GOOD MANUFACTURING PRACTICE

UK CONTRACT QC LABORATORIES CHANGE REPORT - GUIDELINES FOR COMPLETION AND SUBMISSION

Background

Information relating to significant changes within a contract GMP QC laboratory forms part of the MHRA risk based inspection system and is required to be completed by each laboratory named on UK manufacturing and marketing authorisations and licenses.

A Change Report form should be filled in each time a significant change to laboratory activities has occurred, or is planned. Additionally, as part of the inspection planning process laboratories will be asked to confirm that all significant changes have been notified, or to confirm that no such changes have occurred.

Introduction

Ad Hoc Change Report

Change is regarded as either an indicator of an increase or decrease in risk or as a risk itself. For this reason the MHRA should be notified of significant changes to laboratory activities as they occur, or are planned. Inspectors will assess the significance of the reported changes and may amend the planned inspection frequency based on the risk presented by the changes. The risk rating will only be changed after a subsequent inspection.

Pre-Inspection Change Report

This provides the inspector with confirmation of actual changes that have occurred between inspections.
When a laboratory is notified of a forthcoming inspection, they will be asked to complete a Change Report. This is to ensure that the laboratory has the opportunity to confirm that all significant changes have been notified to the MHRA, or that no changes have occurred. Inspectors will assess the significance of the reported changes and may amend the frequency or duration of the planned inspection based on the risk presented by the changes. The risk rating will only be changed after a subsequent inspection.

Guidance on completion of the Change Report

The following information is provided for general guidance for completion of the Change Report. The MHRA are seeking to identify significant changes in a site that would potentially alter, or indicate a change to, the inherent risk to product quality and patient safety resulting from the laboratory activities.

Failure to submit a required Change Report may be assessed by the inspector as an increased risk factor and could affect the risk rating of the laboratory.

Although the following guidance provides an indication of the types of changes that would usually be considered as significant, laboratory management should consider the possible impact of other changes.

Name and Address

The laboratory name and address should be the name and address under which GMP work is undertaken – i.e. the name and address that appear on technical agreements and analytical reports or certificates of analysis. This will also be the name and address that will appear on

any GMP Certificate or related correspondence issued by the MHRA and must be the registered legal entity.

Types of GMP activities undertaken

This information concerns the types of testing undertaken, and the types of samples tested for pharmaceutical clients. Are only human medicines tested, or are both human and veterinary medicines tested?

For the purposes of GMP certification, the types of testing undertaken by the laboratory are considered as falling into one of the four following categories:

- Chemical/Physical testing
- Microbiology: sterility
- Microbiology: non-sterility (includes LAL endotoxin testing and environmental monitoring)
- Biological (tests involving animals or animal derived tissue systems)

If you perform GMP testing that does not seem to fall into any of these four categories please provide more details in the space provided. Any changes to the categories of testing should be notified.

The types of materials subject to chemical/physical, microbiological or biological testing in compliance with GMP will include, but are not necessarily be limited to, the following:

- Finished products (testing of finished products for batch certification by the Qualified Person)
- Investigative Medicinal Products (batch release testing of IMPs for use in human clinical trials)
- Stability testing (for marketed products or IMPs)
- Starting materials or excipients (testing of active or other product ingredients for compliance with raw material specifications)
- Process waters or process intermediates (most frequently testing of water samples)
- Packaging materials
- Samples from environmental monitoring (This will include both the performance of environmental monitoring in production areas, and/or the incubation/assessment of environmental monitoring samples provided by the manufacturing site)
- Identification of microbial isolates
- Other – please give details

Any changes to the types of materials tested, either additional sample types, or cessation of certain test types should be notified.

Contracting out of GMP functions or work

Certain aspects of the laboratory's activities might be contracted out; this could include stability sample storage, use of a consultant for GMP training, IT support etc. Additionally, some specific tests might be contracted out to a third party. Any contracting out of particular services or tests, or bringing them back in-house, should be notified.

The use of contract engineers to service particular pieces of equipment does not need to be identified.

Volume of GMP work undertaken or number of tests performed

Any significant increase, or decrease, in the volume of GMP testing or the number of tests undertaken should be notified.

Facilities and Equipment

The MHRA should be notified if the laboratory will be relocating to new premises, or if there are any changes to the facilities that constitute the contract GMP QC testing laboratory. This will include any additional facilities that are now being used for the conduct of GMP testing, or details of facilities that are no longer used for GMP work. We do not need to be informed of minor refurbishments or relocation of equipment.

Any significant changes to laboratory equipment, e.g. the implementation of a new Laboratory Information Management System (LIMS) should be notified. Acquisition of new or replacement instruments need not normally be notified unless this equipment will be used to conduct additional types of tests (see previous section on types of GMP work)

Personnel

Any significant changes in staff numbers or changes in key laboratory staff should be notified. Who constitute "key personnel" within a laboratory will vary with the size and organisation of the laboratory. For example, the loss and replacement of the only analytical chemist at a small test facility would be significant, but the replacement of one chemist in a team of ten probably would not. It is therefore a matter of judgement as to whether individual members of staff are "key personnel" or not, but in general terms high staff turnover within a year and staff changes within small laboratories are of greater significance.

Other Changes

The types of information that should be recorded here might include the following:

- Any changes in company ownership
- Any changes in the company name or trading style
- Changes to the management or organisation structure

Person Completing the Report

The name and position of the person submitting the change form should be identified. They should provide contact details as any subsequent queries will be addressed to this person.

Person Approving the Report

This person is expected to be the person responsible for the business, e.g. Chief Executive, Managing Director, Site Director or equivalent. If the report is approved by persons other than these, the justification for the suitability/authority to sign should be recorded in the box provided. This signatory is responsible for confirming the accuracy of the changes reported and confirming that no other relevant information has been withheld.

Completion of the form

It is intended that the time taken to complete and submit this change form should not exceed 1 Hour. If it is found to take longer that this, then you should record the actual time taken and provide any additional comments. This information will be used to refine the form or to make other procedural changes to the MHRA risk assessment process.

The completed form should be submitted electronically to the Inspector prior to an inspection or to the GLP mailbox at glp@mhra.gsi.gov.uk using one of the methods outlined on the Report. It would greatly assist administration if this notification could be sent with the subject line "**Changes at *laboratory name***".

MHRA MARCH 2011