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

Policy for Centralized IND/IDE Management

Purpose

The purpose of this policy is to outline how the Clinical Research Support Office (CRSO) centrally manages and monitors all Investigational New Drug applications (INDs) and Investigational Device Exemptions (IDEs) in oncology filed by University of California, San Francisco (UCSF) investigators in the Helen Diller Comprehensive Cancer Center (HDFCCC).

Background

The 2007 National Cancer Institute (NCI) Cancer Center Service Grant (CCSG) competing renewal requires that the UCSF HDFCCC centrally manage all Food and Drug Administration (FDA) IND/IDE submissions. This responsibility is performed by the CRSO housed within the HDFCCC. The CRSO provides centralized regulatory management and oversight for clinical trials conducted at the center and serves as the Office of Record for all INDs and IDEs held by HDFCCC investigators, regardless of program affiliation.

Procedures

Data Capture for New INDs/IDEs

Data for centralized IND/IDE oversight and management are stored in OnCore, the HDFCCC secure electronic clinical trial management system. New IND/IDEs held by HDFCCC investigators are captured at the point of submission to the center's centralized scientific review committee, the Protocol Review Committee (PRC). PRC submission is required for all clinical trials conducted at the HDFCCC, and must be completed in OnCore with the required IND/IDE information.

The CRSO runs monthly OnCore reports to identify new trials with INDs/IDEs held by UCSF investigators. The CRSO ensures that IND/IDE information is completed and updated in OnCore for the life of the trial to include the IND/IDE number, status, responsible FDA division, holder, submission date, and approval date.

Monitoring Annual Progress Reports

The CRSO monitors IND/IDE anniversary dates and ensures annual progress reports are filed within 60 days of the anniversary date. Submissions within 60 days on either side of the anniversary date are considered acceptable based on FDA guidelines. Annual progress reports will be considered late if filed greater than 60 days following the anniversary date. Late annual progress reports identified by the CRSO are escalated to HDFCCC leadership, including the CRSO Medical Director, CRSO Director, Director of Regulatory Affairs and Protocols, HDFCCC Deputy Director, and the Data Safety and

Monitoring Chair. If an annual or progress report will be late due to extenuating circumstances, the responsible party must obtain approval from the Deputy Director and CRSO Director.

Record Keeping

The CRSO ensures that all information and submissions for INDs/IDEs held by UCSF HDFCCC investigators are recorded in OnCore, so that the IND/IDE record in OnCore is complete, accurate, and up to date. All FDA communication dated from October 1, 2010 to present date is housed electronically in the HFDCCC's secure OnCore system. All FDA communication dated prior to October 1, 2010 is housed in paper form in secure HDFCCC location.

Alternate Procedure

None.

Policy Approval

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

DocuSigned by:
Charalambos Andreadis
6F7C7F62042E47D...

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

10/17/2018
Date

DocuSigned by:
Eric Small
7FCB32D327E3438...

Eric Small, MD
Chief Scientific Officer,
Helen Diller Family Comprehensive Cancer Center

10/15/2018
Date

DocuSigned by:
Kate Shumate
80D38159E89D41B...

Kate Shumate, MPA, CCRP
Chief of Staff,
Director, Administration and Planning,
Helen Diller Family Comprehensive Cancer Center

11/15/2018
Date

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

Policy for Summary of Changes

Policy Title: Policy for Centralized IND/IDE Management

Version Date: September 7, 2018

Version Number: Revision 2

Page No.: 1	**Section:** Purpose
Original Text	The 2007 NCI competing renewal review indicated that the University of California, San Francisco (UCSF) Helen Diller Family Comprehensive Cancer Center (hereafter referred to as the HDFCCC) should provide central management for FDA issues and communication. At the HDFCCC this responsibility falls to the Clinical Research Support Office (CRSO), which is housed within the Investigational Trials Resource (ITR). Per NCI guidance, the CRSO is responsible for providing centralized management and oversight functions for coordinating, facilitating, and reporting on, the cancer clinical trials of the center. As part of this NCI mandate, the CRSO provides centralized oversight for all Investigational New Drug applications (INDs) and Investigational Device Exemptions (IDEs) filed by UCSF investigators within the center, regardless of their program of origin. The purpose of this procedure is to outline how the ITR CRSO manages all INDs and IDEs centrally. Detailed instructions on how new INDs and IDEs are identified, how data is entered in the center's secure electronic web-based database, and how documents are stored in the database are found in a separate, non-policy document entitled *ITR CRSO Procedure for Central IND & IDE Management*, which is stored on the CRSO server under *CRSO\Procedures\CRSO\IND & IDE Management\CRSO Procedure for IND & IDE Management*.
New Text	~~The 2007 NCI competing renewal review indicated that the University of California, San Francisco (UCSF) Helen Diller Family Comprehensive Cancer Center (hereafter referred to as the HDFCCC) should provide central management for FDA issues and communication. At the HDFCCC this responsibility falls to the Clinical Research Support Office (CRSO), which is housed within the Investigational Trials Resource (ITR). Per NCI guidance, the CRSO is responsible for providing centralized management and oversight functions for coordinating, facilitating, and reporting on, the cancer clinical trials of the center. As part of this NCI mandate, the CRSO provides centralized oversight for all Investigational New Drug applications (INDs) and Investigational Device Exemptions (IDEs) filed by UCSF investigators within the center, regardless of their program of origin.~~ The purpose of this procedure is to outline how the ITR CRSO manages all INDs and IDEs centrally.~~ Detailed instructions on how new INDs and IDEs are identified, how data is entered in the center's secure electronic web-based database, and how documents are stored in the database are found in a separate, non-policy document~~ entitled *ITR CRSO Procedure for Central IND & IDE Management*, which is stored on the CRSO server under *CRSO\Procedures\CRSO\IND & IDE Management\CRSO Procedure for IND & IDE Management*.~~

	The purpose of this policy is to outline how the Clinical Research Support Office (CRSO) centrally manages and monitors all Investigational New Drug applications (INDs) and Investigational Device Exemptions (IDEs) in oncology filed by University of California, San Francisco (UCSF) investigators in the Helen Diller Comprehensive Cancer Center (HDFCCC).
Reason for Change	Removed Investigational Trials Resource (ITR); Created a Background header and moved text there.

Page No.: 1	**Section:** Background
Original Text	None.
New Text	The 2007 National Cancer Institute (NCI) Cancer Center Service Grant (CCSG) competing renewal requires that the UCSF HDFCCC centrally manage all Food and Drug Administration (FDA) IND/IDE submissions. This responsibility is performed by the CRSO housed within the HDFCCC. The CRSO provides centralized regulatory management and oversight for clinical trials conducted at the center and serves as the Office of Record for <u>all</u> INDs and IDEs held by HDFCCC investigators, regardless of program affiliation.
Reason for Change	Removed Investigational Trials Resource (ITR); Created a Background header and moved text from former Purpose section here.

Page No.: 1	**Section:** Procedures (Intro)
Original Text	For clinical CCSG Programs and non-aligned programs supported by the ITR, the CRSO Protocol Development and Regulatory Unit manages the preparation of all initial IND and IDE applications as well as all annual/progress reports, protocol amendments, and miscellaneous FDA correspondence. Programs in the process of integrating into the ITR manage preparation of their own applications and applicable FDA correspondence. However, the ITR CRSO provides centralized oversight and serves as the Office of Record on all INDs and IDEs held by HDFCCC investigators (regardless of program affiliation).
New Text	~~For clinical CCSG Programs and non-aligned programs supported by the ITR, the CRSO Protocol Development and Regulatory Unit manages the preparation of all initial IND and IDE applications as well as all annual/progress reports, protocol amendments, and miscellaneous FDA correspondence. Programs in the process of integrating into the ITR manage preparation of their own applications and applicable FDA correspondence.~~ ~~However, the ITR CRSO provides centralized oversight and serves as the Office of Record on all INDs and IDEs held by HDFCCC investigators (regardless of program affiliation).~~
Reason for Change	Moved some verbiage to appropriate subsections under procedures; Moved detailed processes to process guideline document.

Page No.: 1 - 2	**Section:** Procedures/ Initial Data Capture
Original Text	<u>Initial Data Capture</u> Initial data on INDs and IDEs is managed electronically in a secure electronic web-based database. The HDFCCC's centralized scientific review committee, Protocol Review Committee (PRC), uses an online application and review process housed in this database. The application process to the PRC requires applicants to enter IND/IDE details in the system. This system captures all clinical research studies pertaining to cancer or subjects at risk for cancer. See the *OnCore PRC (ePRMS) User Manual*, the *UCSF OnCore Wiki* and the *ITR CRSO Procedure for Central IND & IDE Management* document for details on what data is required and how data is entered. The ITR CRSO identifies new trials requiring INDs/IDEs by regularly running a report on new data entered by all PRC applicants, using the secure electronic web-based database. All new trials identified are added to a tracking spreadsheet entitled *IND & IDE Tracking* (stored on the CRSO server under

	CRSO\Reports\INDs & IDEs\IND & IDE Tracking), and the initial FDA correspondence is collected as outlined below under Record Keeping.
New Text	~~Initial Data Capture~~ Initial data on INDs and IDEs is managed electronically in a secure electronic web-based database. ~~The HDFCCC's centralized scientific review committee, Protocol Review Committee (PRC), uses an online application and review process housed in this database~~. The application process to the PRC requires applicants to enter IND/IDE details in the system. ~~This system captures all clinical research studies pertaining to cancer or subjects at risk for cancer. See the *OnCore PRC (ePRMS) User Manual*, the *UCSF OnCore Wiki* and the *ITR CRSO Procedure for Central IND & IDE Management* document for details on what data is required and how data is entered.~~ The ~~ITR~~ CRSO identifies new trials requiring INDs/IDEs by regularly running a report on new data entered by all PRC applicants, using the secure electronic web-based database. ~~All new trials identified are added to a tracking spreadsheet entitled *IND & IDE Tracking* (stored on the CRSO server under *CRSO\Reports\INDs & IDEs\IND & IDE Tracking*), and the initial FDA correspondence is collected as outlined below under Record Keeping.~~ Data Capture for New INDs/IDEs Data for centralized IND/IDE oversight and management are stored in OnCore, the HDFCCC secure electronic clinical trial management system. New IND/IDEs held by HDFCCC investigators are captured at the point of submission to the center's centralized scientific review committee, the Protocol Review Committee (PRC). PRC submission is required for all clinical trials conducted at the HDFCCC, and must be completed in OnCore with the required IND/IDE information. The CRSO runs monthly OnCore reports to identify new trials with INDs/IDEs held by UCSF investigators. The CRSO ensures that IND/IDE information is completed and updated in OnCore for the life of the trial to include the IND/IDE number, status, responsible FDA division, holder, submission date, and approval date.
Reason for Change	Removed Investigational Trials Resource (ITR); Updated wording.

Page No.: 2	**Section:** Procedures/ Effect Date & Anniversary (Renewal) Date Calculation
Original Text	Effect Date & Anniversary (Renewal) Date Calculation If an IND application is exempted, there will be no effect date calculated. For approved IND applications, the effect date is calculated as one of the following, whichever is applicable: • if no communication is received from the FDA for greater than 30 days following FDA receipt of an application (documented in the FDA's receipt letter), then the effect date is 30 days from the FDA's receipt date (or the effect date is the date indicated by the FDA in the FDA receipt letter) • if a Clinical Hold was in place, the effect date is the date the Clinical Hold was lifted • if a Safe to Proceed communication is issued by the FDA, the effect date is the date the FDA issues the Safe to Proceed communication. The anniversary date (known at the HDFCCC as the renewal date) is calculated as one year following the effect date, and annually thereafter until the application is withdrawn.
New Text	~~Effect Date & Anniversary (Renewal) Date Calculation~~ ~~If an IND application is exempted, there will be no effect date calculated. For approved IND applications, the effect date is calculated as one of the following, whichever is applicable:~~ ~~• if no communication is received from the FDA for greater than 30 days following FDA receipt of an application (documented in the FDA's receipt letter), then the effect date is 30 days from~~

	~~the FDA's receipt date (or the effect date is the date indicated by the FDA in the FDA receipt letter)~~ ~~• if a Clinical Hold was in place, the effect date is the date the Clinical Hold was lifted~~ ~~• if a Safe to Proceed communication is issued by the FDA, the effect date is the date the FDA issues the Safe to Proceed communication. The anniversary date (known at the HDFCCC as the renewal date) is calculated as one year following the effect date, and annually thereafter until the application is withdrawn.~~
Reason for Change	FDA Guideline detailed in guideline process document; General summary information moved to Monitoring section.

Page No.: 2-3	**Section:** Procedures/ Monitoring
Original Text	Monitoring The ITR CRSO monitors anniversary (renewal) dates using the tracking spreadsheet entitled *IND & IDE Tracking* (stored on the CRSO server under *CRSO\Reports\INDs & IDEs\IND & IDE Tracking*). The ITR CRSO ensures annual/progress reports are filed within 60 days of the anniversary (renewal) date by issuing email reminders approximately 60 days prior to the anniversary (renewal) date to the appropriate personnel (those preparing the annual/progress reports) to ensure timely submission, monitoring for late annual/progress reports, collecting the relevant documentation, and maintaining consistent data entry for all such submissions. The goal is to have all annual/progress reports filed within 60 days prior to the anniversary (renewal) date, although submission within 60 days on either side of the anniversary (renewal) date is considered acceptable (based on divergent responses from FDA when asked for the definition of "within 60 days"). An annual/progress report will be considered late if it is filed greater than 60 days following the anniversary (renewal) date. There should be no late reports. If the ITR CRSO identifies a late annual/progress report, notification is as follows: if prepared by the ITR CRSO, the CRSO Director and the Regulatory Affairs Unit Supervisor are notified; if not prepared by the ITR CRSO, then the ITR Director, CRSO Director, Principal Investigator and Protocol Project Manager are all notified. If an annual/progress report will be late due to extenuating circumstances, the responsible party must obtain approval from the ITR Director and CRSO Director. Holding an annual/progress report while waiting for a pending protocol amendment is not considered an extenuating circumstance; in such cases the report should describe the expected protocol revisions and advise the FDA that the protocol will be submitted when ready as per 21 CFR 312.30. In addition to annual/progress reports, the ITR CRSO will collect all FDA correspondence pertaining to protocol amendments, addition of investigators, adding protocols, etc., house the documents centrally, and maintain consistent data entry for all such submissions. The sole exception pertains to IND safety reports filed with the FDA under an investigator-held IND or IDE; these are collected and filed by the Data Safety Monitoring Committee (DSMC).
New Text	~~Monitoring~~ The I~~TR~~CRSO monitors anniversary (renewal) dates using the tracking spreadsheet entitled *IND & IDE Tracking* (stored on the CRSO server under *CRSO\Reports\INDs & IDEs\IND & IDE Tracking*). The ~~ITR~~CRSO ensures annual/progress reports are filed within 60 days of the anniversary (renewal)~~ date by issuing email reminders approximately 60 days prior to the anniversary (renewal) date to the appropriate personnel (those preparing the annual/progress reports) to ensure timely submission, monitoring for late annual/progress reports, collecting the relevant documentation, and~~

	~~maintaining consistent data entry for all such submissions. The goal is to have all annual/progress reports filed within 60 days prior to the anniversary (renewal) date,~~ although submission within 60 days on either side of the anniversary (renewal) date is considered acceptable ~~(based on divergent responses from FDA when asked for the definition of "within 60 days").~~ An annual/progress report will be considered late if it is filed greater than 60 days following the anniversary (renewal) date. ~~There should be no late reports. If the ITR CRSO identifies a late annual/progress report, notification is as follows: if prepared by the ITR CRSO, the CRSO Director and the Regulatory Affairs Unit Supervisor are notified; if not prepared by the ITR CRSO, then the ITR Director, CRSO Director, Principal Investigator and Protocol Project Manager are all notified.~~ If an annual/progress report will be late due to extenuating circumstances, the responsible party must obtain approval from the ITR Director and CRSO Director~~. Holding an annual/progress report while waiting for a pending protocol amendment is not considered an extenuating circumstance; in such cases the report should describe the expected protocol revisions and advise the FDA that the protocol will be submitted when ready as per 21 CFR 312.30. In addition to annual/progress reports, the ITR CRSO will collect all FDA correspondence pertaining to protocol amendments, addition of investigators, adding protocols, etc., house the documents centrally, and maintain consistent data entry for all such submissions. The sole exception pertains to IND safety reports filed with the FDA under an investigator-held IND or IDE; these are collected and filed by the Data Safety Monitoring Committee (DSMC).~~ <u>Monitoring Annual Progress Reports</u> The CRSO monitors IND/IDE anniversary dates and ensures annual progress reports are filed within 60 days of the anniversary date. Submissions within 60 days on either side of the anniversary date are considered acceptable based on FDA guidelines. Annual progress reports will be considered late if filed greater than 60 days following the anniversary date. Late annual progress reports identified by the CRSO are escalated to HDFCCC leadership, including the CRSO Medical Director, CRSO Director, Director of Regulatory Affairs and Protocols, HDFCCC Deputy Director, and the Data Safety and Monitoring Chair. If an annual or progress report will be late due to extenuating circumstances, the responsible party must obtain approval from the Deputy Director and CRSO Director.
Reason for Change	Removed Investigational Trials Resource (ITR); Update process; Reword.

Page No.: 3	**Section:** Procedures/ Record Keeping
Original Text	<u>Record Keeping</u> Once new INDs/IDEs are identified, the ITR CRSO collects the available FDA correspondence from the applicant for centralized storage in the Office of Record. Likewise, for all annual/progress reports, protocol amendments, addition of investigators, adding protocols, etc., the ITR CRSO collects all relevant FDA correspondence from the appropriate personnel for centralized storage in the Office of Record. All FDA communication dated prior to October 1, 2010 is housed in paper form in the paper Office of Record files. All FDA communication dated from October 1, 2010 forward is housed electronically in the HFDCCC's secure electronic web-based database. Once the relevant correspondence is centrally housed in the Office of Record, the ITR CRSO ensures consistent data entry within the HFDCCC's secure electronic web-based database. Detailed instructions on how new INDs and IDEs are identified, how data is entered in the database, and how documents are stored in the database

	are found in a separate, non-policy document entitled *ITR CRSO Procedure for Central IND & IDE Management*.
New Text	~~Record Keeping~~ ~~Once new INDs/IDEs are identified, the ITR CRSO collects the available FDA correspondence from the applicant for centralized storage in the Office of Record. Likewise, for all annual/progress reports, protocol amendments, addition of investigators, adding protocols, etc., the ITR CRSO collects all relevant FDA correspondence from the appropriate personnel for centralized storage in the Office of Record.~~ All FDA communication dated prior to October 1, 2010 is housed in paper form in the paper Office of Record files. All FDA communication dated from October 1, 2010 forward is housed electronically in the HFDCCC's secure electronic web-based database~~. Once the relevant correspondence is centrally housed in the Office of Record, the ITR CRSO ensures consistent data entry within the HFDCCC's secure electronic web-based database. Detailed instructions on how new INDs and IDEs are identified, how data is entered in the database, and how documents are stored in the database are found in a separate, non-policy document entitled *ITR CRSO Procedure for Central IND & IDE Management*.~~ <u>Record Keeping</u> The CRSO ensures that all information and submissions for INDs/IDEs held by UCSF HDFCCC investigators are recorded in OnCore, so that the IND/IDE record in OnCore is complete, accurate, and up to date. All FDA communication dated prior to October 1, 2010 is housed in paper form in secure HDFCCC file rooms. All FDA communication dated from October 1, 2010 through April 1, 2018 is housed electronically in the HFDCCC's secure OnCore system. All FDA communication dated after April 1, 2018 is securely stored by IND holder.
Reason for Change	Removed Investigational Trials Resource (ITR); Updated process; Reword; Moved detailed process statements to guideline process document.