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Tech Brief

Integrating Phase-Appropriate Quality Standards

Integrating phase-appropriate quality standards into the development, manufacturing, and control of biopharmaceutical products ensures that GMP requirements are consistently met at every stage. This strategy also supports the achievement of overall development goals through a risk-based approach to late-stage requirements within the quality program. Moreover, adherence to quality standards during technical development supports the preparation of comprehensive and traceable documentation and assures the validity and integrity of data submitted in regulatory dossiers.

A Contract Development and Manufacturing Organization (CDMO) with a proven history in implementing this strategy can help establish clear expectations and requirements while balancing the need for accelerated timelines during product development.

This brief outlines key elements of our approach to phase-appropriate quality standards.

A Systematic Approach Based on Science

Rigorously adhering to cGMP requirements across all clinical phases is essential for ensuring patient safety. This phase-appropriate approach to quality is not about taking shortcuts, but rather about assessing risks and implementing a systematic, science-based, and quality-driven strategy that integrates quality into every aspect of the product's process.

By adopting a phase-appropriate approach, we leverage our deep understanding of both the product and the process, to identify the increasing GMP requirements at each phase. This knowledge allows us to integrate critical late-phase requirements into early-phase processes, setting the stage for the product's long-term success.

Regardless of the phase, however, our process consistently demonstrates a state of control and ongoing improvement. This establishes a robust quality oversight that ensures the safety, efficacy, and compliance of our clients' products throughout the entire development lifecycle.

Early Introduction of Quality

Introducing a strong quality presence early in the product lifecycle ensures that fundamental safety and documentation standards are firmly established from the outset. By embedding quality into the manufacturing and testing of Phase 1 clinical trial materials, a solid foundation is laid for the entire lifecycle of the product, enabling continuous improvement. As the product advances through later phases, including tech transfer and commercial manufacturing, key quality elements—such as process performance, Corrective and Preventative Actions (CAPA) systems, and management review—are applied appropriately and proportionately to each stage. Furthermore, effective knowledge management and the identification of quality risks are crucial in supporting the quality system's goals of achieving product realization, maintaining a state of control, and facilitating ongoing improvement.

Phase-Specific Activities

The knowledge acquired during development phases deepens the understanding and control of the manufacturing process (**Figure 1**). The role of quality relates to conducting evaluations based on a thorough understanding of the process and product, while utilizing a structured risk framework to ensure quality is integrated seamlessly as the product advances from discovery to commercial manufacturing.

Key activities across Phases 1 – 3 are outlined below.

Phase 1

- Critical quality attributes identified with safety are clearly documented
- The process evolves as information is accumulated
- Controls are established for analytical methods

Phase 2

- Processes are characterized and Product Critical Quality Attributes and Critical Process Parameters are identified
- Analytical methods are qualified
- Materials acceptance criteria are defined
- Critical vendors are qualified

Phase 3

- Processes are validated and controlled
- Analytical methods are validated
- Materials have been fully qualified and tested upon receipt as appropriate

Conducting activities in Phase 1 that are aligned with Phase 2 and beyond will consume resources that will be wasted if Phase 1 is not successful. As such, use of resources earmarked for Phase 2 or 3 should be triggered once objectives of the previous phase are met, thus delivering cost effectiveness based on success.

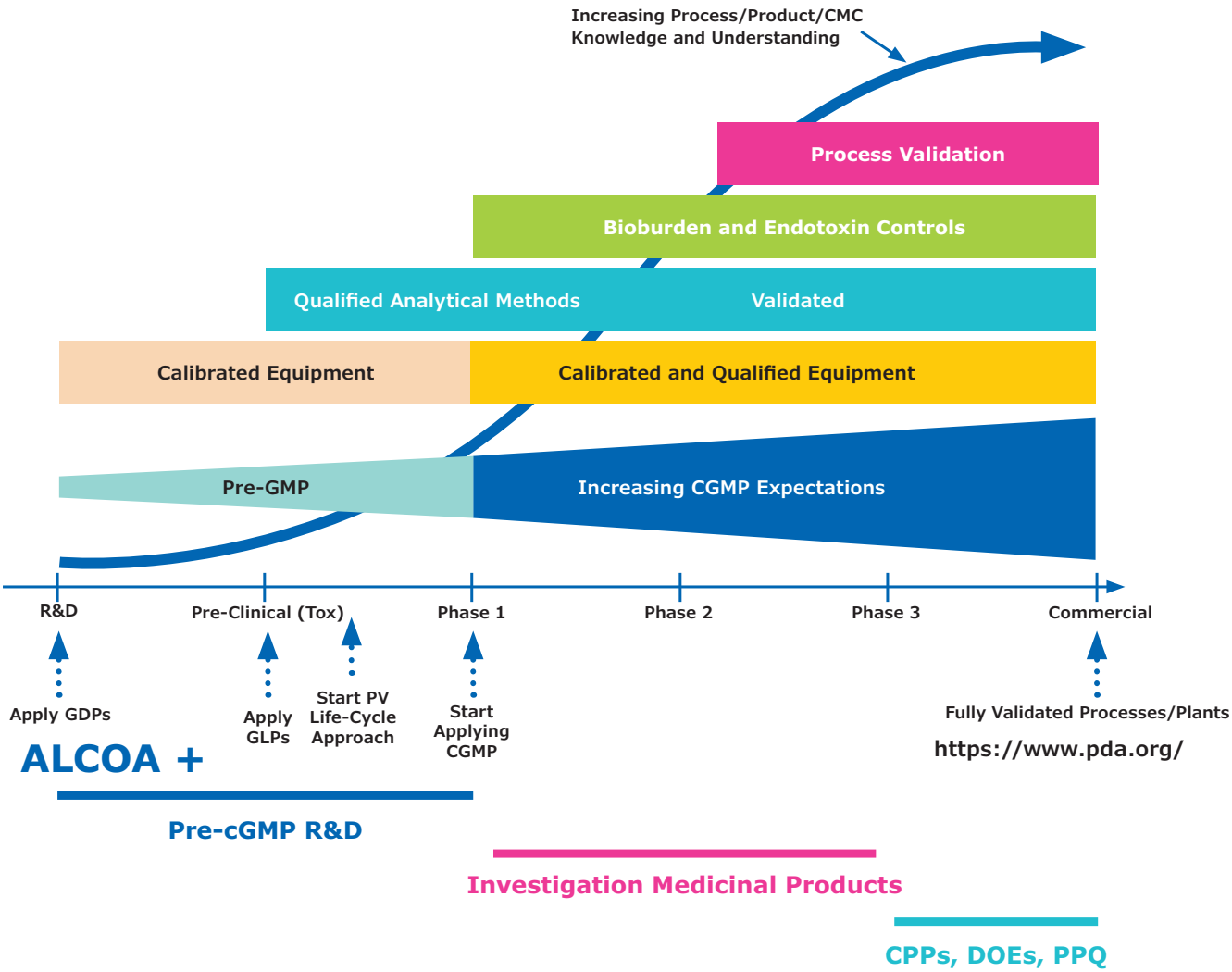

Figure 1. Alignment of activities based on the phase of development.

Table 1 offers examples of how phase-appropriate quality, in alignment with GMP requirements, can be integrated into a process.

One example relates to the evaluation of control equipment used in a Phase 1 process. By applying a phase-appropriate approach, it might be determined that instead of implementing a formal standard operating procedure to control equipment operation, the equipment user manual provides adequate instruction at this stage. For calibration and maintenance, the equipment's risk level can be assessed—whether low, medium, or high—and then a routine calibration schedule based on that risk assessment can be established.

Another example relates to raw materials. If the material can be sourced from an already qualified vendor, that is ideal. However, since this is an early-phase material, when selecting a raw material vendor, it is important to balance current material needs with the potential for future GMP support. While using a fully qualified vendor isn't necessary at this stage, it is advisable to choose a vendor who can achieve provisional qualification—essentially, a vendor who is capable of becoming qualified in the future.

Table 1. Examples of how phase-appropriate quality can be introduced.

Requirement	GMP	Phase Appropriate Quality
Instrument procedure to describe the purpose and scope of the instrument, the installation tests, periodic functional controls and supporting job aids	QA Approved Standard Operating Procedure	User manuals provide sufficient operating instruction. One overarching local equipment SOP is QA approved rather than individual SOPs for each instrument type
Calibrations and maintenance of all equipment to be carried out at periodic intervals to assure reliable and consistent operation of instruments	QA Approved Standard Operating Procedure, PM Schedule, Calibration Schedule, Approved vendor	Equipment can be calibrated on a routine basis based on risk assessment. All analytical instruments are use QC standards as outlined in local site SOP. Instruments identified as medium and high risk (per local procedure) are calibrated internally or externally by vendor.
Choice of the raw materials should ensure supplier is able to be qualified, has capacity to support large scale manufacturing, quality and purity are ensured	QA Approved specification, Approved supplier, part of SQM program	If available, vendor chosen to support future GMP work. Materials sourced from qualifiable vendors for later phase projects as applicable. Use test/bridging study done based on material criticality.

Successfully Navigating Complexity

Navigating the complexities of drug development requires meticulous planning and adherence to quality standards. Choosing the right partner for a phase-appropriate approach is crucial when strategically incorporating quality into development.

We prioritize alignment with our customers to determine what is appropriate for their molecule throughout its development journey. The process also includes:

- Employing a risk-based phased approach to ensure that development goals are met without compromising the program’s late-stage requirements
- Understanding the quick turnaround times needed to meet timelines
- Applying capabilities to support early- and late-phase development
- Harmonizing knowledge transfer to reduce time spent on managing tasks

Partnering with us as your CDMO and applying a phase-appropriate approach to quality ensures that your molecule is ready for scale-up activities, timelines remain on track, and the risk of process rework is minimized as the program advances through subsequent phases.

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