Quality Control Analysis in Research Laboratories: Strategies to Fulfil GMP Requirements in a University Setting

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The Scientific and Technological Centers of the University of Barcelona (CCiTUB) is a research core facility with the main goal to support research and innovation in the areas of chemistry, materials sciences and biosciences. Since 2005, the Center operates under a quality management system certified according to the ISO 9001 standard.

The design, implementation, and maintenance of CCiTUB quality management system is under the responsibility of the Quality Research Unit of the University of Barcelona(QRU-UB).

Main demanded techniques for pharmaceutical products control

- Nuclear magnetic resonance spectroscopy (NMR)
- Test of X-Ray Diffraction
- Test of Differential Scanning Calorimetry (DSC)
- Particle Size Distribution
- Test of Specific Surface area (BET)
- FT-IR microspectroscopy and spectroscopy
- RAMAN spectroscopy
- Scanning Electron Microscopy (SEM-EDX)
- Inductively Coupled Plasma Optical Emission Spectroscopy (ICP-OES)
- Inductively Coupled Plasma Mass Spectrometry (ICP-MS)
- Gas chromatography with different detectors (CG)

How change control is addressed at the Core Facilities of UB?

Treatment of the changes depends on their nature and what they affect:

A) Situations that affect the integrity of the quality system are treated as section 6.3. Planning for changes of ISO 9001 like changes in key personnel, normative or legislative changes, reorganization of activities and spaces, integration of new technologies or techniques, modification of facilities, findings in audits and inspections, nonconformities and complaints, changes in the volume of work, and other strategic changes.

B)Situations that are relevant for service provision to ensure suitability to specified requirements are treated in section 8.5.6. Control of changes of ISO 9001, as follows:

- to equipment, depending on the degree of change, a basic check of the operation of the equipment may be sufficient, or a requalification of the installation or operation and provision may be necessary.
- to a method: modifications are recorded, reviewed and approved before their implementation, e.g. in an SOP or in the records of the particular service.
- to an SOP method agreed with companies with GMP requirements: a new edition of the SOP will be issued where the changes will be marked, reviewed and approved by all parties before their implementation.
- to the staff: it will be necessary to review and adapt their training and competence, if applicable.

ISO 9001- Core facilites of UB

- Scope: support to research
- Customers contract analytical services for quality control of active pharmaceutical ingredients (API) and excipients or for a validation of analytical methods (analysis control of finished product not authorized by Spanish regulations)
- CAPA system

GMP-Method development & Quality control of pharmaceutical sector

- Scope: Quality control or method validation
- Change control procedure
- Out of specifications (OOS) procedure

Quality Assurance Agreement content:

- Analysis will be performed under ISO9001 standard and ICH Q10 guide
- Acceptance of periodic customer audits
- Acces permision to the customer to the relevant documents and facilities to verify compliance
- Agree to undergo inspections of regulatory authorities
- Attach a technical annex that contents:
  - for development of a method: name of the technique,
  - for quality control: product, analyt to be determined, method of analysis and related SOP(if applicable)
- Responsabilities of each parties: method validation, OOS investigation.
- In the case of an OOS, it will be comunicated to CCiTUB, in order to perform the corresponding part of the investigation

ISO 9001 upgrade

- Quality Assurance Agreement
- SOP of analytical method signed by both parties with change control and OOS procedure
- SOP of OOS investigation
- Evaluation by the customer as GMP supplier (audit)

19 active quality agreements
43 SOPs approved by both parties
19 audits between 2019-2022

Standard Operation Procedure content:

- Instructions of the analytical procedure
- Identification of the equipment and materials that have an impact on the quality of the results
- Expression of results
- Change control section mentioning that any change in the method, the equipment or the software will be communicated prior to the customer to assess its impact on the result. If it is deemed necessary, it will be validated and lead to a new edition of the SOP.
- OOS section indicating that in the event that any result of the measurement is out of specification, the investigation corresponding to the part of the analysis carried out by the CCiTUB will be carried out, according to the procedure established in the unit. If the result is confirmed, customer will be informed and CCiTUB will follow its instructions.
- References to Pharmacopoeia or other official methods: customer will inform to CCiTUB if there is an update
- Approval by the Head of the Technical Unit and the Responsible of Quality, as well as by the personnel designated by the customer

Summary and conclusions:

- ✓ Quality control activities to assure the conformity of pharmaceutical products require the compliance of Good Manufacturing Practices (GMP).
- ✓ Pharmaceutical companies outsource some tests to university research core facilities, especially when they require the use of sophisticated analytical instrumentation and a high level of expertise. In these cases, the university laboratory is considered a critical supplier, and the compliance of GMP requirements has to be assured by the pharmaceutical company.
- ✓ The Scientific and Technological Centers of the University of Barcelona (CCiTUB) is a research core facility with a quality management system certified according to ISO 9001 standard, that fulfils most of the requirements of GMP but does not include specific requirements as out of specifications (OOS) management or change control.
- ✓ The Quality Research Unit has designed an upgrade of ISO 9001 to fulfil the GMP requirements required by the customer. In summary, is needed to establish a Quality Assurance Agreement, a SOP of analytical method signed by both parties which contains the control changes and OOS procedure agreed, a SOP of OOS investigation and an audit of the GMP customer to evaluate CCiTUB as a supplier of quality control of APIs and excipients and for provide service of techniques that are used in the development of pharmaceutical products.
- ✓ The CCiTUB has been successfully approved as a critical supplier for more than 20 pharmaceutical companies and has been inspected 3 times by FDA as part of pre-approval inspections of its customers.
- ✓ An added benefit is that the analytical results are obtained in a facility in absence of conflict of interests.