1 Purpose

The purpose of this guideline is to define the general requirements and to provide guidance for the calibration and maintenance of instruments, equipment, facilities, utilities/services and systems.

2 Scope and Applicability

This guideline applies to all instruments, equipment and systems, to be used for GMP activities in R&D and Operations, Manufacturing Functions. It is applicable to all Operational Manufacturing Functions, including API Manufacture, Formulated Product Manufacture, Manufacturing Service Systems, (e.g. water, steam, HVAC, gases,) Packaging activities, QC activities, Monitoring equipment, test equipment, storage and distribution.

For simplicity this guideline uses ótemô as a generic term including any of the foregoing or any sub-part.

The guideline is concerned with the calibration and maintenance requirements of GMP.

3 Definitions

3.2.1 Accuracy

The accuracy of a procedure expresses the closeness of agreement between the value which is accepted either as a conventional true value or an accepted reference value and the value found.

3.2.2 Adjustment (of a measuring instrument – ISO 17025)

Operation of bringing a measuring instrument into a state of performance suitable for its use.

3.2.3 Calibration (ISO 17025)

Set of operations that establish, under specified conditions, the relationship between values of quantities, indicated by a measuring system, or values represented by a material measure or a reference materials, and the corresponding values realized by standards.

3.2.4 Calibration Master Schedule

Information within a controlled document defining agreed calibration and maintenance requirements for GMP critical items. A schedule arising from the initial review of item criticality and kept current in the light of subsequent changes to equipment and facilities. Suitable forms of controlled documents include SOPs, equipment qualification documentation, Service level agreements or critical instrument lists ï if this information exists in such suitable controlled

be related to stated references, usually national or international standards, through an unbroken chain of comparisons all having stated uncertainties.

3.2.14 Unscheduled maintenance (corrective maintenance EN 13306)

Maintenance carried out after a fault recognition and intended to put an item into a state in which it can perform a required function.

4 Responsibilities

It is the responsibility of line management/process owner to:

- Ensure SOPs are in place to support the requirements of this guideline
- To ensure a Service Level Agreement/contract or shared SOP, defining the calibration and maintenance support provided, is in place with the Engineering function and/or other relevant calibration service providers
- Approve calibration master schedules which record commitments to the calibration and maintenance of critical items and manage changes throughout the item lifecycle
- Identify the critical parameters, the process variables, and to derive acceptable limits
- Approve calibration and maintenance results
- Investigate the cause and GMP implications of non-conforming conditions and deviations

It is the responsibility of Engineering, or the line, to:

- Ensure a calibration master schedule is developed in cooperation with relevant experts as defined in local procedures
- conduct calibration and maintenance according to local SOPs , and local work schedules
- To inform the equipment owner of any non-conforming conditions
- Approve the detailed calibration and maintenance procedures prepared for the items
- Approve calibration and maintenance work conducted by contractors to verify the acceptance criteria have been met
- retain calibration and maintenance records

It is the responsibility of Quality Assurance to:

- Approve SOPs for calibration and maintenance
- Approve calibration master schedules for GMP critical items/preventative maintenance to ensure limits are appropriately defined and regulatory requirements are met
- Peview, in collaboration with line/engineering, the implications of out of tolerance results following calibration and/or maintenance activities according to local procedures
- verify that the capabilities of external providers of calibration and maintenance are assured

Calibration and maintenance programs must be conducted according to a written procedure detailing the management of required activities. This will include scheduling of work by the responsible line, Engineering unit or relevant service providers to ensure calibration and maintenance is carried out according to the frequencies and scopes agreed for individual facilities/laboratories. The schedules maintained by the line or Engineering unit must be designed to enable identification of required frequency, due dates and status for calibration and maintenance activities.

Where appropriate the procedure may detail the process for pre-approval of any ‘ad-hoc’ extension to calibration life including the persons responsible (Operations or R&D Manufacturing, Quality Assurance as appropriate).

Calibration and maintenance must be conducted according to written instructions specific to the work being performed. Such written instructions will be in the form of controlled documents approved by Engineering or the line, and must contain an appropriate level of detail to prevent ambiguity.

Reference may be made to existing supplier/vendor/contractor documents as appropriate in order to avoid unnecessary duplication. Critical consumables must be specified where appropriate. Where considered necessary instructions should include requirements for a post-calibration operational check (e.g. when verification of the operation of a probe, when its re-fitting to equipment after calibration, is considered complex).

Instructions must be written in a manner that the work conducted avoids hazard to product or person. This may require inclusion of instructions for avoiding cross-contamination and also the specification of required lubricants and solvents.

Wherever possible calibration must be performed using reference standards traceable to International standards.

5.5 Non-conformance and corrective action

Written procedures will describe the procedure to be followed when a critical item is found not to conform to requirements during recalibration and scheduled maintenance. Procedures will define the persons responsible for investigating the failure (which will include Engineering, line management and Quality Assurance as appropriate).

Investigation must include an assessment of the impact of the non-conformance, identification of any root causes and their corrective actions, as well as repair or re-calibration of the item concerned. Procedures must include revision of schedules following an adverse review of the historic performance of the item.

Procedures must define the actions to be taken in the event of the agreed calibration ‘window’ being exceeded.

Where the non-conformance relates to the calibration of an item of test equipment the investigation must include a review of the implications of all calibrations performed.

