MAN_05 - Integration of the risk analysis techniques and Spearman correlation to support the decision making based in a risk approach of the upstream steps in a therapeutic protein pilot scale

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Introduction: It's well known the advantages of risk management in pharmaceutical industry to incorporate suitable principles in systems starting from the supply chain to the final drug substance processing based on a risk approach according to the Brazilian RDC 658/22 and ICHQ9. Furthermore, procedures based on risk enable process mapping and to define critical risks to be treated, prevented or mitigated to maintain continuous improvement.

Objectives: Integration of risk analysis techniques and Spearman correlation (SC) to support the decision making of 3 different alternatives of upstream process steps to produce a therapeutic protein in pilot scale considering a seed train with working volume of 2,5 L, 8 L, 40 L, and the main production bioreactor to reach 200 L.

Methodology: First, a tool was built using FMEA, HAZOP and risk matrix main characteristics. The process parameters for each step were selected and each deviation was analyzed, identifying the major causes, likelihood, severity of main consequences and monitoring and control elements for biorreators' configuration: (A) = 2 x 2 L, 1 x 5 L, 1 x 50 L and 1 x 200L, B = 2 x 2 L , 1 x 10 L, 1x 50 L and 1x200 L and (C)=1 x 5 L , 1 x 10 L , 1x 50 L and 1x 200 L all in serie. All of them have received a level score previously defined and it's made the risk classification per each deviation as low (L), moderate (M), high (H) and very high(VH). In addition, the Spearman correlation's calculated using the software Jamovi.

Results: 146 deviations for A, 141 for B and 118 for B options were identified. For A, 22% of the risks were classified as VH, 36 % as H, 34% M and 9% L. Moreover, SC showed the strongest positive correlation between severity and likelihood and negative correlation between severity and detectability compared to other options. The B had better results than A, because 20% of risks were VH, 36% H, 35% M and 9% L. The C got the best result compared with other alternatives because, besides having fewer deviations, the risks were classified as 19% VH, 37% H, 35% M and 9% L. However, SC showed a positive correlation between severity and likelihood but weaker than the A. The most critical risks were those that could impact the cultivation process. Main causes of these risks were the possibility of contamination through some hose's connections and absence of gases.

Conclusion: It's possible to establish a decision-based risk approach to choose the C alternative to be used in pilot scale. Therefore, it's clear the potential of using the integration tool within the pharmaceutical industry in decision-making.

Keywords: Risk analysis; Pilot scale; Therapeutic protein