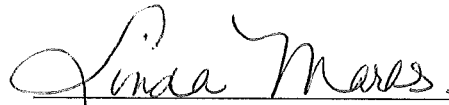


_____ Sutter Health



Approver: SIMR Director – Linda Marks

11-1-2010

Revised Date

SUTTER INSTITUTE FOR MEDICAL
RESEARCH
STANDARD OPERATING PROCEDURES

INTRODUCTION

Following are the standard operating procedures (SOP) that SIMR follows to conduct clinical studies. This is a living document and is updated as procedures are added and revised.

SOPs	Most recent revision
CO-SS.01 to CO-SS.12	November 1, 2010
CO-SM.01 to CO-SM.08	November 1, 2010
QA-PO.01 to QA-PO.06	November 1, 2010
CO-FM.01 to CO-FM.05	November 1, 2010

**SUTTER INSTITUTE FOR MEDICAL RESEARCH (SIMR)
STANDARD OPERATING PROCEDURES (SOP)**

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INTRODUCTION

All research involving human subjects conducted at Sutter Health Sacramento Sierra Region (SHSSR) facilities should be reviewed and approved by the Sutter Institute for Medical Research (SIMR) prior to its implementation. The process includes administrative, clinical, legal and financial review and approval before the research can be initiated. Currently, these SOPs apply to research that is managed through SIMR.

TERMINOLOGY

Following is a list of acronyms that are repeatedly used in these SOPs,

- Adverse event (AE)
- Centralized Institutional Review Committee (IRC)
- Clinical Research Organization (CRO)
- Clinical research associate (CRA)
- Clinical research coordinator (CRC)
- Dietician
- Good clinical practice (GCP)
- Human subjects compliance specialist (HSCS)
- Principal investigator (PI)
- Informed consent form (ICF)
- Investigational drug service (IDS) pharmacist
- Laboratory technician
- Office of research administration (ORA)
- Regulatory compliance technician
- Serious adverse event (SAE)
- Sutter Institute for Medical Research (SIMR)
- Sub-investigator (Sub-I)
- Sutter Health Central Institutional Review Committee (SHCIRC)

CLINICAL OPERATIONS

PURPOSE

This policy establishes the study start-up, study management, and study closure procedures required to ensure proper placement and clinical operations management within Sutter Health.

CO-SS STUDY STARTUP

Study startup may include visits by the sponsor for screening and site selection (pre-start-up), preliminary startup, and study initiation following study approval (prior to enrollment of the first subject).

APPLICABLE REGULATIONS AND GUIDELINES

The following regulations and SOPS apply to all procedures regarding study startup.

21 CFR 312.32	IND safety report
21 CFR 312.33	Annual report
21 CFR 312.60	General responsibilities of investigators
21 CFR 312.62	Record keeping and record retention (investigator)
21 CFR 312.64	Investigator reports
21 CFR 312.66	Assurance of IRC review
45 CFR 46.109	IRC review of research
E6 GCP 3.1	IRC/IEC - Responsibilities
E6 GCP 3.3	IRC/IEC - Procedures
E6 GCP 3.4	IRC/IEC - Records
E6 GCP 4.4	Investigator - communication with the IRC/IEC
E6 GCP 5.11	Sponsor – Confirmation of review by IRC/IEC
NIH – HPPERT – 11/02 Chapter 4	IRC Review
REFERENCES TO SIMR SOPs	
CO - SS.06	Study Preparation
CO - SM.06	Drug Accountability

Reviewed by Regulatory 10-09

CO-SS.01 PROTOCOL FEASIBILITY

POLICY

Studies submitted to SIMR will be evaluated to determine the feasibility of undertaking the study.

PROCEDURE

01.01 There are multiple points of entry in the feasibility process for SIMR Studies including, Administrator, Coordinator and Investigator. Forms that need to be completed for any study should include CDA and Feasibility survey.

01.02 Upon receipt of the protocol synopsis, the CRCs and PI review study for feasibility. If study is determined to be feasible, the appropriate SIMR staff proceeds with sponsor requirements. If site is approved by sponsor, study startup phase begins. All CDAs are signed by SIMR Director level Management or higher except if sponsor's requirements conflict with this policy.

01.03 Studies will be evaluated according to the following guidelines:

- Scientific and clinical merit
- Subject population
- adequate staff to support the study
- Adequate financial compensation
- History of similar studies

CO-SS.02 Regulatory Submission Process

The Sutter Institute for Medical Research has three available options for IRC Submissions. Full, Expedited and Exempt. Each type requires different forms to be submitted to the IRC.

All of these forms are accessible on www.irbnet.org which is accessible by authorized personnel. See Below for detailed forms required by each type of submission.

Full Review

- a. Application
- b. Protocol Summary
- c. IRC Consent Form
- d. Consent Full Guide
- e. IRC Fee Form
- f. Checklist
- g. FDA Form 1572

Expedited Review

- a. Application
- b. Protocol Summary
- c. IRC Consent Form
- d. IRC Fee Form
- e. Checklist
- f. FDA Form 1572

Exempt Form

- a. Application
- b. Checklist
- c. Fee Form
- d. HIPPA Waiver of Request
- e. FDA Form 1572 if applicable

POLICY

The SHCIRC executes the regulatory review process. The SHCIRC exists to protect the rights and welfare of human research subjects in accordance with regulatory guidelines established by the United States Department of Health and Human Services, Office of Human Research Protection, State of California, and the United States Food and Drug Administration (FDA). The Human Subject Compliance Specialist reports the study activity to the SHCIRC. The investigators must obtain approval from SHCIRC to conduct research involving Subjects.

The FDA requires an IRC to review and approve new protocols for clinical trials. There are different processes for submission to the SHCIRC versus a centralized IRC. All IRB submissions are completed and submitted electronically via www.irbnet.org.

PROCEDURE-SHCIRC (LOCAL)

New protocols – Forms are available on www.irbnet.org

- 01.04** Prepare and obtain PI signature on the following documents, protocol signature page, investigators brochure cover page, financial disclosure statement and FDA Form 1572. Sent originals to the study sponsor.
- 01.05** Revise CV in SIMR template, have PI/Subs sign. Must be updated every 2 years. Obtain copy of medical license.
- 01.06** Complete full committee review application. The IRC requires an electronic signature for IRB submission.
- 01.07** IRC Consent form to include: Sutter HIPAA authorization form, and California Experimental Bill of Rights. This will be used to create a consent form implementing sponsors information. The consent must be reviewed and approved by the CRC, and study sponsor before submission to the SHCIRC.
- 01.08** Complete SHCIRC fee form. The fee form is the tool the Financial Analyst uses to initiate billing for SHCIRC services provided.

- 01.09** SHCIRC checklist needs to be completed online.
- 01.10** Submit completed SHCIRC application packet electronically on www.irbnet.org.
- 01.11** IRC coordinator will schedule presentation date and time. PI will present for 10-15 minutes to the SHCIRC Committee.
- 01.12** For the **Expedited committee review** application, the following documents must be completed and submitted.
- Expedited Committee Review Application
 - Expedited Protocol Summary
 - IRC Consent Form
 - Expedited IRC Fee Form
 - Expedited Checklist
 - FDA Form 1572
- PI is required to review and sign the IRC Submission packet electronically
- 01.13** IRC Consent form to include: Sutter HIPAA authorization form, and California Experimental Bill of Rights. This will be used to create a consent form implementing sponsors information. The consent must be reviewed and approved by the CRC, then sent to the study sponsor before it can be submitted to the SHCIRC.
- 01.14** SHCIRC fee form. The fee form is the tool the Financial Analyst uses to initiate billing for SHCIRC services provided.
- 01.15** SHCIRC checklist needs to be completed online.
- 01.16** Submit completed SHCIRC application packet electronically on www.irbnet.org.
- 01.17** For the Exempt review application, the following documents must be completed and submitted electronically.

(a) Exempt Application

- (b) Checklist
- (c) Fee Form
- (d) HIPAA Waiver of Request
- (e) FDA Form 1572 (if applicable)

01.18 Submit completed SHCIRC application packet electronically on www.irbnet.org.

01.19 IRC coordinator will schedule presentation date and time. . PI will present for 10-15 minutes to the SHCIRC Committee.

PROTOCOL AMENDMENTS

Protocol Amendments are to be completed via www.irbnet.org.

01.20 Complete SHCIRC fee form I. The fee form is the tool the Financial Analyst uses to initiate billing for SHCIRC services provided.

01.21 Amendment Form – 8. Complete this form electronically. If the amendment requires revisions to the consent form, this needs to be reviewed and approved by the study sponsor prior to IRC submission.

01.22 Submit completed SHCIRC amendment packet electronically on www.irbnet.org.

01.23 Contingent approval – the study will be contingent upon IRC requested changes to the consent or other IRC requests listed on the IRC contingent letter. These changes to the consent must first be approved by the study sponsor before resubmission to the IRC for final approval. The IRC will review the consent for accuracy and grant final approval. All study documents and approvals must be sent to the study sponsor and filed in the regulatory binder.

IND safety reports

01.24 Submit IND safety reports must be signed and dated by the PI and submitted on a summary table for IRB review. Original documents are filed in the regulatory binder. Electronic submission of safety table is required via www.irbnet.org

Continuing reviews

01.25 Regulatory Technician and CRC prepare and submit reports for continuing review for each study to the SHCIRC at least annually, or more frequently if requested by the SHCIRC. PI must sign and submit electronically.

01.26 If open to enrollment, include the last signed consent of the last subject enrolled in the study.

01.27 A copy of the submission packet is submitted electronically and a copy is stored in the regulatory binder.

Close out reports

01.28 Schedule a study closure visit with the study sponsor.

01.29 Complete and have PI review and sign close out report electronically.

01.30 Review the regulatory binder and all CRFs and correct any outstanding issues.

01.31 File "Records Management" form in the regulatory binder.

01.32 Submit close out report electronically to the SHCIRC only after the study sponsor completes a study closure visit. A permanent closure letter is sent by the SHCIRC.

01.33 Send the IRC close out letter to the sponsor.

Study transfer

A study transfer is defined as the transfer of a study from one site to another.

- 01.34** Complete amendment form and submit via www.irbnet.org notifying IRC of study transfer.
- 01.35** Schedule a study transfer visit with the study sponsor for the current site where the regulatory binder and all CRFs are reviewed and all outstanding issues completed.
- 01.36** File “Records Management” form in the regulatory binder
- 01.37** Submit SHCIRC letter of transfer and file a copy in the regulatory binder and send a copy to the new site.
- 01.38** Send the original regulatory binders and the original CRF binders to the new site. This officially closes the study at SIMR.

PROCEDURE-CENTRAL IRC

Following are the procedures used for submission of all types of documents that may be submitted to a central IRC.

New Protocols

- 01.39** Prepare regulatory documents and obtain PI’s signature on the following:
- FDA Form 1572
 - Protocol signature page
 - PI’s and Sub-I’s CV and medical license
 - Financial disclosure statement
 - IRC questionnaire (site specific)
- 01.40** Submit the following documents:
- Protocol
 - Investigational drug brochure
 - Standardized informed consent
 - Site specific IRC questionnaire
 - Recruitment materials

- PI's and Sub-I's CV, medical license, and financial disclosure statement
- Local laboratory documents (if required)

01.41 SIMR is required to submit other requested documents including; jurisdiction waver of authorization.

01.42 Upon study approval, the central IRC will notify the SIMR clinical trials office.

Protocol amendments and addendums

01.43 Revise the consent to reflect the updated revised protocol for the PI to review.

01.44 The study sponsor may use a CRO when submitting a new protocol to the central IRC. The CRO submits the protocol to the central IRC on behalf SIMR. SIMR is required to submit other requested documents (per central IRC requirements) and consent revisions with SHCIRC language. The revised consent is sent for sponsor approval and then to the central IRC for review.

01.45 A hard copy of the approved documents will be mailed following review. File approved documents in the regulatory binder

IND safety reports for central IRC may be submitted by the study sponsor or the study site, following IRC submission policies.

01.46 Write a letter stating the date that the safety reports were sent to the central IRC following review and signature by the PI.

01.47 For study sponsors using a central IRC, the study sponsor is responsible to submit IND safety reports on SIMRs behalf.

CONTINUING REVIEW

01.48 Complete continuing review form and attach any requested documents.

01.49 The PI for the study completes signs and dates the continuing review form. If the study is still open to enrollment, a copy of the consent form of the last enrolled

subject is included. All forms are returned to the RT. The central IRC may request the return of the original document but a copy is retained in the regulatory binder.

01.50 Documentation from the IRC is sent to the site after continuing review is granted.

Close out reports

01.51 Schedule a study closure visit with the study sponsor. The regulatory binder is reviewed, and outstanding issues resolved.

- Complete Closure form from central IRC website.

01.52 Request a letter of acknowledgement from the IRC that the study has closed. This letter should be filed in the regulatory binder.

Study Transition

A study transition is defined the transfer of a study from one site to another.

01.53 Schedule a study transfer visit with the study sponsor. The regulatory binder and all outstanding issues are resolved.

01.54 File the form "Records Management" with the regulatory technician.

01.55 Submit a letter of transfer to the IRC, if applicable and file a copy of this letter in the regulatory binder.

01.56 Request a letter from the sponsor that states the date that the transfer takes effect.

01.57 Retain a copy of the regulatory binder at the original site.

01.58 Send the original regulatory binders and the original CRF binders to the new site.

01.59 The transfer of the regulatory binders closes the study at SIMR.

CO-SS.03 Maintainence and storage of regulatory DOCUMENTS

POLICY

The regulatory binder is maintained throughout the clinical study. The binder contains pre-study documents and all forms and reports completed during the course of the study.

PROCEDURE

Contents of the regulatory binder

01.60 Include the following materials in the regulatory binder if applicable:

- Pre-study documents
- Form FDA 1572
- Signed and dated financial disclosure form and medical license for the PI and Sub-I
- Current (within 2 years) CV for PI, Sub-I and laboratory director
- Laboratory certification
- IND safety reports
- Protocol (including signature page and synopsis)
- IRC membership list
- IRC approval
- Approved informed consent form
- Advertising material
- Investigators brochure
- Test article inventory and drug accountability record
- Delegation of Authority Form
- CRFs and AE Forms
- Site visit log
- Telephone log
- Master subject list
- Original source documents
- All correspondence to and from the sponsor including additional documents as the study progresses. These may include but are not limited to:
 - a. Updated documents (amendments, addenda, investigator brochures, revised consents)
 - b. Shipping invoices for all test materials, returned goods forms.
 - c. All correspondence pertaining to the study.

Archiving regulatory documents

01.61 All study regulatory documents are stored for a period of 1 year at the SIMR Clinical Trials Office: 2801 Capitol Avenue, Suite 400, Sacramento, CA 95816.

01.62 After 1 year, records are archived at the Sutter Health Records Management at 1650 Cebrian Street, West Sacramento, CA. 95691 for 25 years.

CO-SS.04 Pre-Study Startup Site Selection Visit

POLICY

Each study submitted to SIMR ORA will be evaluated with the sponsor to identify issues that may need to be addressed prior to study placement within SHSSR system facilities.

PROCEDURE

01.63 The sponsor submits a study protocol or protocol synopsis to ORA or the prospective PI for the study.

01.64 The sponsor may request a screening site selection visit, which is arranged with ORA and/or CRC.

01.65 The ORA identifies and facilitates study coordination with ORA and CRC

01.66 Arrange for a tour of the sites where the research is conducted. Areas visited may include:

- Exam rooms
- Laboratory facilities
- Special procedure rooms
- Drug storage facilities
- Study material storage, including CRFs and source documents
- Location of regulatory binders

01.67 A meeting is arranged between the PI, the sponsor, and CRC to discuss clinical issues, answer questions, and present requirements by ORA for protocol review.

01.68 The sponsor notifies ORA and/or PI if the site has been awarded the study.

01.69 If SIMR is awarded the study, the sponsors notify the PI, the CRC and/or the ORA, of locations and dates of required investigator meetings.

01.70 Upon SIMR selection as a study site, the sponsor provides the necessary regulatory documents for IRC submission.

APPLICABLE REGULATIONS AND GUIDELINES

21 CFR312.60	General responsibilities of investigator
21 CFR 312.50	General responsibilities of sponsor
21 CFR 312.55	Informing investigator
21 CFR 312.57	Record keeping and record retention (sponsor)
E6 GCP 5.1	Sponsor – Quality Assurance and Quality Control
E6 GCP 5.12	Sponsor – Information on Investigational Product(s)
E6 GCP 5.14	Supplying and Handling Investigational Product(s)
E6 GCP 8.2	Essential Documents for the Conduct of a Clinical Trial – Before the Clinical Phase of the Trial Commences
REFERENCES TO SIMR SOPs	
CO - SS.05	Study Site Initiation Visit
CO - SS.06	Study Preparation

CO-SS.05 Study Site Initiation Visit

POLICY

The details of a study protocol are given to the PI, CRC, IDS pharmacist and other research team members at the sponsor study site initiation visit. The details of the SIMR internal study activity including but not limited to, finance, billing compliance, budget, regulatory, and recruitment are discussed at the study start up meeting.

SPONSOR SITE INITIATION

PROCEDURE

01.71 Members of the research team may include the PI, CRC, IDS pharmacist and other ancillary staff. The team is notified of the location, date, and time of the visit. The CRC reminds the study team one day in advance of the visit.

01.72 Copies of the research protocol are made available to study team members. For protocols that include investigational drugs, a complete protocol and investigator's brochure is forwarded to the IDS.

01.73 The sponsor meets with the PI and research team to review the protocol, roles, and responsibilities as well as GCP guidelines.

- The sponsor reviews the CRF with the CRC.

01.74 ORA contracts office addresses funding for additional supplies or equipment that need to be provided

01.75 Exceptions:

- (1) The investigator meeting if attended by the PI and CRC, may take the place of the study initiation visit.

- (2) When drug is shipped directly to the PI (not located within a Sutter Hospital), the IDS Pharmacist is not involved in the initiation visit

SIMR INTERNAL STUDY START UP MEETING

PROCEDURE

01.76 Following sponsor site initiation visit, the CRC schedules an internal study start up meeting. The team for this meeting should include finance, billing compliance, contract/budget, recruitment, regulatory.

01.77 The team shares pertinent information including but not limited to :

1. Study Summary – study period, study site, participant issues
2. Study Team information – Investigator issues, names of PI, sub I, backup CRC.
3. Contract/Budget – patient target, budget breakdown, patient stipend, investigator contract, start up fees.
4. Finance Review – Investigator compensation, worksheet
5. Billing Compliance – Form K, and billing instructions
6. Recruitment – various methods of recruitment that will be used including, print and radio advertisement, physician referral, call center, database queries.
7. Regulatory – consent review

01.78

CO-SS.06 Study Preparation

Study preparation time is used to address issues identified during the study initiation visit and prior to study startup.

POLICY

ORA facilitates the preparation for study startup, advertisement, promotion and recruitment of study subjects from SHSSR hospitals, clinics, and the community.

PROCEDURE

- 01.79** The CRC confirms the IRC approval date and reviews any protocol amendments or changes to the consent.
- 01.80** The SIMR contract department confirms the contract and budget approval with the sponsor and solidifies arrangements with off-site subcontractors.
- 01.81** The SIMR contract department solidifies the contract with participating physicians and vendors.
- 01.82** CRC trains a back-up coordinator.
- 01.83** The CRC and regulatory technician resolve any issues regarding storage space or transportation of study materials.
- 01.84** Develop and implement recruitment plan to identify potential subjects. Confirm the date that enrollment starts from the sponsor. Recruitment plans that include direct patient marketing must have approval from an IRC prior to implementation.
- 01.85** In-service and training required by ancillary staff is completed and documented.
Ancillary staff may include:
 - Office staff
 - Pharmacy staff

- Off-site facility staff

01.86 Confirm and record receipt of study drug. Store and file study supplies and IRC study specific approved literature advertisements.

01.87 Purchase and store additional study specific materials or equipment.

APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 56.109	IRC Review of research
21 CFR 56.111	Criteria for IRC approval of research
21 CFR 312.21	Phases of an investigation
21 CFR 312.23	IND content and format
21 CFR 312.60	General responsibilities of investigators
21 CFR 312.68	Inspection of investigator's records and reports
	REFERENCES TO SIMR SOPs
CO-SS.05	Study Site Selection Visit
CO-SM.04	Drug Accountability

CO-SS.07 Adult InfoRmed Consent

POLICY

Informed consent will be administered according to GCP, CFR and HIPAA regulations.

PROCEDURES

01.88 The consent form used must be approved by an IRC and includes SHSSR HIPAA authorization, and a California Experimental Subjects Bill of Rights.

01.89 Study sponsors and their representatives are not involved in the ICF process.

01.90 The PI or the CRC meets with the subject to review each page of the ICF. The following topics must be addressed in the ICF and discussion:

- Purpose of the study
- Number of subjects involved in the trial
- Medication or device involved and probability for random assignment to each treatment
- Description of study procedures and how long subjects will be in the study
- Experimental aspects of the trial
- Risks and benefits
- Alternatives to the study
- Voluntary nature of the study
- Right to withdraw
- Compensation and/or treatments available if the subject is injured
- California Experimental Subjects Bill of Rights
- Expenses from subject participating in the study
- Who to contact for information on rights of trial participants if injury occurs during study
- Stipends for participation
- HIPAA authorization to disclose subjects' information
- A statement regarding how new information about the study will be conveyed to potential subjects
- Questions and concerns of potential study subject

- 01.91** The ICF is written in a language that potential subjects or subjects' representatives understand.
- 01.92** The PI and CRC review the ethical and legal consideration for potential study participants whose first language is not English.
- 01.93** Potential subjects are instructed to read the consent completely and to not sign or date the ICF until questions, comments, and discussions between the PI or designee and potential study subject are addressed.
- 01.94** Potential subjects read the consent alone in a quiet and confidential atmosphere, or are encouraged to take it home and discuss it with family members.
- 01.95** Signatures are obtained on the ICF only when subjects are completely comfortable with the study requirements and have no reservations with signing.
- 01.96** Consent forms are signed and dated by subjects or subjects' representative. The California Experimental Subject Bill of Rights and the HIPAA authorization form are also be signed and dated.
- 01.97** If required, the informed consent process is witnessed.
- 01.98** The CRC documents the informed consent process in the in the source documents and notes that a signed copy of the ICF was given to the subject prior to commencement of the study.
- 01.99** If stipends are provided, subjects complete a W-9 form.
- 01.100** Subjects are given a signed copy of California Experimental Subject's Bill of Rights, HIPAA authorization form, and the W-9 form, if applicable.
- 01.101** If study amendments necessitate revision of the ICF (study procedures are changed, or serious adverse event information becomes available), re-consenting subjects is required. Additional consents need to be obtained as outlined above.

APPLICABLE REGULATIONS AND GUIDELINES

T45 CFR 46.116	General requirements for informed consent
45 CFR 46.117	Documentation of informed consent
50 Subpart B CFR 50.20-50.27	Informed consent of human subjects
E6 GCP 4.8	Investigator – Informed Consent of Trial Subject
http://ohrp.osophs.dhhs.gov/	
http://www.fda.gov/oc/ohrt/IRCs/faqs.html	
45 CFR 46.116	General requirements for informed consent
45 CFR 46.117	Documentation of informed consent

CO-SS.08 SURROGATE CONSENT

POLICY

Surrogate consent is administered according to the guidelines provided by the Sutter Health Legal Advisory and SHCIRC.

PROCEDURES

The following procedures apply to the non-emergency room environment, emergency room environment, and to mentally alert potential subjects unable to sign a consent form.

- 01.102** Research staff conducting the consent discussion must find an impartial 3rd party to witness the consent process. When potential subjects indicate they want to participate in the study, the 3rd party signs the ICF for subjects.
- 01.103** The 3rd party must document their own name (legibly written) and an explanation regarding why they signed the ICF for the subject.
- 01.104** The Coordinator and/or PI signs and verifies why the subject couldn't sign the ICF when available.
- 01.105** Subjects who are able, indicate they have agreed to participate in the research study by making a mark on the ICF.

APPLICABLE REGULATIONS AND GUIDELINES

The following regulations and guidelines apply to CO-SS.08, CO-SS.09, and CO-SS.10

50 Subpart D CFR 50.50-50.56	Additional Safeguards for Children in Clinical Investigations
REFERENCES TO SIMR SOPs	
CO – SS.07	Adult Informed Consent

CO-SS.09 Pediatric Informed Consent

POLICY

For research subjects under the age of 18, informed consent is obtained from the minor's parent or legal guardian as described in the Adult Informed Consent SOP. Assent should be sought when in the judgment of the IRC; children are capable of understanding the nature of their participation in the research. The following guidelines are used when obtaining pediatric informed consent.

GUIDELINES

01.106 Minors may participate in research when the IRC finds the study meets one of the following criteria:

- a. Does not involve greater than minimal risk to the minor.
- b. Involves greater than minimal risk but presents the prospect of direct benefit to the individual subject.
- c. Involves greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalized knowledge about the subject's disorder or condition.

01.107 The parent(s) or legal guardian must be at least 18 years old or an emancipated minor.

01.108 The parent(s) or legal guardian must be capable of understanding the research study.

01.109 Consent from only one parent or legal guardian is required if the research involves no more than minimal risk.

01.110 Consent from only one parent or legal guardian is required if the research involves greater than minimal risk but presents the prospect of direct benefit to the individual subject.

01.111 Consent from both parents or legal guardians is necessary only if the research involves greater than minimal risk and does not hold out the prospect of direct benefit to the individual subject. This is likely only to occur in oncology studies.

01.112 Study materials must be provided in a language understood by the parent or legal guardian.

CO-SS.10 Pediatric Assent

POLICY

Pediatric assent is required when in the judgment of the IRC, children are capable of understanding the nature of their participation in the research. The NIH National Commission recommends that assent generally be obtained from children who are seven years of age or older.

GUIDELINES

01.113 Pediatric assent is not required if the research directly benefits the subject and the intervention is available only through research.

01.114 Information must be given to child in age-related and developmentally appropriate language where the format is simple and short.

CO-SS.11 CONTRACT preparation and management

PURPOSE

The purpose of this SOP is to document the process for completion of a clinical research site contract.

POLICY

It is the policy of Sutter Health that all studies conducted on the premises or involving a Sutter facility within the SHSSR are managed through SIMR. All contracts are reviewed by a contracts specialist (CS) according to Sutter Health guidelines and are processed in a timely manner. The CS works with a contracts team that may include the PI, CRCs, DO, regulatory technician, compliance and contract coordinator, Sutter's Risk Services Department, and Sutter's legal counsel.

BUDGET REVIEW

The budget and contract may occur simultaneously or consecutively. The sequence of events is dependent upon the sponsor. An agreement with the sponsor can be signed before a budget is in place. However, in accordance with the Stark law, payments to physicians must be agreed upon prior to signing a contract with physicians.

PROCEDURE

- 01.115** Receive notification of a new study and obtain sponsor contact information.
- 01.116** Study schema is reviewed with members of the contracts team to determine billable hours for each visit and other potential costs associated with the protocol such as labs, diagnostic tests, other medical personnel, or equipment needed.
- 01.117** subcontracts are created for the following: :

- a. Principal and Sub Investigator Agreements.
- b. Sutter Affiliate Agreements.
- c. Sutter Vendors

CONTRACT REVIEW

The sponsor's draft contract is reviewed with the Sutter's legal department and makes required changes to reflect Sutter Health policies. Contract development is dependent upon the number of changes required by the sponsor as well as Sutter Health. As a result, the contract may go through several revisions until it satisfies the needs of the sponsor and Sutter Health. Once the contract is approved, then a copy of the fully executed contract is scanned into Tract Manager, Tract manager number is entered onto the lower right hand corner of first page of contract in red and SIMR finance logs document for billing purposes.

CO-SS.12 SUBJECT Recruitment

Effective recruitment methods provide rapid enrollment of qualified research subjects into a clinical research study. For each clinical research study, a plan is developed using a wide range of recruitment methods. Recruitment methods are implemented according to GCP and HIPAA regulations (reference SHSSR Policy On Use and Disclosure of Protected Health Information (PHI) for Research Under HIPAA)

POLICY

A variety of recruitment methods are used to assist with subject recruitment to meet sponsor-required timelines. The research team develops a recruitment plan that is specific for each research study. Recruitment goals are established, reviewed, and revised on an ongoing basis throughout the course of the study. Only IRC approved recruitment materials are used to for subject recruitment. Subject recruitment activities are conducted in compliance with state and federal laws, GCP, IRC requirements and HIPAA. Effective April 14, 2003, SHSSR research personnel uses and discloses potential research patients PHI with proper authorization

SIMR implements recruitment strategies designed to meet individual site needs. SIMR utilizes the SIMR Call Center, direct advertising such as radio and print ads and community networking in addition to querying databases of patients treated at Sutter facilities to market currently available clinical trials.

PROCEDURES

- 01.118** During the protocol feasibility stage SIMR determines whether or not Sutter has the patient population to successfully meet enrollment goals for a clinical trial. Lab, pharmacy, and/or billing databases may be used to determine an appropriate Sutter PI for the study and to determine if Sutter has a patient population with the medical condition required for the study.

01.119 Prior to study enrollment, the research team develops a recruitment plan. Brainstorming sessions among the clinical research team are conducted to generate recruitment strategies.

01.120 The research team creates recruitment and screening forms, physician to patient letters, and phone screen questionnaires. These are submitted to the IRC and the sponsor for approval prior to use.

Methods of subject recruitment may include:

- Call Center
- Advertising
- Accessing Sutter PHI
- Accessing lab, pharmacy, and/or billing databases
- Performing chart screens SHSSR facilities
- Performing chart screens at non-SHSSR facilities
- Accessing SIMR's Research Database
- Inviting other physicians, and office staff to participate in subject recruitment and enrollment

Direct Advertising

01.121 The availability of funds for direct advertising and sponsor-approved recruitment materials is confirmed with the sponsor.

01.122 The research team contacts Sutter Health Marketing to assist in the recruitment campaign.

01.123 The sponsor, IRC, and Sutter Health Marketing approve the recruitment materials prior to distribution.

01.124 Direct advertising methods may include:

- Newspaper ads
- Radio scripts
- Television scripts
- Public service announcements
- Press releases
- Posters and flyers,
- Sutter Health Regional Update

- Sutter Insights Newsletter
- Newspaper human interest and medical columns
- SIMR and other appropriate website listings
- Participation in local health fairs and trade shows.

Recruitment of patients treated at SHSSR facilities

01.125 The SIMR research team follows the SHSSR Policy on Use and Disclosure of PHI for Research Under HIPAA during all recruitment activities

01.126 Recruitment of patients treated at SHSSR facilities may include:

- Accessing the lab, pharmacy, and/or billing databases
- Performing chart screens or accessing an electronic medical record (EMR) at outpatient SHSSR facilities
- Performing chart screens or accessing an EMR at inpatient SHSSR facilities
- Performing chart screens at non-SHSSR facilities
- Accessing SIMR's Research Database
- Inviting site physicians office staff members to participate in subject recruitment and enrollment
- Reviewing the PI and Sub-I's daily schedules for patients who may meet study criteria

Recruitment at non-SHSSR facilities

01.127 SIMR staff may review the medical records' of potential research subjects' at non-SHSSR facilities with proper authorization from the treating physician.

01.128 Treating physicians at non-SHSSR facilities are required to follow the facility's HIPAA policy.

APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 50.2021	General requirements for informed consent
21 CFR 56.10921	IRC review of research
21 CFR 312.60	General responsibilities of investigators
21 CFR 312.62	Investigator record keeping and record retention
	SSHR Policy on Use and Disclosure of PHI for Research, August 2004
45 CFR 160 & 164	US department of HHS/ Health Insurance Portability and Accountability Act of 1996 (HIPAA)

CO-SM STUDY MANAGEMENT

Standard operating procedures outlined below provide continuity and guidelines during the conduct of clinical studies. These policies include sponsor-initiated monitoring visits, reporting AEs, progress reports, and drug accountability requirements.

APPLICABLE REGULATIONS AND DOCUMENTS

The following regulations and guidelines apply to all SOPs that address study management.

21 Subpart D CFR 312.50 – 312.70	Responsibilities of Sponsors and Investigators
E6 GCP 4.6	Investigator – Records and Reporting
E6 GCP 4.9	Investigator – Progress Reports
E6 GCP 5.18	Sponsor – Monitoring
E6 GCP 5.15	Sponsor – Record Access
E6 GCP 8.3	Essential Documents for the Conduct of a Clinical Trial – During the Clinical Conduct of the Trial

CO-SM.01 RECORDS AND CASE REPORT FORMS

POLICY

The PI is responsible for all data reported on CRFs. CRCs or designee completes CRFs using the following guidelines.

PROCEDURES

- 01.01** CRFs should be completed using a black or black ink pen (if paper).
- 01.02** Data reported on CRFs, which are derived from source documents (HP, lab results, imaging reports) should be consistent with the source documents, or the discrepancies should be explained.
- 01.03** Any change or correction to the CRF should be lined out without obscuring original entry, dated, initialed, and explained if necessary. Directions from the individual study sponsor should be followed.
- 01.04** Original source documents should be made available for comparison with the CRFs at monitoring visits.

CO-SM.02 SPONSOR MONITORING VISITS

POLICY

The ORA and CRCs will facilitate a monitoring visit in which all materials are accessible, complete, and accurate. A successful monitoring visit allows the site to reinforce or revise logistics according to the protocol and GCPs. ORA will provide adequate space for the proper conduct of the monitoring visit.

PROCEDURES

Prior to the monitoring visit, the CRC is responsible for:

- 02.01** Notification of all research team members, including the PI and regulatory technician, of monitoring visit date, time, and place.
- 02.02** Assurance of a space to work, phone, FAX, copy machine, and computer if requested.
- 02.03** Review of the CRF and all applicable documents for accuracy.
- 02.04** Notification of the IDS pharmacist of impending meeting and requesting copies of all required documentation to be forwarded to the CRC.

The monitoring visit consists of the following.

- 02.05** Reviewing the CRF with the study monitor.
- 02.06** A meeting between the PI and study monitor to sign required documents.
- 02.07** Addressing questions, corrections, and clarifications.

APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 312.50	General responsibilities of sponsors
21 CFR 312.56	Review of ongoing investigation
21 CFR 312.59	Disposition of unused supply of drug
21 CFR 312.60	General responsibilities of investigators
21 CFR 312.62	Investigator record-keeping and record retention
21 CFR 312.64	Investigator reports
21 CFR 312.66	Assurance of IRB review
21 CFR 312.68	Inspection of investigator's records and reports

CO-SM.03 ADVERSE EVENT REPORTING

POLICY

Adverse events (AEs) that occur during the course of a research study are reported to the IRB and the study sponsor.

PROCEDURE

- 03.01** An AE is defined as a medical complaint, change or possible side effect of any degree of severity that may or may not be attributed to the test article. AEs may or may not need to be reported to the sponsor.
- 03.02** Record AEs immediately in source documents, include the following information: start and stop date of adverse reaction, severity of adverse event, action taken, if any with start and stop dates; and causality.
- 03.03** The PI or Sub-I determines the causality between the AE and the study device or drug.
- 03.04** The severity of the AE is determined based on the criteria noted in the study protocol.

APPLICABLE REGULATIONS AND GUIDELINES

The following regulations and guidelines apply to CO-SM.03 and CO-SS.04

21 CFR 312.32	IND safety reports
21 CFR 56.108	IRB functions and operations
21 CFR 56.109	IRB review of research
21 CFR 56.115	IRB records
E6 GCP 4.11	Investigator – Safety Reporting
E6 GCP 5.16	Safety Information
E6 GCP 5.17	Adverse Drug Reaction Reporting
Clinical Safety Data Management	

CO-SM.04 SERIOUS ADVERSE EVENT REPORTING

POLICY

A serious adverse event (SAE) is defined as any untoward medical occurrence that results in death, is life threatening requires in-patient hospitalization or prolongs existing hospitalization; results in persistent or significant disability or incapacitation; or is a congenital anomaly/birth defect. An important medical event may be considered an SAE when, based upon appropriate medical judgment, the event may jeopardize the patient and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. An AE is considered an SAE when defined as any occurrence that is not consistent with the current investigator brochure or study protocol. SAEs are reported by the investigator to the IRB and study sponsor to comply with applicable regulations and sponsor requirements. The FDA and IRB require that SAEs be reported as soon as possible but not later than 10 days following notification of an event. Most sponsors require SAEs to be reported to them within 24 hours following notification of an event.

PROCEDURE

- 04.01** Access all medical information pertaining to SAE (i.e. medical records, statements, documentation)
- 04.02** Contact the sponsor within 24 hours of knowledge of an SAE or unexpected AE by phone or FAX, unless sponsor has provided different instructions. The sponsor is required to report unexpected AEs to the FDA within 24 hours of notification.
- 04.03** Complete SAE form provided by the sponsor and fax to sponsor and Central IRB (if applicable), within 24 hours of knowledge of serious or unexpected AE.
- 04.04** If applicable, complete Form H to report SAE and submit to SHCIRC within 10 business days of knowledge of serious adverse or unexpected event.
- 04.05** In a blinded study, the PI in conjunction with the sponsor determines whether the blind needs to be broken. The blind is not disclosed unless instructed by the sponsor.
- 04.06** Subjects with an SAE may or may not be removed from the study. Any subject who is unblinded will be removed from further participation in the study.

04.07 Removal of a subject with an SAE depends on the nature of the event and is determined by the PI and sponsor.

04.08 Submit follow-up reports or information to the sponsor and IRB as soon as possible.

CO-SM.05 DRUG ACCOUNTABILITY

The investigational drug service (IDS) pharmacy is responsible for the proper receipt, storage, distribution, accountability and disposition of study drug according to policies, state and federal requirements. This procedure describes the procedure for receipt, distribution, accountability, and disposition of drugs for outpatient studies. The Policy and Procedures on Investigational Drugs for hospitalized patients undergoing research through SIMR will be followed as applicable. They also contain documents applicable to drug receipt, storage, delivery, and transfer.

POLICY

The IDS pharmacy, under the supervision of the IDS pharmacist, will participate as a voting member of the SHCIRC, and inform the medical staff, through the pharmacy and therapeutics committee of all approved investigational drug studies. The IDS pharmacist is responsible for the safe distribution and control of investigational drugs on protocols with SHCIRC/IRB approval. The IDS pharmacist will develop ongoing educational programs for pharmacy, and administrative staff in the dispensing, administration and associated clinical implications of study medications and agents. Exceptions to this policy will be discussed among the IDS pharmacist, CRC, and study sponsor prior to study start-up.

PROCEDURES

- 05.01** The IDS pharmacy assumes responsibility for investigational protocol agents, dispense to outpatient subjects per investigator's instructions or the entities listed under drug dispensing as applicable, maintain drug accountability logs, and obtain unused drug returns for final disposition.
- 05.02** The IDS pharmacist maintains and updates on a monthly basis a protocol list with drug, location of drug stock, and CRC. This list is distributed throughout study drug locations and a copy sent to SIMR ORA.
- 05.03** The following addresses are used to receive drug shipments:

Sutter Memorial Hospital Pharmacy

5151 F Street
Sacramento, CA 95819

Sutter General Hospital Pharmacy

2801 L Street
Sacramento, CA 95816

Sutter Midtown Pharmacy

2800 L Street, Suite 450
Sacramento, CA 95816

Outpatient physician offices and clinics (non-SMCS)

Investigational drugs may also be shipped to the offices of PIs provided that they have adequate facilities for proper receipt, accountability, and storage of drug. SIMR updates IDS protocol list.

Documentation of Delivery

- 05.04** The movement of drug shipment from the IDS pharmacy is documented.
- 05.05** If drug needs to be transported from IDS Pharmacy to a remote study site (i.e. Sutter Roseville, Infusion Center, etc) without the CRC or pharmacist, obtain approval from the study sponsor to use the current SHSSR delivery system.
- 05.06** All drugs are stored in a secure, locked cabinet or designated pharmacy with access only to authorized personnel. Each drug is stored separately by protocol. If a drug is used for more than one protocol, the drug is stored separately for each protocol.

Drug dispensing

- 05.07** Drug is dispensed from the IDS pharmacist or PI to:
 - The CRC
 - The Sutter satellite pharmacy servicing the clinic
 - Directly to the hospital pharmacy servicing the subject's nursing unit
 - Pediatric HMO infusion clinic
 - Cancer center ambulatory infusion clinic
- 05.08** All required documentation and drug accountability logs are completed in black ink by all individuals handling investigational drugs and forwarded to the IDS pharmacy when completed.

Drug returns

05.09 The CRC is responsible for acquisition of any unused drug from the patient and return to the IDS pharmacist.

05.10 The IDS pharmacist is responsible for study drug accountability.

APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 312.50	General responsibilities of sponsors
21 CFR 312.59	Disposition of unused supply of drug
21 CFR 312.60	General responsibilities of investigators
21 CFR 312.61	Control of the investigational drug
21 CFR 312.62	Investigator record keeping and record retention
21 CFR 312.68	Inspection of investigator's records and reports
21 CFR 312.69	Handling of controlled substances
E6 GCP 4.6	Investigator – Investigational Product (s)
E6 GCP 5.12	Sponsor – Information on Investigational Product(s)
E6 GCP 5.14	Sponsor – Supplying and Handling Investigational Product(s)
SMCS Pharmacy Procedure	Drugs from SMP to RINC
SMCS Pharmacy Policy	Policy on Investigational Drugs
SMCS Pharmacy Procedure	Procedure on Investigational Drugs
SMCS Pharmacy Procedure	Procedure on Investigational Drugs from another Institution
SMCS Pharmacy SOP #40	Medication Disposition and Disposal
SMCS Pharmacy SOP #760	Disposing of Pharmaceutical Waste

CO-SM.06 SPECIMEN PROCESSING

POLICY

It is the policy of SIMR to comply with all state and federal laws pertaining to the processing and shipping of laboratory specimens. Department managers determine the occupational exposure and required training for each employee.

PROCEDURE

- 06.01** “*Shipping Infectious and Diagnostic Specimens*” Certification is maintained by SIMR research staff involved with shipping lab specimens. Certification is updated every 2 years, as required by law.
- 06.02** Research staff receives yearly training regarding blood borne pathogens, as required by law. This training is included in the *Sutter Medical Center Annual Environment of Care (Safety) Education Checklist*.
- 06.03** Employees have access to the *Sutter Health Infection Control/Blood Borne Pathogen Manual*, as required by law. The SIMR safety officer maintains the manual and provides required training. The safety officer I also contacts the Sutter Health Safety Department to obtain yearly updates regarding blood borne pathogens and protocols.
- 06.04** Department managers update the employee occupational hazard classification annually.
- 06.05** Needlestick injuries are reported to Occupational Health (7:00-4:00) or the Emergency Department (for non-business hours). All follow-up visits are with Occupational Health.
- 06.06** Non-Needlestick injuries are reported to the regional disability manager the next business day
- 06.07** A report of injury log (*OSHA 300*) log is maintained and kept current within 14 days and is posted at each site for one month during the year.

APPLICABLE REGULATIONS AND GUIDELINES

29 CFR 1910.1030	Bloodborne pathogens
	California Code of Regulations Title 17
	SHSSR – Environment of Care Manual
	SHSSR – Infection Control Manual
	SHSSR – Policy Guidelines for Work Related Employ Injuries
49 Subtitle B Parts 105-180	RESEARCH AND SPECIAL PROGRAMS ADMINISTRATION, DEPARTMENT OF TRANSPORTATION

CO-SM.07 STUDY RECORD RETENTION/DESTRUCTION

POLICY

SIMR ORA will retain study records in accordance with Title 21 CFR or sponsor's contractual agreement; whichever is more stringent.

PROCEDURE

07.01 All study records are delivered to the SIMR regulatory technician for processing in a Bankers box supplied by Sutter Health's records management department and includes:

- All patient CRFs
- Patient research charts
- Regulatory binder(s)
- Investigators' brochure (including all versions)
- Investigator's binder (if available)
- Blank CRF
- Copy of blank source documents

07.02 Insert a copy of the completed "Record of Deposit" form in the box and include the following:

- Sponsor, protocol number, PI and study close out date on the first line of each page. List only one study per page.
- An individual list of all contents of the box (include patient initials and patient number).

07.03 A label the end of the box with the following information:

- Facility name (location of research)
- Department
- Record types (i.e patient records)
- Sponsor and study name
- Protocol number (if available)
- Study close out date

07.04 Study records for closed studies will be maintained on-site for a minimum of one year.

07.05 After a minimum of one year, study records are retained off- site by Sutter Health Records Management, for a period of 25 years.

CO-SM.08 STUDY CLOSURE

PROCEDURE

- 08.01** Collect drugs or devices from subjects, inventory supplies, and reconcile drug or device accountability log for each patient.
- 08.02** Follow sponsors' instructions on destruction of study drugs. IDS pharmacy provides these services, or sponsor will have drug shipped back to them at their expense for destruction.
- 08.03** Study sponsor conducts close- out visit.
- 08.04** When all queries have been resolved, the sponsor provides a letter closing the study. If no letter is received, the CRC contacts the sponsor to confirm all data have been received and documents the contact.
- 08.05** PI sends letter to IRB closing the study.

APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 312.50	Review of ongoing investigations
21 CFR 312.56	General responsibilities of sponsors
21 CFR 312.56	General responsibilities of sponsors
21 CFR 312.59	Disposition of unused supply of drug
21 CFR 312.60	Investigator record keeping and record retention
21 CFR 312.62	Investigator report
21 CFR 312.64	Investigator reports
21 CFR 312.66	Assurance of IRB review
E6 GCP 4.13	Investigator Final Report(s)
E6 GCP 4.22	Sponsor – Clinical Trial/Study Reports
E6 GCP 8.4	Essential Documents for the Conduct of a Clinical Trial – After Completion of Termination of the Trial
REFERENCES TO SIMR SOPs	
CO-SM 05	Drug Accountability

QUALITY ASSURANCE

INTRODUCTION

Clear quality standards, operating processes and procedures, and oversight procedures have been established to provide guidance for SIMR to meet its goal of promoting and ensuring quality in all aspects of its operations.

The purpose of this policy is to describe the procedures in place that demonstrate SIMR's practices to ensure adherence to the policies and regulations mandated by the ICH Good Clinical Practice guidance and FDA regulations.

QA-PO PROGRAM OVERSIGHT

Program oversight includes the oversight procedures SIMR has put in place to maintain billing compliance and monitor the quality of the studies conducted at SIMR.

QA-PO.01 BILLING COMPLIANCE

POLICY

Any claim for services rendered to a participant of a clinical trial must be compliant with federal regulations and policies. To obtain this objective, departments, coordinators, and principal investigators must cooperate with SIMR Administration, provide any necessary documentation, and strictly follow any written instructions throughout the course of the clinical trial.

PURPOSE

The purpose of this policy is to describe the process that allows for the accurate processing of claims involving inpatient charges for services rendered to patients enrolled in clinical trials at SIMR. The policy also ensures that Sutter remains compliant with applicable regulations pertaining to the processing of claims for clinical trial participants.

PROCEDURE – PREPARATION FOR BILLING COMPLIANCE

- 01.1** A copy of the study budget, protocol or study schema, and Form X is obtained from the contracts and compliance coordinator or designee. The CCC collects the information from the specific department including SHC IRC administrative office, regulatory technician (RT), PI and/or CRC. If information is omitted or not properly completed on the Form X, this form is returned to the CRC for further processing.
- 01.2** For an investigational device exemption (IDE) the CCC is required to notify Sutter's fiscal intermediary (FI) prior to billing for costs associated with the clinical study.
- 01.3** The PI includes the FDA approval letter in the submission to the IRB. The FDA approval letter includes the category of the device. The categories of devices are as follows:
 - Category A (experimental)
 - Category B (non-experimental)
- 01.4** Category A (experimental): The safety and effectiveness of Category A devices are not established and cannot be billed to Medicare.

- 01.5** Category B (non-experimental): The safety and effectiveness of Category B devices are assured and can be covered by Medicare.
- 01.6** For Category B devices only, the CCC submits required information to Sutter's FI, Palmetto GBA for approval. Palmetto GBA requires the following information:
- FDA approval letter (either conditional or final/full approval letter)
 - Device Category B (specified in the first letter issued by the FDA)
 - Name of device (both trade, common or usual name, and classification name)
 - Narrative description of the device
 - Action taken to confirm to any applicable FDA special controls
 - Statement that indicates how the device is similar to and/or different from other comparable device(s)
 - Provider's protocol for obtaining the patient's informed consent specific to clinical trial
 - The SHCIRC authorization/approval letter
 - Name of the facility and it's Medicare provider number where the clinical trial will be conducted

PROCEDURE – BILLING COMPLIANCE PROCEDURES

- 01.7** The CCC writes specific requirements for billing for these studies. This includes using the appropriate revenue code and including the IDE number. The device is included on the bill either as a non-covered charge or as a covered charge depending upon the determination.
- 01.8** The specific billing requirements accompany the approval letter sent from the FI after processing the provider's submission.

- 01.9** Investigational new drug studies (IND) are automatically qualified and it is not necessary to notify the FI for these studies.
- 01.10** CCC or designee determines the non-billable or protocol induced procedures from the information in the protocol document. The PI, CRC, other appropriate personnel, and CBO are included in this process to accurately complete this task.
- 01.11** The CCC or designee creates clear and precise billing instructions using the billing instruction and Form K templates. This information is distributed to the CRC and applicable staff within each department involved in the study.
- 01.12** The CCC or designee adds SIMR (3108) as a primary payer code upon receipt of each Form K in the “billing revisions screen” in MS4 (Sutter’s primary billing system). In the “insurance verification screen”, the CCC or designee adds SIMR (3108) as the primary carrier by moving the patient’s insurance(s) into the secondary, tertiary or fourth carrier slots. The CCC or designee updates notes in the “patient account notes screen” by informing CBO that SIMR has been designated as the primary payer and that the patient is a participant in SIMR clinical trial. CBO is instructed to follow the billing instructions pertaining to the trial.
- 01.13** If the patient’s bill is not received within 10 business days after their discharge date, the CCS or designee follows up with CBO.
- 01.14** Upon receipt of the patient bill, the CCC removes any protocol that includes labs, x-rays, or procedures ordered specifically for the clinical trial from the patient’s bill prior to submitting it to the insurance company.
- 01.15** Study related charges are removed regardless of whether or not the sponsor's budget covers the cost of these items. If the device is provided at no charge, then it cannot be included on the patient’s bill. Other sponsor provided supplies are coded appropriately and are not billed to the patient’s insurance.
- 01.16** If the sponsor does not supply the device and the provider has the approval from the FI, then insurance can be billed for the device. The charge must be comparable to that of an approved device serving the same medical purpose.

- 01.17** If the FI determined that the trial was not “qualified” and did not approve billing for the study, then the device and any related services required in preparation, use, and aftercare of the device is not billable to insurance.
- 01.18** Qualified Clinical Trials include:
- Trials funded or supported by the National Institutes of Health (NIH), Center for Disease Control (CDC), Agency for Health Care Quality (AHRQ), Center for Medicare and Medicaid Services (CMS), Department of Defense (DOD), Veterans Administration (VA).
 - Investigational New Drug Application (IND) reviewed by the FDA.
 - An IND Exemption under 21 CFR 312.2 [b], are considered “deemed” until qualifying and certifying processes are in place.
- 01.19** If the provider is receiving funds for standard of care through the study budget, these items or services cannot be included on the patient bill.
- 01.20** The CCC or designee removes study related procedures from the bill, makes a copy of the bill, sends one copy to CBO and one copy to SIMR’s financial analyst. CBO invoices all remaining charges to the patient’s insurance company.
- 01.21** To ensure billing instructions are followed, accounts are audited as per CO-QA.2.

APPLICABLE REGULATIONS AND GUIDELINES

42 CFR 405-207	Services Related to a Non-covered Device
42 CFR 405-209	Payment for a Non-experimental /Investigational (Category B) Device
42 CFR 411.406	Procedures for Medicare Contractors in Making Coverage Decisions
National Coverage Decision	Section 30-1, Routine Costs of Clinical Trials
Medicare Bulletin 402 (Clinical Trials-Medical Devices)	
Transmittal AB-00-89 (Claims Processing Instructions for Carriers, DMERCS, Intermediaries and Regional Home Health Intermediaries (RHHs) for Claims Submitted for Medicare Beneficiaries Participating in Medicare Qualifying Clinical Trials	
Transmittal AB-01-142 (Revised Guidelines for Processing Claims for Clinical Trial Routine Care Services	
REFERENCES TO SIMR SOPs	
CO-QA.2	Auditing Study Quality

01.22

QA-PO.02 AUDITING STUDY QUALITY

PURPOSE

The National Institutes of Health (NIH) require all institutions conducting clinical research to establish an internal mechanism by which their research conduct and data collection is reviewed and confirmed as meeting federal regulations and International Conference on Harmonization GCP. The Research Compliance Officer (RCO) has the responsibility of conducting institutional audits on clinical trials conducted at SHSSR. The categories of audits are:

- Protocol Compliance
- Billing Compliance
- Informed Consent
- Regulatory Compliance

The RCO is supported by the SIMR Medical Director (MD), Director, SIMR Operations (Dr) ,, and IDS pharmacist,. The RCO that will have the knowledge and ability to audit all of the above processes. The RCO will contact the personnel required in order to conduct the audit and will make arrangements to spend an appropriate amount of time auditing the selected study. Personnel contacted may include the PI, CRC, and appropriate study staff.

During the audit, the RCO refrains from discussing findings with the PI, CRC and/or the RT. However, if vital information is not available it is appropriate for the RCO to question the PI, CRC, and/or the RT to confirm its existence.

02.1 Protocol Selection Process

Any category of audit may be conducted on a study. The RCO along with the MD and DO determines the protocols selected for an audit. The three types of audits that may be performed are: 1) For cause, 2) Random selection, and 3) Directed selection.

- For cause: An audit for cause is performed for studies that are identified as having grave study conduct issues defined to be in violation of the ICH GPC guidance.
- Random selection: Any open study is subject to be selected for a random audit.
- Directed selection: A directed selection audit may be conducted on studies that are complex due to the nature of the patient population of study, standard of care, or research billing configuration.

02.2 Patient Selection Process

A random sample of 10% of the patient population is selected for auditing. When a 10% sample is less than 5 patients, the percentage is increased to include at least 5 patients in each audit sample. If a study has enrolled less than 5 patients, all patients are audited.

PROTOCOL COMPLIANCE AUDIT

The purpose of the protocol compliance audit is to ensure the study has been conducted appropriately and adheres to the federal regulations and GCP including verification that the study conduct corresponds to the protocol and all amendments as written.

PROCEDURE

Once a study has been selected for auditing, the RCO:

- 02.3** Notifies the PI and CRC of the intent to audit the study via a formal letter and e-mail. The PI and CRC are asked to assist the auditors to provide information that might not be readily available or to make known the location of study specific data that might not be obvious to the RCO..
- 02.4** Notifies the RT of the intent to audit the study via e-mail. The RT is asked to provide the protocol and all amendments to the auditor to document the evolution of the study.

- 02.5** Creates audit forms to collect the study's required information. Customized audit forms are created for each study. The exception to this is the regulatory audit, which has a standard audit form available to the auditors (Appendix E).
- 02.6** The IRB, PI, and sponsor are immediately notified when major violations are found during an audit.

BILLING COMPLIANCE AUDIT

The purpose of the billing compliance audit is to ensure that charges for study related procedures, exams, or tests generated during the study are billed to the appropriate party.

PROCEDURE

- 02.7** When a study has been selected for an audit, the RCO or designee notifies the SIMR Contracts and Compliance Specialist (CCS) of the intent to audit the study via a formal letter and e-mail.
- 02.8** The RCO can obtain a copy of the Form K, billing instructions and patient invoices for the study period.
- 02.9** The CRC, CCC and the Central Billing Office (CBO) are notified immediately when billing compliance issues are identified.

INFORMED CONSENT AUDIT

The purpose of the informed consent audit is to ensure that the consent forms were signed and dated appropriately by the patient or patient representative and a valid study consentor. This audit also compares the date of the consent against the study start date to confirm that the patient was consented prior to initiation of the research.

PROCEDURE

- 02.10** The RCO notify the PI and CRC of the intent to audit the study via a formal letter and e-mail. The PI and CRC may be asked to assist the auditors in providing information about the filing of the consent form.
- 02.11** The RCO obtain study start information to verify that the consent was signed prior to the study intervention.
- 02.12** Protocol regulatory information is obtained to ensure that study participants have signed the correct version of the consent.
- 02.13** The signature of the person conducting the consent process is validated.

REGULATORY COMPLIANCE AUDIT

The purpose of the regulatory compliance audit is to ensure all appropriate and required regulatory documentation is available in the regulatory binders, all protocol amendments are consistent between the sponsor and the IRB submissions, and that all information in the regulatory binder is updated and current.

PROCEDURE

- 02.14** The RCO notifies the PI, CRC, and the RT of the intent to audit the study via e-mail and formal letter.
- 02.15** The RCO obtains a standard regulatory audit form and modifies this as needed.
- 02.16** The RCO requests a date, time and place to review the regulatory binder from the RT.
- 02.17** The IRB, PI, and sponsor are notified when major violations are identified.

AUDIT FINDINGS

- 02.18** The results of all audits are summarized in an audit report prepared by the RCO (Appendix E). The report is signed and dated by the RCO and DO.

- 02.19** An audit findings letter and report is sent to the PI for review and comments.
- 02.20** The PI is given the opportunity to respond to the findings within a specified period of time.
- 02.21** The PO reviews the PI's responses and signs and dates a final letter and issues it to the PI, MD, and IRB.
- 02.22** The IRB keeps the RCO and DO informed of actions and outcomes directly related to the information provided by the audit.
- 02.23** All information provided by the IRB is documented and included in the study's audit file.
- 02.24** The results of all audits are included in the semiannual report to the Medical Policy Committee.

APPLICABLE REGULATIONS AND GUIDELINES

ICH GCP 4.5	Protocol Compliance
ICH GCP 4.8	Informed Consent of Trial Subjects
ICH GCP 4.9	Records and Reports
ICH GCP 4.11	Safety Reporting
ICH GCP 8.1	Essential Documents – Before the Clinical Phase of Trial Commences
ICH GCP 8.2	Essential Documents – During the Clinical Conduct of Trial
ICH GCP 8.3	Essential Documents – After Completion or Termination of the Trial
21 CFR 50.20	General Requirements of the Informed Consent (IC)
21 CFR 50.23	Exceptions from General Requirements (IC)
21 CFR 50.27	Documentation of the Informed Consent (IC)
REFERENCES TO SIMR SOPs	
CO-SS.02	Regulatory Submission Process
CO-SS.07	Adult Informed Consent
CO-SS.08	Surrogate Consent
CO-SS.09	Pediatric Informed Consent
CO-SS.10	Pediatric Assent
CO-SM.01	Records and Case Report Forms
CO-SM.03	Adverse Event Reporting
CO-SM.03	Serious Adverse Event Reporting

CO-QA.01	Billing Compliance
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QA-PO.03 WORKLOAD BALANCE

PURPOSE:

- In Accordance with Sutter Health Standards for Business Conduct, SIMR is implementing guidelines that address workload issues and concerns. This process is to encourage and facilitate communication and teamwork among staff members. There are many options to assist staff with workload variances including support from manager or coworkers, and various educational opportunities through company sponsored programs as necessary. It is ok and encouraged by management to ask for assistance.
- It is expected that these guidelines be used for all areas within SIMR including but not limited to administration, front office, coordinators, regulatory staff, research services staff, lab staff and clinical staff. Ultimately, all staff is responsible for their own workload, and accountability is required.
- All currently trained employees should mentor new staff members as necessary in any areas of need. Each employee will be given various training opportunities to take classes by a Sutter sponsored or outside vendor if needed.
- Professionalism and Accountability – Unbalanced Workload may contribute to a stressful work environment. Staff members are responsible for conducting themselves in a professional manner and according to Sutter Health Standards for Business Conduct. It is important that stress levels not override professional behavior within the workplace.

PROCEDURES:

- Assess when Assistance May be needed – You are responsible for handling your workload in a professional manner. Getting assistance with your workload may require reworking your strategy.
- **Steps to take:**

Prioritize workload, clearly taking into account timelines and approaching deadlines. Regularly, present a report to your manager of time allocation and resources needed to accomplish your

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tasks against real time available. Microsoft Outlook is a tool that can be used to assist with resource allocation and schedules. In addition to one on one discussion with management, both SIMR CRC and SIMR Staff Meetings will include in the agenda, time to discuss “workload balance” issues. An opportunity will be given to discuss openly at the meetings upcoming challenges so the department can lend support where necessary and make the decision to reallocate resources if needed. Communicate day to day needs to co-workers by describing your issues, concerns and how someone can best assist you.

Action Item lists and deadlines should be adhered to and reviewed regularly

APPLICABLE REGULATIONS AND GUIDELINES

Sutter Medical Center, Sacramento Organizational Ethics Statement
Sutter Medical Center, Sacramento Human Resources Policy Guidelines for Disruptive Behavior and Prevention of Workplace Violence

QA-PO.04 FDA INSPECTION SITE VISIT

PURPOSE:

This SOP describes the responsibilities of SIMR staff when preparing for and participating in an US FDA site inspection. Applies to all SIMR personnel

PROCEDURES:

Upon notification of an impending US FDA inspection, the clinical research personnel who first receives notification will inform the principal investigator (in most cases, the PI is first contacted). The CRC or site manager will immediately notify the sponsor. In the case that notification comes from the sponsor, the above individuals will be notified as stated.

The principal investigator must be available during the US FDA inspection. If the proposed date of the inspection is in conflict with the principal investigator's schedule, the principal investigator or designee may contact the US FDA inspector to request rescheduling at a mutually agreed time. The IRB is to be notified as well.

Initial contact with US FDA representative

Upon initial contact and introduction to the US FDA inspector, the greeting staff member will:

1. Ask for the ID of the inspector and the purpose of the visit. (agent will produce an ID card and/or badge) You may not touch or take a copy of the ID/badge.
2. Unless the greeting staff is the study CRC/PI/Site manager, no additional conversation will be initiated.
3. Staff member will contact CRC/PI/Site Manager to continue audit procedures.

All Staff

At least one (1) SIMR employee should be available at all times for the US FDA inspector. The CRC or Site Manager is to escort the agent to a prepared room where it will be appropriate for document retrieval and confidential discussions.

Continue business as usual. All staff should be aware of the audit and be prepared for call by SIMR CRC to participate in inspection as needed.

Copy only what inspector asks for, keep a copy of every document given to inspector, never volunteer information to the inspector.

Answer questions honestly without elaboration.

Ask for clarification if you do not understand the question being asked.

Schedule close out meetings to discuss any findings once the investigation is completed. This meeting must include the PI.

If a form 483 has been issued begin corrective action planning if necessary as soon as possible (within 15 days of the close/review meeting. A Form 482 may not be issued, however a letter from the US FDA may be received at a later date with findings or corrective actions, this too needs to be responded to within 15 days of receipt of the letter or actions.

Conduct Mock US FDA inspections yearly

APPLICABLE REGULATIONS AND GUIDELINES

- ICH GCP 1.29
- 21 CFR 812 - Investigational Device Exemptions
- 21 CFR 50 - Protection of Human Subjects
- 21 CFR 54 – Financial Disclosure
- 21 CFR 56 - Institutional Review Boards
- www.fda.gov/CDRH/DEVADVICE/ide/enforcement.shtml

QA-PO.06 SIMR EMERGENCY PROCEDURE

PURPOSE

The purpose of this policy is to provide a responsive mechanism for employees of Sutter Institute for Medical Research (SIMR) in the event of an emergency and/or disaster that may impact or have implications on our research facility or infrastructure. This Policy defers to the Sutter Medical Center Sacramento, Emergency Management Program in all situations. This SIMR policy is supplemental and only relative once the situation has been reviewed and approved by Sutter. The goal is to ensure a seamless coordination and collaboration between the groups.

SCOPE

Applies to all SIMR Clinical Trials personnel and SIMR Research Services personnel.

ABBREVIATIONS:

SIMR– Sutter Institute for Medical Research

PI- Principal Investigator

CRC- Clinical Research Coordinator

SMCS – Sutter Medical Center Sacramento

MSDS – Material Safety Data Sheet

VELOS- VELOS eResearch <https://sutter.veloseresearch.com/eres/jsp/ereslogin.jsp>

PROCEDURE

Once Sutter has authorized departments to go to work, **SIMR Safety Captain** is to assess the impact of the emergency on the SIMR Clinical Trials and SIMR Research Services personnel and contact staff with proper plan to follow including the following:

Communicate to SIMR staff about significant steps and roles using an audit checklist. Contact each employee responsible for a site location and use checklist.

MSDS information to be given to all staff

Contact the facilities where equipment is located and assess condition of facility, (i.e., drug refrigerators, freezers, storages, computers, monitors, source documents). This includes drug stored with the Research Pharmacist. Assess patient data, source data, sponsor data, drug logs, and condition of each.

Safety Captain to assess Resource allocation for each project area and report to Director the resource needs. Contact all Sponsors that we are working with and advise them of status.

CO-FM SIMR FINANCE MANAGEMENT

PURPOSE

The purpose of this SOP is to document the management of SIMR's revenue and expenses.

POLICY

Sutter Regional Finance follows an accrual based accounting system. This means that revenue is recognized upon completion of study activities rather than upon receipt of payment.

SCOPE

This document covers the financial operations within Sutter Institute for Medical Research. The document is divided into several sections

CO-FM.01	Accounts Payable- Section
CO-FM.02	Financial Tracking and Reporting
CO-FM.03	Deferred Revenue
CO-FM.04	Accounts Receivable
CO-FM.05	Cost Analysis

CO-FM.01 ACCOUNTS PAYABLE

INTRODUCTION

Accounts payable are liabilities that SIMR owes to suppliers, vendors, and investigators. For SIMR to pay its bills, a check request is sent to Sutter Finance Accounts Payable Department (Accounts Payable) who processes the check so that the recipient is paid by the payment due date. For all types of payments, the original check request is sent to Accounts Payable and a copy of the check request is placed in the appropriate study contract finance file or general office file drawer. Director approval is obtained for all vendor invoices and expense reports before submission to Accounts Payable.

There are 4 general types of payments:

1. Recurring monthly payments of the same amount each month. A check request for the entire fiscal year (or contract period) generates the payment.
2. Payments for study related procedures usually by receipt of an invoice from the vendor.
3. Employee reimbursements on expense reports.
4. PI payments for visits that have occurred where the invoice is generated by SIMR on behalf of the PI.

RECURRING MONTHLY PAYMENTS

Medical Director Stipend

01.01 A contract is signed by Chief Medical Officer and the Medical Director which states the time period of payments and the amount of the payment.

01.02 The Medical Director completes, signs, and dates a physician activity report (PAR) each month.

01.03 Chief Medical Officer signs the report and forwards to the financial analyst who submits the PAR to the Accounts Payable Manager each month.

01.04 The previously done check request for recurring monthly payments allows the check to be processed.

PAYMENTS TO VENDORS FOR ADMINISTRATIVE SERVICES

01.05 Approval is obtained by the Director on the invoice or check request form prior to submitting the check request to Accounts Payable.

PAYMENTS FOR STUDY RELATED PROCEDURES

01.06 Invoices received for study-related procedures are approved by the Director and reconciled with the vendor contract (if applicable).

EMPLOYEE REIMBURSEMENTS

01.07 Employees complete an expense form and obtain the required approval signatures according to the instructions and code the entries to reflect the correct activity number for each expense. All receipts should be attached to the expense report.

01.08 Reports need to be submitted to Financial Analyst no later than the Tuesday of the close of the pay period in order to receive the reimbursement with the paycheck on that Friday.

01.09 A copy of the expense report is kept in the general office payables file drawer.

PAYMENTS TO INVESTIGATORS

Prior to study enrollment, an investigator agreement is developed between SIMR and the principal investigator (PI) that defines the responsibilities of the PI and payment schedule for study related procedures. Subject enrollment should not begin until both parties sign the agreement. Investigators are compensated for research related activity in the month after the work was completed. The payment period is generally between the 26th of the month prior to the study activity through the 25th of month that the activity occurred which is the time period that the Coordinators report study visits.

01.10 The SIMR Director works with the PI to complete the investigator agreement.

01.11 Prior to signing a study contract, a review of the study schema is done and negotiation of the study budget with the study sponsor to obtain a budget that will cover study expenses.

01.12 The Financial Analyst prepares the study accrual worksheet using information from the study contract. The worksheet is populated at the end of each month with information from the Coordinator's logs to show the current month's visits and therefore revenue accruals.

01.13 The Financial Analyst generates an invoice on behalf of the PI by the end of the second week of the month. The invoice details the patient initials and date of the study-related activity performed and is submitted to the accounts payable department who cuts checks to the respective investigator or to SMF if the PI is an SMF employee. SMF will pay the PI in the next quarterly SMF payment.

01.14 A letter and copy of the invoice is sent to each investigator after the invoice has been sent to Accounts Payable. An additional copy is sent to SMF when applicable such as departments where the PI funds are kept by SMF.

CO-FM.02 FINANCIAL TRACKING AND REPORTING

Study revenue and expenses are documented in the month that the activity occurred as opposed to when the cash is received.

02.01 Review the budget and contract to understand the revenue and expenses associated with each clinical study.

02.02 The Financial Analyst creates a spreadsheet based on study related activity stated in the contract and study budget. This information is used for the Accounts Receivable Schedule (called Attachment C in the Monthly Close documents) and the Accounts Payable Schedule (called Attachment D in the Monthly Close documents).

02.03 The Financial Analyst and the SIMR Director review the spreadsheet to validate its accuracy at the beginning of the study.

02.04 The Financial Analyst prepares a summary sheet at the end of the study when all activities are completed and all revenue has been received to show the overall revenue versus expenses. The information for this summary is obtained from Lawson. It is report AC290.

SEMI-ANNUAL REPORT TO INVESTIGATOR

The semi-annual report keeps study investigators updated on the payments to the investigators on their studies. Semi-annual reports are compiled and sent to every physician participating in a clinical trial for the six months ending, June 30, and December 31 for each year.

02.05 The report contains the following information; The date and amount paid to the PI for each study visit each month

02.06 A cover letter for the report is also sent to the investigator.

ACTIVITY BASED ACCOUNTING OF STUDY RELATED ACTIVITES

SIMR tracks its study-related revenue and expenses using accounting units and activity codes. Following are SIMR's accounting units. New studies are assigned an activity code under one of the accounting units based on the funding source of the study:

- SMF Clinical Trials 227080. This accounting unit will be phased out beginning in 2007. New SMF clinical trials will be given the accounting unit 227085.

- Clinical Trials 227085
- Federal Funded Trials 227066

02.07 New studies are assigned an activity code under the appropriate accounting unit based on the source of funding and whether the PI is an SMF employee. After 2007, the 227080 accounting unit will not be used so it will be immaterial if the PI is a SMF employee.

02.08 Employees spending time on study-related activities charge their time to the appropriate accounting unit and activity code by entering this in Kronos.

02.09 Grant funding that is currently in SIMR deferred revenue will not be booked as income until employees' charge their time to the study or there are vendor expenses for study related activity.

Tracking of SIMR overhead costs

SIMR includes a line item in all of its study budgets for study overhead. Overhead is designed to cover the cost of contract management, financial management, and administrative support.

SIMR Administration (228610) does not accrue revenue. However, the overhead amount from the studies, are transferred from the activity-based accounting units into the SIMR Administrative account number 228610-68400. There is one administrative cost center and 4 additional cost centers that define departments within SIMR.

SHC-IRC 228611

SIMR Training lab 227060

Pharmacy 227064

Research Services 227063

SIMR Administration 228610

SHC-IRC, SIMR Training lab, and Pharmacy are self-contained departments. This means that all revenue and expenses for these departments remain with these cost centers.

The Research Services cost center does not accrue revenue. Employees of the Research Services department may also charge time to study-related activity numbers.

MONTHLY CLOSE DOCUMENTS

At the end of each month, the Financial Analyst prepares the Monthly Close documents to be sent to Sutter Finance. These documents record the study financial transactions for the month. These documents are due by the 2nd work day of the following month. The documents consist of the following:

- a. Close Cover Page which lists the activity numbers opened that month, inpatient payables, SMCF transfers to studies, deferred revenue transfers to studies, and miscellaneous transfers from other departments to SIMR studies or the training lab invoices.
- b. Bank Deposit Log
- c. Schedule of Accounts Receivable
- d. Accounts Payable Schedule
- e. Pharmacy transfer payments
- f. Backup documents for inpatient payables, SMCF transfers, deferred revenue transfers and miscellaneous transfers

CO-FM.03 DEFERRED REVENUE

Deferred revenue refers to any advance payment for study procedures that have not yet been performed. Grant money currently in deferred in previous years will remain in deferred revenue until employees charge their time to the study. New checks received from extramural grants will not be deposited by SIMR but given to Sutter Medical Center Foundation (SMCF) for deposit.

Because SIMR's policy is to accrue revenue when study-related activity occurs, deferred revenue cannot be considered income until the activity occurs for which the revenue was marked by the Sponsor. This policy is in place so that in the event that the activity does not occur, SIMR has funds available to reimburse the Sponsor. It is also in place so that SIMR can ensure that grants received are sent to SMCF for deposit and used for the purpose that they are intended.

03.01 Deferred revenue is recorded in the Deferred Revenue Spreadsheet maintained by Sutter Finance. Checks that are to be deferred are recorded on the Bank Deposit Log (called Attachment A in the Monthly Close documents) are coded to Accounting code 221000-21035-0001 by the Finance Department.

03.02 When study related activity occurs, the funds needed to cover the cost of the activity are subtracted from this account and added to the Accounts Receivable Schedule and also recorded the Monthly Close Cover document. This is when the revenue is booked as income. Sutter Finance will subtract the funds from the Deferred Revenue Spreadsheet.

03.03 Each month the amount of remaining deferred revenue is printed out. It is reviewed during the month for any study related activities that have occurred and need the deferred funds. This is called recognition of the deferred funds.

CO-FM.04 ACCOUNTS RECEIVABLE

INTRODUCTION

Accounts receivable are revenue that is owed to SIMR based on completion of activities documented in a study contract but where payment has not actually been received. The dollar value of the study activities are based on the contract budget. As patient visits, surgeries, procedures, etc. occur, the dollar values of these activities are accrued as revenue to the study. Study visits and surgeries are paid by the Sponsor at their schedule upon completion of Case Report Forms (CRFs) by the CRCs.

04.01 The CRCs maintain a subject-tracking log and enter the information in the software program called Velos eResearch to document patient visits and other interactions that the CRC has with study subjects. The subject tracker log is also given to the SIMR Financial Analyst at the end of each month

Payments requiring invoicing

04.02 Study visits and surgeries are paid by the Sponsor without an invoice being sent by SIMR. Those items that require an invoice from SIMR in order for SIMR to receive payment are:

- * Study startup fees
- * IRB fees
- * Special projects
- * Reimbursements for expenses by SIMR or patient not covered in the visit prices.

04.03 The SIMR Financial Analyst generates an invoice in MS Word that states that payment is due within 30 days of the invoice date.

04.04 After sending the invoice to the Sponsor, a copy is made and placed in the outstanding invoices binder. Once paid, the check copy and invoice copy is pulled from the outstanding invoices binder and filed in finance section of study file.

04.05 The outstanding invoices binder has a cover sheet listing all the current outstanding invoices. This cover sheet is updated monthly.

The following occurs at the end of each month by the financial analyst:

04.06 Data entry on the study worksheet for each study that contains a list of all study activities that require sponsor payment. Creation of a new spreadsheet when there are first visits on a study.

04.07 Discrepancies between the CRC patient-tracking log and the study worksheet are reconciled at this time.

04.08 Preparation of the Accounts Receivable Schedule to determine the appropriate amount to be accrued based on the information provided by study coordinators, the training lab, and IRC submission.

04.09 Update of the report to remove accounts receivable as cash is received or deferred money recognized.

COLLECTION OF DELINQUENT PAYMENTS

Definition of delinquent payments

04.10 Payments requiring invoicing are considered delinquent if they are not received after 60 days.

04.11 Study activity payments are considered delinquent if they are not received after 90 days of the activity.

Awareness of delinquent payments

04.12 The SIMR finance department becomes aware of delinquent payments through:

- Review of the accounts receivable schedule that occurs at the end of each month.
- Review of the outstanding invoices binder.

Collection of delinquent payments

04.13 To collect delinquent payments, the SIMR Financial Analyst contacts the company that owes payment. The date calls or e-mails are made and the outcomes of the calls are recorded on the invoice in the outstanding invoices binder.

04.14 If the company is not able to make payments, the SIMR director meets with the company representative to discuss a payment plan or potential write-off.

RECEIPT OF REVENUE

04.15 The SIMR Financial Analyst records checks and electronic fund transfers (EFTs) received into the Bank Deposit Log (called Attachment A in the Monthly Close documents). Training Lab checks and IRB checks are also recorded in the Training Lab Invoice Table and IRB Invoice Table respectively.

04.16 Checks are deposited with 7 days of receipt. Checks exceeding \$10,000 are deposited on the day that they are received.

04.17 All payments are to be fully reconciled to the study activities. Often checks arrive with a payment detail document from the Sponsor. If the purpose of the check is unknown, a call or e-mail is made to the Sponsor for explanation and/or a payment detail document. Sometimes the payment detail is received before the check. The payment detail is held until the check arrives and is then matched up to the check.

04.18 A check reconciliation form is completed and attached to the check copy in the financial section of the study contract folder. The reconciliation form explains the study activities that are paid by the check. Any payment detail information sent by the Sponsor is also attached to the check copy.

04.19 The payment-tracking log located in the financial section of the study contract folder is updated at the end of the month.

CO-FM.05 COST ANALYSIS

Upon completion of a study, a cost analysis is conducted to determine if the study budget met the cost requirements of the study. Information obtained from a post-study cost analysis provides useful feedback to be used for developing budgets for future studies.

LAWSON report AC290 is run at the end of the study for each fiscal year of the study activities. The data is entered on the Closed Study Fiscal Summary spreadsheet.

The revenue versus the expenses for the study is reviewed by the Financial Analyst, SIMR Director and SIMR Medical Director.

For studies where the overall expenses exceeded the revenue, SIMR can request up to \$5,000 from SMCF to cover the excess expenses.

An AC290 report can be run at any time during the study to examine the current financial status.

Standard operating procedures outlined below provide continuity and guidelines during the conduct of clinical studies. These policies include sponsor-initiated monitoring visits, reporting AEs, progress reports, and drug accountability requirements.