Automated Surface Swab Sampling: A Statistical Comparison of a Novel Approach to Existing Methods.

Presented by:

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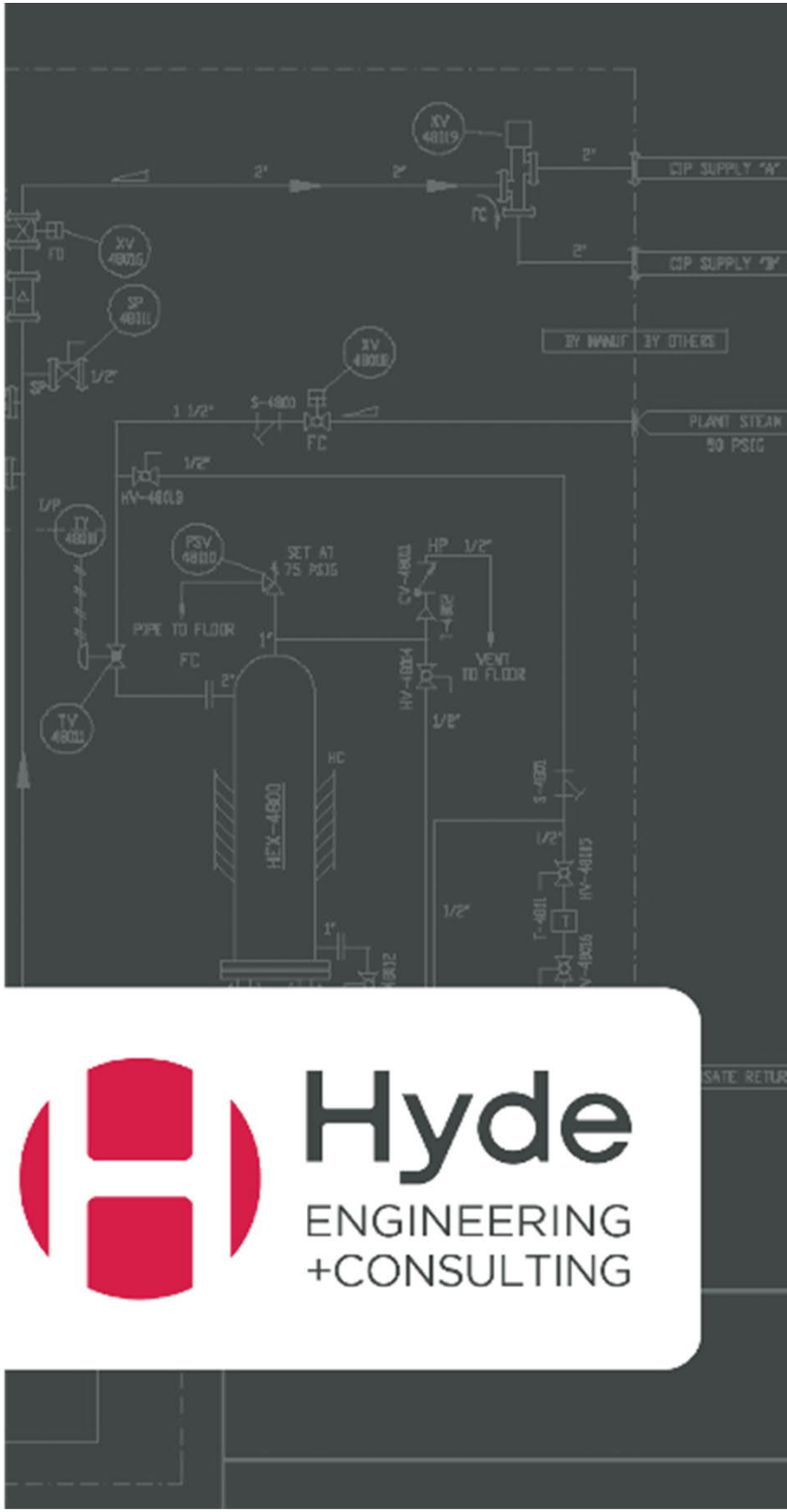
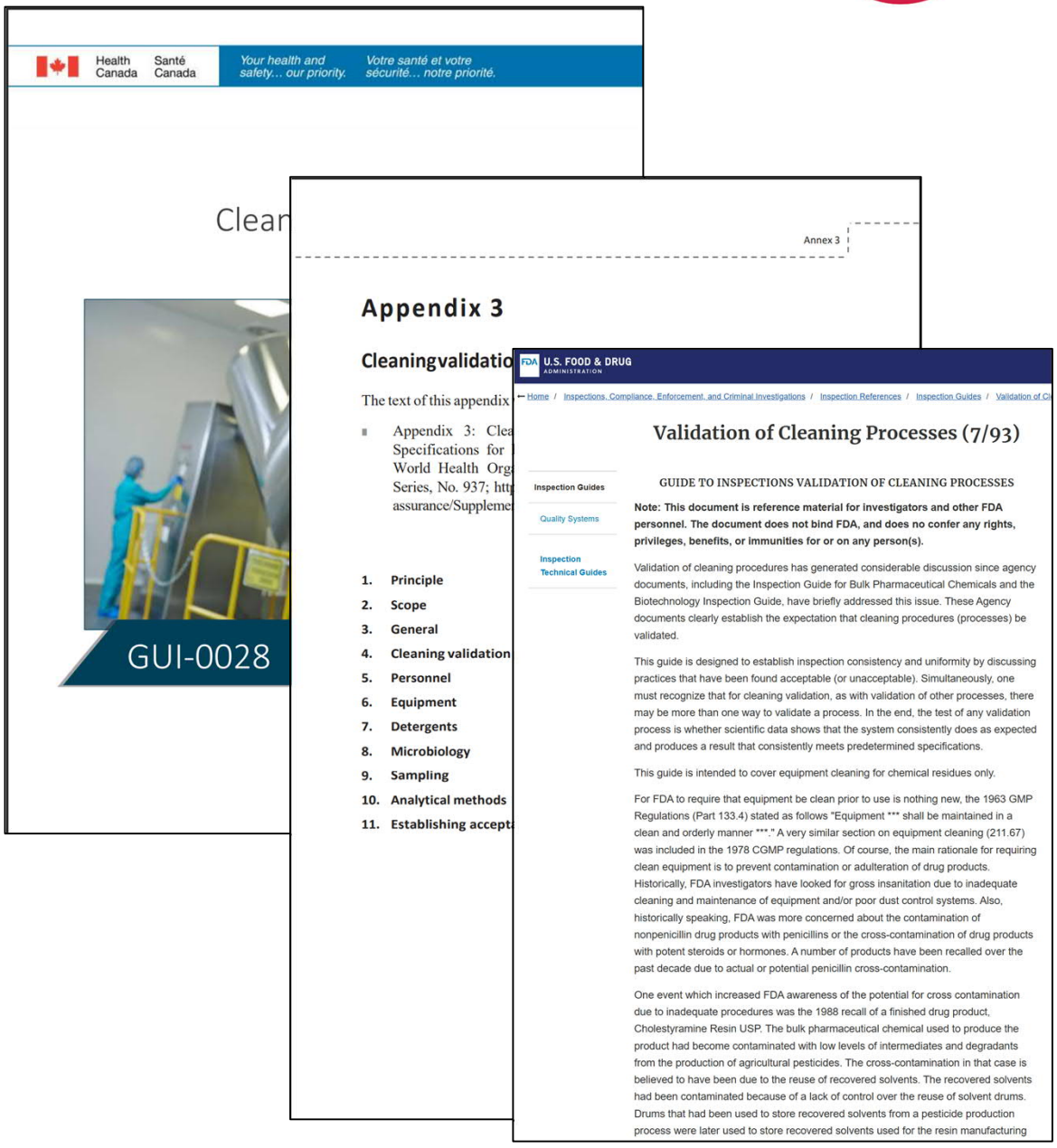


Direct Sampling

- Regulatory Health Authorities suggest the use of direct and indirect samples for cleaning validation
  - Health Canada, Cleaning Validation Guide [1]
  - World Health Organization, Good Manufacturing Practices, Appendix 3, Cleaning Validation [2]
  - US FDA, Validation of Cleaning Processes [3]
  - Eudralex Volume 4, Annex 14 [4]
- While it's possible, depending on product and process characteristics, to rely on rinse sampling, most regulators expect surface swab sampling



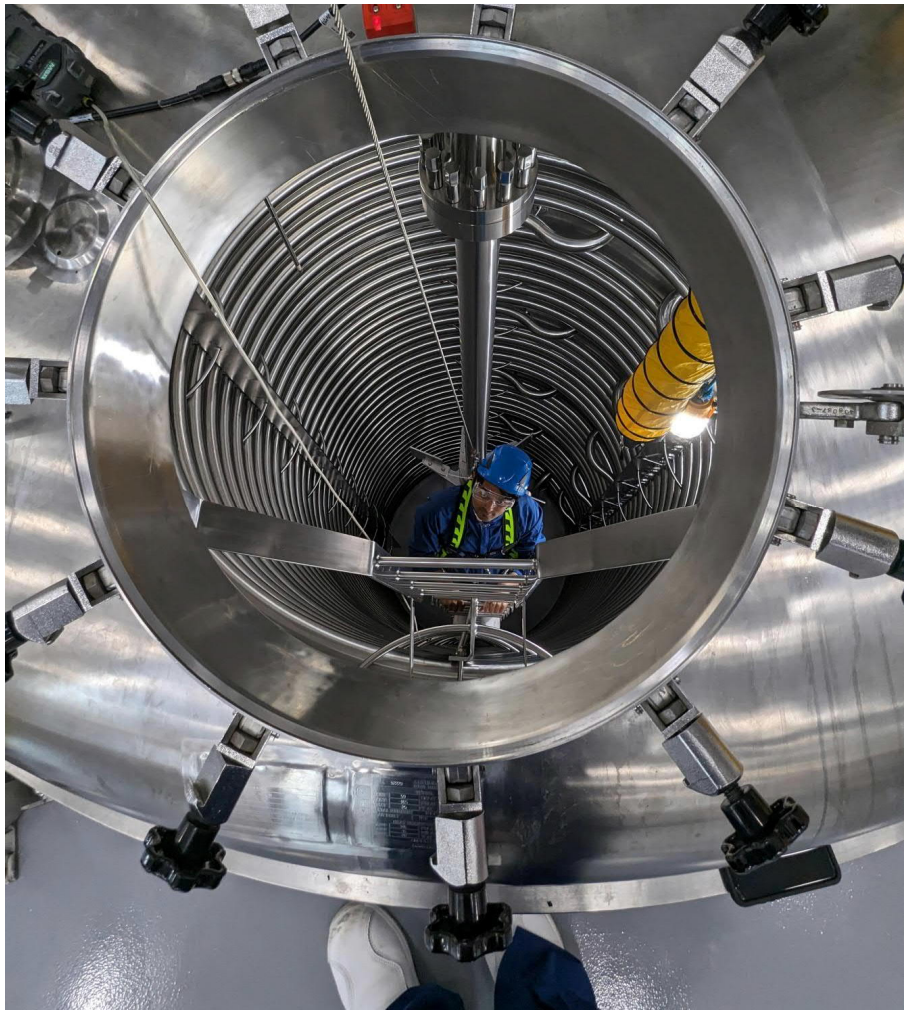
Sampling Considerations

Confined Space and Manual Swabbing vs. Remote Sampling Methods

- Sampling Sites Often Difficult to Reach and Require Confined Space Entry
- Confined Space Entry Increases Safety Risks as well as the Possibility of Equipment Damage
- Remote Devices Can be Validated and Used for Sample Collection

Confined Space Entry Considerations

- Fall Protection
- Crane
- Entry Ladders
- Atmospheric Monitoring
- Forced Ventilation
- Additional Attendants
- EMS Personnel
- Confined Space Entry Increases the Likelihood of Sample Contamination



Industry Approach to Remote Sampling

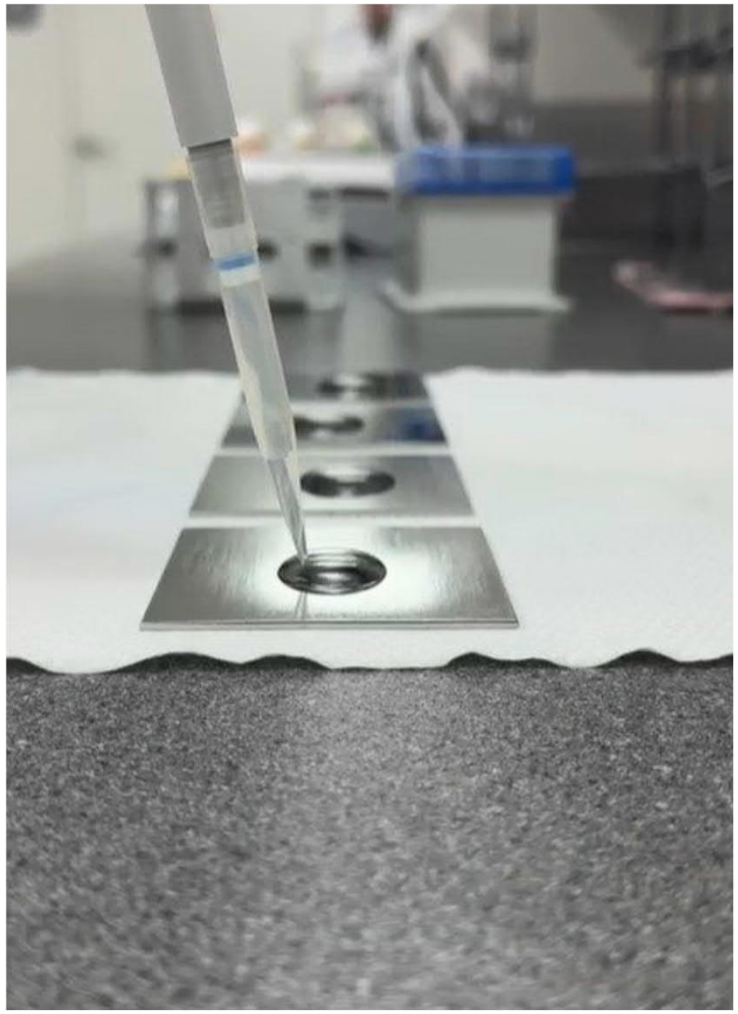
Recovery should be shown to be possible from all product contact materials sampled in the equipment with all the sampling methods used.

Development and Qualificationof Remote Method

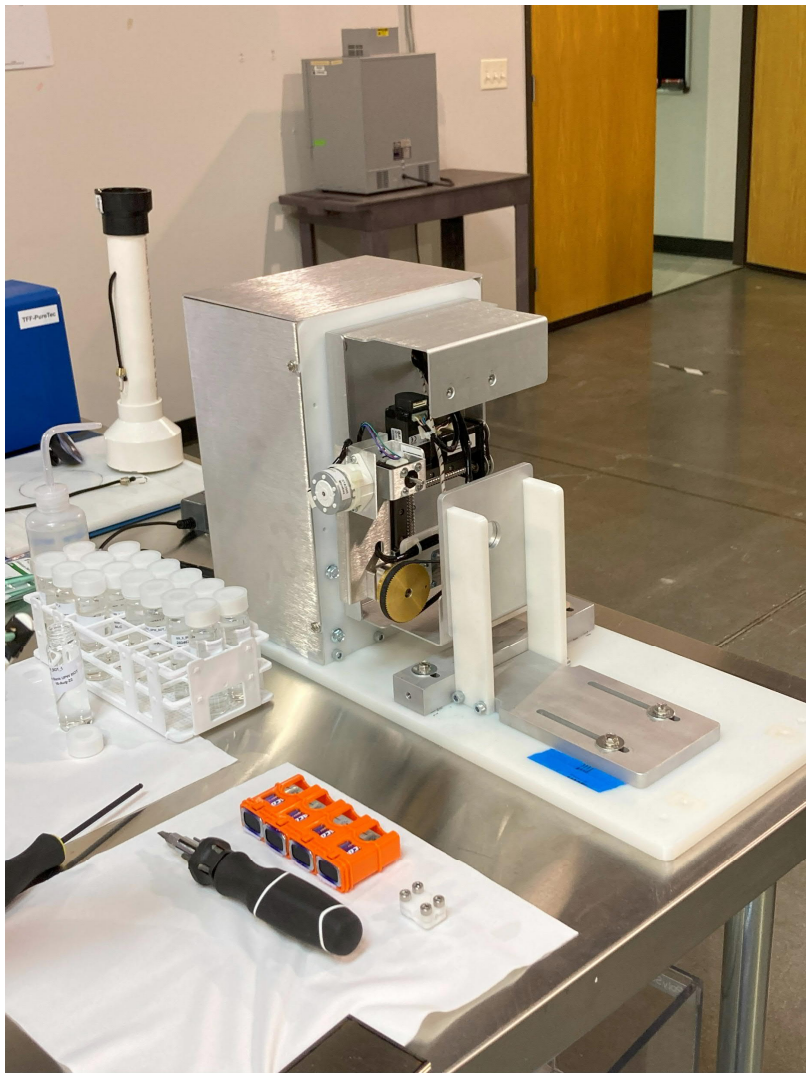
- Control of the Swab Extension Pole is Difficult
- Inconsistent Coverage and Sampling Pattern
- Variable Pressure on the Swab Head can Impact Recovery
- Training, Practice, and Requalification are of Paramount Importance

Study Design

- Hyde compared three different swab methods
  - Manual or hand swabbing
  - Swabbing with an extension pole
  - Swabbot's prototype automated swabbing device
- To ensure that the solutions used for the recovery performance characterization study are reliable
  - Carbon content characterization was performed for sucrose and bovine serum albumin solutions.
  - Three concentrations as well as blanks samples were analyzed.



Study – Materials and Methods



Sucrose (ACS Grade)

- Blank (4x)
- 0.5 µg/cm² (4x)
- 1 µg/cm² (4x)
- 5 µg/cm² (4x)

BSA (1 mg/mL)

- Blank (4x)
- 0.5 µg/cm² (4x)
- 1 µg/cm² (4x)
- 5 µg/cm² (4x)

Coupons

- 316L Stainless Steel
- 20 Ra Surface Finish
- 2.5” x 2.5”

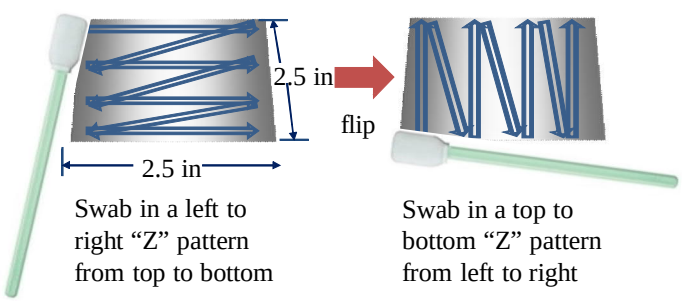
Total Organic Carbon

- Sievers M9
- Acid Flowrate (1.0 µL/min)
- Oxidizer Flowrate (1.0 µL/min)

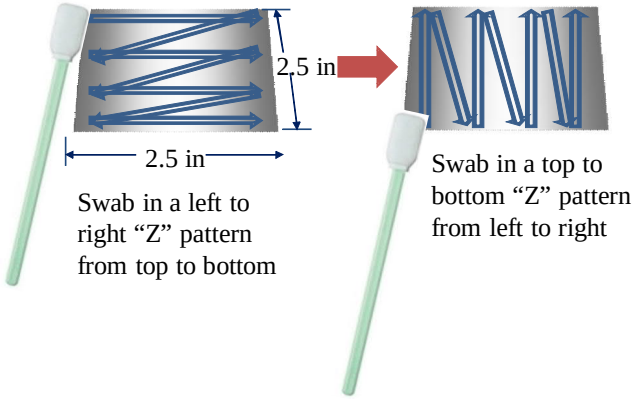
Data Analysis

- % Recovery
  - Blank adjusted / Based on positive controls
- One-Way ANOVA

Swab Patterns

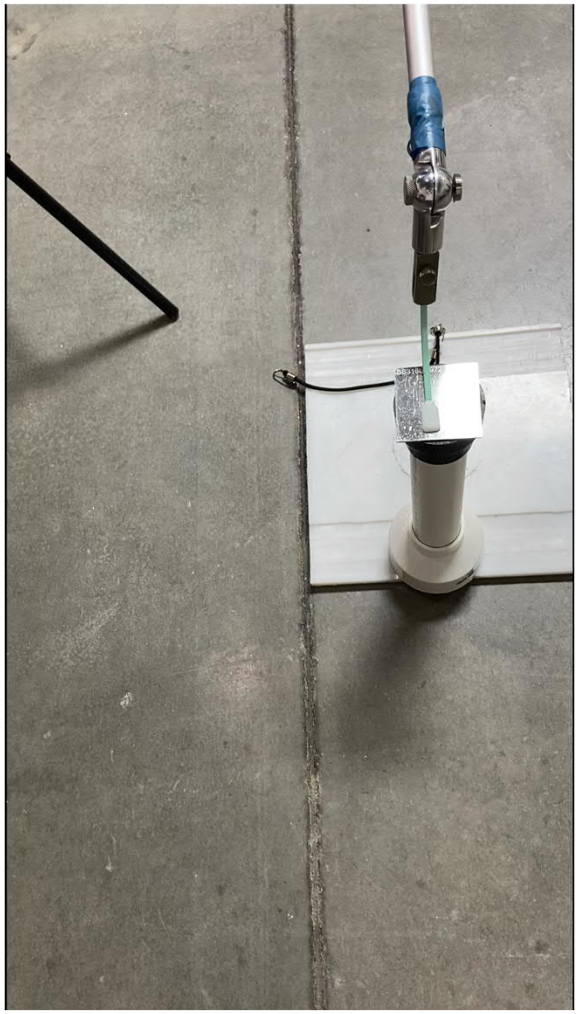


Manual and Automated Swabbing



Remote Swabbing

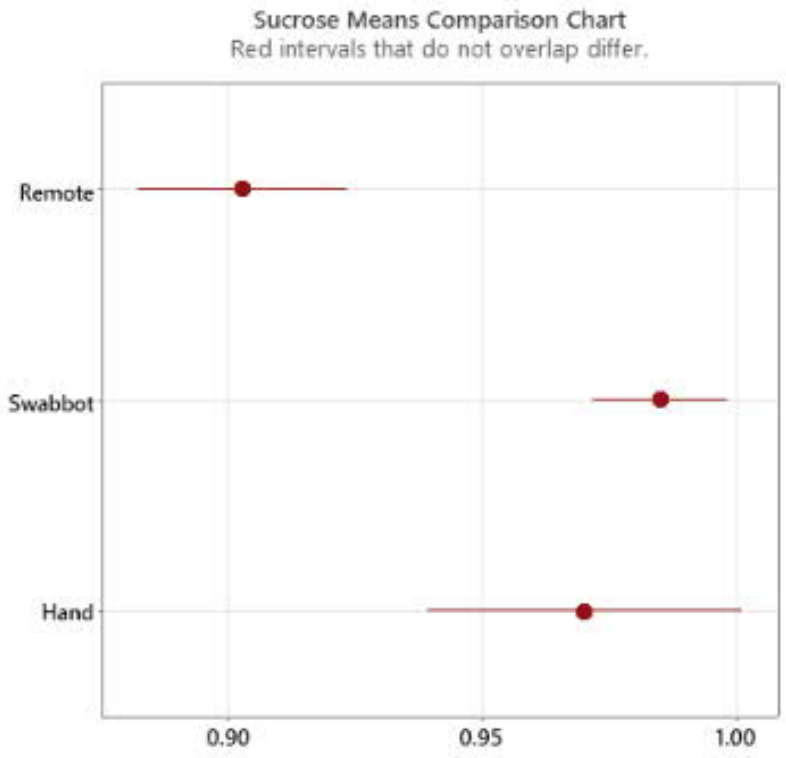
Remote Swab Sampling

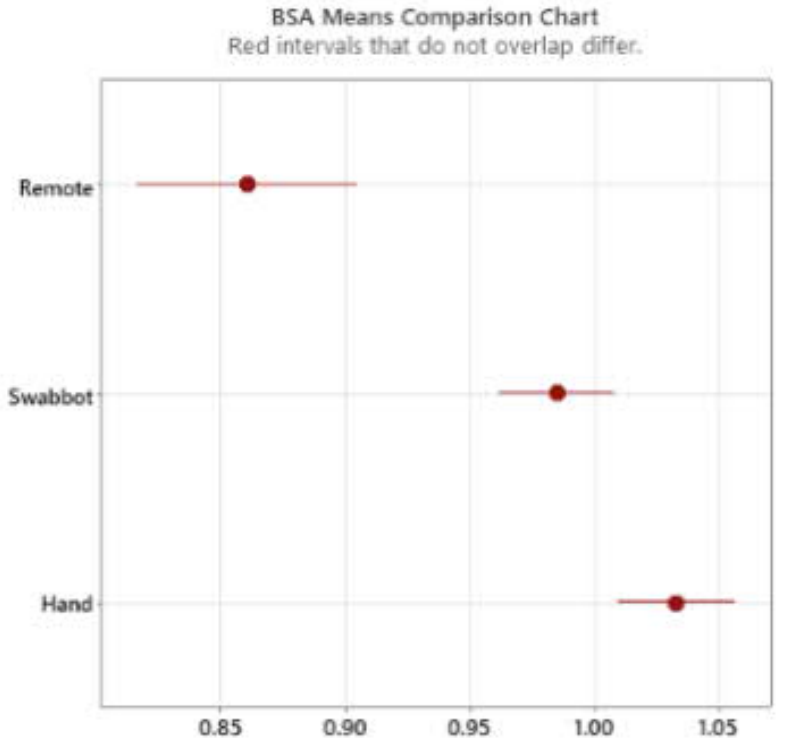


Study Results

Swab Sampling Results Summary (316L Stainless Steel)							
Expected Concentration (ppm C)	Method	Average Recovery (%)		Average Recovery % SD		% Difference from Swabbot	
		Sucrose	BSA	Sucrose	BSA	Sucrose	BSA
0.5	Hand	100	107	1	3	1	6
1	Hand	95	102	7	6	3	3
5	Hand	96	101	7	2	3	5
0.5	Remote	89	90	3	4	11	11
1	Remote	90	86	5	10	8	14
5	Remote	92	82	5	8	7	16
0.5	Swabbot	99	101	1	3		
1	Swabbot	98	99	1	4		
5	Swabbot	99	96	1	6		

Study Results



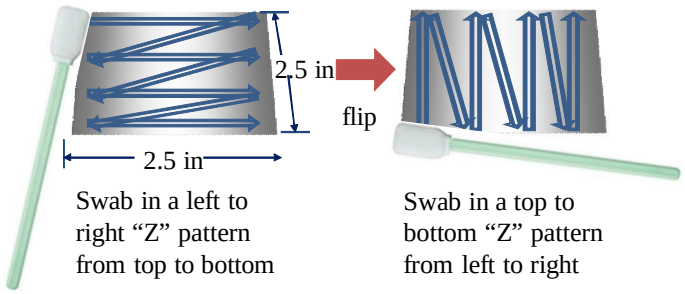


Using Recovery Data to Improve Instrument Design

A comparison of swabbing patterns for data-driven instrument footprint reduction

Swab Pattern Comparison

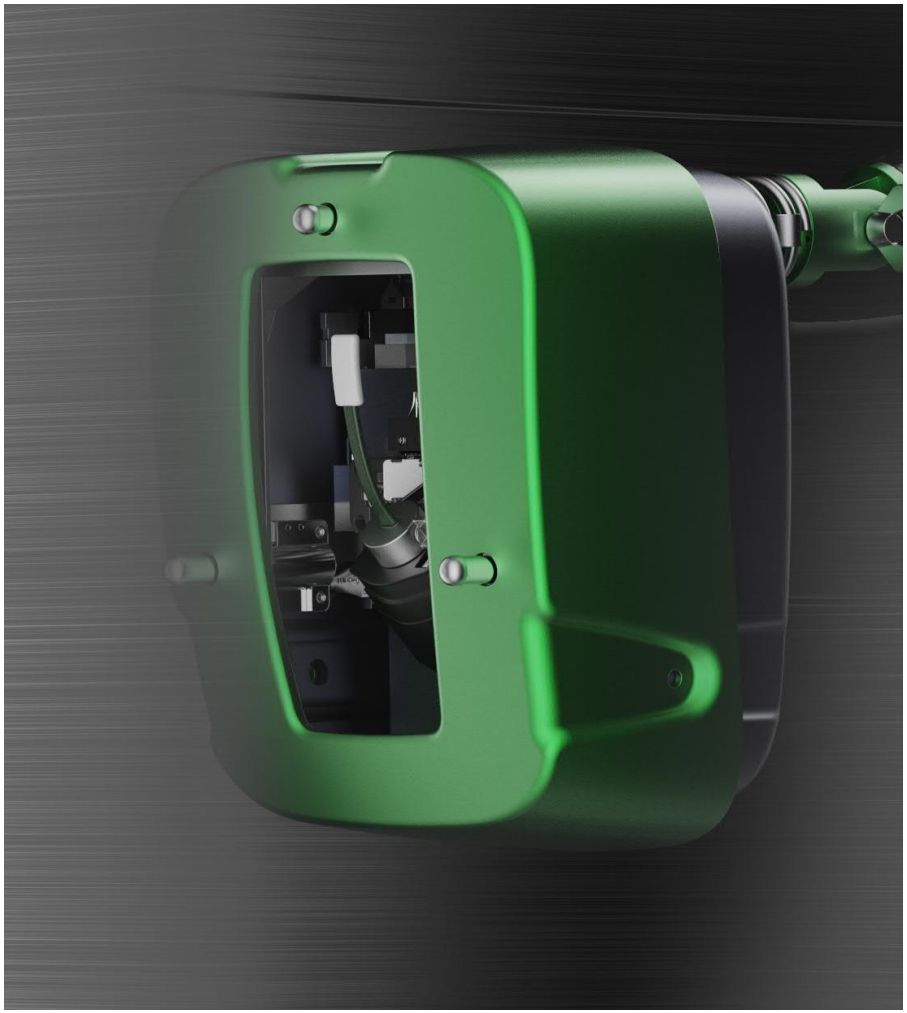
- Initial Prototype Design used the Pattern Shown Below
- Rotation of the Swab to a Perpendicular Orientation Required More Components and Operational Space
- Determine if the Pattern Used for Swab Extension Poles is Comparable to Rotation



Section Break

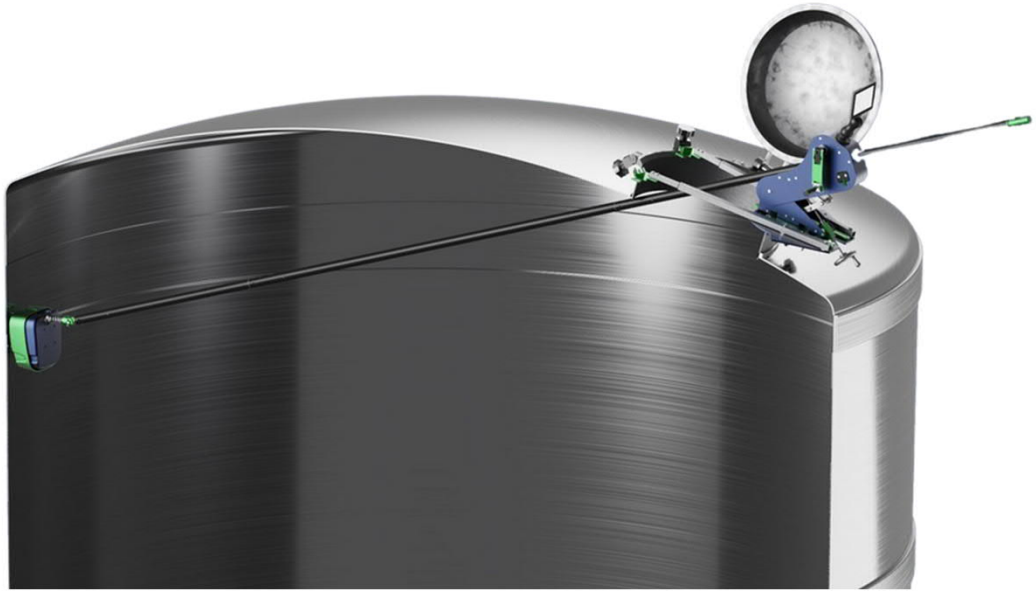
316L SS Swabbot Sampling Method Summary Table				
Expected Concentration (ppm C)	**Sampling Method**	**Avg Corr TOC (ppm C)**	**Recovery**	**Repeatability Recovery SD**
0.5	Original	0.453	97%	3%
1	Original	0.907	93%	2%
5	Original	4.77	91%	2%
0	Stable Orientation	0.0824	N/A	N/A
0.5	Stable Orientation	0.477	102%	1%
1	Stable Orientation	0.928	95%	1%
5	Stable Orientation	4.86	93%	1%
0	No Flip	0.0834	N/A	N/A
0.5	No Flip	0.456	98%	3%
1	No Flip	0.850	87%	1%
5	No Flip	4.63	89%	3%

Resulting Design



- Cleanable enclosure
- Silicone Bumpers as Point of Contact with Equipment to Prevent Damage
- Resulting Design Weighs Less than 3 Kilograms
- The instrument is mounted on a carbon fiber extension pole.
- The instrument is deployed to the sample site using an equipment access system designed to facilitate positioning and prevent contamination or equipment damage.

Deployment Examples



Acknowledgements

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- Founder, Swabbot, Inc.

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Michael Lund

- Senior Scientist, Hyde Engineering

References

1. Health Canada's Cleaning validation guide (GUI-0028), https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/good-manufacturing-practices/validation/cleaning-validation-guidelines-guide-0028/document.html#s9-1, accessed November 14, 2022
2. The FDA Guide to Inspections : Validation of Cleaning Processes states https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/inspection-guides/validation-cleaning-processes-793
3. WHO TRS 1019 - Annex 3: Good manufacturing practices: guidelines on validation, Appendix 3 https://cdn.who.int/media/docs/default-source/medicines/norms-and-standards/guidelines/production/who-good-manufacturing-practices-guidelines-on-validation.pdf?sfvrsn=9440a5c_0&download=true, accessed November 14, 2022
4. PICS Annex 15 " in section 10.12, https://picscheme.org/docview/4590