

REFERENCES

- Aranda, R., Dineen, S. M., Craig, R. L., Guerrieri, R. A., & Robertson, J. M. (2009). Comparison and evaluation of RNA quantification methods using viral, prokaryotic, and eukaryotic RNA over a 10(4) concentration range. *Analytical biochemistry*, 387(1), 122–127.
<https://doi.org/10.1016/j.ab.2009.01.003>
- Chaudhary, N., Weissman, D., & Whitehead, K. A. (2021). mRNA vaccines for infectious diseases: principles, delivery and clinical translation. *Nature reviews. Drug discovery*, 20(11), 817–838.
<https://doi.org/10.1038/s41573-021-00283-5>
- Czochor, J., & Turchick, A. (2014). Introduction. Vaccines. *The Yale journal of biology and medicine*, 87(4), 401–402.
- Forsyth, R. J. (2016). Best practices for cleaning validation swab recovery studies. *Pharmaceutical Technology*, 40(9), 40-53.
- Gouveia, B. G., Rijo, P., Gonçalo, T. S., & Reis, C. P. (2015). Good manufacturing practices for medicinal products for human use. *Journal of pharmacy & bioallied sciences*, 7(2), 87–96.
<https://doi.org/10.4103/0975-7406.154424>
- Haidar Ahmad, I. A., & Blasko, A. (2017). Failure of Cleaning Verification in Pharmaceutical Industry Due to Uncleanliness of Stainless Steel Surface. *Journal of visualized experiments : JoVE*, (126), 56175. <https://doi.org/10.3791/56175>
- Hedman, J., Akel, Y., Jansson, L., Hedell, R., Wallmark, N., Forsberg, C., & Ansell, R. (2021). Enhanced forensic DNA recovery with appropriate swabs and optimized swabbing technique. *Forensic Science International: Genetics*, 53. <https://doi.org/10.1016/J.FSIGEN.2021.102491>
- Hogan, M. J., & Pardi, N. (2022). MRNA Vaccines in the COVID-19 Pandemic and Beyond. In *Annual Review of Medicine*, 73, 17–39. <https://doi.org/10.1146/annurev-med-042420-112725>
- Iwasaki, A., & Omer, S. B. (2020). Why and How Vaccines Work. *Cell*, 183(2), 290–295.
<https://doi.org/10.1016/j.cell.2020.09.040>
- Jones, L. J., Yue, S. T., Cheung, C. Y., & Singer, V. L. (1998). RNA quantitation by fluorescence-based solution assay: RiboGreen reagent characterization. *Analytical Biochemistry*, 265(2), 368–374. <https://doi.org/10.1006/abio.1998.2914>
- Kalelkar, S., & Postlewaite, J. (2013). Sampling for Cleaning Validation — Analytical Considerations. *Cleaning and Cleaning Validation*, 2, 393–410. www.pda.org/bookstore
- Koley, D., & Bard, A. J. (2010). Triton X-100 concentration effects on membrane permeability of a single HeLa cell by scanning electrochemical microscopy (SECM). *Proceedings of the National*

Academy of Sciences of the United States of America, 107(39), 16783–16787.

<https://doi.org/10.1073/pnas.1011614107>

Lamei Ramandi, S., & Asgharian, R. (2020). Evaluation of Swab and Rinse Sampling Procedures and Recovery Rate Determination in Cleaning Validation Considering Various Surfaces, Amount and Nature of the Residues and Contaminants. *Iranian journal of pharmaceutical research : IJPR*, 19(3), 383–390. <https://doi.org/10.22037/ijpr.2020.1101173>

National Center for Biotechnology Information (2022). PubChem Compound Summary for CID 5590, Triton X-100. Retrieved July 10, 2022 from <https://pubchem.ncbi.nlm.nih.gov/compound/Triton-X-100>.

Nguyen, T. T., Tran, V. T., & Mia, M. (2020). Multi-response optimization of electrical discharge drilling process of SS304 for energy efficiency, product quality, and productivity. *Materials*, 13(13). <https://doi.org/10.3390/ma13132897>

Pardi, N., Hogan, M. J., Porter, F. W., & Weissman, D. (2018). mRNA vaccines - a new era in vaccinology. *Nature reviews. Drug discovery*, 17(4), 261–279. <https://doi.org/10.1038/nrd.2017.243>

Park, J. W., Lagniton, P., Liu, Y., & Xu, R. H. (2021). mRNA vaccines for COVID-19: what, why and how. *International journal of biological sciences*, 17(6), 1446–1460. <https://doi.org/10.7150/ijbs.59233>

Pélabon, C., Hilde, C. H., Einum, S., & Gamelon, M. (2020). On the use of the coefficient of variation to quantify and compare trait variation. *Evolution letters*, 4(3), 180–188. <https://doi.org/10.1002/evl3.171>

Plotkin S. (2014). History of vaccination. *Proceedings of the National Academy of Sciences of the United States of America*, 111(34), 12283–12287. <https://doi.org/10.1073/pnas.1400472111>

Pluta, P. L. (2013). *A REVIEW ON SWAB SAMPLING AND RINSE SAMPLING PROCEDURE USED IN PHARMACEUTICAL INDUSTRY* | PharmaTutor. Davis Healthcare International Publishing. <https://www.pharmatutor.org/articles/a-review-on-swab-sampling-and-rinse-sampling-procedure-used-in-pharmaceutical-industry>

Reed, G. F., Lynn, F., & Meade, B. D. (2002). Use of coefficient of variation in assessing variability of quantitative assays. *Clinical and diagnostic laboratory immunology*, 9(6), 1235–1239. <https://doi.org/10.1128/cdli.9.6.1235-1239.2002>

Riedel S. (2005). Edward Jenner and the history of smallpox and vaccination. *Proceedings (Baylor University. Medical Center)*, 18(1), 21–25. <https://doi.org/10.1080/08998280.2005.11928028>

Sung, K., Khan, S. A., Nawaz, M. S., & Khan, A. A. (2003). A simple and efficient Triton X-100 boiling and chloroform extraction method of RNA isolation from Gram-positive and Gram-negative

bacteria. *FEMS Microbiology Letters*, 229(1), 97–101.

[https://doi.org/10.1016/S0378-1097\(03\)00791-2](https://doi.org/10.1016/S0378-1097(03)00791-2)

Texwipe. (2011). *Swabs for Cleaning Validation in Pharmaceutical Manufacturing*. TEXWIPE.

<https://www.texwipe.eu/swabs-for-cleaning-validation-in-pharmaceutical-manufacturing>

APPENDICES

Appendix 1. Calculation for Rinse Sampling Method

I. Determination of Detected Concentration

Since 25 ng/mL standard curve solution is diluted with 0.1% Triton X-100 solution at a 1:1 ratio, the concentration of RNA that will be detected is:

$$n = \frac{12,5 \text{ ng/mL}}{2}$$

$$n = 6,25 \text{ ng/mL}$$

Appendix 2. Calculation for Swab Sampling Method

I. Determination of Sample Amount

The sample concentration made for the swab sampling method is 10 µg/mL. The amount of sample needed to obtain a concentration of MACO value is done with the following equation:

$$n = \frac{m}{V}$$

Where n is the concentration (ng/mL); m is mass (µg or ng); and V is volume (mL).

Rearranging the equation gives:

$$V = \frac{m}{n}$$

To calculate the required amount of 10 µg/mL sample, m shall be substituted with the MACO value of the swab sampling method and n shall be substituted with the concentration of the sample solution as shown:

$$V = \frac{304 \text{ ng}}{10 \text{ ug/mL}}$$

$$V = \frac{304 \text{ ng}}{10,000 \text{ ng/mL}}$$

$$V = 0,0304 \text{ mL}$$

$$V = 30,4 \text{ uL}$$

II. Determination of Detected Concentration

Since 30,4 µL of 10 µg/mL sample is tested onto the swabs, the concentration of RNA in the 10 mL Triton X-100 solution shall:

$$n = \frac{m}{V}$$

$$n = \frac{304 \text{ ng}}{10 \text{ mL}}$$

$$n = 30,4 \text{ ng/mL}$$

Taking into consideration of the Quant-iT addition on the microplate, the concentration that will be detected is:

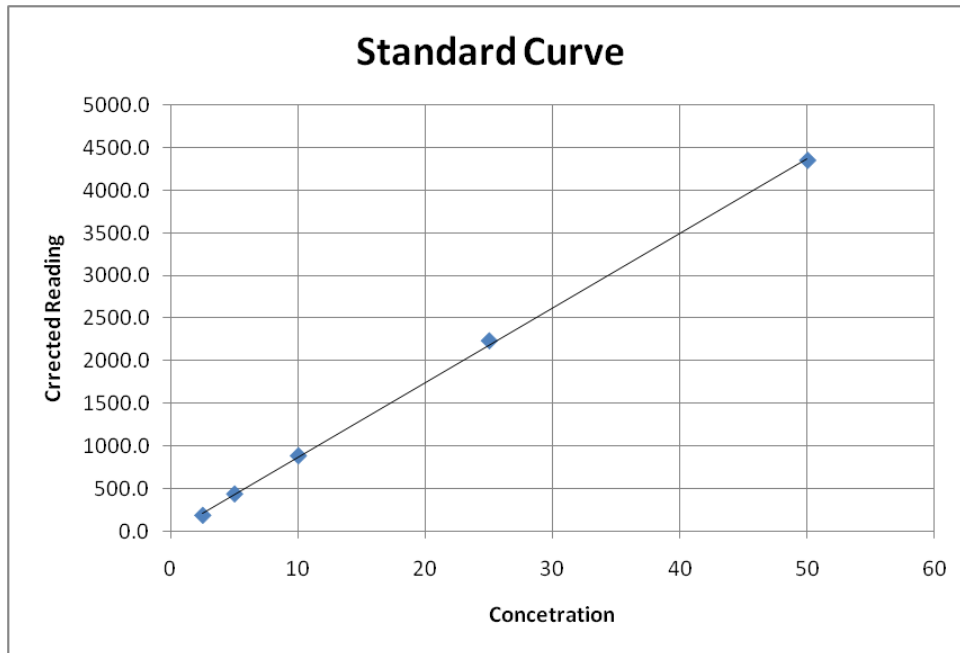
$$n = \frac{30,4 \text{ ng/mL}}{2}$$

$$n = 15,2 \text{ ng/mL}$$

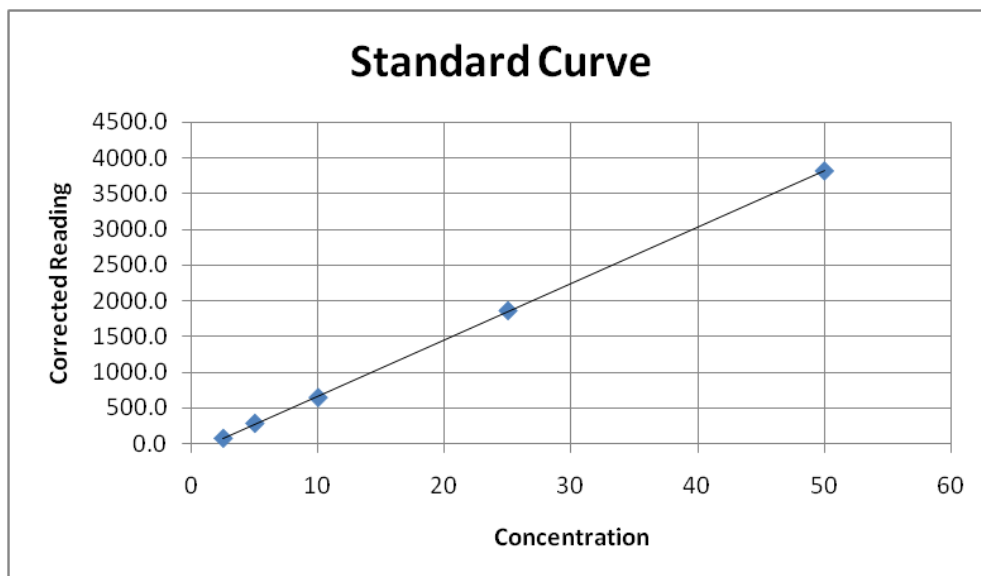
Appendix 3. Calculation for Percentage (%) CV

To determine the Percentage (%) CV of the obtained results, the following formula can be used:

$$CV (\%) = \left(\frac{\text{Standard deviation}}{\text{Mean}} \right) \times 100$$



Appendix 4. Standard Curve 1 for Rinse and Swab Sampling Methods (Determination of Swab Sampling Material)

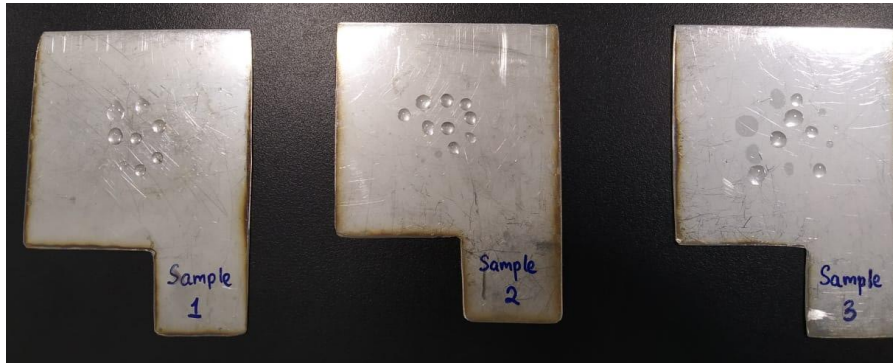


Appendix 5. Standard Curve 2 for Swab Sampling Methods (Detection of mRNA Residue with Swab Sampling Method)

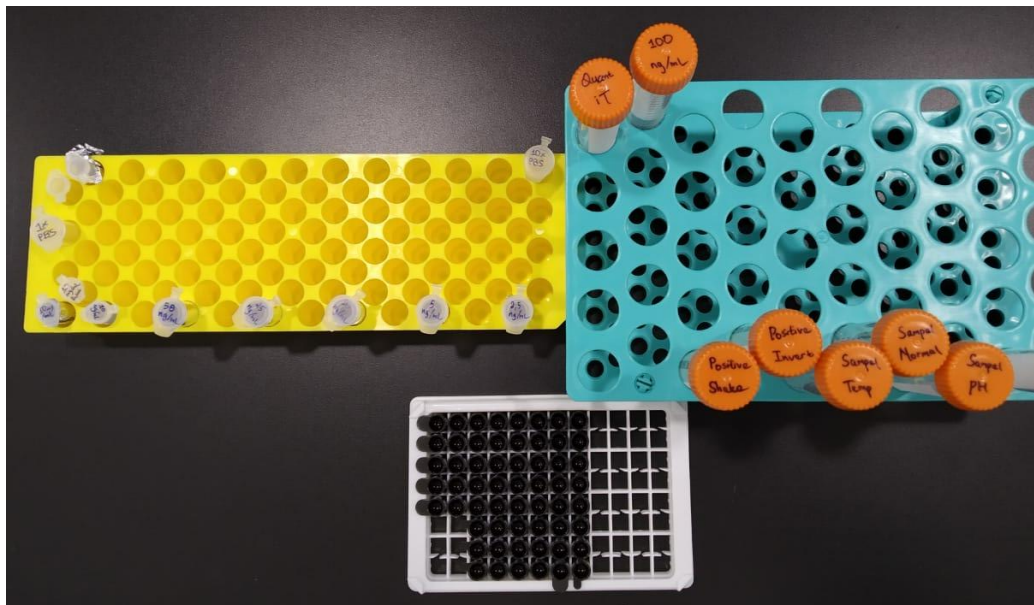
Appendix 6. List of the Standard Equation and R^2 values of the Standard Curves

Standard Curve No.	Standard Equations	R^2
1.	$y = 87,59x - 5,239$	0,999
2.	$y = 78,98x - 124,4$	0,999

DOCUMENTATION



Documentation 1. Samples on plate for the swab sampling method



Documentation 2. Preparations for the rinse and swab sampling method



Documentation 3. Bio-Tek FLX800T Microplate Fluorescence Reader