VAC_26 - From bench to pilot plant: mapping the nanoencapsulation process of mRNA to develop a control strategy and transfer the technology

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Introduction: Transferring messenger RNA encapsulation technology from development to pilot production scale can be a complex task. Developing a control strategy based on risk management facilitates this process and helps to ensure product quality. The control strategy is designed to ensure that products are of the desired quality, both in process and final form. This document is applied to product processing as described in the International Harmonization documents ICH Q7, Q8, and Q10 Guides, Quality Risk Management as described in ICH Q9, ICH Q13, and applicable current guidelines.

Objectives: Map and classify the parameters of the naked mRNA encapsulation process based on risk analysis and define the criticality to mitigate the impacts of the process on the drug substance.

Methodology: The mRNA encapsulation process was mapped, and meetings were held between the nanoencapsulation platform and quality assurance to define criteria, acceptance ranges, and impact mitigation based on previous experience of the platform operators. The parameters were listed and individually ranked according to criticality. Parameters that could interfere with critical attributes of the encapsulated mRNA were classified as critical (CPP); parameters that did not interfere were classified as non-critical (NCPP); and steps that required control during processing were classified as in-process control (IPC).

Results: A total of 78 parameters were described, of which 64 were classified as non-critical, 13 as critical, and 1 as in-process control. In addition, analytical methods were developed and formalized to describe the output measurements and to ensure product quality at this stage. Operating protocols were developed to describe the steps and a product specification document was developed to describe the encapsulated mRNA and its specifications that will go into the final vaccine formulation.

Conclusion: According to the risk analysis carried out, it was possible to develop a control strategy to ensure the quality of the encapsulated mRNA, in addition to achieving greater robustness throughout the documentation at this stage. This approach will enable the transfer of developed technology from the bench to the pilot facility and mitigate any potential impact on the quality of the drug substance.

Keywords: Messenger RNA vaccine; Nanoencapsulation; control strategy