antineoplastic drugs, traces, antineoplastics, service providers, sampling, cytotoxics, and tests. We included all service providers that could analyze trace amounts of antineoplastics for Canadian institutions and that replied to at least one email message from our group requesting additional information and clarification.

Contact methods

We contacted each service provider by email between June 3rd and June 15th, 2020. We specified the objective of our study and described the information needed and the variables of interest with standardized questions. Additional questions were sent by emails or via teleconferences.

Study variables

The following data were collected from service providers’ websites and their direct responses: service provider’s name, country where the service provider are available, type of provider, ISO certification, antineoplastic drugs tested, number of samples per kit, minimum number of samples to be analyzed per invoice, sampling materials used (e.g. tissues, filter paper, sampling swabs), size of sampling materials, solvent used, template to delineate the wiping area, suggested surface area to be sampled (cm²), sampling technique, suggested sampling sites and description, suggested timing of sampling, analytical method, limit of detection (LOD) (min–max in ng/cm²), detailed LOD (ng/cm²), limit of quantification (LOQ), recovery rates, requirement for shipment on dry ice (to maintain drug stability), waiting time to obtain results, relative price range for services offered to Canadian institutions, and published references associated with the service provider. Prices were categorized in relative terms, as +, ++, or +++ (most expensive) according to the costs publicly disclosed on their website or provided to our research team. The term “+” was used for prices of approximately under 100$CA per sample for a single drug, the term “++” was between 200$CA and 300$CA per sample and the term “++=” was used for more than 300$CA per sample.

Analysis

The data were tabulated to allow comparison of the services offered by providers and their sampling requirements. No statistical analyses were performed.

Results

We identified six providers offering services to Canadian hospitals, either based in Canada or in the United States.
Five of these providers were private companies and one was a public organization.

Each service provider was able to measure trace contamination of 3–17 antineoplastic drugs (Table 2). Five of the providers quantified drugs using ultra-performance liquid chromatography coupled with tandem mass spectrometry (UPLC-MSMS), which allowed for lower LODs. The sixth provider offered quantification by immunoassay, which has higher LODs, but offers near real-time results; the surface area to be sampled with this method was also smaller than with UPLC-MSMS (Table 2, 3).

The services offered varied among the service providers. The information about LODs supplied by each provider was often insufficient and the units were not standardized.

A cost per drug quantified could not be obtained, because of variability in the scenarios involved (e.g. drug selection to be quantified, number of samples, nondisclosure of ancillary costs).

Four of the six service providers were unable to report LOQ values. Most providers did not provide recovery rates or values that were exploitable.

Table 1: Profile of the environmental monitoring services offered.

| Variable                              | BCE Pharma™ | BD® | Bureau Veritas (ChemoAlert) | ChemoGLO™ | HealthMark (SafeChemo™) | INSPQ |
|---------------------------------------|-------------|-----|-----------------------------|-----------|--------------------------|-------|
| Country providers                     | Canada      | Canada and United States | Canada and United States | Canada and United States | Canada and United States | Canada |
| Provider type                         | Private company | No  | Private company            | Private company | Private company | Public organisation |
| ISO certification                     | No          | No  | Yes                         | No        | Yes                      | Yes   |
| Number of antineoplastic drugs tested | 18          | 3   | 17025                       | 14        | 17                       | 15    |
| Number of samples per kit             | 1–10        | 1–20| 1–10                        | 1–10      | 1–12                     | 1–13  |
| Minimum number of samples to be analyzed | 1           | 1   | 1                           | 6         | 1                        | 1     |
| LOD intervals (minimum-maximum), ng/cm² | 0.002–0.13a | 0.1–0.5 | NA                         | 0.01–4.35 | 0.0005–0.01             | 0.001–0.3 |
| Shipping conditions                   | Room temp   | Room temp | NA                         | NA        | NA                      | Room temp |
| Waiting time to obtain results        | 3–4 weeks   | <10 min | NA                         | 10–15 working days | 30 days | 10–15 working days |
| Price rangeb                          | ++          | ++    | +++                        | +++       | +++                     | +     |
| Historical results available (web-based) | Yes        | No   | No                         | No        | No                      | Yes   |
| Studies that used this provider       | NA          | NA   | NA                         | [15, 19, 20] | NA                      | [14, 17, 18, 21, 22] |

ISO, International Organization for Standardization; INSPQ, Institut national de santé publique du Québec; UPLC-MSMS, ultra-performance liquid chromatography coupled with tandem mass spectrometry; NA, not available; LOD, limit of detection. aFor BCE Pharma, LOD values were provided as nanograms per wipe of 225 cm²; the LOD in nanograms per square centimetre was derived from the following calculation, for instance for cyclophosphamide: 0.5ng/225 cm² = 0.002 ng/cm². bPrices were categorized in relative terms, as + (least expensive), ++, or +++ (most expensive).

Discussion

Characteristic of service providers

To our knowledge, this is the first published comparison of providers of wipe sampling services for antineoplastic drugs in North America.

There were some commonalities among the six North American service providers that we identified. Five of the six providers used a UPLC-MSMS analytical approach. This generated LODs that were at least 10 times lower than what was possible with the lateral flow immunoassay method. Environmental monitoring involves the identification of very small (trace) quantities and a detection method with higher LODs can create a false sense of security. Thus, the UPLC-MSMS method is recommended for conducting environmental monitoring, and the lateral flow immunoassay method could be reserved for accidental spills or particular situations.

Not all of the service providers supplied easily comparable LOD values; different units were used (e.g. ng/cm² or ng/wipe). While limits can be converted, this ratio is only valid for the area to be sampled which has been validated by the provider.
| Variables                  | BCE Pharma™ | BD® | Bureau Veritas (ChemoAlert) | ChemoGLO™ | HealthMark (SafeChemo™) | INSPQ |
|---------------------------|-------------|-----|-----------------------------|-----------|--------------------------|------|
| Analytical method         | UPLC-MSMS   |     | UPLC-MSMS                   | UPLC-MSMS | UPLC-MSMS                |      |
| Sampling material          | Filter paper| Cotton swab | Tissue (polyester Texwipe® TX714A) | Cotton swabs | Tissue (polyester)       | Tissue (WypAll® X-60) |
| Size of sampling material | 55 mm diameter | NA | NA                          | NA | NA                       | 6 cm × 8 cm |
| Solvent                   | NA          | NA  | NA                          | Proprietary blend containing isopropylic alcohol | NA | 10 mL of extracting solution and internal standards added to each tube |
| Template to delineate the wiping area | Yes | Yes | Yes | Yes | Yes | Yes |
| Suggested surface area to be sampled, cm² | 225 | 930 | 100 | 930 | 465 | 600 |
| Sampling technique         | 2 times (once horizontally and once vertically) | One time (vertically) | Two times (once horizontally with one swab and once vertically with another swab) | Two times (once horizontally with one swab and once vertically with another swab) | Two times (once horizontally with one swab and once vertically with another swab) | Four times (twice horizontally and twice vertically with the same swab) |
| Suggested sampling sites and description | Yes Pharmacy and outpatient oncology clinic; surfaces in other locations | Yes Pharmacy and outpatient oncology clinic | No | Yes Pharmacy and outpatient oncology clinic | Yes Reception area, compounding area, hood, sink, computer, floor, patient bed area | Yes Six locations in pharmacy and six locations in outpatient oncology clinic |
| Suggested sampling period  | After cleaning | Before cleaning | No | Before or after cleaning | Before or after cleaning | Before or after cleaning |

ISO, International Organization for Standardization; INSPQ, Institut national de santé publique du Québec; UPLC-MSMS, ultra-performance liquid chromatography coupled with tandem mass spectrometry; NA, not available; LOD, limit of detection.
Table 3: Limits of detection and limit of quantification for each provider.

| Antineoplastic drug | BCE Pharma™ | BD® | Bureau Veritas (ChemoAlert) | ChemoGLO™ | HealthMark (SafeChemo™) | INSPQ |
|---------------------|-------------|-----|---------------------------|-----------|-------------------------|-------|
| 5-Azacitidine       | NA          | NA  | NA                        | NA        | NA                      | NA    |
| 5-Fluorouracil      | 0.008       | NA  | 5 ng/sample               | NA        | 0.01                    | 0.04  |
| Busulfan            | NA          | NA  | 5 ng/sample               | NA        | 0.14                    | NA    |
| Cyclophosphamide    | 0.002       | 0.5 | NA                        | NA        | 0.01                    | 0.001 |
| Cytarabine          | 0.01        | NA  | 5 ng/sample               | NA        | 0.01                    | NA    |
| Daunorubicin        | NA          | NA  | 5 ng/sample               | NA        | NA                      | NA    |
| Docetaxel           | 0.13        | 0.1 | NA                        | NA        | 0.01                    | 0.3   |
| Doxorubicin         | 0.04        | NA  | 5 ng/sample               | NA        | 0.01                    | NA    |
| Epirubicin          | 0.04        | NA  | 5 ng/sample               | NA        | NA                      | NA    |
| Etoposide           | 0.008       | NA  | 5 ng/sample               | NA        | 0.01                    | NA    |
| Gemcitabine         | 0.002       | NA  | 5 ng/sample               | NA        | 0.01                    | 0.001 |
| Ifosfamide          | 0.002       | NA  | 5 ng/sample               | NA        | 0.01                    | 0.004 |
| Irinotecan          | 0.008       | NA  | 5 ng/sample               | NA        | NA                      | 0.003 |
| Melphalan           | 0.004       | NA  | 5 ng/sample               | NA        | NA                      | NA    |
| Methotrexate        | 0.04        | 0.1 | NA                        | NA        | 0.01                    | 0.002 |
| Mytomycin C         | NA          | NA  | 5 ng/sample               | NA        | NA                      | 0.006 |
| Paclitaxel          | 0.04        | NA  | 5 ng/sample               | NA        | NA                      | 0.04  |
| Pemetroxed          | 0.008       | NA  | 5 ng/sample               | NA        | NA                      | 0.012 |
| Platin              | 0.002       | NA  | 5 ng/sample               | NA        | 0.0005                  | NA    |
| Vinblastine         | 0.04        | NA  | 5 ng/sample               | NA        | NA                      | NA    |
| Vincristine         | NA          | NA  | 5 ng/sample               | NA        | 0.01                    | NA    |
| Vinorelbine         | NA          | NA  | 5 ng/sample               | NA        | NA                      | 0.012 |

INSPQ, Institut national de santé publique du Québec; NA, not available; LOD, limit of detection. *For BCE Pharma, LOD values were provided as nanograms per wipe of 225 cm²; the LOD in nanograms per square centimetre was derived from the following calculation, for instance for cyclophosphamide: 0.5 ng/225 cm² = 0.002 ng/cm².
That area may vary between providers. Most literature will present results in ng/cm², according to Connor et al. [13] it is the standardized unit to reporting results. For the results to be interpretable, the client must accurately measure and record the area sampled.

**Choice of service provider**

A client’s choice of service provider will depend on their needs. A structured approach is needed. This approach would include a call for tenders from the various services providers available, outlining the specific criteria to be included in the contract. Considering the differences in methods, different results would be obtained with different providers, so caution should be used to interpret results if the provider is changed over the years. Criteria to consider include:

- Validation of analytical method (ISO certification, low limit of detection)
- Choice of antineoplastic drugs to be quantified (how many, which)
- Choice if sampling sites (how many, which)
- Understanding the sampling method and its limit (sampling size)
- Price
- Results interpretation

The provider chosen should have a validated analytical method (e.g. ISO certification) and questions should be asked to understand the recovery on different surface types. Limits of detection and quantification must be shared to interpret the results accurately. A low limit of detection is needed to adequately represent the workers’ exposure.

For some clients, it may be important to use the provider that can analyze the greatest number of antineoplastic drugs; for others, it may be important to select the provider with the most flexibility; yet others may seek the lowest-cost supplier. Centers should select at least three of their most used antineoplastic drugs for their environmental monitoring. Some drugs are more frequently detected than others for various reasons, e.g. they are more persistent of surfaces, degradation products of the drug remain on surfaces, not the parent drug.

Each healthcare facility must designate someone to obtain environmental monitoring samples according to instructions from the service provider. Ideally, the same person should do this task each time, so that sampling is carried out consistently over time. Connor et al. proposed good practices for the performance of wipe sampling for detection of surface contamination by antineoplastics [13].

Some surfaces are typically more contaminated than others [12, 13, 17, 18]. Frequently contaminated areas that may be sampled include counters were the drugs are handled (received, stored), compounding areas (biological safety cabinets), storage areas (pharmacy and healthcare units), drug administration areas (chairs, infusion pumps, patient rooms), waste management (waste bins, toilets) and administrative areas (computers, desks). Sampling 6–12 different sites can identify problematic areas. A designated person should collaborate with other stakeholders to choose the sites (e.g. pharmacist, pharmacy technician, nurse, physician, allied health personnel).

The service providers used different sampling methods (e.g. type of wipes, solvent used, area sampled). It is important that the center understands the limits of the method chosen to interpret the results correctly. Regardless of the service provider chosen, several conditions must be met to ensure the quality of environmental monitoring. One person within the facility should be designated to follow up on the monitoring schedule (e.g. every 6 or 12 months). It appears useful to create a spreadsheet where the following data can be recorded: date and time of sampling, personnel responsible, sampling locations (accompanied by photographs), results obtained, and applicable LODs and LOQ indicated in the service provider’s report. Less formal record-keeping may not allow longitudinal analysis. The documentation tool should include a history of actions taken (e.g. annual or biennial major cleaning or decontamination, changes of layout, changes of equipment, implementation of training). Like Connor et al. [13], it is important for us that laboratory had a quality certification and accreditation (ISO 17025).

Prices are presented differently, and they cannot be easily compared between providers because prices per drug will vary depending on the total number of drugs quantified and ancillary costs.

The environmental monitoring process should include appropriate feedback to any personnel who have been exposed to antineoplastics. Result interpretation is not easy because there are no safe exposure thresholds. Comparing the results from year to year can help identify if a problem arises. Comparing a centers’ result with national data helps interpreting them; however, the use of different sampling sites or service providers limits the comparability. Results may also be compared with the literature, keeping in mind that, in addition to differences in methods, results obtained in a research setting may not represent the true workers’ exposure and may be biased.

**Limits**

We limited our search to organizations based in North America, and we obtained data for six service providers. Further
research might identify other Canadian or North American players. Service providers were not all willing to share all the information that a client needs to make an informed choice. Service providers’ claims were not verified. Other relevant elements were not evaluated: e.g. ease of use, clarity of instructions, clarity of reports, interactions with the provider.

Conclusions

Few data are available from Canadian service providers concerning the characteristics of wipe sampling methods for antineoplastics. This study identified six north American providers. Their characteristics were very heterogeneous. Criteria to consider when choosing a provider include the validation of their analytical method, a low limit of detection, the choice of drugs to be quantified and the sites to be sampled, obtaining details about the method and understanding its limits, and price. This should be part of a structured multidisciplinary approach in each center.

Research funding: None declared.

Author contributions: All authors have accepted responsibility for the entire content of this manuscript and approved its submission.

Competing interests: Claire Chabut and Jean-François Bussières from the pharmacy practice research unit at CHU Sainte-Justine, Montreal are independent but do collaborate with Institut national de santé publique du Québec (INSPQ) on an annual surveillance program in Canada. While hospitals assume the cost of analyses performed by INSPQ, benchmarking analyses are offered free of charge to participating hospitals by the pharmacy practice research unit.

Informed consent: Not applicable.

Ethical approval: Not applicable.

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