

## Guideline for Developing a Manual of Operations (MOO)- RPG-05

### Guideline

#### Purpose

The purpose of this Guideline is to provide advice to investigators and study staff regarding development of a study specific Manual of Operations.

#### Definitions

A study Manual of Operations (MOO) is a document that outlines the details of how to operationalize the scientific protocol and conduct all study-specific procedures. It is an essential tool that ensures accuracy and consistency in study implementation across different study sites and research staff over time. The MOO is also an important tool for the initial training of study staff and an invaluable reference when staff turnover occurs. All final approved versions of the study MOO should be dated in the footer and maintained in electronic format.

### Procedure

A study MOO is highly recommended for all clinical research investigations. A study MOO must be developed by CRC staff working in collaboration with the study investigators for all studies where the CRC is funded to serve as the data coordinating center.

#### Contents

The content of the MOO may vary significantly depending upon the type of research study, the scope of the study and the number of sites involved in the study. At a minimum, the following areas should be included or described in the MOO, as appropriate:

- **Study Overview:** This section should include a brief overview of the study and the study aims and objectives. An abstract prepared for the grant or proposal, might serve as the study overview.

- **Study Organization and Staff Roles and Responsibilities:** Contact information for all study staff including study coordinators and project management should be included in this section. In addition, staff members' roles and responsibilities in the study should be described. For multi-site studies, the governing structure and role of committees and subcommittees should be detailed.
- **Subject Recruitment:** This section should explain in detail how subjects are to be recruited for the study, including how subjects will be informed about the study, who will approach subjects for recruitment, where the study population will be found, and type of pre-screening activities that will take place. This section should include details on how and when informed consent will be obtained and the URL link to the CHB Informed Consent Library (<http://chbcfapps.tch.harvard.edu/cfapps/cci/ICLIBUserside/index.cfm>). For additional information, refer to CRC Guideline for Recruitment, RPG-09.
- **Screening:** The instructions in this section should further define the study population, specify the study Inclusion and Exclusion Criteria, and describe the study screening activities. Details should be provided to illustrate how and when each eligibility criterion should be evaluated prior to enrollment.
- **Subject Enrollment:** This section should include the step-by-step instructions that should be followed to enroll a subject into the study once s/he meets all eligibility criteria.
- **Randomization Procedures (for randomized trials only):** This section of the MOO should explain the randomization procedure for the study. If the study is blinded, the MOO should include the procedures required to maintain blinding and steps that must be followed in the event of intentional or inadvertent unblinding. For more specific information, refer to CRC Guideline for Developing Randomization Procedures, RPG-03.
- **Study Visit Schedule:** This section should specify the number and schedule of study visits with target dates for each visit relative to the enrollment date along with acceptable windows of time within which study visits should occur. This section should also include the study procedures/measurements that will be completed at each specific visit, and procedures to follow if a study visit is missed.
- **Study Measurements:** Detailed procedures should be provided to study staff to specify how to conduct study measurements. For example, these may include systematic procedures for measuring height, weight, head circumference, or blood pressure and the instruments that should be used. If special education, licensure, or protocol specific training is required to complete the measure, it should be described in this section.
- **Study Medication/Pharmacy Procedures (for drug treatment protocols):** This section should include details as to how the study medication is stored, how the drug is dispensed to the subject, and the role of the Research Pharmacy. For specific information, refer to CRC Guideline for Developing Pharmacy Procedures for Clinical Trials, RPG-10.

- **Case Report Forms (CRF):** All data collection tools should be included in the Study MOO. Although there may be numerous versions and different drafts of the study CRFs over time, only the currently approved versions of the master CRFs should be included in the MOO. All outdated versions of the CRFs should be archived in a restricted access location. Master CRFs should only be accessible to study staff as PDF documents to prevent inadvertent or intentional alteration of the data collection instruments.
- **Question by Question (QxQ) Instructions:** A question-by-question instruction guide (QxQ) should be written for each CRF. Each QxQ should include an introduction of general instructions regarding what the specific CRF is designed for; at which study visits it should be completed; and who should complete it. The instruction guide should also specify the primary source for the data recorded on the form, i.e. hematology lab report, discharge summary, operative notes, etc For more specific information, refer to CRC Guideline for Developing Case Report Forms, RPG-02.
- **Adverse Event Reporting:** The instructions provided in this section should describe the process of reporting adverse events. For more specific information, refer to CRC Guideline for Developing Adverse Event Reporting Procedures, RPG-01 and the CCI.
- **Sample Collection and Processing:** This section should include comprehensive instructions regarding how biologic samples are collected and processed, including shipping instructions where appropriate. It should include step-by-step instructions regarding all aspects of how the sample is to be collected, the supplies needed, how the sample is to be labeled and how the sample is to be processed to prepare for the analyses. If applicable, the instructions should also describe how the sample should be packaged and shipped and procedures for maintaining a shipping log and specimen receipt log. This section should be as detailed as possible and include timing issues, temperature specifications, a list of specific supplies needed, in addition to any other information that might be relevant to reduce the chance of error in processing. For specific information, refer to CRC Guidelines for Developing Laboratory Procedures for Clinical Trials, RPG-26.
- **Data Management:** The Data Management procedures should describe how data is to be collected and managed. This includes how study identifiers are assigned; where the ID assignment logs are located; the structure of the subject ID numbers; the modes of data collection; how data forms are completed, reviewed and filed or stored; and information on how missing data or invalid data on case report forms are addressed and resolved. In addition, contact information should be provided, when applicable, regarding where data should be sent.
- **Quality Assurance Procedures:** This section should explain how quality assurance is maintained among study staff throughout the duration of the study. This customarily includes a description of study training and certification procedures, communication procedures and maintenance of a communication log, reproducibility studies, approaches to ensure the integrity of the data collected such as valid value and range checks during data entry and data security, regulatory and data verification

audits, and on-going staff performance monitoring including site visits for multi-site studies.

### **Development**

The development of the study MOO should be a collaborative effort between the Principal Investigator of the study and the relevant study staff. When the CRC is funded to serve as the data coordinating center, CRC staff should also collaborate in the development of the MOO. The MOO should be developed after reviewing the study protocol and outlining all the information that is needed to implement the study protocol. Details of these procedures are then developed by various staff with the appropriate expertise, and reviewed and approved by the study Principal Investigator.

The contents of the MOO might be maintained as electronic documents or as hard copy. Customarily, the MOO is divided into functional sub-sections that contain specific information relevant to the various procedures and measurements. The first page of the MOO should include a Table of Contents detailing the sections and associated page number within the master document. Each section should be page numbered independently to facilitate future changes. A footer should be included on each page and contain the title of the section, the version date, and the page number.

### **Implementation**

Once completed, the MOO should be made available to investigators and study staff working on the research project. When the CRC is funded to serve as the data coordinating center, the MOO will be maintained by the CRC Project Director assigned to the study. Other research staff working on the project will have access to relevant sections of the MOO based upon what role they have in conducting the research. A list of MOO recipients should be maintained by the study coordinator.

Changes to the MOO must be reviewed and approved by the PI and made to the master electronic document. All approved versions must be dated and maintained in the study archive. All hard copy Manuals in distribution must be updated by the study coordinator. All outdated hard copy versions of the MOO should be kept in the study archive by key study staff as a reference.

# Related Content

## Table of Contents – General Guidelines

### I. Study Overview

- A. Study Aims and Objectives – Basis for study outcomes.
- B. Background and Rationale – Describe study rationale; detail previous findings related to illness/disease; define relative terms, acronyms, and abbreviations related to illness/disease.

### II. Study Organization

- A. Participating Centers – Coordinating and study center(s), laboratories, etc.
- B. Administration and Governance – Committees, funding agencies, and data and safety monitoring boards.
- C. Roles and Responsibilities – Responsibilities of investigators and study staff defined.

### III. Recruitment

- A. Inclusion and Exclusion Criteria – Eligibility criteria defined.
- B. Recruitment Approaches – Strategies for approaching and recruiting potential subjects.
- C. Informed Consent – Outline procedures for obtaining informed consent.

### IV. Study Visits

- A. Study Visit Schedule – Visit schedule and activities entailed in each visit, baseline vs. follow-up visits, and visit windows.
- B. Treatment protocol – describe the intervention or treatment to be given where applicable.
- C. Randomization Procedures – Procedures to randomize subjects or groups to different study treatments and approaches for blinding where applicable.
- D. Study Close-out – Explanation of end-of-study activities, post-study follow-up.

### V. Study Measurements and Data Collection Procedures

- A. Medical record abstracts.
- B. Administering surveys/questionnaires.
- C. Procedures and examinations.
- D. Specimens and sample collection procedures.

### VI. Adverse Event Reporting

- A. Definitions, documentation.
- B. Reporting and follow-up procedures.

### VII. Pharmacy and Drug Handling

- A. Research pharmacy procedures.
- B. Drug handling and administration procedures.
- C. Compliance with Hospital Policy – Research using drug/therapeutic agent implemented in a standardized way, in accordance with hospital policy.

### VIII. Study Forms and Instructions for Form Completion

- A. Study forms.
- B. Question x Question instructions for completing the study forms.

### IX. Data Management Procedures

- A. Overview of data flow.
- B. Data entry procedures.
- C. Form completion tracking.
- D. Data entry error resolution and editing procedures.

### X. Quality Control

- A. Training and Certification– Teaching standardized methods of data collection.
- B. Staff Performance Monitoring/Site Visits – Oversight and periodic reviews.
- C. Equipment calibration.
- D. Laboratory quality control.
- E. Communication procedures.

XI. Appendices

- A. Recruitments materials.
- B. Letters to study subjects, primary care providers, etc.

## **Example: Study Specific Table of Contents**

- I. STUDY OVERVIEW
  - A. Specific Aims and Hypotheses
  - B. Project Summary
  - C. Time Line
  - D. Coordinating Site Contact Information
  - E. Study Collaborators
  - F. Roles and Responsibilities
  
- II. STUDY VISIT SCHEDULE AND FOLLOW-UP PROCEDURES
  - A. Screening Visit
  - B. Pouchoscopy Visit
  - C. Study Drug Initiation and Pharmacokinetics
  - D. Telephone Contact: Study Drug At One Week
  - E. Study Midpoint (Two Weeks) Visit
  - F. Telephone Contact: Study Drug at Three Weeks
  - G. Exit Pharmacokinetics Visit (Four Weeks)
  - H. Exit Pouchoscopy Visit (Four Weeks)
  - I. Telephone Contact: Open-Label at Two Weeks
  - J. Open Label Conclusion Visit

## **STUDY MEASUREMENTS AND DATA MANAGEMENT**

- I. Introduction
- II. Data Collection
- III. Data Management
- IV. Study Monitoring
- V. Adverse Events Monitoring

## **SECTION D: RANDOMIZATION PROCEDURE**

### **SECTION E: FORMS AND QUESTION – BY – QUESTION SPECIFICATIONS**

- I. General Instructions
- II. Telephone Pre-Screening - Form 1
- III. Screening Visit - Form 2
- IV. Labs – Form 3
- V. Pouchitis Disease Activity Index (Pdai) – Symptom – Form 4
- VI. Rating Form Of IBD Patient Concerns (Rfipc) - Form 5
- VII. Pouchitis Disease Activity Index (Pdai) Pathology/History – Form 6
- VIII. Inclusion Exclusion Criteria – Form 7
- IX. Pharmacokinetics – Form 8
- X. Telephone Follow-Up – Form 9
- XI. Visit Follow-Up - Form 10
- XII. Midpoint Visit - Labs – Form 11
- XIII. Inclusion Exclusion Criteria – Open Label – Form 7a
- XIV. Telephone Follow-Up Open Label Period – Form 12
- XV. Open Label Physical Exam - Form 13
- XVI. Adverse Events - Form 14
- XVII. Serious Adverse Events - Form 15
- XVIII. Withdrawal Form - Form 16

## **SECTION F: STUDY DRUG CHEMISTRY, MANUFACTURING AND CONTROL INFORMATION**

# References

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<b>Approved</b>	<table style="width: 100%; border: none;"> <tr> <td style="width: 50%; border: none; vertical-align: top;"> <p><b><u>SIGNATURE ON FILE</u></b>                      Stavroula Osganian, MD, ScD, MPH                      Co-Chief, Clinical Research Center</p> </td> <td style="width: 50%; border: none; vertical-align: top;"> <p><b><u>SIGNATURE ON FILE</u></b>                      Ellis Neufeld, MD, PhD                      Associate Chief, Division of                      Hematology/Oncology</p> </td> </tr> </table>			<p><b><u>SIGNATURE ON FILE</u></b>                      Stavroula Osganian, MD, ScD, MPH                      Co-Chief, Clinical Research Center</p>	<p><b><u>SIGNATURE ON FILE</u></b>                      Ellis Neufeld, MD, PhD                      Associate Chief, Division of                      Hematology/Oncology</p>
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**Disclaimer:** Should Hospital and CRC policies conflict, Hospital policy will supersede CRC policy in all cases.