Qualité

Availability of New Study Templates

In keeping with the PCR SOP changes, several study document templates have been developed to aid investigator-initiated studies with creating essential documents. Concurrently, a significant number of existing study document templates has also been revised.

The new study document templates are listed below.

New Template Available	Purpose of Template
Corrective Action & Preventive Action Plan (CAPA) Template	The CAPA template may be used to detail the corrective actions and preventive actions taken to address study findings detailed in study review reports. The study team should work together to complete the CAPA, which should be submitted to the study reviewer by the stipulated deadline.
Note to File Template	This template may be used to document explanations or supplement inadequate information in the study documentation. The completed note to file should be retained in the study file.
Template for Documentation of Adverse Event in Medical Records	This template format may be directly entered into the subject medical records by the investigator performing the documentation. The template serves as a guide on the necessary fields and details that should be documented pertaining to the adverse event(s) experienced by the subject.
Adverse Event / Serious Adverse Event Tracking Log	This template helps investigators track the adverse events (AEs) or serious adverse events (SAEs) that occur during the study, particularly for the purpose of determining whether these event(s) qualify for expedited reporting to the sponsor and / or regulatory authorities.
Investigational Product Dispensing & Accountability Log (Multiple Subjects)	This template is used to document the receipt, supply and return of the investigational product(s) used in a clinical trial. Two different formats of the same template are available to cater to different study requirements.
Investigational Product Dispensing & Accountability Log (Per Subject)	
Subject Identification Log	This template is used to document the personal particulars of all subjects participating in the study.
Temperature Log	This template is used to document the temperature monitoring records of the premises in which the investigational product is stored.
Study Initiation Meeting Attendance Log	This log serves as a record of the study staff who attended the study initiation meeting. This log also constitutes documentation of study-related training records.

Principal investigators and all research staff are advised to read the above-mentioned PCR SOPs in their entirety to obtain a better understanding of the SOP changes. The new and revised study document templates are also available for downloading from the NHG research website. Researchers may adapt and customise the various templates to suit the individual study requirements.

To access the full listing of PCR SOPs and study document templates, please refer to the following link: http://www.research.nhg.com.sg/wps/wcm/connect/romp/nhgromp/resources/research+sops

References

4. NHG Proper Conduct of Research Standard Operating Procedures (PCR SOP) 501-A02 – Responsibilities of the Research Team
5. NHG Proper Conduct of Research Standard Operating Procedures (PCR SOP) 501-C01 – Informed Consent Form and Process
6. NHG Proper Conduct of Research Standard Operating Procedures (PCR SOP) 501-B05 – Documentation

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GCP Frequently Asked Questions – How to Write a CAPA

In our last issue, we introduced readers to the scope and directives of the Research Quality Management unit under the Office of Human Research Protection Program (OHRPP). The attentive reader may recall one of the core functions of RQM introduced – that is, the conduct of study reviews on research studies that are currently ongoing in NHG and partner institutions. Principal investigators whose research studies have undergone study reviews would be issued a study review report by RQM. To address the findings in the study review report, the principal investigator would be tasked to submit a corrective action and preventive action plan (CAPA) by the stipulated deadline.

What is a CAPA?

Based on the ISO 9000 definition, corrective actions are steps taken to eliminate the causes of existing non-conformities in order to prevent recurrence of the deviation. Consequently, preventive actions are steps taken to prevent the occurrence of non-conformities or undesirable situations that do not yet exist. Occurrence is prevented by eliminating the potential causes of such situations. Originally a Good Manufacturing Practice (GMP) concept, the use of CAPAs has been adopted in the clinical research industry as a compliance and quality improvement strategy.

Creating a CAPA

As the CAPA can be an effective way to address non-compliances within a research study, it is typically requested for by the relevant authorities following an audit and / or inspection visit. In creating a CAPA, the following important steps should be considered:

1. **Determine the problem**
   Review the finding raised by the auditor / inspector, as well as the evidence cited to substantiate the finding, to pinpoint the nature of the non-compliance.

2. **Determine the corrective actions to be taken**
   Identify the action(s) that can be taken to rectify the problem, as well as the person(s) responsible for implementing the corrective actions proposed. In instances where the non-compliance has already occurred and cannot be corrected or reversed, the only action that can be taken is to document the problem by means of a file note or protocol deviation report.

3. **Conduct a root cause analysis**
   Determine the root cause of the finding, particularly to establish if it is a systematic or isolated problem. A systematic problem could mean that other studies may also be affected. Examples of systematic problems include lack of training, or inadequate standard operating procedures (SOPs).

4. **Determine the preventive measures that may be taken**
   Propose solutions to address the root cause of the problems, taking into account existing regulations, guidelines and resources that may be allocated for the study. Again, an accountable person should be appointed to oversee the implementation process.

5. **Set realistic deadlines**
   Consider the manpower and resources that can be assigned to implement the corrective and preventive measures proposed above. A reasonable time frame for achieving these measures should be proposed and documented on the CAPA.

A Collective Effort by the Study Team

Completion of the CAPA should never be a lone effort. Conversely, it is recommended that the principal investigator and his / her study team collaborate closely to address study findings following a study review visit. In instances where the protocol non-compliances are significant, the study team may approach the auditor(s) / inspector(s) for advice or additional guidance on proposed actions that can sufficiently address the problem.

Resources for More Information

A CAPA template has been developed by NHG's Research Quality Management (RQM) unit for investigators' use and reference. The CAPA template is available for download from the NHG research website, at: http://www.research.nhg.com.sg/wps/wcm/connect/romp/nhgromp/resources/research+sops

References

1. Resources, NHG Research Website. Accessed on 26 Jun 2013. http://www.research.nhg.com.sg/wps/wcm/connect/romp/nhgromp/resources/research+sops
2. Here are quick tips on corrective action plans. (2011).Clinical Trials Administrator. Retrieved from http://search.proquest.com/docview/908312855?accountid=12763; http://sirious.library.unsw.edu.au:9003/sfx_local?url_ver=Z39.88-2004&rft_val_fmt=info:ofi/fmt:kev:mtx:journal&genre=article&sid=ProQ:ProQ%3Ahealthcompleteshell&atitle=Here+are+quick+tips+on+corrective+action+plans&title=Clinical+Trials+Administrator&issn=15448460&date=2011-12-018&volume=&issue=&spage=&au=&isbn=&jtitle=Clinical+Trials+Administrator&btitle=
3. Guidance for Formulating Responses to GCP Inspection Findings. (06 Jun 2007). Medicines and Healthcare Products Regulatory Agency (MHRA), UK. Website accessed on 26 Jun 2013. http://www.mhra.gov.uk/home/groups/is-insp/documents/websiteresources/con2031399.pdf
4. Writing an Effective Corrective Action Plan. Northwestern University Institutional Review Board. Website accessed on 26 Jun 2013. http://irb.northwestern.edu/policies/compliance/corrective-action-plan
5. ISO 9000, 9001 and 9004 Plain English Definitions. Praxiom Research Group Limited. Website accessed on 26 Jun 2013. http://www.praxiom.com/iso-definition.htm#Corrective action

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Non-Compliance Report: Major Deviations in Study Conduct from the DSRB-Approved Protocol

Background

The National Healthcare Group (NHG) Research Quality Management (RQM) team conducts regular and random study reviews on ongoing clinical research studies carried out in NHG and its partner institutions, under the oversight of the NHG Domain Specific Review Board (DSRB).

The purpose of these study reviews is to increase awareness among investigators and their study staff on proper research practices and documentation techniques; and ultimately, to safeguard the rights, safety and well-being of trial subjects.

Study Review Findings

A recent study review visit by the RQM team revealed that a study team had conducted study procedures differently from how they had been described in the DSRB-approved protocol.

Pertinent findings identified had included:

The number of times that blood had to be taken from each subject had not been clearly stated in the informed consent form.

The quantity of blood collected from each subject was different from that specified in the approved protocol, constituting a protocol deviation.

Useful Tips & Recommendations

Here are some practical tips that investigators can take note of to avoid similar lapses in their research studies:

1. **Start with a well-written protocol:**
   Before initiating a trial, the Principal Investigator (PI) should ensure that the protocol clearly describes the procedures to be performed on subjects, and that the procedures described are practically feasible to carry out. Information included in the informed consent form should correspond with that in the study protocol and DSRB application form.

2. **Have a process in place for identifying, tracking, reporting and correcting protocol deviations/violations:**
   It is the PI's responsibility to document and explain any deviation(s) from the DSRB-approved protocol. Processes should also be established to evaluate and determine if any corrective action is required to rectify the deviation, or whether a protocol amendment is needed. Protocol non-compliances should be reported by completing the ROAM Online DSRB Non-Compliance / Protocol Deviation Form, which should be submitted within a week of first knowledge of the deviation. To reduce the incidence of study deviations, it is recommended that routine meetings be held with study staff to discuss study-related issues, review trial progress and update study team members on any changes to the protocol study procedures.

3. **Ensure that research staff are appropriately trained and qualified:**
   It is the PI's responsibility to ensure that all study team members involved in the research are appropriately qualified and trained on the study protocol. All investigators and study staff are also required to meet the minimum training requirements set by DSRB [e.g. Good Clinical Practice (GCP) training, Collaborative Institutional Training Initiative (CITI) programme].

4. **Acquaint oneself with the guidelines and regulations governing the conduct of research:**
   Besides having good knowledge of the protocol details, PIs and study team members are strongly encouraged to familiarise themselves with institutional guidelines, standard operating procedures and regulatory requirements governing research. It is the PI's responsibility to ensure that research is conducted in compliance with all applicable guidelines and regulations.

5. **Keep the DSRB informed of any study amendments:**
   Only the approved protocol and research documents should be implemented. Where the need for a protocol amendment arises, the PI is responsible for informing the DSRB via the Study Amendment Cover Note. The amended documents should also be submitted for approval. The PI may only implement the protocol amendments after written approval from DSRB has been obtained.

References

1. Singapore Guideline for Good Clinical Practice (SG GCP)
2. NHG Proper Conduct of Research Standard Operating Procedures (PCR SOP) 501-A02 – Responsibilities of the Research Team
3. NHG Proper Conduct of Research Standard Operating Procedures (PCR SOP) 501-A03 – Training and Education
4. NHG Proper Conduct of Research Standard Operating Procedures (PCR SOP) 501-B04 – Interactions with Domain Specific Review Board

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