GUIDANCE FOR FORMULATING RESPONSES TO GCP INSPECTION FINDINGS

Introduction

The GCP Inspectorate have assessed many responses to GCP inspection reports. Responses that require amendment/clarification lead to additional time spent by the inspector and the inspected organisation in order to close the inspection. This document aims to give assistance in how to respond to the GCP inspection report findings, increase awareness of the GCP Inspectors' expectations and aid formulation of an acceptable response.

Only findings in the inspection report need a response. Whether observations and recommendations within the report are acted upon is up to the organisation unless it is stated that a response is required.

Evaluation and Root Cause of the Finding

The finding should be reviewed to determine the issue that the inspector has raised. The inspector is likely to have cited evidence to support the finding and this has the potential for correction. The finding issue applies to (at least) the cited evidence. If an organisation does not understand the finding or needs further clarification, then the contact person for the organisation should contact the lead inspector.

Ensure that the finding is reviewed to determine the root cause of it. The root cause analysis should be comprehensive and broad. Inspectors are often presented with 'human error' or 'lack of training' as the root cause, but these are commonly not the overall root cause of an issue. Determine whether the finding is systematic (could other trials be affected) or isolated. What was the cause of the finding? Was it a genuine error or oversight? Was there was a lack of training (individual/all)? Was there no documented procedure? If there was a documented procedure was it not followed or was it inadequate?

Corrective Action

On reviewing the evidence, the organisation should decide whether the evidence supporting the issue can be corrected or whether the problem requires documentation only (e.g. in a file note, deviation record etc). Consideration should be given to the need to correct any clinical study report or publication associated with the trial(s) that are affected by the finding.

Preventative Action

This should include details of any planned amendments to referenced documented systems/procedures. It may also require training to be undertaken. Will there be methods to assess the effectiveness of your preventative action?

EXAMPLE 1

"Control of database access post database lock was inadequate. For study XXX the database was frozen FEB20. However, the Data Manager was able to (and did) delete a SAS dataset during the Inspection."

In this finding the SAS dataset was meant to be secure due to controls on the folder in which it resided. The SAS dataset was, for this organisation, the final database. The evidence is highlighted in green. The SAS dataset tested was not secure – this would need to be investigated and could be corrected. Other SAS datasets that were not looked at by the inspector may also have the same problem generating more corrective actions. The issue in the above finding is highlighted in red text. Why wasn't the database secure as the organisation intended? This needs to be investigated and action taken as a preventative measure.

EXAMPLE 2

"There was evidence that the regulatory green light (RGL) process for IMP was not robust. Whilst a checklist of essential documents was prepared and signed off by clinical operations and QA, this was not linked to the ability to order the IMP release from the contractor/sponsor to the investigator site, as this could be done independently by the Project Manager. For example, for study 1, the instruction to ship to investigator site was made on 06MAR19, but the checklist of essential documents was not approved by QA until the 07MAR19, the day the IMP was received at investigator site."

The issue is in red text and this would need to be addressed as a preventative measure. In this case, however, the evidence (in green text) cannot be corrected as it has already happened. The only thing that can be done is to document the problem (i.e. file note/deviation record).

Timescales

Timescales for corrective and preventative actions should be given. These should be as prompt as possible, but realistic and achievable.

Effectiveness Checks

There needs to be details of the process that would be used to determine that the implementation of preventative actions is effective.

Findings relating to other parties (e.g. CRO, Sponsor Investigator Sites)

Some of the findings in the report may be related to the systems/procedures of another party involved in the clinical trial. A response along the lines of "The point raised has been noted and has been brought to the attention of the XXXXX" is insufficient. The GCP inspector will expect the inspected organisation to supply responses for all findings (i.e. liaise with the other party).

Disputed Findings

If the organisation believes the inspection finding is wrong and disputes it, the response should clearly state why this is the case and provide evidence to support the decision.

Format of Response

The inspection report contains fields (with highlighted yellow text) for completing the response to the inspection.

Inspected Organisation's Response - 01			
Evaluation & Root Cause	[organisation to complete]		
Corrective Action(s)	[organisation to complete]	**Due Date**	DD/MM/YY
Preventative Action(s)	[organisation to complete]	**Due Date**	DD/MM/YY

ACCEPTABLE RESPONSE EXAMPLE

FINDING:

"The IMP recall procedure has not been tested."

Inspected Organisation's Response - 01			
Evaluation & Root Cause	*XXXX acknowledge that the IMP recall procedure has not been tested. The IMP recall procedure is described in SOP10 "Complaints and Product Recall", however, on review this currently has no requirement for testing.*		
Corrective Action(s)	*A mock recall will be carried out following part 1 & 2 of preventative action, according to the revised SOP10*	**Due Date**	31/03/22
Preventative Action(s)	*SOP10 will be updated by the SOP Review Team to contain a requirement for regular testing of the IMP recall*	**Due Date**	31/12/21
	Training of relevant personnel in SOP10(and documentation of this) will be provided by the "job title"		31/01/22
	Compliance with the regular testing requirements of SOP10 will determined by commencing audits by the internal QA group		31/03/22

Inspector Review

The GCP Inspector will review responses and provide feedback to the organisation regarding any finding responses that are not adequate by completing the MHRA response field in the inspection report. Remember, however, that the Inspector is NOT a consultant and will not have time to provide detailed review of SOPS etc. so do not expect this.

The organisation is given ONE opportunity to provide clarification of responses and additional information by completing a further response in the inspection report. Inadequate responses will be documented in the report and in the inspection closing documentation and should these responses be to major findings, this may cause early re-inspection. If there are inadequate responses to critical findings, these will be dealt with by the Inspection Action Group.

Next Inspection

The organisation will be assessed at next inspection in terms of whether the corrective and preventative actions have been implemented and maintained – has the organisation done what they said they would? If previous major findings have not been addressed, then a critical finding may be given.