Process Validation
PDA Technical Report No. 60
as a practical guideline

By Thomas Peither

The Technical Report No. 60 “Process Validation: A Lifecycle Approach” was recently published by The Parenteral Drug Association (PDA).

Since 2008 a PDA task force has been working on this technical report which has long been anticipated. Despite the fact that the lifecycle approach to process validation has been favored by the FDA (U.S. Food and Drug Administration) and the EMA (European Medicines Agency) it has rarely been implemented in the industry.

The unsatisfactory situation was caused by a lack of consensus regarding implementation. This is about to change with the new guidance: 28 authors from different companies have contributed to this document. It was definitely worth the effort.

In the document all aspects for an up-to-date process validation strategy are being discussed.

Structure of the Technical Report

In general the technical report follows the U.S. FDA Guideline about Process Validation 2011.

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The document is not only based on the FDA und EMA guidelines. It also takes the ICH documents into consideration which are essential for the interpretation of the overall context. These correlations are mentioned in the first chapter (introduction).

The glossary offers different interpretations by the FDA and EMA as well as definitions of terms from other guidelines, e.g. ISPE. A short list of abbreviations completes this chapter.

The three stages
- Building and capturing process knowledge,
- Process qualification and
- Continued process verification

are required for the life cycle approach.

The document offers extensive and valuable information on all three stages.

Stage 1: Process design

It is listed which documents are to expect when a product enters the marketing phase coming from development. Considering common practice in the past and present the list serves as a valuable reference in the mutual understanding of product development and manufacturing. This shows the involvement of people with hands on experience in the compilation of this report.

Specific topics are
- Critical Quality Attributes
- Defining the Manufacturing Process
- Analytical Methods
- Risk Assessment and Critical Process Parameters
- Process Characterization
- Product Characterization
- Control Strategy
- Clinical Manufacturing Experience
- Process Design Report
- Process Validation Master Plan
- Manufacturing and Technology Considerations

All information are not only contemplated theoretically but are also illustrated with examples, figures and flow charts.
Stage 2: Process qualification

Process qualification is the topic of two parts which is in accordance to the FDA philosophy:

¬ Facility and equipment qualification  
¬ Process Performance Qualification (PPQ)

This chapter offers examples and valuable tips. It is highlighted that already qualified facilities, which have applied account risk assessments, are treated differently than new production sites.

A list of documents that can be expected when passing through step 2 might be used as a checklist for the expectations represented within the company. A simple comparison illustrates the company’s own position.

It has not been widely appreciated that different approaches can be followed for PPQ studies. The PDA Technical Report introduces many different concepts along with short descriptions and illustrates them with corresponding examples.

Of course key documents are covered, e.g.

¬ PPQ plans and  
¬ PPQ reports.

Stage 3: Continued process verification

The third stage Continued Process Verification (CPV) is illustrated with many figures. It is especially mentioned that the CPV already starts in stage 1 and has to be developed along with the control strategy.

This chapter focuses especially on

¬ documentation  
¬ existing products  
¬ CPV Monitoring Plan  
¬ data analysis and trending  
¬ control loops  
¬ data review and reporting

Overall this chapter offers detailed information that can rarely be found in such clarity.

Enabling systems and technologies

Of all systems enabling process validation risk management is the dominating one. Furthermore analytical instruments like PAT (Process Analytical Technology), technology transfer and last but not least knowledge management are discussed in a detailed manner. All these systems support and facilitate the implementation of a lifecycle approach.

Examples, appendices and references

Supported by examples (from the area of biotechnology (large molecules) and from parenteral manufacturing (small molecules)) it is demonstrated how process validation could practically be implemented.

In both examples all three stages are discussed and a clear picture of a life cycle approach is provided.

The appendices contain additional information useful for the different stages of process validation. The references are a source for further literature.

Summary

This Technical Report No. 60 ought to become a compulsory reading for all those involved in the implementation of new process validation approaches. The different stages and processes are illustrated with examples, figures and tables and numerous questions are answered.

In the near future implementation of a life cycle approach for process validation is indispensable. This technical report serves as an essential component of this process which can accelerate the development and implementation.

Source


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