

GUIDANCE FOR FORMULATING RESPONSES TO GCP INSPECTION FINDINGS

Introduction

GCP Inspectorate have assessed many responses to GCP inspection reports and 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 provide assistance in how to formulate a response.

Assessment of the finding and Corrective Action

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

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.

On reviewing the evidence, the organisation should decide whether the evidence supporting the issue can actually be corrected or whether the problem requires documentation only (e.g. in a file note, deviation record etc).

EXAMPLE 1

“Control of database access post database lock was inadequate. For study XXX the database was frozen FEB06. 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 06MAR06,** but the checklist of essential documents was not approved by QA until the 07MAR06, 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).

Analysis of the Finding

Ensure that the finding is reviewed to determine the root cause of it. 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 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?

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?

Timescales

Timescales for corrective and preventative actions should be given.

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 not sufficient. 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.

ACCEPTABLE RESPONSE EXAMPLE

FINDING:

“The IMP recall procedure has not been tested.”

RESPONSE:

“XXXX acknowledge that the IMP recall procedure has not been tested. The IMP recall procedure described in SOPXXXX “Complaints and Product Recall” is currently under review and will be updated. Following this a mock recall will be carried out to test this procedure. Action will be completed by DD/MM/YY.”

AN IMPROVED RESPONSE:

XXXX acknowledge that the IMP recall procedure has not been tested. The IMP recall procedure is described in SOPXXXX “Complaints and Product Recall”, however, on review this currently has no requirement for testing.

Corrective Action

A mock recall will be carried out following part 1 & 2 of preventative action, according to the revised SOPXXX. This will be undertaken by DD/MM/YY.

Preventative Action

- 1. SOPXXX will be updated by the SOP Review Team by DD/MM/YY to contain a requirement for regular testing of the IMP recall.*
- 2. Training of relevant personnel in SOPXXXX (and documentation of this) will be provided by the “job title” and completed by DD/MM/YY.*
- 3. Compliance with the regular testing requirements of SOPXXX will determined by audit by the internal QA group. The first audit is planned to take place by DD/MM/YY.*

Inspector Review

The GCP Inspector will review responses and provide feedback to the organisation regarding any finding responses that are not adequate. 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. Inadequate responses will be documented in the post-inspection summary 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 – has the organisation done what they said they would? If previous major findings have not been addressed then a critical finding may be given.