

# Opportunities to Support a Robust 'R2P-To-Research' Framework for Managing Health Risks Associated with Hazardous Drug Handling

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# Agenda

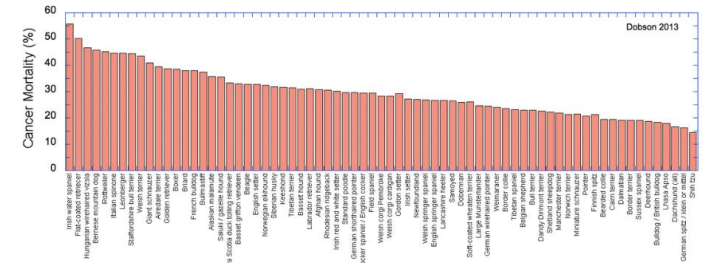
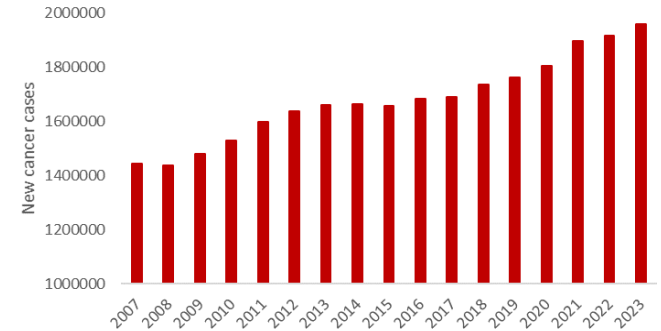
- Introduction
- Qualitative Research
- Quantitative Research
- Gaps and Opportunities

# Introduction - burden

## Increasing antineoplastic drug environmental exposure

- Estimated 1.9 million cancer cases in 2023
  - Increase of 25% over the last 15 years
  - 58 million patient oncology clinic visits
- Estimated 1/3 dogs will develop cancer
  - Leading cause of death
  - Increase in chemotherapy administration

ACS reported cancer incidence



## Introduction - need

Complex and stubbornly persistent exposures and potential health risks

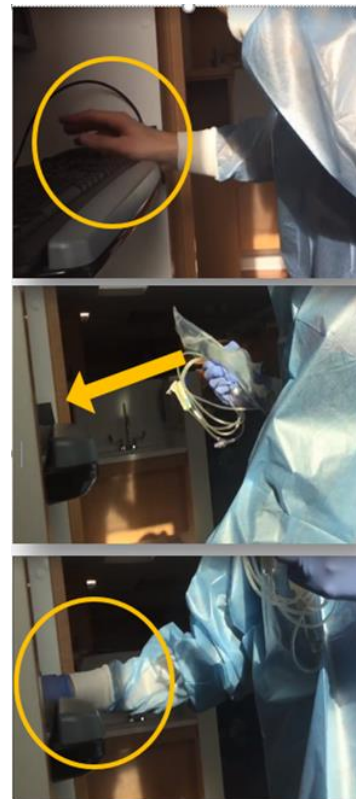
- No standardized protocols for surveillance or decontamination
- Robust evidence of surface contamination of parent AD
  - What about breakdown products?
  - Are there tools to monitor these scenarios?
- We have developed and implemented tools to identify and quantify antineoplastic drug contamination in various occupational and environmental settings

*Can we better inform the workforce to reduce the risk of exposure?*

# Qualitative research - Observational study



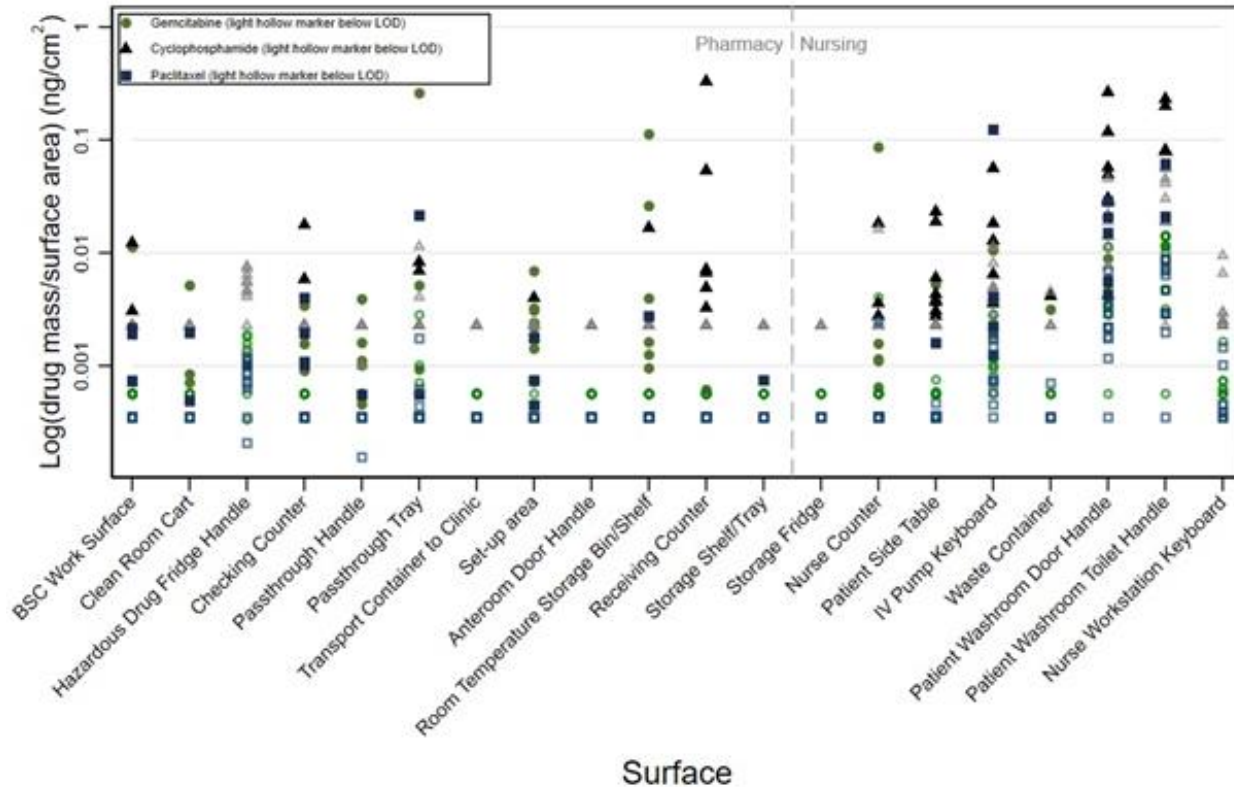
Top 5 surfaces touched in BSC



## Qualitative research - Veterinary oncology surveys

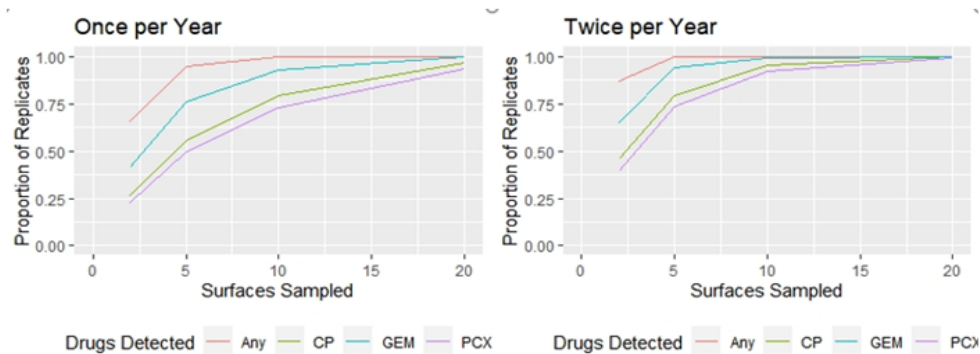
- Survey of practices, n = 80 respondents from Can & U.S.
- 24% (19/80) ever administered AD
- 82% (66/80) of never administered referred patients for treatment
- 98% of participating practices had never undertaken any assessments of potential antineoplastic drug residues on surfaces
- **68% (13/19) who administer ADs never received formal safe handling training**
- **17% (4/23) clinics reported AD prepared in general clinic area,** while only 13% (3/23) reported having a designated preparation room

# Quantitative research - SURFACES longitudinal study



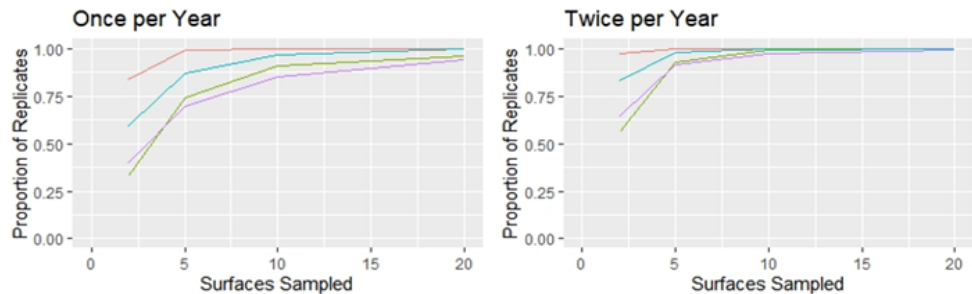
# Quantitative research - Sampling strategy guidance

## Random



CP: cyclophosphamide  
GEM: gemcitabine  
PCX: Paclitaxel

## Sentinel

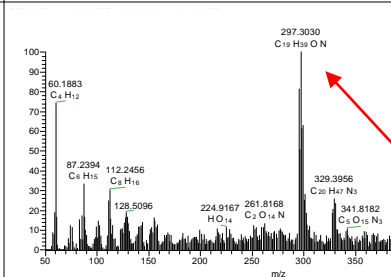
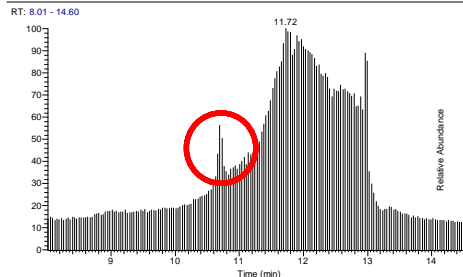
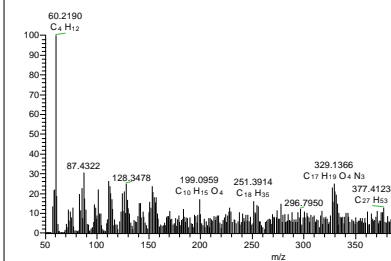
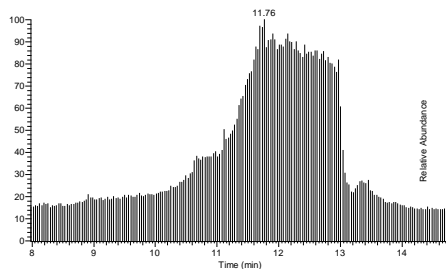




# Quantitative research

## Surfaces cleaning pilot study

- Characterize byproducts formed during the decontamination of antineoplastic drugs and cleaning products using High Resolution Mass Spectrometry
- Commonly used drugs:
  - Cyclophosphamide
  - Doxorubicin
  - 5-Fluorouracil
- Commonly used cleaning products:
  - Bleach (NaOCl)
  - Peridox RTU (H<sub>2</sub>O<sub>2</sub>)



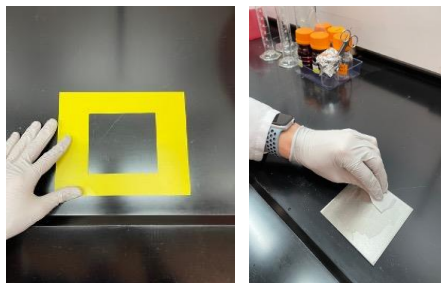
# Quantitative research

## LC-SRM-MS/MS and wiping method development

- Developed an LC-SRM-MS/MS for the simultaneous detection of chemotherapy drugs
- Optimized and validated a surface wipe sampling protocol

### Surface Wipe Sampling

- 10cm x 10 cm
- stainless steel plates
- clinical surfaces

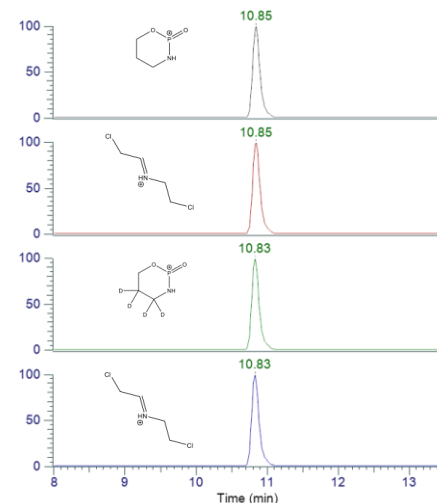
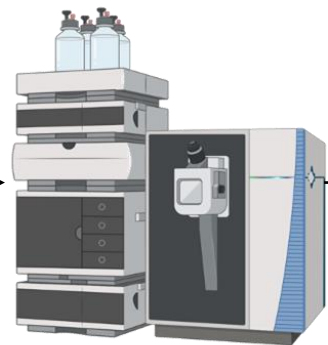


### Wipe desorption



### Targeted Method

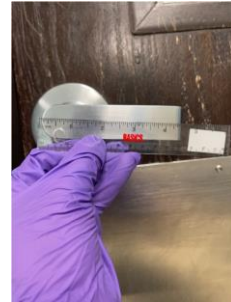
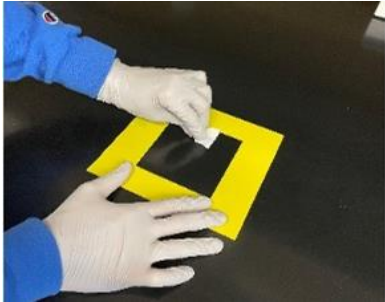
- Parent ions
- Fragmentation ions



# Quantitative research

## Veterinary oncology surveillance surface wipe sampling

- Surface wipe sample collection in a veterinary oncology clinic
- Canine-patients treated with either:
  - cyclophosphamide (Cytosan, oral administration)
  - doxorubicin (Adriamycin, intravenous administration)



# Quantitative research

## Veterinary oncology surveillance surface wipe sampling

- Identify and quantify cyclophosphamide and doxorubicin on clinical surfaces.

Areas Sampled	Cyclophosphamide (pg/cm <sup>2</sup> )
Door handle	17.4
Treatment table	6.8
Small treatment table	Not detected
Pharmacy Bag	Not detected
Oral drug administration	14.0
Blanket	Not detected
Hazardous waste bin	11.4

Areas Sampled	Doxorubicin (pg/cm <sup>2</sup> )
Door handle	40.3
Treatment table	20.5
Small treatment table	13.5
Pharmacy Bag	19.1
Syringe	35.8
Blanket	15.4
Hazardous waste bin	18.0

# Quantitative research

## Veterinary oncology surveillance canine-patient sampling

- Canine-patient wipe sample collection in a veterinary oncology clinic for the identification of antineoplastic drugs using a LC-SRM-MS/MS method.



# Quantitative research

## Veterinary oncology surveillance canine-patient sampling

- Identify and quantify cyclophosphamide and doxorubicin on clinical surfaces and canine-patients.

Areas Sampled	Cyclophosphamide (ng/sample)
Kennel Floor	Not detected
Kennel Mat	Not detected
Dog 5hr	4.2 – 8.6
Dog 24hr	Below LOQ

Areas Sampled	Doxorubicin (pg/cm <sup>2</sup> )
Kennel Floor	18
Kennel Mat	1655
Dog 5hr	Not detected
Dog 24hr	Not detected

# Looking forward - knowledge gaps and opportunities

## Gaps

- health based OEL-Surface Limits
- clear understanding of determinants of exposure
- evidence-based interventions
- others?

## Opportunities

- invitation to provide input & collaborate on (proposed) intervention study
- contact Susan Arnold [arnol353@umn.edu](mailto:arnol353@umn.edu)

# Appendix

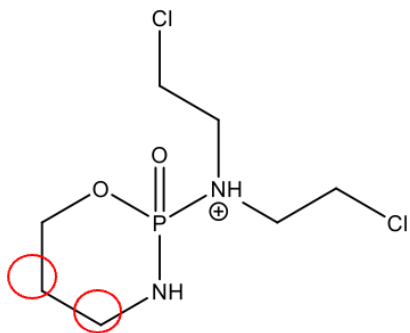


# Masses of Drugs and Internal Standards

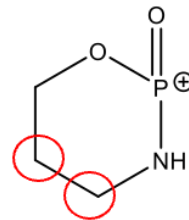
Drugs	Mass	Labeled Internal Standards	Mass
Cyclophosphamide	261.04	Cyclophosphamide-d4	265.06
5-Fluorouracil	129.02	5-Fluorouracil-13C,15N2	132.02
Methotrexate	455.21	Methotrexate-methyl-d3	458.22
Etoposide	606.20	Etoposide-d3	609.277
Paclitaxel	854.32	Paclitaxel-d5	859.32
Doxorubicin	544.18	Daunorubicin (analog)	528.19

# Target antineoplastic drug ion selection

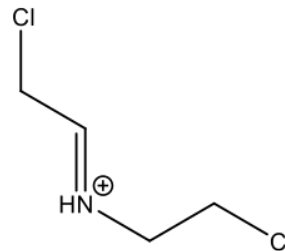
## Cyclophosphamide



Chemical Formula:  $C_7H_{16}Cl_2N_2O_2P^+$   
Exact Mass: 261.03210  
Molecular Weight: 262.09021



Chemical Formula:  $C_3H_7NO_2P^+$   
Exact Mass: 120.02089  
Molecular Weight: 120.06721



Chemical Formula:  $C_4H_8Cl_2N^+$   
Exact Mass: 140.00283  
Molecular Weight: 141.01445

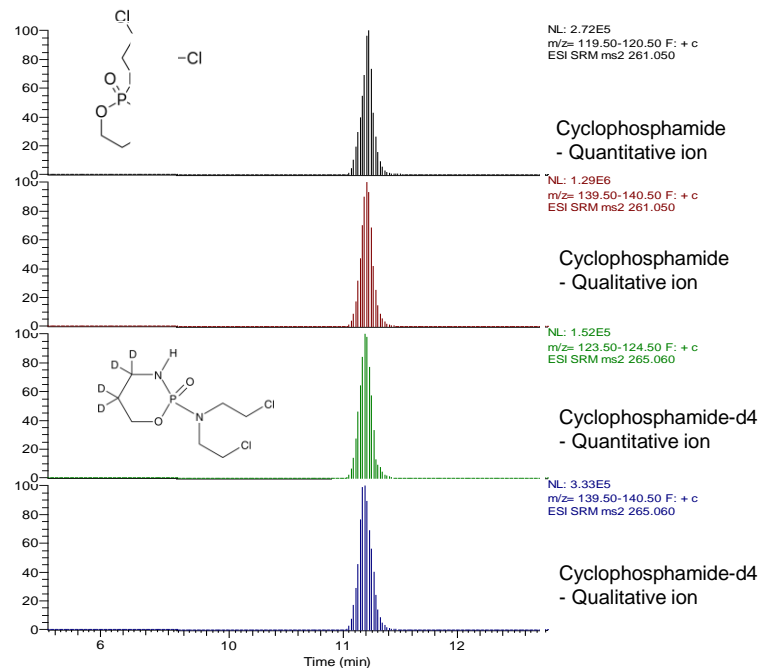
# LC-MS method development process

Instrument: Triple Quadrupole

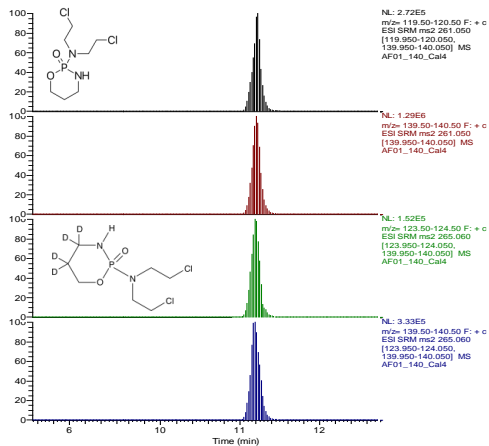


Direct infusion

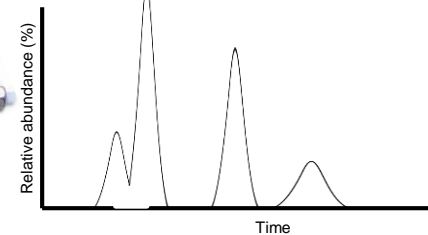
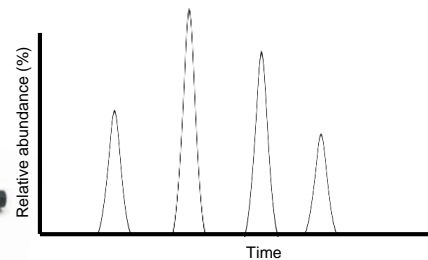
Identification of parent ion and fragment ions



# LC-MS method development process



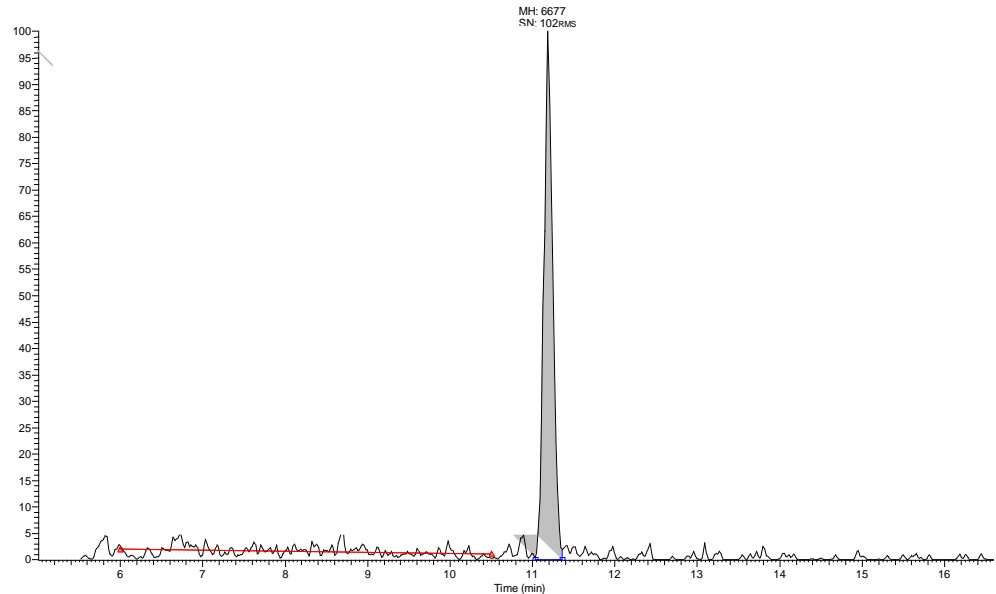
Testing LC-MS Parameters  
(mobile phases, columns,  
injection volume)



# LC-SRM-MS/MS method LOD and LOQ

- LOD = Concentration \*3 / signal to noise ratio (SN)
- LOQ = Concentration \*10 / SN

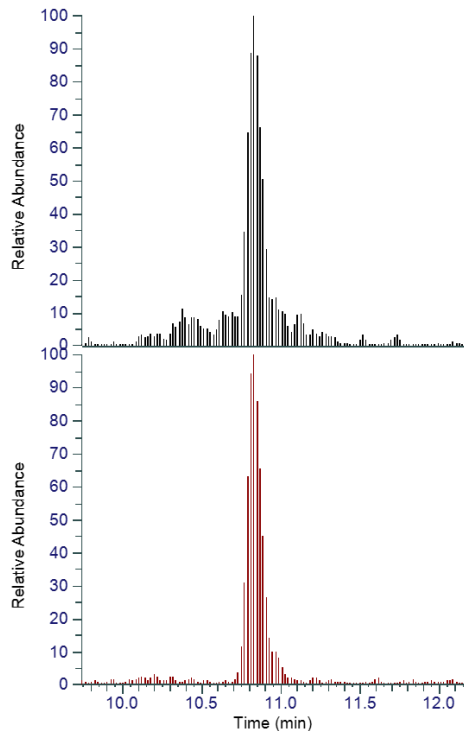
Drugs	LOD	LOQ
Cyclophosphamide	0.003	0.013
5-Fluorouracil	0.17	0.71
Methotrexate	0.009	0.031
Etoposide	0.013	0.043
Paclitaxel	0.002	0.010
Doxorubicin	0.005	0.015



All concentrations are in ng/mL

# Cyclophosphamide detected on canine patient wiping samples

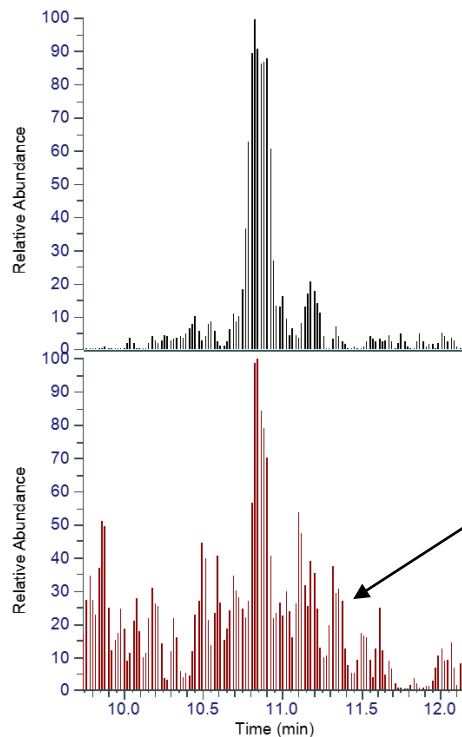
5H dog wiping sample



261 → 120  
Quantitative ion

261 → 140  
Qualitative ion

24H dog wiping sample



261 → 120  
Quantitative ion

261 → 140  
Qualitative ion