Comprehensive Approach for Annex 1 Gap Assessments

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RESILIENCE GENE THERAPY

Abstract

Since the current version of European Union (EU) GMP Annex 1 took effect on 25 August 2023, sites across the world have been assessing their adherence to the Annex 1 regulations to meet the European market patient demand. Here at Resilience Research Triangle Park, we have taken a comprehensive approach to assessing three-hundred and sixty (360) Annex 1 requirements against our processes and procedures. Each gap was identified through a risk-based approach and categorized by topic area (i.e.-single use systems, equipment, utilities etc.) and ranked as Low, Medium, or High based on impact to product quality against existing site controls. The following sections describe our strategy for methodically assessing the alignment between Annex 1 and our current processes and procedures.

Introduction

The current version of the EU GMP Annex 1 includes additional requirements that are aligned with modern pharmaceutical manufacturing practices, intended to ensure a high level of sterility assurance. Revision has included incorporation of modern technologies, risk management approaches, and addressing new industry challenges. However, alignment with the current Annex 1 EU requirements presents challenges for companies to assess and implement.[1] Here at Resilience RTP a comprehensive approach was used to conduct a thorough gap assessment for Annex 1 compliance.

Materials & Methods

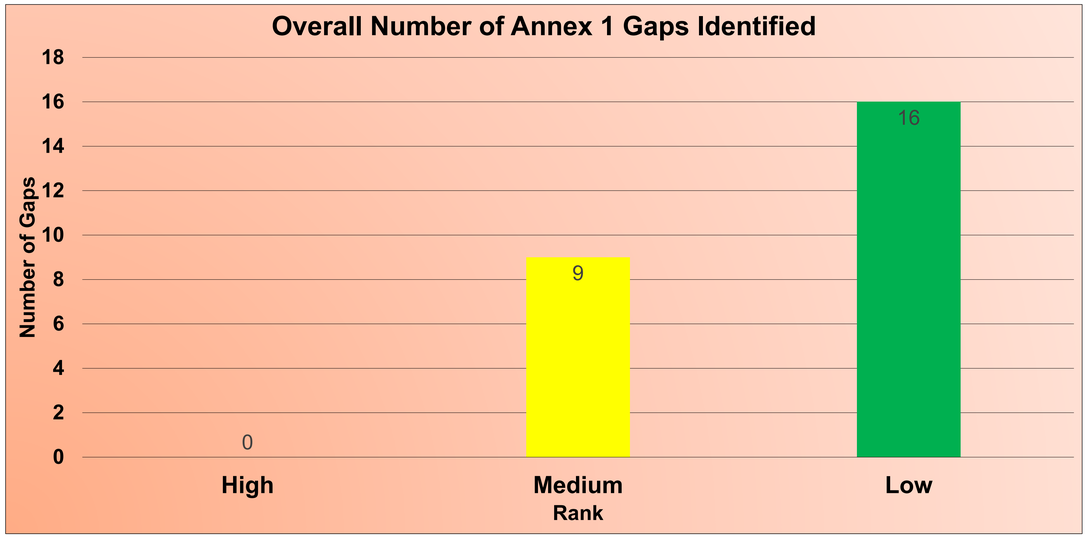
A gap assessment template was created to evaluate each Annex 1 section against existing site controls to determine if each requirement is met. A site Annex 1 core team was identified based on their role, site knowledge, and industry expertise, to facilitate and lead the gap assessment. Upon identification of gaps, the team leveraged industry quality risk management principles to rank overall risk level.

Item No.	Topic Area	Section Reference	Requirement	Site Assessment (Aligned, GAP, N/A) *** If a GAP is identified, add a short description*	Site or Global Document Reference(s) that Addresses Requirement at Site	Site GAP Action ***Include any Quality System References*	Gap Owner	CAPEX Impact (Y/N) *** Add estimated amount, if known)*	Target Completion Timeline	Interim Control and Timeline (if needed) ***Include any Quality System References*
H1	General	9.1	The site's environmental and process monitoring programme forms part of the overall CCS and is used to monitor the controls designed to minimize the risk of microbial and particle contamination. It should be noted that the reliability of each of the elements of the monitoring system (viable, non-viable and APS) when taken in isolation is limited and should not be considered individually to be an indicator of asepsis. When considered together, the results help confirm the reliability of the design, validation and operation of the system that they are monitoring.	Aligned	SOP- ABC SOP-XYZ	None	Department	N/A	N/A	N/A

Upon completion of the assessment, the risk team members ranked gaps on severity utilizing quality risk management principles. The ranking criteria focused on impact to product quality and the presence of existing controls.

Overall Risk Level	Required Action for Initial Rating	Acceptable for Residual Risk
Low	No action, or minor document revision. Existing controls provide adequate justification / requirements to meet gap.	No risk or risk is acceptable. No impact on Product Quality. Process or procedures are in place.
Medium	Requires mitigating action(s) or documented justification for Resilience practices.	Risk is acceptable with written justification. Potential impact on Product Quality. Partial or no Process or Procedure in place.
High	Requires mitigating action(s) to establish controls and procedures to meet requirement.	Risk is unacceptable. There is an impact to Product Quality. No Process, Procedure, or controls in place.

Results



- Total number of Requirements Assessed: 360
- High Risk: 0.0%
- Medium Risk 2.5%
- Low Risk 4.4%

Conclusion

Performing the gap assessment for Annex 1 alignment was achievable through categorization and ranking of the various gaps identified. The executed gap assessment produced 11 action items for the cross-functional team to address the identified gaps.

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References 1.Dimont, Xenia. Are Annex 1's CCS Requirements Still Challenging You?, Bioprocess Online, June 5, 2024