

Introduction of major change for new premises, equipment and process of raw materials grinding in production of solid dosage forms

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Introduction

Premises and equipment must be located, designed, constructed and maintained to suit the operations to be carried out. Their layout and design must aim to minimize the risk of errors and permit effective cleaning and maintenance in order to avoid cross-contamination. During the construction of new premises and procurement of new equipment URS are prepared. New systems and equipment should pass through all stages of qualification including design qualification (DQ), installation qualification (IQ), operational qualification (OQ) and performance qualification (PQ) as appropriate. Changes such as introducing a new premises or equipment in production must go through the change management system.

Background

The continued suitable performance of equipment is important to ensure batch-to-batch consistency. Therefore, critical equipment should be qualified. The manufacturer should have a qualification policy for systems and equipment. The relevant documentation associated with qualification including standard SOPs, specifications and acceptance criteria and certificates should be maintained and the results of the qualification should be recorded and reflected in qualification reports.

Pharmaceutical quality system

The Pharmaceutical Quality System is based on International Standards Organisation (ISO) quality concepts and includes applicable Good Manufacturing Practice (GMP) regulations and complements ICH Q8 “Pharmaceutical Development” and ICH Q9 “Quality Risk Management”. The objective is to assure that manufacturing site continuously provides products with the highest standards for quality, safety and efficacy fit for their intended use.

Change management system

In order to evaluate, approve and implement changes regarding equipment and premises properly, a company should have an effective change management system to provide a high degree of assurance there are no unintended consequences of the changes. This change was evaluated by an expert team contributing the appropriate expertise from relevant areas to ensure that it is technically justified. After implementation, an evaluation of the change will be made to confirm the change objectives were achieved and that there was no deleterious impact on product quality (EU GMP Guideline Annex 15).

Critical utilities

Introducing new premises and equipment could affect the qualification status of the critical utilities such as PW, compressed air, dedusting etc. In this particular case the HVAC is subjected to PQ, new AHU unit was installed and

the system for distribution of purified water was extended to the new premises in production which are part of oral solid dosage forms where the new equipment for grinding of raw materials was installed.

Quality risk management

Quality risk management is a systematic process for the assessment, control and review of risks to the quality of the medicinal product across the product lifecycle (ICH guideline Q9). The scope and extent of equipment qualification and process validation was determined by using a documented risk assessment approach. QRM is applied to determine appropriate actions preceding the implementation of a change, e.g., additional testing, (re)qualification, (re)validation or communication with regulators. In this case it was determined that equipment qualification and process validation are necessary.

User requirements

During the construction of new premises and procurement of new equipment user requirement specifications are prepared in which users specify the requirements regarding the performance of the equipment/system, critical parameters of the equipment and operating rank, cleaning requirements, necessary documents from manufacturer/supplier and qualification requirements (EU GMP Guideline Annex 15). URS was prepared before procurement of the new equipment.

Premises and equipment qualification

The equipment was qualified prior to be brought into routine use to provide documented evidence that it is fit for its intended purpose (EU GMP Guideline Annex 15). The extent of the qualification was based on the criticality of the equipment. The premises is situated in an environment which presents minimal risk of causing contamination of materials or products.

Process validation

Process validation is the verification that a process meets the requirements imposed on its process results (EU GMP Guideline Annex 15). The cGMP regulations require that manufacturing processes be designed and controlled to assure that in-process materials and the finished product meet predetermined quality requirements and do so consistently and reliably (EU GMP Guideline Chapter 5). Process validation is required, in both general and specific terms, by the cGMP regulations. In this case, due to the

introduction of new equipment and process of raw materials process validation will be performed.

Cleaning validation

Cleaning validation is a procedure of establishing evidence that cleaning processes for manufacturing equipment prevents contamination and cross-contamination. A pharmaceutical manufacturing plant compliant with cGMP must have cleaning validation protocol and program in place to establish documented evidence that the cleaning processes will consistently ensure that the products manufactured will meet expectations for purity, safety and quality (ICH guideline Q10). Regarding this shared product equipment, cleaning validation will be performed according company's validation strategy with a worst case product approach.

Conclusion

In conclusion, in order for a new premises, equipment and process to be introduced in a production plant they must undergo a series of activities including qualification, process validation and cleaning validation to ensure the processes carried out are compliant with cGMP and regulatory requirements and to assure the quality of the products, as well as patient's safety. All these activities should be documented and evaluated within the Change control process as part of the Pharmaceutical Quality System.

References

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