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NUTRITIONAL COMPOUNDING FACILITY, EUROPE

CONTAMINATION CONTROL

GENERATION OF A CONTAMINATION CONTROL STRATEGY

CASE STUDY: COMPLIANCE & REGULATORY ISSUES

Contamination Control: Generation of a Contamination Control Strategy

A small-scale parenteral nutritional compounding facility in Europe engaged CAI to support remediation efforts required by its local Regulatory Authority. One key initiative was the development of a Contamination Control Strategy (CCS) document for the client site, an essential compliance task that had remained unaddressed despite the adoption of Eudralex Volume 4, Annex 1 (Revision 1) on the 'Manufacture of Sterile Medicinal Products' in August 2023.

PROJECT OVERVIEW

The client site had been operational for several years, with experienced management staff. However, a comprehensive contamination control document, outlining all critical control points and assessing the effectiveness of control and monitoring measures, had yet to be established. In the absence of this overarching document, the client lacked a holistic view of their compliance as well as regulatory expectations. Following a gap assessment alongside the revised Annex 1 guideline further control measures were foreseen.

To address this, a senior CAI agent was placed on-site to collaborate directly with client personnel responsible for developing the CCS document. The agent provided expertise and coaching on regulatory requirements and helped identify critical control points where contamination risks were most significant. Through direct observation of processing operations, product testing activities and cleaning procedures, the CAI agent facilitated knowledge transfer, ensuring full engagement and swift resolution of any emerging issues.

The project began with the identification of key 'pillars' representing the fundamental aspects of contamination control at the site, referred to as the House of Contamination Control. The identified pillars included facility design, covering material and personnel flows, control measures established through procedures and practices, environmental monitoring and validation strategies and risk assessment of potential contamination sources.

Understanding the available information also informed the decision on the format of the Contamination Control Strategy (CCS) document. CAI, leveraging its access to various suitable templates, collaborated with the client to select a document format suitable to their company needs. This template outlined the key elements considered potential contamination sources and risk-based control measures in a CCS document, such as plant design, equipment, personnel, utilities and raw materials. It incorporated the regulatory requirements from Annex 1, along with a summary referencing the company's compliance status and identifying any gaps requiring further action.

Where gaps were identified, corrective and preventive actions (CAPA) were documented. Although the selected template did not assign a specific risk rating to issues, the CAPA process provided risk categorization, ensuring that all omissions were assessed and addressed appropriately.

A comprehensive requirements document was then developed, with the CAI agent compiling readily available information from reports, procedures, training programs, process flows and monitoring programs to demonstrate compliance with Annex 1 requirements.

Where gaps were identified, the CAI agent collaborated with relevant personnel to assess whether the necessary information was available. If gaps were confirmed, remediation actions were documented and corrective and preventive actions (CAPAs) were recorded within the quality management system and associated timelines assigned to each CAPA. Risk rankings for these CAPAs were assigned based on potential severity, detectability and the likelihood of occurrence, ensuring a structured approach to addressing deficiencies.

CHALLENGES

Throughout the project, several challenges arose. One of the primary difficulties in achieving a first draft of the CCS document stemmed from competing site priorities, which led to a lack of engagement from key site personnel, which led to a subsequent delay in the initial meeting the initial target due date. To ensure progress and adherence to timelines, the CAI agent initiated regular one-on-one meetings with relevant department stakeholders, securing their focused input on the sections for which they were responsible. By sharing key sections in advance, these meetings remained concise and targeted, minimizing disruptions while maximizing engagement. These meeting insights were invaluable in refining document inputs, ensuring their practicality and effectiveness.

Early resistance from the client regarding the CCS document's function also posed challenges. While its necessity as a regulatory requirement was acknowledged, the CAI agent emphasized its role as a living document that required active review in response to changes and emerging issues. Moreover, it served as a driver for continuous improvement in manufacturing and control methods. These discussions revealed the need for an additional governance pillar within the Quality Management System to sustain long-term regulatory compliance. The implementation of measurable effectiveness checks was identified as a crucial indicator of this pillar's success.

Determining the risk rating for remediation actions presented another hurdle, as team members were initially disengaged from the process of risk categorization in accordance with Quality Risk Management (QRM) principles. To address this, the CAI agent updated the client's QRM procedure to align with the revised ICH Q9 Guideline. Comprehensive mentoring and training were provided to all personnel, establishing a clear baseline for stakeholders on risk assessment. This clarity facilitated the accurate classification of risk ratings for each action, which were subsequently documented as CAPAs.

Additionally, many of the existing procedures and processes at the client site required updating, as they were not fully aligned with current regulatory expectations or technological advancements in sterile product manufacturing. One such requirement was the Pre-Use Post-Sterilization Integrity Test (PUPSIT) outlined in Annex 1. Meeting these evolving expectations necessitated budgetary and resource investment. As part of the CCS document development, the CAI agent collaborated with stakeholders to define remediation actions and ensure that associated implementation costs were identified and approved within the client's budget. By the project's completion, all remediation actions requiring investment had been accounted for and successfully incorporated into the approved budget.

PROJECT SUCCESS

CAI brought deep expertise in Quality Compliance and Regulatory Affairs, combined with a strong collaborative relationship with the client, enabled the successful authoring, review and approval of the CCS document, delivered on time and within budget. The document was submitted to the regulatory authority which was accepted without further comment.

Beyond its creation, the CAI agent established a structured procedure for the periodic review of the CCS document, ensuring the ongoing maintenance of the highest safety standards. To reinforce its significance, a dedicated training module was developed in collaboration with the CAI agent, emphasizing the critical role of the contamination control strategy. As a result, the client incorporated CCS review elements into their internal audit program. Staff were actively encouraged to report any concerns or propose improvements, fostering a culture of continuous enhancement driven by their increased understanding of contamination control.

Operating under tight time constraints, CAI successfully delivered a comprehensive Contamination Control Strategy document, securing the highest standards of safety and quality for the life-saving parenteral nutritional products manufactured at the site. The pragmatic solutions focussed approach by CAI and their 'Can-Do' approach facilitated seamless integration of all relevant information into a cohesive document. More importantly, it fostered engagement and alignment across stakeholders, supporting both Operational Readiness and a longer-term vision of Operational Excellence

LESSONS LEARNED

The most significant lesson learned by all stakeholders in this project was the critical importance of engagement and collaboration throughout every stage of the CCS document's creation, review, approval and implementation. Developing a comprehensive CCS document can be a complex and demanding process, particularly for a site where none previously existed.

In this case, limited governance and oversight within the quality framework led to a reactive focus on meeting daily production targets, often at the expense of strategic planning for regulatory and technological developments. This posed a risk to long-term compliance and operational stability. Through targeted support and guidance provided by CAI, the site addressed these gaps, implemented necessary improvements, and established a structured process that promotes sustainable compliance. These outcomes directly contributed to enhanced Operational Readiness and laid the groundwork for continuous improvement aligned with Operational Excellence.

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