VAC_13 - Implementation of a Control Strategy for DNA linearization in the technological development used for mRNA synthesis of the COVID-19 vaccine

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Introduction: The Control Strategy is designed to ensure that products have the desired quality, both in process and final form. The development of a Control Strategy is possible due to an integrated approach, considering aspects described in the International Harmonization documents ICH Q7, Q8, and Q10 Guides, Quality Risk Management described in ICH Q9, ICH Q13, and applicable current guidelines. The linearization of plasmid DNA is a critical step in the production of the mRNA vaccine for COVID-19 developed at Bio-Manguinhos, and ensuring its quality is a key component for the product's effectiveness.

Objectives: To design a Control Strategy by risk assessment of the plasmid DNA linearization process in experimental development through mapping and classifying process parameters regarding their criticality.

Methodology: The DNA linearization process was mapped and meetings between the technical-scientific team of the Molecular Biology Platform and Quality Assurance were held to define the criticality of each process parameter. Aspects such as Material Attributes, Process Monitoring and Control, Holding Time, and Critical Process Parameters were evaluated in this Control Strategy. Team members defined criticality based on prior experience with DNA processing.

Results: A total of 39 parameters were classified according to their criticality in the process. Of these 39 parameters, 4 were classified as critical and 35 as non-critical. Three output measurements were classified as Key Process Attributes, with purity and linearization efficiency being evaluated as Critical Quality Attributes and two analytical methods established and described for the analyses. A Product Specification document was generated to specify the linearized DNA. As a result, a Risk Assessment Report was prepared containing all the information mentioned and the Control Strategy established for the linearization of plasmid DNA in experimental development. This document will be subject to review and updating according to internal Technological Transfer during scaling of production and use of updates in the composition of registration documents by ANVISA for the Bio-Manguinhos Messenger RNA COVID-19 Vaccine.

Conclusion: This is the first Control Strategy designed at Bio-Manguinhos and allowed to map critical parameters that could interfere with the effectiveness of the DNA used in the messenger RNA synthesis. Thus, it is possible to visualize when risk mitigation actions will be carried out and the final quality of the product will be assured, as well as it will be possible to use the document to compose documentation for registration of the COVID-19 vaccine in Brazil regulatory agency.

Keywords: Messenger RNA; Vaccines; Control strategy