UCSF Helen Diller Family Comprehensive Cancer Center

University of California, San Francisco
Helen Diller Family Comprehensive Cancer Center

Clinical Research Activation Policy for Industry Trials

Process and workflows for clinical research activation of industry trials

Table of Contents

Purpose 1
Scope 2
Background 2
Procedures 2
1.0 Study Activation – Submission Process 2
2.0 Site Committee Submission and Review 2
3.0 Protocol Review and Monitoring Committee (PRMC) Submission 3
4.0 Office of Clinical Trial Activation (OCTA) 3
5.0 Industry Contracts Division (ICD), Office of Sponsored Research 4
6.0 Institutional Review Board (IRB) 4
7.0 Mid-Activation Protocol Amendments 4
8.0 Activation Holds 5
9.0 Sponsor Communication 5
10.0 E-Regulatory Systems and E-Source 5
11.0 HDFCCC Policies 6
Policy Exemptions 6
References 6
Appendices 6
Policy Approval 7
Appendix 1 – HDFCCC Activation Workflow for Industry Trials 8
Summary of Changes 9

Purpose

The purpose of this Helen Diller Family Comprehensive Cancer Center (HDFCCC) policy is to outline the activation workflows and requirements for interventional clinical research studies sponsored by industry. This policy governs the clinical research start-up (also referred to as activation) process as it pertains to both UCSF study teams, and study sponsors.

Scope

This policy applies to all cancer center interventional studies, both single and multi-center, sponsored by industry.

Definitions

- *Activation:* activities involved in the start-up of clinical research studies starting at Site Committee review and ending with the study being open to accrual.
- *Interventional Clinical Trial:* As defined by the National Cancer Institute (NCI), Interventional Clinical Trials are those trials in which "individuals are assigned prospectively by an investigator based on a protocol to receive specific interventions. The participants may receive diagnostic, treatment, behavioral, or other types of interventions. The assignment of the intervention may or may not be random. The participants are followed and biomedical and/or health outcomes are assessed."

Background

The HDFCCC seeks to activate interventional industry trials in a timely manner. A workflow has been established to ensure activation proceeds through the required steps, and is reviewed for scientific rigor, feasibility and ethical considerations. Failure to follow these workflows or meet specified requirements may result in delayed study activation.

Procedures

1.0 Study Activation – Submission Process

A schematic of the study activation workflow can be found in Appendix 1. Descriptions of the offices and departments involved in study activation are provided in subsequent sections below. Following Site Committee approval (see section 2.0), the study team will start the activation process by submitting to the Protocol Review and Monitoring Committee (see section 3.0), the Office of Clinical Trial Activation (OCTA) (see section 4.0) and the Institutional Review Board (IRB) (see section 6.0). OCTA will route the study to the Industry Contracts Division (ICD) (see section 5.0) as appropriate.

2.0 Site Committee Submission and Review

The disease/discipline-focused Site Committees review studies for scientific merit, feasibility, and prioritization. The process for Site Committee review is governed by the HDFCCC PRMS Site Committee Review Policy. In order to receive full review at Site Committee, a near- final version of the protocol is required. Site Committees may make the decision to not participate in the study at any point up to PRMC submission.

Questions from Site Committee members regarding feasibility, scientific merit, or operations may be asked of the sponsor. Sponsors are expected to reply to these queries within 1 week of the request.

3.0 Protocol Review and Monitoring Committee (PRMC) Submission

The PRMC performs a mandatory centralized review of studies for scientific merit and feasibility. The process for PRMC review is governed by the HDFCCC PRMS Site Committee Review Policy. PRMC submission is the start of the activation timeline at the HDFCCC. Studies will not be accepted by the PRMC for review until the following documents have been received:

- Final protocol
- Investigator's brochure or packaging insert (if applicable)
- All Site Committee review forms and Protocols in Development list
- Site Committee Competing Protocols list (if applicable)
- Lab manual (if not stated in protocol)
- Pharmacy manual (if not stated in protocol)
- Imaging manual (if not stated in protocol)

Failure to include all above study documents will result in the study being returned to the Site Committee without review. Questions from PRMC members regarding feasibility, scientific merit, or operations may be asked of the sponsor. Sponsors are expected to reply to these queries within 1 week of the request.

Additional study activation-related documents that should be available at the time of PRMC submission:

- Informed consent form template(s)
- Clinical Trial Agreement (CTA) template
- Draft budget and/or fee schedule (if applicable)
- Patient facing documents (i.e., drug diaries, subject information cards) (if applicable)
- DSMC Charter (if applicable; draft acceptable)
- FDA Study May Proceed Letter (i.e., IND approval letter--if IND# not included in protocol)

Once all documents have been received the study team may submit the study to PRMC for review.

4.0 Office of Clinical Trial Activation (OCTA)

OCTA is a centralized UCSF unit responsible for building the study calendar in our Clinical Trial Management System (CTMS) OnCore©, Medicare Coverage Analysis (MCA) and budget. The study team will be in regular communication with the relevant analysts at OCTA to keep the study moving along the activation queue. Draft MCA and budgets will be provided by OCTA to the study team and Principal Investigators (PI) for review. Both the study team and OCTA will review and provide comments back to drafts within 7 days. If the PI or study team is unresponsive to OCTA's communication, study activation may be de-prioritized.

The PI may delegate the review and approval of draft MCAs and budgets to co-PIs or appropriate study personnel in the roles of (or equivalent to): Clinical Research Managers (CLIN RSCH SUP 2), Clinical Research Supervisors (CLIN RSCH SUP 1), Senior Clinical Research Coordinators or Protocol Project Managers (Sr. CRCs). All study staff delegated to review and approve draft MCAs and budgets will be trained appropriately and their qualifications will need to be on record with OCTA.

Once study team approval is obtained, OCTA will subsequently work with the sponsor on the

budget. Sponsors are expected to complete budget approval within 35 days. If the sponsor is unresponsive to OCTA's communication, study activation may be de-prioritized.

5.0 Industry Contracts Division (ICD), Office of Sponsored Research

ICD is a centralized UCSF unit within the Office of Sponsored Research that reviews, negotiates and executes all industry sponsored research contracts. These include agreements for non-disclosure/confidentiality, material transfers, data use, research agreements, collaborations, clinical trials, and other agreements that may be funded by an industry sponsor. Master contracts are feasible, and sponsors should connect with the ICD Director for further discussion. If a master contract is available, every effort will be made to add the new study to the master contract. ICD will work with the sponsor on the contract and expects responses to questions and redlines within 10 business days. If the sponsor is unresponsive to ICD's communication, study activation may be de-prioritized.

6.0 Institutional Review Board (IRB)

UCSF IRB workflows, policies and meeting schedules are available on the UCSF IRB website. Every effort is made to complete initial IRB review within 45 days of IRB submission. Please be aware of informed consent template language mandated by UCSF as changes to this language may delay our ability to submit the study.

If an external IRB will be used, sponsors must notify the study team before submission to PRMC to ensure adequate time to confirm that the study meets the UCSF criteria for using an outside IRB; the appropriate fees can be added to the study budget; and, the IRB reliance application can be submitted to the UCSF IRB.

7.0 Mid-Activation Protocol Amendments

Other than administrative amendments, protocol amendments submitted mid-way through the activation process will cause substantial delays in the overall activation timeline, since all workflows in the activation pipeline have to be re-visited to ensure updates are appropriately reflected in the OnCore calendar, MCA, budget, IRB approval and CTA. Because of this disruption to the workflow, overall, it is more efficient for mid-activation amendments to be addressed and approved AFTER the original protocol is approved.

For this reason, it is **strongly recommended** that mid-activation amendments (other than administrative amendments) be held until the original protocol is approved. UCSF study teams are instructed to prioritize approval of the original protocol, even if it means to hold on enrollment, while an amendment is subsequently addressed. Mid-cycle amendments that are deferred until after approval of the original protocol will be prioritized.

NOTE: To submit an amendment to the UCSF activation pipeline, a red-line version of the protocol, summary of changes and revised budget (if applicable) are required. Failure to do so will significantly delay the activation process.

8.0 Activation Holds

Protocol status should be updated to ON HOLD in OnCore, if a sponsor or PI puts the protocol on hold for any reason *prior* to opening the study to accrual.

Studies are placed on hold in the activation process if the activation workflows are impacted by events or restrictions external to the University activation process. In general, the On Hold status should be used if the study team anticipates delays longer than 14 calendar days (unless otherwise specified below) and results in the activation process being halted (PRMC, MCA, budget, IRB or contracting).

Examples include but are not limited to:

- Mid-activation amendment is pending from the sponsor and UCSF cannot proceed with the current version. All activation work on the current protocol is stopped;
- Sponsor requests a hold;
- Change in study drug formulation or delays in procurement of study drug or device;
- FDA hold or FDA delays > 30 days;
- Contract signed by sponsor but the sponsor is not ready to activate the site yet (i.e., has not issued the activation letter or conducted the site initiation visit);
- Reduced staffing in a clinical research program, which results in the delay in submission to the OCTA pipeline.

If there is another event (other than listed above) that the study team or PI believes warrants the status of On Hold, the study team must reach out to the CRSO Director for adjudication. The CRSO Director will adjudicate along with the CRSO Medical Director, PRMS Manager and PRMS Chair. Sponsors will be notified of the On Hold status by the study teams and the proposed timeline to re-start activation.

9.0 Sponsor Communication

HDFCCC study teams will maintain close communication with sponsors and relevant Clinical Research Organizations. Sponsors are expected to be responsive to communications and requests for information and feedback. If a sponsor (or its representative Clinical Research Organization) does not respond to or acknowledge requests within 7 days, the HDFCCC reserves the right to put study activation on hold or terminate the study (in the case of egregious lack of communication).

10.0 E-Regulatory Systems and E-Source

All HDFCCC industry sponsored studies may use Complion as an e-regulatory system. Use of the e-regulatory system allows for remote monitoring of all regulatory files and source documents not available through the UCSF electronic medical record. As of June 2020, sponsors may request access to the UCSF electronic medical record system (APeX) to view source documents directly in APeX. Sponsors must discuss the use of e-source and e-regulatory systems with the study team during the activation process, since appropriate agreements must be put in place.

11.0 HDFCCC Policies

All HDFCCC policies are available on the HDFCCC website. Sponsors must familiarize themselves with the HDFCCC policies at the start of the activation process and ask questions early so that all issues are addressed prior to budget and contract negotiation.

Policy Exemptions

None

References

None

Appendices

Appendix 1: HDFCCC Activation Workflow for Industry Trials

Policy Approval

This policy document was approved by the following personnel on the following dates:

DocuSigned by:
Eric Small
7ECB32D327E3438...

12/21/2021

Eric Small, MD
Deputy Director
Helen Diller Family Comprehensive Cancer Center

Date

DocuSigned by:
Kate Shumate
80D38159E89D41B...

12/17/2021

Kate Shumate, MBA CCRP
Director, Administration and Planning
Helen Diller Family Comprehensive Cancer Center

Date

DocuSigned by:
Charalambos Andreadis
6E7C7F82042E47D...

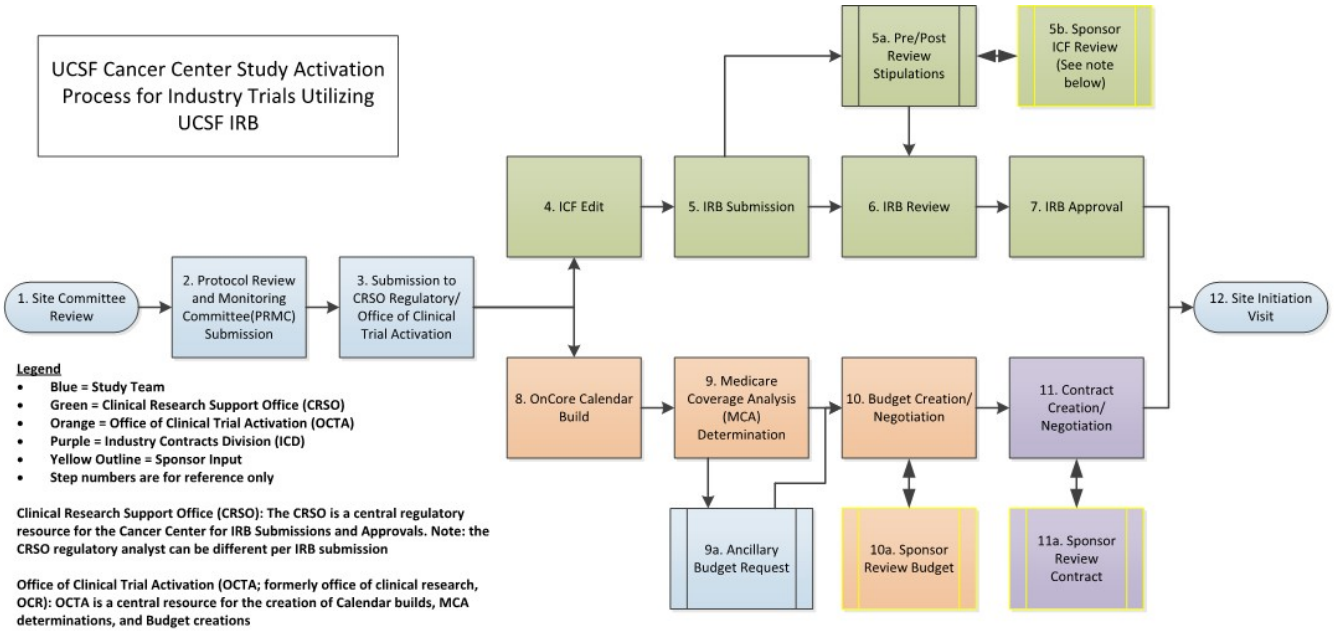
12/19/2021

Charalambos Andreadis, MD
Clinical Research Support Office Medical Director
Helen Diller Family Comprehensive Cancer Center

Date

Policy contact:
Andrea Skafel, Clinical Research Support Office Director
Andrea.skafel@ucsf.edu; +1 415 502 5805

Appendix 1 – HDFCCC Activation Workflow for Industry Trials



Legend

- **Blue = Study Team**
- **Green = Clinical Research Support Office (CRSO)**
- **Orange = Office of Clinical Trial Activation (OCTA)**
- **Purple = Industry Contracts Division (ICD)**
- **Yellow Outline = Sponsor Input**
- **Step numbers are for reference only**

Clinical Research Support Office (CRSO): The CRSO is a central regulatory resource for the Cancer Center for IRB Submissions and Approvals. Note: the CRSO regulatory analyst can be different per IRB submission

Office of Clinical Trial Activation (OCTA; formerly office of clinical research, OCR): OCTA is a central resource for the creation of Calendar builds, MCA determinations, and Budget creations

Protocol Review and Monitoring Committee = Scientific Review Committee

Notes to Sponsor:

- A finalized protocol and Investigator's Brochure is required to initiate Step 1.
- The following items are required to complete Step 2: **Protocol, Investigator Brochure(s), ICF Template(s), CTA Template, Draft Budget or Fee Schedule, Lab Manual (if not stated in protocol), Pharmacy manual, Imaging Manual (if applicable). Patient handouts including reimbursement materials (if applicable), FDA IND Approval to Proceed Letter.**
- In order to expedite the activation process, Sponsor's ICF comments will be submitted with post-IRB review stipulations.
- IRB Approval and OnCore Calendar Build/MCA/ Budget/Contracts development occur in parallel. However, the CTA cannot be fully executed without IRB Approval
- Budget and contracts analysts are not typically assigned until step 10 and 11 respectively.
- Institutional Biosafety Committee (IBC) submissions typically occur during Step 3 and do not need to be approved prior to IRB submission, but must be approved prior to IRB approval
- IRB approval will not be provided until PRMC and IBC approval is obtained

Clinical Research Policy Revision
Summary of Changes

Policy Title: Clinical Research Activation Policy for Industry Trials
Version Date: December 16, 2021
Version Number: Revision 1

Section(s)	Summary of Change	Rationale
3.0	Separated documents required for PRMC versus other activation processes e.g. OCTA submission.	Provided clarity as to what committee/departments require which documents
8.0	Changed time frame for putting study on an activation hold from 30 days to 14 days. Included sponsor unresponsiveness as a reason for hold.	External delays longer than 14 days are unexpected during standard activation processes. When delays longer than 14 days occur, it is assumed activation process is on hold.

DocuSign

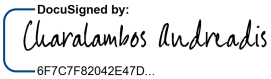
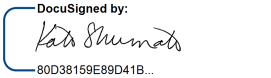
Certificate Of Completion

Envelope Id: DC20B5376ACE48EB91CDE96E4A49E622
Status: Completed
Subject: Please DocuSign: HDFCCC_Activation_Policy_for_Industry_Trials_FINAL_revision 1_2021DEC16.pdf
Source Envelope:
Document Pages: 9
Signatures: 3
Certificate Pages: 2
Initials: 0
AutoNav: Enabled
EnvelopeId Stamping: Disabled
Time Zone: (UTC-08:00) Pacific Time (US & Canada)

Envelope Originator:
Andrea Skafel
1855 Folsom St
Suite 566
San Francisco, CA 94103
andrea.skafel@ucsf.edu
IP Address: 128.218.42.80

Record Tracking

Status: Original
12/16/2021 1:50:03 PM
Holder: Andrea Skafel
andrea.skafel@ucsf.edu
Location: DocuSign

Signer Events	Signature	Timestamp
Charalambos Andreadis charalambos.andreadis@ucsf.edu MD University of California, San Francisco Security Level: Email, Account Authentication (Optional)	DocuSigned by:  6F7C7F82042E47D... Signature Adoption: Pre-selected Style Using IP Address: 157.131.221.151	Sent: 12/16/2021 1:52:21 PM Viewed: 12/19/2021 7:57:27 PM Signed: 12/19/2021 7:57:40 PM
Electronic Record and Signature Disclosure: Not Offered via DocuSign		
Eric Small eric.small@ucsf.edu Professor University of California, San Francisco Security Level: Email, Account Authentication (Optional)	DocuSigned by:  7FCB32D327E3438... Signature Adoption: Pre-selected Style Using IP Address: 98.42.87.27	Sent: 12/16/2021 1:52:20 PM Viewed: 12/21/2021 9:03:48 AM Signed: 12/21/2021 9:03:56 AM
Electronic Record and Signature Disclosure: Not Offered via DocuSign		
Katherine Shumate kate.shumate@ucsf.edu Chief of Staff, Director of Administration University of California, San Francisco Security Level: Email, Account Authentication (Optional)	DocuSigned by:  80D38159E89D41B... Signature Adoption: Uploaded Signature Image Using IP Address: 128.218.42.138	Sent: 12/16/2021 1:52:20 PM Viewed: 12/17/2021 10:29:04 AM Signed: 12/17/2021 10:29:18 AM
Electronic Record and Signature Disclosure: Not Offered via DocuSign		

In Person Signer Events	Signature	Timestamp

Editor Delivery Events	Status	Timestamp

Agent Delivery Events	Status	Timestamp

Intermediary Delivery Events	Status	Timestamp

Certified Delivery Events	Status	Timestamp

Carbon Copy Events	Status	Timestamp

Witness Events	Signature	Timestamp

Notary Events	Signature	Timestamp

Envelope Summary Events	Status	Timestamps
Envelope Sent	Hashed/Encrypted	12/16/2021 1:52:21 PM
Certified Delivered	Security Checked	12/17/2021 10:29:04 AM
Signing Complete	Security Checked	12/17/2021 10:29:18 AM
Completed	Security Checked	12/21/2021 9:03:56 AM

Payment Events	Status	Timestamps