

VAC.08 - Yellow fever vaccine: development of an optimized freezing dryer cycle in industrial scale

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Introduction:

Although Brazil is the biggest Yellow Fever Vaccine (YFV) producer worldwide, there is still a risk of supply discontinuity to meet the demand in the country and Africa if the epidemiological scenario gets worse. Fiocruz YFV production needs a lyophilization process step to stabilize the final product, however, in terms of process management, it is a bottleneck constraining the increase of the production of YFV during outbreaks. To decrease the lead-time from production to the market of YFV, this work aims to demonstrate the results of an accelerated and 41 months stability study of an optimized freeze-drying cycle time. Three experiments in industrial scale were carried out with a lyophilization cycle 15 hours shorter than the original cycle.

Objective:

Demonstrate the results of an optimized lyophilization cycle in industrial scale of YFV decreasing the manufacturing lead-time and increase production capacity.

Methodology:

The methodology is based on three industrial scale batches produced in 2014 with a 15h less lyophilization cycle that were performed following the same YFV raw materials, production procedures and validations times used in commercial batches. Modifications were done only in physical properties of the current freeze-drying cycle temperature and time. The batches were analyzed by Bio-Manguinhos Quality Control Department and a six months accelerated stability studied and a 41 months of real time stability study were conducted.

Results:

Cake appearance was approved after 100% visual inspection. Thermo stability (14 days at 37°C) results range from 4,56 to 4,74 Log₁₀ UI/dose.

Six months accelerated stability test at 25°C, the minimum potency result was 4,73 Log₁₀ UI/dose and maximum residual moisture 1,64% among the batches.

Real time stability study from 2°C to 8°C and -20°C was conducted up to 41 months and results from aspect, pH, residual moisture, potency were within the specifications and average residual moisture presents a maximum value of 1,6% and potency a minimum value of 4,11 Log₁₀ UI/dose among the batches. Maximum potency loss was 0,53 log₁₀ UI/DH for real time stability study.

All the results are within the specifications and no tendency was observed when compared with the real time stability results from commercial batches.

Conclusion:

All batches in industrial scale are within the specifications of ANVISA and WHO. The results from stability studies demonstrate the viability of the optimized lyophilization cycle and confirm no changes in safety, quality and efficiency of YFV. The development of an optimized lyophilization cycle 15h shorter than the original one can improve Fiocruz capacity at the yellow fever production facility, decreasing the product time to market. These improvements are aligned with the strategies of Bio-Manguinhos/Fiocruz, contributing to increase the global stockpile of vaccines for emergency outbreaks, especially in African Countries and Latin American countries to contain the spread of the disease.

Keywords: Yellow Fever Vaccine; Freeze Dryer; Optimization