



CASE  
COMPREHENSIVE  
CANCER CENTER

# **Case Comprehensive Cancer Center Standard Operating Procedures**

## **June 2011 (1<sup>st</sup> Edition)**

**(Revisions: October 2012; November 2012; December 2012; January 2013;  
February 2013; October 2013; September 2014; November 2014;  
April 2015; May 2015; December 2015; July 2016; October 2016;  
December 2016; April 2017; October 2017)**

**Case Comprehensive Cancer Center  
11100 Euclid Avenue, Wearn 152  
Cleveland, Ohio 44106-5065**



A Cancer Center Designated by the  
National Cancer Institute

**Case Comprehensive Cancer Center  
Standard Operation Procedures for Clinical Research**

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**INTRODUCTION**

Standard Operating Procedures (SOPs) apply to those members of the clinical research team who are involved in conducting cancer research and clinical trials at the Case Comprehensive Cancer Center. The Cancer Center implements and enforces all SOPs across consortium institutions – Case Western Reserve University, Cleveland Clinic Foundation and University Hospitals.

The clinical research team includes the following personnel: Principal Investigator; Co-Investigator; Site Investigator; Research Nurse; Clinical Research Associate / Coordinator; Regulatory Coordinator; Data Analyst / Coordinator; Quality Assurance Manager; Biostatistician; Support Staff; Other Personnel, as applicable.

**CONTACTS**

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**ABBREVIATIONS**

ADE	Adverse Drug Event/Experience
ADR	Adverse Drug Reaction
AE	Adverse Event
Case CCC	Case Comprehensive Cancer Center
CCF	Cleveland Clinic Foundation
CFR	Code of Federal Regulations
COI	Conflict of Interest
CRA	Clinical Research Associate
CRC	Clinical Research Coordinator
CRF	Case Report Form
CRO	Case CCC Clinical Research Office
CRO	Contract Research Organization
C-ROC	Clinical Research Operations Committee
CTRP	Clinical Trials Reporting Program
CTU	Clinical Trials Unit
CTWG	Clinical Trials Working Group
CWRU	Case Western Reserve University
DSM	Data and Safety Monitoring
DSMB	Data and Safety Monitoring Board
DSMP	Data and Safety Monitoring Plan
DSTC	Data Safety and Toxicity Committee
FDA	Food and Drug Administration
GCP	Good Clinical Practice
IBC	Institutional Biosafety Committee
ICF	Informed Consent Form
ICH	International Conference on Harmonization
IDE	Investigational Device Exemption
IND	Investigational New Drug
IRB	Institutional Review Board
NCI	National Cancer Institute
NCT	National Clinical Trial
OBA	Office of Biotechnology Activities
OHRP	Office for Human Research Protections
OnCore®	Clinical Trials Management System
PI	Principal Investigator
PRMC	Protocol Review and Monitoring Committee
QA	Quality Assurance
QC	Quality Control
QOL	Quality of Life
SAE	Serious Adverse Event
SOP	Standard Operating Procedure
UH	University Hospitals

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**SECTION 1: GENERAL ADMINISTRATION (GA)**

**Case Comprehensive Cancer Center  
Standard Operation Procedures for Clinical Research**

**Title: Procedure for the Development, Review, Approval, Updating and Maintaining of Standard Operating Procedures (SOPs)**  
**SOP #: GA-1.1.0**  
**Version #: 4.0**

<b>Original Approval Date:</b>	<b>May 3, 2011</b>
<b>Effective Date:</b>	<b>July 3, 2011</b>
<b>Revision Dates:</b>	<b>January 7, 2013 April 7, 2015 May 16, 2017</b>

**1.0 Standard Operating Procedure Statement/ Purpose/Background**

To define parameters and a process for establishing and maintaining all of Case Comprehensive Cancer Center (Case CCC) clinical research guidelines and procedures. To define expectations regarding harmonization between Case CCC institutional research policies.

**2.0 Scope**

All cancer research activities and processes that involve any Case CCC institution, department and institute.

**3.0 Responsibility**

Case CCC Clinical Research Operations Committee (C-ROC).

**4.0 Definitions**

- 4.1 Definitions: Terminology to clarify intent of message.
- 4.2 SOP Number: Alphanumeric number of SOPs reflecting the SOP category and number within that category.
- 4.3 Original Approval Date: Date of the C-ROC meeting when a given SOP was approved.
- 4.4 Effective Date: The date when the policy became active.
- 4.5 Revisions Dates: Date of the C-ROC meeting when revisions were approved.
- 4.6 SOP Statement/Purpose/Background: An SOP general statement and a brief description of the SOP purpose and/or background.
- 4.7 Procedure: A predetermined course of action established as a guide/instructions towards acceptable actions and objectives.
- 4.8 References: Any/all references to support the SOP.
- 4.9 Appendices: Supplemental documents in support of the SOP.

**5.0 Procedure**

**5.1 Policy Development, Review and Approval**

- 5.1.1** All elements provided in the Definitions section 4.0 above are required as applicable.

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- 5.1.2 SOP format will include a statement of purpose, background, scope and responsibility, and an overview of procedures. Definitions, references, appendices and other documentation may be included.
- 5.1.3 Any member of the Case CCC Clinical Trials Working Group (CTWG) may propose, develop and draft a new SOP or revise current SOPs and forward it to the CTWG for review and approval. Members of CTWG will collectively propose and agree on guidelines that will hold both institutions, Cleveland Clinic (CC) and University Hospitals (UH) accountable for established SOPs.
- 5.1.4 Whenever feasible and applicable, research staff outside the CTWG will be given an opportunity to review and evaluate the SOPs for completeness and appropriateness in reference to their departments' and institutes' policies and procedures.
- 5.1.5 SOPs should be clear, concise, and well defined to a specific area of practice within the conduct of clinical research, however generic enough to allow flexibility by both institutions.
- 5.1.6 All research SOPs are to be reviewed at least annually or more frequently, if needed, and revised as applicable.
- 5.1.7 CTWG will forward SOPs to the C-ROC for review and approval.
- 5.1.8 C-ROC will review and approve all new and revised SOPs. The Chair of the C-ROC or designee will have the signatory authority for all new and revised SOPs.

**5.2 SOP Implementation**

- 5.2.1 A PDF version of each SOP is be placed in the Case CCC SOP Manual on the Case CCC website. Paper copies of the current and archived SOPs will be retained and maintained by Case CCC Clinical Research Office.
- 5.2.2 Sponsors, their representatives, and other approved internal or external persons may review SOPs on-site. SOPs will not be copied for external distribution.
- 5.2.3 New and/or revised SOPs will be effective within 30 days after posting on the Case CCC website, unless otherwise indicated.
- 5.2.4 Training and education about new or revised SOPs will be conducted prior to the SOP effective date and will be the responsibility of respective institutions and departments.

**6.0 References:** None.

**7.0 Appendices:** None.

<b>SOP #: GA-1.1.0; Version #: 4.0</b>	
<b>Approved by:</b> Name: Mikkael Sekeres, MD	
Position: Deputy Associate Director of Clinical Research; Director of Clinical Trial	
Signature: 	Date: 09-05-2017



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**SECTION 2: EDUCATION AND TRAINING (ET)**

**SECTION 3: ONCORE CLINICAL TRIALS  
DATABASE (OC)**

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**Title: Registration of Case CCC Personnel in the OnCore® Database**  
**SOP #: OC-3.1.0**  
**Version #: 3.0**

<b>Original Approval Date:</b>	<b>October 4, 2011</b>
<b>Effective Date:</b>	<b>November 4, 2011</b>
<b>Revision Dates:</b>	<b>November 6, 2012 November 21, 2012 December 4, 2012 February 5, 2013 (Appendix I) June 21, 2017</b>

**1.0 Standard Operating Procedure Statement / Purpose / Background**

To provide access and register Case Comprehensive Cancer Center (Case CCC), Case Western Reserve University (CWRU), University Hospitals (UH) and Cleveland Clinic personnel in the OnCore database.

**2.0 Scope**

The OnCore database contains data for all the cancer clinical trials conducted by the Case CCC. Case CCC, CWRU, UH and Cleveland Clinic personnel, as described in Section 5.1.4 below, that request access to the OnCore database to either input information or utilize information for research purposes, will need to undergo vetting process as per this SOP in order to be considered to be registered and granted access in the OnCore database.

**3.0 Responsibility**

It is the responsibility of the OnCore Registration Coordinator to register personnel. The OnCore registration coordinator can be reached at [oncore-registration@case.edu](mailto:oncore-registration@case.edu).

**4.0 Definitions**

- 4.2** OnCore® Clinical Trials Management System (referred to as OnCore): database to track information from clinical trials conducted by the Case CCC.
- 4.3** HIPS: The Health Information Privacy and Security.
- 4.4** OnCore Learning Portal: training videos and documents for the OnCore database.
- 4.5** SRE: Secure Research Environment
- 4.6** CWRU [U]Tech: CWRU information technology services
- 4.7** Tenant Coordinator: SRE account manager

**5.0 Eligible Users**

- 5.1** The following personnel can request and may receive access to OnCore database based on their employment, qualifications and needs: Case CCC members; people actively involved in conducting and managing research studies and clinical trials at CWRU, UH and Cleveland Clinic and their satellites; respective IRB offices staff, and IRB Chairs and Co-Chairs.

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- 5.2** Any other CWRU, UH and Cleveland Clinic faculty and/or staff outside the above listed categories will be required to write a letter addressed to the Case CCC Associate Director for Clinical Research and copy the Registration Coordinator, requesting and justifying his/her specific access to OnCore. Requests will be reviewed by the Case CCC Associate Director for Clinical Research and Registration Coordinator. Access will be considered on a case by case basis.

**6.0 Procedure**

- 6.1** Complete the SRE User Enrollment and OnCore Access Form on the Case CCC website: <http://cancer.case.edu/research/clinical-research-office/oncore/>. (Appendix I)
- 6.1.1** E-mail accounts are required to be institutionally provided, i.e. case.edu, ccf.org, uhhospitals.org (accounts such as yahoo, g-mail, etc. cannot be used).
  - 6.1.2** The supervisor must sign off on the Form, provide his/her contact information and check the appropriate role/roles for the new user.
  - 6.1.3** Email completed form to: [oncore-registration@case.edu](mailto:oncore-registration@case.edu).
- 6.2** Activate CWRU Network ID and Complete CITI HIPS Training
- 6.2.1** The OnCore registrar will acquire a CWRU ID for the new user.
  - 6.2.2** The new user will receive an email from network-id@case.edu with their CWRU ID and instructions to set up a password for their CWRU account.
  - 6.2.3** The new user will set up their CWRU email account (<https://www.case.edu/utech/cwru-email/>).
    - 6.2.3.1** This email address can be forwarded to your primary email account
  - 6.2.4** Set up DUO login with CWRU:
    - 6.2.4.1** Instructions at: <https://www.case.edu/its/information-security/duo/>
  - 6.2.5** Email oncore-registration@case.edu when Duo Security and CWRU account are set up.
  - 6.2.6** All Case CCC consortium members must submit their CITI HIPS training certification to [oncore-registration@case.edu](mailto:oncore-registration@case.edu) and submit continuing renewals every 3 years.
- 6.3** Activate SRE account:
- 6.3.1** Upon completion of the above steps (6.1 and 6.2) the OnCore registrar will apply for an SRE account for the user with CWRU [U]Tech.
    - 6.3.1.1** Registrar will complete page 2 of the SRE User Enrollment and OnCore Access Form and send it to CWRU [U]Tech. An electronic copy will be kept in OnCore
    - 6.3.1.2** [U]tech service will create the new user's account and provide an SRE password sent to their work email.
- 6.4** Training
- 6.4.1** The new user will be contacted via e-mail or phone to set up training.
    - 6.4.1.1** Cleveland Clinic employees should contact Cleveland Clinic OnCore administrator.
    - 6.4.1.2** UH and CWRU employees will be contacted by the OnCore administrator
  - 6.4.2** Once training is complete the trainer will sign the sections of the training log appropriate to the user's roles (Appendix II)
  - 6.4.3** Upon completion of training the user will receive a login and password to OnCore with their assigned roles.
- 6.5** Maintenance of OnCore Users

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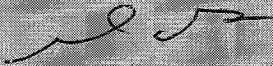
- 6.5.1 A report (Inactive Users 120 Days) is run every 6 months from the OnCore database. This report lists users that have not logged into OnCore in the past 120 days. These users will be inactivated, disabling their login to OnCore. The purpose of this is to update and delete users that are no longer active.
- 6.5.2 SRE and CWRU affiliate accounts expire annually and must be renewed by the OnCore Registrar
  - 6.5.2.1 Once a month, CWRU [U]Tech will send the OnCore Registrar a list of all SRE users with account expiration dates
  - 6.5.2.2 OnCore Registrar will use the SRE Bulk Access Change form to renew all active OnCore User accounts expiring in the next 60 days (Appendix III)
  - 6.5.2.3 Affiliate CWRU accounts should be renewed at the same time as the SRE account. This can be done at: <https://its-services.case.edu/my-case-identity/affiliates/request/>
  - 6.5.2.4 30 days prior to an SRE password expiring, CWRU [U]Tech will send OnCore Registrar and user reminders to update the passwords. Passwords expire every 6 months.

**7.0 References**

- [oncore-registration@case.edu](mailto:oncore-registration@case.edu): Registration, new password and help with OnCore
- <https://sreportal.case.edu> : SRE Server (gateway to OnCore)
- <https://www.citiprogram.org/default.asp> : HIPS training
- <http://cancer.case.edu/research/clinical-research-office/oncore/>: access form
- <https://its-services.case.edu/my-case-identity/affiliates/request/>: Affiliate CWRU ID request form
- 216-368-HELP: Case IT for help with CWRU or SRE issues

**8.0 Appendices**

- Appendix I: SRE User Enrollment and OnCore Access Form
- Appendix II: Training Log
- Appendix III: SRE Bulk Access Change Form

<b>SOP #: OC-3.1.0; Version #: 3.0</b>	
<b>Approved by:</b>	
Name: Mikkael Sekeres, MD	
Position: Deputy Associate Director of Clinical Research; Director of Clinical Trials	
Signature: 	Date: 09-13-17

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**APPENDIX I**

**SRE User Enrollment and OnCore Access**

**1. SRE Access Requested**

Role:

- Researcher  
 Clinician  
 Admin (Research Support)  
 Nurse

Application:

- OnCore  
 Labmatrix  
 APEX

Request Type:

- New User  
 Renewal  
 Access Modification

**2. SRE User Information**

Last Name                      Middle Initial                      First Name                      Case Net ID  
Work Email                      Work Phone                      Alt. Phone  
Work Address                      City                      ZIP Code  
DOB

Department:                      Job Title

Employer: UH CC CWRU Other (specify)                      Title Credentials: MD   
DO PhD RN

**3. SRE Applicant Acknowledgement (read and sign)**

- You must be located physically at an SRE approved facility.
- You agree to complete a "Securing the Human" training.
- You agree to use SRE in accordance with all applicable laws and Case's "Acceptable Use of Computing and Information Technology Resources" policy:  
<http://www.case.edu/its/security/docs/aup.html>
- By signing below, a SRE applicant acknowledges that the information they have provided is accurate and that they will follow applicable policies and standards.
- The SRE is not connected to the Internet. In order to provide a secure controlled environment there is no outside connectivity to websites and other network resources. This includes email, web search, social media, reference sites such as wikis, or any other web property.
- Data transmissions are monitored. By default the SRE is monitored for malicious activity. This includes gaining access to systems that you are not authorized to use. Please report any misuse to the ITS help desk.
- I will not log on to the system in order to provide another person access to the system.
- I agree to abide by Federal and Institutional HIPAA and HITEC guidelines and related activities concerning data and patient information.

\_\_\_\_\_  
Printed **SRE User Name**  
Date

\_\_\_\_\_  
SRE User Signature

**4. Supervisor Information**

\_\_\_\_\_  
Printed **Supervisor Name**                      \_\_\_\_\_ Phone Number  
Supervisor Signature \_\_\_\_\_

To be completed by Supervisors (indicate access rights)

- Registering Subject     Regulatory     Read     Data Entry     Financial

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**APPENDIX II**

**TRAINING LOG**

Instructions: Log into the SRE website at <https://sreicboncore.case.edu> using the CWRU id and SRE password given to you. Click on the ICB OnCore link. Log in using your OnCore id and OnCore password. You will be asked to change your password. Once training is complete return this signed log to [oncore-registration@case.edu](mailto:oncore-registration@case.edu). Upon receipt your new role will be assigned.

<b>User Name:</b>		
<b>Document File Name</b>	<b>Date</b>	<b>Signed</b>
<b><i>ALL Users</i></b>		
General Tips & Navigation Reference		
OnCore Personalization - Home Screen Configuration		
OnCore Searches: Protocol, Subject, and Document		
<b><i>Audit (AUDIT)</i></b>		
Audit Console Tutorial		
<b><i>Clinical Research Associate (CRA)</i></b>		
New Subjects Registration		
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Subject Administration		
Subject Search Overview		
Subject Visit Tracking and Forms		
<b><i>Data Manager (DMAN)</i></b>		
Subject Visit Tracking and Forms		
Online Forms Monitoring Overview (DM Console)		
<b><i>Data Safety and Monitoring (DSMC)</i></b>		
DSMC Audit Overview		
DSMC Console Overview		
OSR Management Overview		
<b><i>Finance (FIN)</i></b>		
Financial Console Overview		
Charge Master Overview		
<b><i>Regulatory (REG); (PRMC)</i></b>		
Protocol Administration Overview		
SIP Product Overview		
Managing Protocol task lists		
<b><i>Protocol Investigator (PI)</i></b>		
PI Console		
<b><i>Statistician (ST)</i></b>		
Biostat Console Overview		
Access Log Overview		
Accrual Monitoring Overview		
<b><i>Biospecimen Management (BSM)</i></b>		
<b>OnCore Admin Sign off:</b>		

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**APPENDIX III**

**SRE Bulk Access Change Form**

Case Western Reserve’s University’s Secure Research Environment (SRE) is intended to be used by authorized individuals for the purpose of securely handling research data. SRE user access shall not exceed 365 days without Study Official review and reauthorization of access.

SRE access for the individuals listed below is expected to expire in the near future. Please review the information below to determine appropriate renewal status.

Acknowledge access renewals by placing an X next the appropriate SRE ID.

The SRE Bulk Access Change Form facilitates the bulk renewal of account access for 365 days. User access renewals requiring specific changes to access and resources should use the “SRE Enrollment and Access Change Form”.

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Renew	NetID	First Name	Last Name	Training Confirmation

**Tenant Coordinator Acknowledgement**

By signing below, the study coordinator acknowledges that they have reviewed the provided information, verified required training completion, and renewed SRE access for selected individuals for a period of 365 days.

\_\_\_\_\_  
Printed Tenant Coordinator  
Name

\_\_\_\_\_  
Tenant Coordinator Signature

\_\_\_\_\_  
Date



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**Title: Registration of Non-Case CCC Personnel in the OnCore® Database**  
**SOP #: OC-3.2.0**  
**Version #: 1.0**

<b>Original Approval Date:</b>	<b>August 1, 2017</b>
<b>Effective Date:</b>	<b>September 1, 2017</b>
<b>Revision Dates:</b>	

**1.0 Standard Operating Procedure Statement / Purpose / Background**

To provide access and register users from institutions outside of the Case Comprehensive Cancer Center (Case CCC) in the OnCore Database. All OnCore users from outside Case CCC must be working on studies sponsored by Case CCC.

**2.0 Scope**

The OnCore database contains data for all the cancer clinical trials conducted by the Case CCC. Users outside of the Case CCC consortium, that request access to the OnCore database to either input information or utilize information for research purposes, will need to undergo vetting process as per this SOP in order to be considered to be registered and granted access in the OnCore database.

**3.0 Responsibility**

It is the responsibility of the OnCore Registration Coordinator to register personnel. The OnCore registration coordinator can be reached at [oncore-registration@case.edu](mailto:oncore-registration@case.edu).

**4.0 Definitions**

- 4.2 OnCore Clinical Trials Management System (referred to as OnCore): database to track information from clinical trials conducted by the Case CCC.
- 4.3 HIPS: The Health Information Privacy and Security.
- 4.4 OnCore Learning Portal: training videos and documents for the OnCore database.
- 4.5 SRE: Secure Research Environment
- 4.6 CWRU [U]Tech: CWRU information technology services
- 4.7 VDI: Virtual desktop infrastructure. Used to access OnCore from outside Case CCC
- 4.8 Tenant Coordinator: SRE account manager

**5.0 Procedure**

- 5.1 Complete the SRE User Enrollment and OnCore Access Form, available on the Case CCC website: <http://cancer.case.edu/research/clinical-research-office/oncore/>. (Appendix I)
  - 5.1.1 E-mail accounts are required to be institutionally provided (accounts such as yahoo, g-mail, etc. cannot be used).
  - 5.1.2 The supervisor must sign off on the Form, provide his/her contact information and check the appropriate role/roles for the new user.
  - 5.1.3 Email completed form to: [oncore-registration@case.edu](mailto:oncore-registration@case.edu).
- 5.2 Activate CWRU Network ID
  - 5.2.1 The OnCore registrar will acquire a CWRU ID for the new user.

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- 5.2.2 The new user will receive an email from network-id@case.edu with their CWRU ID and instructions to set up a password for their CWRU account.
- 5.2.3 The new user will set up their CWRU email account (<https://www.case.edu/utech/cwru-email/>).
  - 5.2.3.1 This email address can be forwarded to your primary email account
- 5.2.4 Set up DUO login with CWRU:
  - 5.2.4.1 Instructions at: <https://www.case.edu/its/information-security/duo/>
- 5.2.5 Email oncore-registration@case.edu when Duo Security and CWRU account are set up.
- 5.3 User must submit CITI HIPS training certification to [oncore-registration@case.edu](mailto:oncore-registration@case.edu). If CITI HIPS training is not available, training will be requested for the user by the OnCore Registrar from the CWRU Compliance Office. Both CITI training or the provided security training must be renewed every 3 years.
- 5.4 Activate SRE account:
  - 5.4.1 Upon completion of the above steps (6.1-6.3) the OnCore registrar will apply for an SRE account for the user with CWRU [U]Tech.
    - 5.4.1.1 Registrar will complete page 2 of the SRE User Enrollment and OnCore Access Form and send it to CWRU [U]Tech. An electronic copy will be kept in OnCore
    - 5.4.1.2 [U]tech service will create the new user's account and provide an SRE password sent to their work email.
    - 5.4.1.3 If the user has arranged to work through the SRE web portal, the user's IP address must be provided to [U]Tech with submission of the SRE Access form
    - 5.4.1.4 If user will be using the virtual desktop infrastructure (VDI) to access OnCore, no IP address is required.
    - 5.4.1.5 Users within the VDI cannot save or print from OnCore
- 5.5 Training
  - 5.5.1 The new user will be contacted via e-mail or phone to set up training.
    - 5.5.1.1 Users working with a Cleveland Clinic led study should contact Cleveland Clinic OnCore administrator.
    - 5.5.1.2 Users working with a UH or CWRU led study will be contacted by the OnCore registrar
  - 5.5.2 Once training is complete the trainer will sign the sections of the training log appropriate to the user's roles (appendix II)
  - 5.5.3 Upon completion of training the user will receive a login and password to OnCore with their assigned roles.
- 5.6 Maintenance of OnCore Users
  - 5.6.1 A report (Inactive Users 120 Days) is run every 6 months from the OnCore database. This report lists users that have not logged into OnCore in the past 120 days. These users will be inactivated, disabling their login to OnCore. The purpose of this is to update and delete users that are no longer active.
  - 5.6.2 SRE and CWRU affiliate accounts expire annually and must be renewed by the OnCore Registrar
    - 5.6.2.1 Once a month, CWRU [U]Tech will send the OnCore Registrar a list of all SRE users with account expiration dates
    - 5.6.2.2 OnCore Registrar will use the SRE Bulk Access Change form to renew all active OnCore User accounts expiring in the next 60 days (Appendix III).

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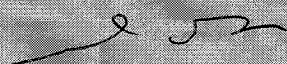
- 5.6.2.3 Affiliate CWRU accounts should be renewed at the same time as the SRE account. This can be done at: <https://its-services.case.edu/my-case-identity/affiliates/request/>
- 5.6.2.4 30 days prior to an SRE password expiring, CWRU [U]Tech will send OnCore Registrar and user reminders to update the passwords. Passwords expire every 6 months

**6.0 References**

- [oncore-registration@case.edu](mailto:oncore-registration@case.edu): Registration, new password and help with OnCore
- <https://sreportal.case.edu> : SRE Server (gateway to OnCore)
- <https://www.citiprogram.org/default.asp> : HIPS training
- <http://cancer.case.edu/research/clinical-research-office/oncore/>: access form
- <https://its-services.case.edu/my-case-identity/affiliates/request/>: Affiliate CWRU ID request form
- 216-368-HELP: Case IT for help with CWRU or SRE issues

**7.0 Appendices**

- Appendix I: SRE User Enrollment and OnCore Access Form
- Appendix II: Training Log
- Appendix III: SRE Bulk Access Change Form

<b>SOP #: OC-3.2.0; Version #: 1.0</b>	
<b>Approved by:</b>	
Name: Mikkael Sekeres, MD	
Position: Deputy Associate Director of Clinical Research; Director of Clinical Trials	
Signature: 	Date: 09.13.17

**Case Comprehensive Cancer Center  
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**APPENDIX I**

**SRE User Enrollment and OnCore Access**

**1. SRE Access Requested**

Role:	Application:	Request Type:
<input type="checkbox"/> Researcher	<input type="checkbox"/> OnCore	<input type="checkbox"/> New User
<input type="checkbox"/> Clinician	<input type="checkbox"/> Labmatrix	<input type="checkbox"/> Renewal
<input type="checkbox"/> Admin (Research Support)	<input type="checkbox"/> APEX	<input type="checkbox"/> Access Modification
<input type="checkbox"/> Nurse		

**2. SRE User Information**

Last Name	Middle Initial	First Name	Case Net ID
Work Email	Work Phone	Alt. Phone	
Work Address DOB	City	ZIP Code	
Department:	Job Title		
Employer: <input type="checkbox"/> UH <input type="checkbox"/> CC <input type="checkbox"/> CWRU <input type="checkbox"/> Other (specify)		Title Credentials: <input type="checkbox"/> MD <input type="checkbox"/> DO	
<input type="checkbox"/> PhD <input type="checkbox"/> RN			

**3. SRE Applicant Acknowledgement** (read and sign)

- You must be located physically at an SRE approved facility.
- You agree to complete a “Securing the Human” training.
- You agree to use SRE in accordance with all applicable laws and Case’s “Acceptable Use of Computing and Information Technology Resources” policy:  
<http://www.case.edu/its/security/docs/aup.html>
- By signing below, a SRE applicant acknowledges that the information they have provided is accurate and that they will follow applicable policies and standards.
- The SRE is not connected to the Internet. In order to provide a secure controlled environment there is no outside connectivity to websites and other network resources. This includes email, web search, social media, reference sites such as wikis, or any other web property.
- Data transmissions are monitored. By default the SRE is monitored for malicious activity. This includes gaining access to systems that you are not authorized to use. Please report any misuse to the ITS help desk.
- I will not log on to the system in order to provide another person access to the system.
- I agree to abide by Federal and Institutional HIPAA and HITEC guidelines and related activities concerning data and patient information.

\_\_\_\_\_  
Printed **SRE User Name**  
Date

\_\_\_\_\_  
SRE User Signature

**4. Supervisor Information**

\_\_\_\_\_  
Printed **Supervisor Name**  
Supervisor Signature \_\_\_\_\_

\_\_\_\_\_  
Phone Number

To be completed by Supervisors (indicate access rights)  
 Registering Subject  Regulatory  Read  Data Entry  Financial

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**APPENDIX II**

**TRAINING LOG**

Instructions: Log into the SRE website at <https://sreicboncore.case.edu> using the CWRU id and SRE password given to you. Click on the ICB OnCore link. Log in using your OnCore id and OnCore password. You will be asked to change your password. Once training is complete return this signed log to [oncore-registration@case.edu](mailto:oncore-registration@case.edu). Upon receipt your new role will be assigned.

<b>User Name:</b>		
<b>Document File Name</b>	<b>Date</b>	<b>Signed</b>
<b>ALL Users</b>		
General Tips & Navigation Reference		
OnCore Personalization - Home Screen Configuration		
OnCore Searches: Protocol, Subject, and Document		
<b>Audit (AUDIT)</b>		
Audit Console Tutorial		
<b>Clinical Research Associate (CRA)</b>		
New Subjects Registration		
Pre-Screening Overview		
Subject Administration		
Subject Search Overview		
Subject Visit Tracking and Forms		
<b>Data Manager (DMAN)</b>		
Subject Visit Tracking and Forms		
Online Forms Monitoring Overview (DM Console)		
<b>Data Safety and Monitoring (DSMC)</b>		
DSMC Audit Overview		
DSMC Console Overview		
OSR Management Overview		
<b>Finance (FIN)</b>		
Financial Console Overview		
Charge Master Overview		
<b>Regulatory (REG); (PRMC)</b>		
Protocol Administration Overview		
SIP Product Overview		
Managing Protocol task lists		
<b>Protocol Investigator (PI)</b>		
PI Console		
<b>Statistician (ST)</b>		
Biostat Console Overview		
Access Log Overview		
Accrual Monitoring Overview		
<b>Biospecimen Management (BSM)</b>		
<b>OnCore Admin Sign off:</b>		

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**APPENDIX III**

**SRE Bulk Access Change Form**

Case Western Reserve’s University’s Secure Research Environment (SRE) is intended to be used by authorized individuals for the purpose of securely handling research data. SRE user access shall not exceed 365 days without Study Official review and reauthorization of access.

SRE access for the individuals listed below is expected to expire in the near future. Please review the information below to determine appropriate renewal status. Acknowledge access renewals by placing an X next the appropriate SRE ID.

The SRE Bulk Access Change Form facilitates the bulk renewal of account access for 365 days. User access renewals requiring specific changes to access and resources should use the “SRE Enrollment and Access Change Form”.

-----  
-----

<b>Renew</b>	<b>NetID</b>	<b>First Name</b>	<b>Last Name</b>	<b>Training Confirmation</b>

**Tenant Coordinator Acknowledgement**

By signing below, the study coordinator acknowledges that they have reviewed the provided information, verified required training completion, and renewed SRE access for selected individuals for a period of 365 days.

\_\_\_\_\_  
Printed Tenant Coordinator  
Name

\_\_\_\_\_  
Tenant Coordinator Signature

\_\_\_\_\_  
Date

**Case Comprehensive Cancer Center  
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**SECTION 4: TRIAL REGISTRATION (TR)**

**Case Comprehensive Cancer Center  
Standard Operation Procedures for Clinical Research**

**Title: National Cancer Institute Clinical Trials Reporting Program (CTRP)**  
**SOP #: TR-4.1.0**  
**Version #: 4.0**

<b>Original Approval Date:</b>	<b>July 5, 2011</b>
<b>Effective Date:</b>	<b>August 5, 2011</b>
<b>Revision Dates:</b>	<b>September 4, 2012</b> <b>May 5, 2015</b> <b>June 21, 2017</b>

### **1.0 Standard Operating Procedure Statement / Purpose / Background**

To document the process for registering and maintaining protocols with the National Cancer Institute (NCI) Clinical Trials Reporting Program (CTRP).

### **2.0 Scope**

As a NCI-designated comprehensive cancer center, the Case Comprehensive Cancer Center (Case CCC) is required to register all interventional clinical cancer trials (investigator-initiated (IIT) and proprietary) that were open to accrual as of January 1, 2009. NCI-designated cancer centers are also required to report accrual data for IIT and proprietary trials for studies open to accrual as of January 1, 2012.

### **3.0 Definitions**

- 3.1 OnCore® Clinical Trials Management System (referred to as OnCore):** Database to track information from clinical trials conducted by the Case CCC.
- 3.2 CTRP Registration Coordinator:** Person responsible for registering and maintaining trials. Member of the Clinical Research Office.
- 3.3 Proprietary Trials:** Industry-sponsored trials.
- 3.4 Study Personnel:** Personnel responsible for entering data into OnCore. Required fields in OnCore for CTRP registration are listed in Appendix I.

### **4.0 Procedure**

The Case CCC Clinical Research Office CTRP registration coordinator is responsible for registering trials with CTRP.

- 4.1 Communication:** New trials are put into the OnCore database by the Protocol Review and Monitoring Committee (PRMC) manager. Notification of PRMC approval is automatically sent to the CTRP registration coordinator through the OnCore database. As trials are reviewed and approved by the University Hospitals IRB and the Cleveland Clinic IRB, the approval information is entered into OnCore. IRB notification is generated by the regulatory coordinator in OnCore and is sent to the CTRP registration coordinator. IIT Trials are registered in the CTRP database after IRB approval. Trials not sponsored by Case CCC are registered after PRMC approval. Trials are required to be registered prior to enrolment of the first subject.



## **Case Comprehensive Cancer Center Standard Operation Procedures for Clinical Research**

- 4.2 Sponsors other than Case CCC:**
- 4.2.1 Cooperative Group trials:** These groups are responsible for registering their respective trials in CTRP. Therefore, these trials are not registered by Case CCC registration coordinator.
  - 4.2.2 Outside Investigator Initiated Trials (IIT):** When Case CCC is participating on an IIT sponsored by another institution, the lead institution is responsible for adding Case CCC as a site in CTRP and any accrual to the CTRP accrual website.
    - 4.2.2.1** When another institution is participating on a Case CCC investigator initiated trial, Case CCC is responsible for adding all participating sites to CTRP and any accrual from these sites to the CTRP accrual website.
  - 4.2.3 Proprietary trials:** If the trial is not already in CTRP, these trials can be uploaded by the registration coordinator at any of the participating sites from ClinicalTrials.gov
    - 4.2.3.1 Participating Site for proprietary trials:** The CTRP registration coordinator is responsible for adding Case CCC to trials already registered in CTRP.
- 4.3 Registration of Case CCC sponsored trials:** All information and the required documents (IRB approval letter, protocol and consent form) are obtained from OnCore after initial IRB approval. Study personnel are responsible for entering this information in OnCore ( Appendix I). Upon acceptance of a trial registration in CTRP, a NCI # is assigned to the protocol. The NCI # is entered in the management screen of OnCore by the CTRP registration coordinator.
- 4.4 Review Information:** Registration confirmation emails are sent within 24 hours from CTRP to the registration coordinator. Within 8-10 business days CTRP sends a Trial Summary Report (TSR) and xml file to the registration coordinator. The registration coordinator reviews the TSR and sends corrections, as applicable, to CTRP at [ncictro@mail.nih.gov](mailto:ncictro@mail.nih.gov). The xml file may be used for Clinicaltrials.gov registration.
- 4.5 Maintenance:** Protocol amendments and status changes are entered in OnCore by study personnel and notification is then sent to the CTRP registration coordinator. Amendment and status updates are registered with CTRP upon notification. Amendments are required to be registered with CTRP within 20 days of IRB approval. Revised protocol, consent, IRB approval letter and summary of changes documents are sent with the amendment update. Protocol status definitions are listed in Appendix II.
- 4.5.1** Amendment changes may include PI, title, sites, objectives/outcomes, study design and eligibility criteria.
  - 4.5.2** All dates of the CTRP registration and maintenance processes are recorded on an OnCore checklist.
- 4.6 Accrual Reporting:** required quarterly to the CTRP accrual website (<https://trials.nci.nih.gov/accrual/home.action>)
- 4.6.1 Proprietary Trials:** only requires summary accrual
  - 4.6.2 Investigator-initiated Trials:** report from OnCore is exported for all trials open during any part of a quarter. This report includes demographic information for individual subjects including the

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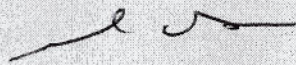
following: study subject ID, zip code, country code, date of birth (YYYY/MM), gender, ethnicity, registration date (YYYY/MM/DD), registering group, disease site, race.

**5.0 References**

- <https://oncore.cwru.edu> (Case CCC database for clinical trials)
- <https://trials.nci.nih.gov> (NCI-CTRP registration site)
- <https://trials.nci.nih.gov/accrual/home.action> (NCI\_CTRP accrual reporting site)
- <http://www.cancer.gov/clinicaltrials> (NCI public website)
- [ncictro@mail.nih.gov](mailto:ncictro@mail.nih.gov) (CTRP email contact)

**6.0 Appendices**

- Appendix I: Required OnCore Data Fields for NCI-Clinical Trials Reporting Program (CTRP)
- Appendix II: Protocol Status Definitions

<b>SOP #: TR-4.1.0; Version #: 4.0</b>	
<b>Approved by:</b>	
Name: Mikkael Sekeres, MD	
Position: Deputy Associate Director of Clinical Research; Director of Clinical Trial	
Signature: 	Date: 09-06-17

**Case Comprehensive Cancer Center  
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**Appendix I**

**Required OnCore Data Fields for NCI-Clinical Trials Reporting Program (CTRP)**

1. Lead organization trial identifier
2. Title
3. Phase
4. Trial type (intervention or non-interventional)
5. Primary Purpose (treatment, prevention, supportive care, screening, diagnostic, health services research, basic science, other)
6. Accrual disease terminology (e.g. ICD9)
7. Lead Organization
8. Principal Investigator
9. Sponsor
10. Responsible Party (sponsor, investigator, sponsor-investigator)
11. Data Table 4 funding sponsor type (institutional, national group, externally peer-reviewed, industrial)
12. Data Table 4 funding sponsor
13. NIH grant information
  - a. Funding mechanism (e.g. P30)
  - b. Institution code (AA, AE, CA, etc.)
  - c. Serial Number
  - d. NCI Division/Program Code (OD, CCR, CIP, etc.)
14. Trial Status
  - a. Status Date
  - b. Status
15. Start Date
16. Primary Completion Date
17. IND information (if applicable)
  - a. IND/IDE type
  - b. IND/IDE number
  - c. IND/IDE Grantor (CBER, CDRH, CDER)
  - d. IND/IDE Holder Type (industry, investigator, NCI, etc.)
  - e. NIH Institution
  - f. Expanded Access (yes/no)
    - i. If yes, expanded access type
  - g. Exempt (yes/no)
18. Oversight Authority country
19. Trial Oversight authority organization (institutional review board, FDA)
20. FDA regulated intervention indicator (yes/no)
21. Section 801 indicator (yes/no)
22. Delayed posting indicator (yes/no)
23. Data monitoring committee (yes/no)
24. Protocol: must include principal investigator's contact information: name, address, phone number, email *and* sponsor organization: name, address, email *and* lead organization: name, address, email
25. IRB approval letter
26. Summary of changes for amendments
27. Informed Consent

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**Appendix II  
Protocol Status Definitions**

<b>CTRP</b>	<b>Clinicaltrials.gov</b>
<b>In Review:</b> Trial is currently under IRB review	<b>Not yet recruiting:</b> participants are not yet being recruited. <i>This also applies to approved studies in CTRP</i>
<b>Approved:</b> Trial has been IRB approved	
<b>Withdrawn:</b> Trial has been withdrawn from development and review prior to enrollment of first participant. **	<b>Withdrawn:</b> trial halted prematurely, prior to enrollment of first participant **
<b>Active:</b> Trial is open for accrual	<b>Recruiting:</b> participants are currently being recruited
<b>Temporarily Closed to Accrual:</b> Trial is temporarily not accruing. **	<b>Suspended:</b> recruiting or enrolling participants has halted prematurely but potentially will resume **
<b>Temporarily Closed to Accrual and Intervention:</b> Trial is temporarily not accruing. Participants are not receiving intervention. **	
<b>Closed to Accrual:</b> Trial has been closed to participant accrual. Participants are still receiving treatment/intervention.	<b>Active, not recruiting:</b> study is ongoing (i.e., patients are being treated or examined), but participants are not currently being recruited or enrolled
<b>Closed to Accrual and Intervention:</b> Trial has been closed to participant accrual. No participants are receiving treatment/intervention, but participants are still being followed according to the primary objectives of the study.	
<b>Administratively Complete:</b> Trial has been completed <b>prematurely</b> (for example, due to poor accrual, insufficient drug supply, IND closure, etc.) **	<b>Terminated:</b> recruiting or enrolling participants has halted <b>prematurely</b> and will not resume; participants are no longer being examined or treated **
<b>Complete:</b> Trial has been closed to accrual and follow-up. Participant treatment/intervention has been completed and participants are no longer monitored for trial endpoints (i.e., last patient's visit has occurred). The trial has met its objectives.	<b>Completed:</b> The study has ended normally, and participants are no longer being examined or treated (that is, the "last subject, last visit" has occurred).
<b>Primary Completion Date:</b> date that the final subject was examined or received an intervention for the purposes of final collection of data for the <b>primary outcome</b> , whether the clinical trial concluded according to the pre-specified protocol or was terminated.	<b>Primary Completion Date:</b> date that the final subject was examined or received an intervention for the purposes of final collection of data for the <b>primary outcome</b> , whether the clinical trial concluded according to the prespecified protocol or was terminated.
<b>Completion Date:</b> The date that the trial has been closed to accrual and follow-up. Participant treatment/intervention have been completed and participants are no longer monitored for trial endpoints. The trial has met its objectives	<b>Study Completion Date:</b> Final date on which data was (or is expected to be) collected.
** Reason must be stated as to why trial stopped.	** Reason must be stated as to why study stopped.

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<b>Title: Registration of Clinical Trials on ClinicalTrials.Gov</b> <b>SOP #: TR-4.2.0</b> <b>Version #: 4.0</b>
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<b>Original Approval Date:</b>	<b>May 3, 2011</b>
<b>Effective Date:</b>	<b>July 3, 2011</b>
<b>Revision Dates:</b>	<b>September 4, 2012</b> <b>April 7, 2015</b> <b>June 21, 2017</b>

**1.0 Standard Operating Procedure Statement / Purpose / Background**

To document the process for registering and maintaining trials with Clinicaltrials.gov.

**2.0 Scope:** The U.S. Food and Drug Administration (FDA) is the government agency that requires registration of clinical trials. The ClinicalTrials.gov website is maintained by the National Library of Medicine (NLM) at the National Institutes of Health (NIH)

**2.1** The Food and Drug Administration Amendments Act of 2007 (FDAAA or US Public Law 110-85) passed on September 27, 2007 requires mandatory registration and results reporting for certain clinical trials of drugs, biologics, and devices. Case Comprehensive Cancer Center (Case CCC) is required to register applicable clinical trials within 21 days of enrollment of first participant. Results from the clinical trials must be registered within 1 year of completing data collection for the pre-specified primary outcome. The purpose of this law is intended to facilitate enrollment in clinical trials, allow for tracking of the progress of such trials and address problems with the lack of timely dissemination of research findings.

**2.2** The International Committee of Medical Journal Editors (ICMJE) requires all interventional trials (including all phases, surgical, behavioural and other interventions) to be registered in ClinicalTrials.gov. All trials must be registered prior to enrollment of first participant.

**3.0 Responsibility:** The Case Comprehensive Cancer Center registration coordinator registers all applicable clinical trials and reports results.

**4.0 Definitions:**

**4.1** Applicable clinical trials: Trials of Drugs and Biologics; Controlled, clinical investigations, other than Phase I investigations, of a product subject to FDA regulation; Trials of Devices: Controlled trials with health outcomes of a product subject to FDA regulation (other than small feasibility trials) and pediatric post-market surveillance trials.

**4.2** Registration Coordinator: Person(s) responsible for registering and maintaining trials.

## **Case Comprehensive Cancer Center Standard Operation Procedures for Clinical Research**

- 4.3 Sponsor: Initiator and owner of the study data, grant recipient, IND holder (if applicable).
- 4.4 CTRP: The National Cancer Institute Clinical Trials Reporting Program [Refer to SOP TR-4.1.0, National Cancer Institute Clinical Trials Reporting Program (CTRP)]
- 4.5 OnCore<sup>®</sup> Clinical Trials Management System (referred to as OnCore): Database to track information from clinical trials conducted by the Case CCC.
- 4.6 Study Personnel: Personnel responsible for entering data into OnCore.

### **5.0 Procedure**

The Case CCC maintains a central office with a registration coordinator responsible for registering and maintaining trials within the Case CCC ClinicalTrials.gov account.

- 5.1 **Interventional Treatment Trials**: To be compliant with FDAAA and ICMJE regulations, all interventional clinical trials are registered after approval by the Protocol Review and Monitoring Committee (PRMC). A PDF file is sent to the PI for approval of the information. (See ClinicalTrials.gov website for required data elements.)
  - 5.1.1 **IND trials**: If the PI is the IND holder, then he/she is the responsible party. The registration coordinator will set up an account in clinicaltrials.gov for the PI to approve and release the study.
  - 5.1.2 **Once the protocol is approved and “released,”** personnel at ClinicalTrials.gov will review and post comments on the Case CCC account at ClinicalTrials.gov. Corrections can be made, as needed, and the trial can be re-released. If there are no review comments the trial is released to the public website within 2 business days.
- 5.2 **Maintenance**: Per FDA regulations, trials must be updated every six months. Clinicaltrials.gov notifies the registration coordinator’s account of which trials are due for updates. Changes are made on an ongoing basis as the registration coordinator gets notifications of amendment and status updates.
- 5.3 **Results reporting**: see SOP#: TR-4.3.0: Clinical Trials Results Reporting with ClinicalTrials.gov

### **6.0 Penalties for non-compliance**

- 6.1 Up to \$10,000 per day fine for unreported results
- 6.2 Withholding of NIH grant funding
- 6.3 ICMJE may refuse to publish work associated with the trial

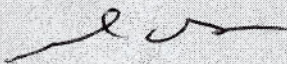
### **7.0 References**

- <https://sreportal.case.edu> (Gateway to Case CCC database for clinical trials)
- <https://register.clinicaltrials.gov> (ClinicalTrials.gov registration site)
- <http://prsinfo.clinicaltrials.gov/s801-fact-sheet.pdf> (public law info)
- <http://clinicaltrials.gov> (ClinicalTrials.gov public website)
- <http://prsinfo.clinicaltrials.gov/definitions.html> (data element definitions)
- <https://trials.nci.nih.gov> (NCI-CTRP registration site)
- <http://www.cancer.gov/clinicaltrials> (NCI public website)

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- [ncictro@mail.nih.gov](mailto:ncictro@mail.nih.gov) (CTRP email contact)

**8.0 Appendices:** None.

<b>SOP #: TR-4.2.0; Version #: 4.0</b>	
<b>Approved by:</b>	
Name: Mikkael Sekeres, MD	
Position: Deputy Associate Director of Clinical Research; Director of Clinical Trials	
Signature: 	Date: 09-06-17

**Case Comprehensive Cancer Center  
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**Title: Clinical Trials Results Reporting with ClinicalTrials.gov**  
**SOP #: TR-4.3.0**  
**Version #: 4.0**

<b>Original Approval Date:</b>	<b>October 2, 2012</b>
<b>Effective Date:</b>	<b>December 6, 2012</b>
<b>Revision Dates:</b>	<b>February 3, 2014</b> <b>April 7, 2015</b> <b>June 21, 2017</b>

**1.0 Standard Operating Procedure Statement / Purpose / Background**

To document the process for reporting clinical trial results with ClinicalTrials.gov.

**2.0 Scope:** The U.S. Food and Drug Administration (FDA) is the government agency that requires registration and results reporting of clinical trials. The ClinicalTrials.gov website is maintained by the National Library of Medicine (NLM) at the National Institutes of Health (NIH)

**2.1 ClinicalTrials.gov:** The Food and Drug Administration Amendments Act of 2007 (FDAAA or US Public Law 110-85) passed on September 27, 2007 requires mandatory registration and results reporting for certain clinical trials of drugs, biologics, and devices. Results are required for all phases other than Phase I and small feasibility trials.

**2.2 Case Comprehensive Cancer Center (Case CCC)** is required to register applicable clinical trials within 21 days of a trial activation or “opening to accrual”. Results from the clinical trials must be registered within 1 year of completing data collection for the pre-specified primary outcome. The purpose of this law is intended to facilitate enrolment in clinical trials, allow for tracking of the progress of such trials and address problems with the lack of timely dissemination of research findings.

**2.3 All NIH funded interventional trials, regardless of phase, must report results within 1 year of completing data collection for the pre-specified primary outcome or risk loss of funding.**

**3.0 Responsibility**

The Case CCC registration coordinator registers all applicable clinical trials and reports results.

**4.0 Definitions**

**4.1 Applicable Clinical Trials:** Trials of Drugs and Biologics: Controlled, clinical investigations, other than Phase I investigations, of a product subject to FDA regulation; Trials of Devices: Controlled trials with health outcomes of a product subject to FDA regulation (other than small feasibility trials) and pediatric postmarket surveillance trials. CTRP: The National Cancer Institute Clinical Trials Reporting Program [Refer to SOP TR-4.1.0, National Cancer Institute Clinical Trials Reporting Program (CTRP)].



**Case Comprehensive Cancer Center  
Standard Operation Procedures for Clinical Research**

- 4.2 Registration Coordinator:** Person(s) responsible for registering and maintaining trials. The registration coordinator is also an administrator of the Case CCC ClinicalTrials.gov account.
- 4.3 Sponsor:** Initiator and owner of the study data, grant recipient, IND holder (if applicable).
- 4.4 OnCore® Clinical Trials Management System (referred to as OnCore):** Database to track information from clinical trials conducted by the Case CCC.
- 4.5 Study Personnel:** Personnel responsible for entering data into OnCore.

**5.0 Procedure**

The Case CCC maintains a central office with a registration coordinator responsible for results reporting with ClinicalTrials.gov.

Information for results reporting comes from the Principal Investigator, statistician(s) and the OnCore database. It is critical that data in OnCore are maintained and updated on an on-going basis by PIs and study staff.

- 5.1** The primary completion date (PCD) determines the time frame for results reporting. The primary completion date is the date when the final subject was examined and/or received an intervention for the purposes of final collection of data for the pre-specified primary outcome (as per protocol), regardless whether the clinical trial was completed or terminated. The sponsor has one year from this date to enter trial results.
  - 5.1.1** Patient status dates and primary outcome time frame determines the primary completion date.
  - 5.1.2** The registration coordinator receives notification once a study is closed to accrual. The registration coordinator will then monitor the patient status (on treatment, off treatment, off study) to determine the PCD. This date can be entered in ClinicalTrials.gov as “anticipated” and updated as the study moves forward. Once the date is set as “actual” then the sponsor has 1 year from this date to enter results.
  - 5.1.3** The primary completion date field is updated in OnCore by the registration coordinator.
  - 5.1.4** The registration coordinator will contact the PI and study team to confirm the primary completion dates.
- 5.2 Results Modules:** there are five modules of data required.
  - 5.2.1 Participant Flow:** Description of the number of research participants starting and completing the study, including exclusions and dropouts, for *each arm* or comparison group
  - 5.2.2 Baseline Characteristics:** Demographic and baseline data for the study population and *each arm* or comparison group
  - 5.2.3 Outcome Measures and Statistical Analyses:** Table of outcome measure values for *each arm* or comparison group, including appropriate statistical analyses. For all pre-specified primary and secondary outcome measures: name and description; unit of

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measurement; time frame; analysis population; and summary data, total and by arm.

**5.2.4 Adverse Events:** Number and frequency of all serious adverse events and other adverse events exceeding a specified frequency threshold in *each arm* or comparison group, grouped by organ system.

**5.2.5 Documents:** The final protocol and statistical analysis plan is required at the time results are submitted. The protocol must include the official title, NCT number, version date, and summary table of all global IRB amendments. If a statistical analysis plan is not included in the protocol, it must be submitted separately. Study names, addresses, and other personally identifiable information may be redacted from the document.

### **5.3 Process for clinical trials results registration.**

**5.3.1** The registration coordinator will contact the study data manager prior to entering results to confirm that all data has been entered into the OnCore system

**5.3.2** The registration coordinator will enter applicable information on a template from the OnCore database, using the DSMC and Biostats Consoles (Appendix I).

**5.3.3** The registration coordinator will send the template to the PI and study team requesting additional required information. The completed template is returned to the registration coordinator for reporting results in ClinicalTrials.gov.

**5.3.2** If necessary the PI, statistician and/or study staff will be contacted to discuss clarifications. Please note that for trials with already published manuscripts, while the manuscripts are useful, they do not replace the template.

**5.3.3** After all the data are entered in ClinicalTrials.gov and reviewed and verified by the PI and statistician, the information can be formally submitted (released). IND trials must be released by the PI.

**5.3.4** ClinicalTrials.gov will review the submission and post comments for corrections/clarifications. Depending on the nature of corrections, these can be done by the registration coordinator and/or PI, as necessary. Once the review process is complete, ClinicalTrials.gov will send notification to the registration coordinator (and to PI, if PI is an IND holder) that the submission of study results has been approved and will be published on the ClinicalTrials.gov website within 2 business days.

**5.3.5** Secondary outcome results, if not reported at initial results submission, are reported when data have been analyzed and tabulated. Anticipated posting dates must be included at the time of primary outcome results entry. The PI and statistician are responsible for communicating this information to the registration coordinator.

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**6.0 Penalties for non-compliance**

6.1 Up to \$10,000 per day fine for unreported results

6.2 Withholding of NIH grant funding

6.3

**7.0 References**

- <https://oncore.cwru.edu> (Case CCC database for clinical trials)
- <https://register.clinicaltrials.gov> (ClinicalTrials.gov registration site)
- <http://clinicaltrials.gov> (ClinicalTrials.gov public website)
- <http://prsinfo.clinicaltrials.gov/s801-fact-sheet.pdf> (public law info)
- [http://prsinfo.clinicaltrials.gov/results\\_definitions.html](http://prsinfo.clinicaltrials.gov/results_definitions.html) (results data element definitions)
- <https://trials.nci.nih.gov> (NCI-CTRP registration site)
- <http://www.cancer.gov/clinicaltrials> (NCI public website)
- [ncictro@mail.nih.gov](mailto:ncictro@mail.nih.gov) (CTRP email contact)

**8.0 Appendices**

- Appendix I: CTGOV Results Reporting Template.

**SOP #: TR-4.3.0; Version #: 4.0**

**Approved by:**

Name: Mikkael Sekeres, MD

Position: Deputy Associate Director of Clinical Research; Director of Clinical Trials

Signature:



Date:

09.06.17

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APPENDIX I

**CTGOV Results Reporting Template**

CASE XXXX: Title/PI

**Participant Flow:** Description of the number of research participants starting and completing the study, including exclusions and dropouts, for each arm or comparison group (frequently reported as a CONSORT diagram in a journal article) and for each period/milestone.

**Period(s) \***

Definition: Discrete stages or interval of trial activity of a clinical trial during which numbers of participants at specific significant events or points of time are reported. If only one period, use *Overall Study* for "Period Title." Example of two periods: sertraline then placebo; placebo then sertraline; double blind then open blind. (Time Change)

**Milestone(s) \***

Definition: Specific events or time points in the trial when the numbers of participants are reported. While there is no limit to the number of milestones that may be used in a single period, data are required for two milestones, STARTED and COMPLETED, within each period. (Population Change)

	ARM/GROUP 1	ARM/GROUP 2
<b>START</b>		
Period/milestone		
<b>COMPLETED</b>		
<b>Reason not completed</b>		
<b>ADVERSE EVENT</b>		
<b>WITHDRAWAL by SUBJECT</b>		
<b>DEATH</b>		
<b>LACK of EFFICACY</b>		
<b>LOST to FOLLOW-UP</b>		
<b>PHYSICIAN DECISION</b>		
<b>PREGNANCY</b>		
<b>PROTOCOL VIOLATION</b>		
<b>OTHER (EXPLAIN)</b>		

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**Baseline characteristics:** Demographic and baseline data for the study population and each arm or comparison group (frequently reported as “Table 1” in a journal article).

**Study-Specific Baseline Measure:** clinical measures relevant to the study

- Clinical characteristics, including baseline values of outcome measures
- Prior and concurrent treatment characteristics

AGE	ARM/GROUP 1	ARM/GROUP 2
Continuous (Mean +/- SD)		
20-29		
30-39		
40-49		
50-59		
60-69		
70-79		
80-89		
GENDER		
Female		
Male		
RACE		
American Indian or Alaska Native		
Asian		
Native Hawaiian or Other Pacific Islander		
Black or African American		
White		
More than one race		
Unknown or Not Reported		
ETHNICITY		
Hispanic or Latino		
Not Hispanic or Latino		
Unknown or Not Reported		
STUDY SPECIFIC BASELINE MEASURE (title, unit of measure, measure type*, dispersion/precision)		

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<b>type*)</b>		

**\*Measure Type:**

- Number
- Mean
- Median
- Least Squares Mean
- Geometric Mean
- Log Mean

**\*Measure of Dispersion:**

- Not Applicable
- Standard Deviation
- Inter-Quartile Range
- Full Range

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**Outcome Measures and Statistical Analyses:** Table of outcome measure values for each arm/comparison group, including appropriate statistical analyses. For all pre-specified primary and secondary outcome measures: name and description; unit of measurement; time frame; analysis population; and summary data, total and by arm.

**Analysis Population Description:**

Definition: Explanation of how the number of participants for analysis was determined. Indicate whether the analysis was "per protocol", "intention to treat (ITT)", or another method.

<b>PRIMARY OUTCOME</b>		
Time Frame		
Analysis Population Description		
No. Participants Analyzed		
MEASURE (title, unit of measure, measure type*, dispersion/precision type*)	<b>ARM/GROUP 1</b>	<b>ARM/GROUP 1</b>
<b>Statistical Analysis (provide only one): P value, Confidence Interval OR Estimated Value</b>		
<b>P value</b> Method		
<b>Confidence Interval</b> Number sides Lower limit Upper limit Parameter Dispersion Type		
<b>Estimated Value</b> Parameter		

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<b>SECONDARY OUTCOME</b>		
Time Frame		
Analysis Population Description		
No. Participants Analyzed		
MEASURE (title, unit of measure, measure type*, dispersion/precision type*)	<b>ARM/GROUP 1</b>	<b>ARM/GROUP 2</b>
<b>Statistical Analysis (provide only one): P value, Confidence Interval OR Estimated Value</b>		
<b>P value</b> Method		
<b>Confidence Interval</b> Number sides Lower limit Upper limit Parameter Dispersion Type		
<b>Estimated Value</b> Parameter		

**\*Measure Type:**

Number  
Mean  
Median  
Least Squares Mean  
Geometric Mean  
Log Mean

**\*Measure of Dispersion:**

Not Applicable  
Standard Deviation  
Inter-Quartile Range  
Full Range



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**ADVERSE EVENT DATA WILL BE EXTRACTED FROM ONCORE**

**Time Frame for Adverse Event Reporting:** Period in which the reported adverse event data were collected (e.g., 1 year, 6 months)

**Serious Adverse Events** include adverse events that result in death, require either inpatient hospitalization or the prolongation of hospitalization, are life-threatening, result in a persistent or significant disability/incapacity or result in a congenital anomaly/birth defect. Other important medical events, based upon appropriate medical judgment, may also be considered Serious Adverse Events if a trial participant's health is at risk and intervention is required to prevent an outcome mentioned.

**Serious Adverse Events:** A table of *all* anticipated and unanticipated serious adverse events, grouped by organ system, with number and frequency of such events in each arm of the clinical trial.

**Other (Not Including Serious) Adverse Events:** A table of anticipated and unanticipated events (not included in the serious adverse event table) that exceed a frequency threshold within any arm of the clinical trial, grouped by organ system, with number and frequency of such events in each arm of the clinical trial.

**Other (Not Including Serious) Adverse Events** are those that are not Serious Adverse Events that exceed a frequency threshold.

**Frequency Threshold for Reporting Adverse Events:** Overall number of participants affected by one or more Other (Not Including Serious) Adverse Events above the specified Frequency Threshold (e.g., 5%) reported in the table.

**COMMENTS/QUESTIONS:**

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**SECTION 5: PROJECT MANAGEMENT (PM)**

**Case Comprehensive Cancer Center  
Standard Operation Procedures for Clinical Research**

**Title: Transfer of the Lead Institution Responsibilities to the Secondary Institution for Joint Cancer-Related Research Studies**  
**SOP #: PM-5.1.0**  
**Version #: 2.0**

<b>Original Approval Date:</b>	<b>May 3, 2011</b>
<b>Effective Date:</b>	<b>July 3, 2011</b>
<b>Revision Dates:</b>	<b>May 5, 2015</b>

**1.0 Standard Operating Procedure Statement/ Purpose/Background**

To document the process for transferring lead institution responsibilities for joint research.

**2.0 Scope**

All cancer-related research studies.

**3.0 Responsibility**

Principal Investigators; Regulatory Managers; Regulatory Coordinators.

**4.0 Definitions:** None.

**5.0 Procedure**

Transfer of lead site responsibilities will only occur by mutual agreement between the two institutions.

- 5.1 Principal Investigators (PIs) at both institutions must agree in writing (e-mail acceptable) to transfer responsibilities.
- 5.2 The logistical plan to transfer responsibilities must be approved by the PIs at both institutions, as well as managers at both institutions.
- 5.3 The coordinators at both institutions are responsible for determining the logistics of transferring responsibilities, including timing of transfer, , and document sharing, as applicable. The prospective lead site is responsible for submitting an amendment to accept responsibilities of the study to their local IRB. The prospective lead site must receive IRB approval before the outgoing lead site can close the study with their IRB.
- 5.4 The prospective lead site will be responsible for updating IRB approval and transfer of responsibilities in OnCore.
  - 5.4.1 Update Primary Institution in the Managing Group on the Management tab.
  - 5.4.2 Clearly document the submission in the Reviews screen.
  - 5.4.3 Update Role of study staff for outgoing site to “inactive”.
  - 5.4.4 Update Stop Date for each staff of the outgoing site.

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**6.0 References**

<https://oncore.cwru.edu> (OnCore)

<http://cancer.case.edu/researchadmin/prmc> (PRMC instructions and forms-password protected)

<http://casemed.case.edu/ora/irb/irbpolicy.cfm> (Case Cancer IRB SOPs)

**7.0 Appendices:** None.

**SOP #: PM-5.1.0; Version #: 2.0**

**Approved by:**

Name: Mikkael Sekeres, MD

Position: Deputy Associate Director of Clinical Research; Director of Clinical Trial

Signature:



Date:

5/13/15

**Case Comprehensive Cancer Center  
Standard Operation Procedures for Clinical Research**

**Title: Responsibilities of the Lead Institution for Joint Cancer-Related Research Studies**  
**SOP #: PM-5.2.0**  
**Version #: 1.0**

<b>Original Approval Date:</b>	<b>May 3, 2011</b>
<b>Effective Date:</b>	<b>July 3, 2011</b>
<b>Revision Dates:</b>	

**1.0 Standard Operating Procedure Statement/ Purpose/Background**

To document the process for determining the lead institution for joint research studies and to outline the responsibilities of the lead institution.

**2.0 Scope**

All cancer-related research studies.

**3.0 Responsibility**

Principal Investigator; Regulatory Managers; Regulatory Coordinators.

**4.0 Definitions:** None

**5.0 Procedure**

All cancer-related research studies are subject to oversight by the Case Comprehensive Cancer Center (Case CCC). The Case CCC is comprised of three institutions, University Hospitals, Cleveland Clinic and Case Western Reserve University. There are two clinical institutions, Cleveland Clinic and University Hospitals. These institutions are expected to work jointly, and one institution will be considered the lead institution for each trial.

- 5.1** All cancer-related research studies must be reviewed by the Protocol Review and Monitoring Committee (PRMC) and the Case Cancer Institutional Review Board (Case Cancer IRB).
- 5.2** The institution that initiates the review process is called the “lead institution” and is responsible for communicating activity to the other institution.
- 5.3** The lead institution must identify if the other institution would like to participate and clarify with the sponsor if the additional institution is permitted to participate. If yes, the following steps are the responsibility of the lead institution:
  - 5.3.1** Notify the PRMC (and subsequently the Case Cancer IRB) of the institution’s planned participation.
  - 5.3.2** Notify the other institution that they are permitted to participate and relay sponsor contact information.
  - 5.3.3** It is the responsibility of the non-lead institution to contact the sponsor to initiate their start-up process.
- 5.4** The lead institution is responsible for securing PRMC approval and subsequently submitting the study to the Case Cancer IRB.

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- 5.5** The lead institution must notify the sponsor to distribute study materials (e.g. regulatory binders, lab manuals, kits, etc.) to each institution separately.
- 5.6** All internal Serious Adverse Events (SAEs) and internal protocol deviations are to be processed and submitted to the Case Cancer IRB and the Data Safety and Toxicity Committee (DSTC) by the institution where the SAE/protocol deviation occurred. SAEs and deviations are entered into OnCore. A copy of the IRB submission must be sent to the other institution (all SAEs should be shared with both institutions; the lead institution should have a copy of all deviations).
- 5.7** It is the responsibility of the lead institution to keep OnCore updated, including the institution, management, status and IRB submission screens. Documents should be attached for IRB submission, the protocol, and IRB approved, stamped consent(s).
- 5.8** Each site is responsible for entering and updating each of their patient's demographics, consent, eligibility, on/off study date, sequence number, on/off treatment (as applicable), follow-up fields, SAEs and protocol deviations in OnCore.
- 5.9** The lead institution is responsible for submitting all protocol amendments to the Case Cancer IRB (and PRMC if appropriate). A copy of the Case Cancer IRB submission must be distributed to the other participating institution. The paperwork to add or remove study staff should be completed by the site adding/removing the staff. The paperwork is then sent to the lead site for submission to the IRB. The lead site is responsible for updating the Protocol Staff on the Management screen in OnCore upon IRB approval.
- 5.10** The lead institution is responsible for submitting all continuing reviews to the Case Cancer IRB. It is the responsibility of the non-lead institution to provide all relevant data to the lead institution in a timely manner. A copy of the IRB submission must be distributed to the other participating institution. This can be accomplished by attaching the document in OnCore with the Document Type IRB Approval Letter and notify via email the opposite institution.
- 5.11** The lead institution is responsible for processing IRB defined external SAEs.
- 5.12** Internal processing of external safety letters is per institutional policy; however, only the lead institution will submit external safety letters to the IRB and/or DSTC. If external safety letters meet IRB reporting guidelines, a copy of the IRB submission must be distributed to the other participating institution. If immediate action is required for an external safety letter, the lead institution is responsible for submission to the DSTC and for notifying any participating sites that were not already notified by the sponsor.

Should the lead site decide to terminate their participation in a joint study, they should follow the SOP PM-5.1.0, Transfer of the Lead Institution Responsibilities to the Secondary Institution for Joint Cancer-Related Research Studies.

**6.0 References**

<https://oncore.cwru.edu> (OnCore)  
<http://cancer.case.edu/researchadmin/prmc>(PRMC instructions and forms-password protected)  
<http://casemed.case.edu/ora/irb/irbpolicy.cfm> (Case Cancer IRB SOPs)

**7.0 Appendices: None**

**Case Comprehensive Cancer Center  
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**Approved by:**

Name: John Sweetenham, MD

Position: Deputy Associate Director of Clinical Research; Director of Clinical Trials

Signature:



Date:

5/23/11

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**SECTION 6: SUBJECT MANAGEMENT (SM)**



**CaseComprehensiveCancerCenter  
Standard Operation Procedures for Clinical Research**

**Title: Secondary Review of Eligibility for Therapeutic Clinical Trials**  
**SOP #: SM-6.1.0**  
**Version #: 4.0**

<b>Original Approval Date:</b>	<b>May 3, 2011</b>
<b>Effective Date:</b>	<b>July 3, 2011</b>
<b>Revision Dates:</b>	<b>January 7, 2013</b> <b>December 7, 2015</b> <b>July 5, 2016</b>

**1.0 Standard Operating Procedure Statement/ Purpose/Background**

In order to ensure that patients meet all eligibility requirements for a therapeutic study, it is required that the Inclusion and Exclusion criteria be reviewed by a second person, and that supporting documentation be available as source documents for each inclusion/exclusion criteria.

**2.0 Scope**

All cancer-related therapeutic clinical trials.

**3.0 Responsibility**

Any research personnel involved in patient enrollment to therapeutic clinical trials. The secondary review of eligibility is not required for non-therapeutic trials as defined by the NCI.

**4.0 Definitions: None.**

**5.0 Procedure**

- 5.1 Creation of the Inclusion/Exclusion Worksheet.**
  - 5.1.1** For Investigator-initiated studies, or if a worksheet is not provided, an Inclusion/Exclusion worksheet may be created by the regulatory coordinator or the Principal Investigator's designee, or the inclusion/exclusion pages from the protocol will be used.
- 5.2 Completion of the Inclusion/Exclusion Worksheet**
  - 5.2.1** At screening, the research nurse/study coordinator will fill out an Inclusion/Exclusion worksheet for the potential patient, indicating each Inclusion and Exclusion criteria response, ensuring that source documentation for each criterion is available.
  - 5.2.2** Once the Inclusion/Exclusion worksheet is completed, it will be given to the institution's designated personnel for review of secondary eligibility and signature.
- 5.3 The Site Principal Investigator or Co-Investigator must confirm eligibility status by signing and dating the Inclusion/Exclusion worksheet prior to the patient registration.**
  - 5.3.1** A total of three (3) reviews are required for the study eligibility confirmation and one must be by the Principal Investigator or Co-Investigator.

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**5.3.2** If consensus agreement on patient eligibility is not met, the institute/program research director or designee who is not an investigator on the study will make the final determination.

**5.3.2.1** Note: Per Case Comprehensive Cancer Center policy, no eligibility waivers are accepted.

**5.4** The responsible research personnel will enter the patient information into OnCore.

**5.4.1** On the Eligibility tab, the responsible research personnel will enter the following fields:


- a) Version Date: This denotes the version date of the protocol eligibility criteria.
- b) Verified By: The name of the person performing the secondary review of the eligibility, as outlined above, shall be entered here. The name of the person shall be used, not just initials.
- c) Status Date: The date of secondary eligibility review shall be entered here.
- d) Eligibility Status: If the patient has met the Inclusion/Exclusion criteria, then they will be marked as "Eligible".
- e) If the patient is determined to be ineligible, then the responsible research personnel shall mark the patient status in ONCORE as "Ineligible".

**6.0 References**

**6.1** NCI clinical protocol types.

**6.2** Case Comprehensive Cancer Center eligibility waiver policy.

**7.0 Appendices:** None.

<b>SOP #: SM-6.1.0; Version #: 4.0</b>	
Approved by:	
Name: Mikkael Sekeres, MD	
Position: Deputy Associate Director of Clinical Research; Director of Clinical Trials	
Signature: 	Date: 07-13-16

**Case Comprehensive Cancer Center  
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**Title: Verification and Confirmation of Independent Review of Patients' Responses on Investigator-Initiated Clinical Trials**  
**SOP #: SM-6.2.0**  
**Version #: 2.0**

<b>Original Approval Date:</b>	<b>October 1, 2013</b>
<b>Effective Date:</b>	<b>November 21, 2013</b>
<b>Revision Dates:</b>	<b>December 5, 2016</b>

**1.0 Standard Operating Procedure Statement/ Purpose/Background**

To outline the process for confirmation of responses for Case Comprehensive Cancer Center (Case CCC) investigator-initiated trials (IITs).

The process of reviewing sets of comparative measurements is an essential Quality Assurance (QA) function of an academic medical center. In NCI-designated Cancer Centers, the data safety oversight is performed on all investigator-initiated clinical trials by the Data Safety and Toxicity Committee (DSTC).

The DSTC oversight includes the review of the process in which an independent reviewer(s) confirmed that patients had a response (solid tumor and hematologic response) following cancer treatment on an investigator-initiated investigational studies. The DSTC review of the process is critical for: 1) QA; 2) compliance with federal NCI regulations; and 3) assurance of independent review to avoid conflict of interest and bias.

The written reply from the DSTC regarding its review of the response will follow the DSTC meeting when the response is presented and discussed. The DSTC will also assist to facilitate the process for additional reviews in cases when the independent review does not confirm readings by the Principal Investigator (PI). The PI or the research coordinator will provide the DSTC with the appropriate imaging and response documents necessary to complete the response confirmation process.

It is the responsibility of each Principal Investigator to ensure that the process of independent review takes place and that applicable information and documents are submitted to the DSTC in a timely fashion.

**2.0 Scope**

All Case CCC cancer-related IITs.

**3.0 Responsibility**

The Principal Investigator (PI) for each Case CCC cancer-related investigator-initiated treatment clinical trial.

**4.0 Definitions:** None.

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**5.0 Procedure**

- 5.1 Solid tumor and hematologic responses will be confirmed as follows: responses must be determined by the treating physician or PI and must be confirmed (or not) by a second physician.
- 5.2 Principal Investigator and/or study team will enter required information regarding the responses into OnCore.
- 5.3 Principal Investigator and/or study team will submit information on responses to the Case CCC DSTC on an ongoing basis.
- 5.4 The DSTC prepare quarterly reports using OnCore to ensure that all responses have been submitted to DSTC for review of the response confirmation.  
For solid tumor responses the following information and documents must be submitted to the DSTC: 1) a completed tumor measurement form. Responses must be determined by the treating physician or PI and must be confirmed (or not) by a second physician; 2) all source documents that support the conclusion (e.g. MRI report, CT report, etc.); and 3) the section of the protocol delineating the response criteria to be used.  
For hematologic responses the following information and documents must be submitted to the DSTC: 1) the source documentation that demonstrates a response (e.g. bone marrow pathology report, laboratory reports etc.); 2) a note from the treating physician or PI describing the response events; and 3) a note from the second physician reviewer stating concordance or discordance with the primary response review; and 4) the section of the protocol delineating response criteria to be used.
- 5.5 The written reply from the DSTC regarding its review of the response will be sent to the PI following the meeting when the response was presented.

**6.0 References**

- 6.1 Case Comprehensive Cancer Center Clinical Trials Operations Manual.

**7.0 Appendices: None.**

<b>SOP #: SM-6.2.0; Version #: 2.0</b>	
Approved by:	
Name: Mikkael Sekeres, MD	
Position: Deputy Associate Director of Clinical Research; Director of Clinical Trials	
Signature: 	Date: 12-07-2016

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**5.0 Procedure**

- 5.1 Tumor responses will be independently confirmed in the following ways:
  - 5.1.1 UH solid tumor response: designated radiologist or radiation oncologist reads base, initial and confirmatory scans (primary source documents) and confirms (or not) initial measurements done by the investigator.
  - 5.1.2 UH hematologic response: two hematology physicians (investigator and one additional physician) are needed for confirmation.
  - 5.1.3 CCF solid tumor response and hematologic response: CCF will assign *ad hoc* reviewers (from a selected group of faculty) to participate in the process of response confirmation.
- 5.2 Principal Investigator and/or study team will enter required information regarding the responses into OnCore.
- 5.3 Principal Investigator and/or study team will submit information on responses to the Case CCC DSTC on an ongoing basis.
- 5.4 The DSTC will be preparing quarterly reports using OnCore to ensure that all responses have been submitted to DSTC for review of the response confirmation.
- 5.5 For solid tumor responses the following information and documents have to be submitted to the DSTC: 1) a completed tumor measurement form from both the treating physician and one physician not participating in the study; 2) all source documents that support the conclusion (e.g. MRI report, CT report, etc.); and 3) the protocol response section of the protocol.
- 5.6 For hematologic responses the following information and documents have to be submitted to the DSTC: 1) the source documentation that demonstrates a response (e.g. bone marrow pathology report, laboratory reports etc.); 2) the section of the protocol that describes and discusses responses; and 3) a note from the treating physician, as well as a note from a second physician not participating in the study, that states that he/she agrees that a response has occurred.
- 5.7 The written reply from the DSTC regarding its review of the response will be sent to the PI following the meeting when the response was presented.

**6.0 References**

- 6.1 Case Comprehensive Cancer Center Clinical Trials Operations Manual.

**7.0 Appendices: None.**

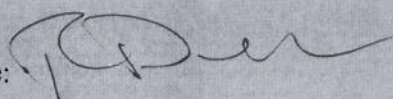
SOP #: SM-6.2.0; Version #: 1.0

Approved by:

Name: Robert Dreicer, MD

Position: Deputy Associate Director of Clinical Research; Director of Clinical Trials

Signature:



Date:

10/7/13

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**SECTION 7: DATA SAFETY AND  
MONITORING COMMITTEE (DSTC)  
&  
DATA SAFETY AND MONITORING (DSM)**

**Case Comprehensive Cancer Center  
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**Title: Submission of Documents to the Data Safety and Toxicity Committee**  
**SOP #: DSTC/DSM-7.1.0**  
**Version #: 1.0**

<b>Original Approval Date:</b>	<b>September 2, 2014</b>
<b>Effective Date:</b>	<b>November 2, 2014</b>
<b>Revision Dates:</b>	

**1.0 Standard Operating Procedure Statement / Purpose / Background**

To document the requirements, process, and timeline for submitting objective responses, audit and monitoring results, continuing reviews, serious adverse events, and major deviations to the Data Safety and Toxicity Committee and the process and timeline for notification of approval.

**2.0 Scope**

The purpose of the DSTC is to oversee all aspects of data monitoring and safety for institutionally sponsored, investigator-initiated interventional trials and those trials that do not have external monitoring that are active at the Case CCC.

**3.0 Responsibility**

It is the responsibility of the committee to review objective responses, audit results, monitoring results that are questionable or unacceptable, continuing reviews, serious adverse events, and major deviations in terms of data integrity and patient safety.

**4.0 Definitions**

- 4.1 Case CCC: Case Comprehensive Cancer Center
- 4.2 CR: Continuing Review
- 4.3 Deviation: Any variation from the protocol requirements
- 4.4 DSTC: Data Safety and Toxicity Committee
- 4.5 OnCore™: Clinical Trials Management System (referred to as OnCore): database to track information from clinical trials conducted by the Case CCC
- 4.6 PI: Principal Investigator
- 4.7 SAE: Serious Adverse Event

**5.0 Procedures**

- 5.1 All internal SAEs and external SAEs under Investigator-initiated trials purview will be reviewed on a twice monthly basis at the meeting following their receipt by the DSTC.
  - 5.1.1 SAE submission should include an SAE report per the protocol requirements with a matching entry in OnCore per the respective IRB reporting requirements.
    - 5.1.1.1 The DSTC will only review SAEs that occur after initiation of protocol treatment and fall within the defined SAE parameters specified in the protocol.
- 5.2 Major protocol deviations; for example, ineligibility, consent form issues, treatment error or a treatment that is not within the guidelines of the protocol will be reviewed on a twice monthly basis at the meeting following their receipt by the DSTC.

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- 5.2.1** Submission of major deviations should include a detailed OnCore entry including an “Action Taken” per the respective IRB reporting requirements.
- 5.2.2** Deviations deemed to be minor are reviewed by the DSTC at the continuing review.
- 5.3** It is strongly recommended that CRs are sent annually to the DSTC for any investigator initiated trials that have had activity of accrual, had active patients, and/or SAEs during the reporting time frame at least 30 calendar days prior to submission to the IRB. (Refer to Case CCC SOP: DSTC/DSM-7.2.0: *Submission of Continuing Reviews to the Data Safety and Toxicity Committee*)
- 5.4** Objective responses (partial and complete responses) of the Case CCC investigator-initiated trials, and those trials that the physician requests an unbiased review, will be confirmed based on the criteria for response defined in the protocol. (Refer to Case CCC SOP: SM-6.2.0: *Verification and Confirmation of Independent Review of Patients’ Responses on Investigator-Initiated Clinical Trials*)
  - 5.4.1** Responses must be confirmed by the treating MD and an independent reviewer, and submitted to DSTC to be considered reportable.
  - 5.4.2** Submission of responses should occur as soon as possible after confirmation of best response.
    - 5.4.2.1** All results will be entered in OnCore into the Review section under DSMC Action History by each institution’s coordinator.
- 5.5** All audit reports should be submitted to the DSTC as soon as possible either after the receipt by PI and study team of an acceptable report from the auditor or after submission of response and corrective action plan to the auditor.
- 5.6** Other items requiring prompt submission to the DSTC include protocol specific special safety reviews, safety concerns and issues referred by either PRMC or monitoring committees for high risk clinical trials, and internal SAEs on behavioral trials and should be forwarded to the DSTC site coordinator within 14 calendar days of submission to the respective IRB.
- 5.7** Following submission of any of the aforementioned materials, the DSTC will notify the PI with a copy to any appropriate parties, such as regulatory specialist, research nurse specialist, etc. of confirmation, denial, or questions regarding material submission within 7 calendar days of the DSTC meeting and review.
  - 5.7.1** The DSTC reserves the right to request, as appropriate, changes in the consent form to inform patients of previously unrecognized risks, changes in dose modifications, schedules or toxicity monitoring.
- 5.8** Any delinquency in submission or receipt of the aforementioned materials will be directed to the Administrative Director of the Case CCC Clinical Research Office.

**6.0 References**

Case CCC Data and Safety Monitoring Plan

**7.0 Appendices**

None



**Case Comprehensive Cancer Center  
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**SOP #: DSTC/DSM-7.1.0 Version #: 1.0**

**Approved by:**

Name: Robert Dreicer, MD

Position: Deputy Associate Director of Clinical Research; Director of Clinical Trials

Signature: 

Date: 2/15/14

**Case Comprehensive Cancer Center  
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**Title: Submission of Continuing Reviews to the Data Safety and Toxicity Committee  
SOP #: DSTC/DSM - 7.2.0  
Version #: 1.0**

<b>Original Approval Date:</b>	<b>September 2, 2014</b>
<b>Effective Date:</b>	<b>November 2, 2014</b>
<b>Revision Dates:</b>	

**1.0 Standard Operating Procedure Statement / Purpose / Background**

To document the requirements, process, and timeline for submitting continuing reviews to the Data Safety and Toxicity Committee and the process and timeline for notification of approval.

**2.0 Scope**

The DSTC receives IRB continuing review reports for treatment investigator-initiated trials—interventional trials that are open to accrual or those that have been open and closed to accrual with the 1 year timeframe reported—that have had activity of accrual, had active patients, deviations and/or SAEs.

**3.0 Responsibility**

It is the responsibility of the committee to review accrual goals, toxicity, response, study conduct to ensure data integrity, and safety. The DSTC determines whether an early stopping toxicity endpoint has been met and whether protocol and consent form modifications are needed.

**4.0 Definitions**

- 4.1 Case CCC: Case Comprehensive Cancer Center
- 4.2 CR: Continuing Review
- 4.3 CRO: Clinical Research Office
- 4.4 CTO: Clinical Trials Office
- 4.5 Deviation: Any variation from the protocol requirements
- 4.6 DSMC: Data Safety and Monitoring Coordinator (OnCore role)
- 4.7 DSTC: Data Safety and Toxicity Committee
- 4.8 IRB: Institutional Review Board
- 4.9 OnCore™: Clinical Trials Management System (referred to as OnCore): database to track information from clinical trials conducted by the Case CCC
- 4.10 PI: Principal investigator
- 4.11 SAE: Serious adverse event

**5.0 Procedures**

- 5.1 It is strongly recommended that continuing reviews are sent annually to the DSTC for any investigator initiated trials that have had activity of accrual, had active patients, and/or SAEs during the reporting time frame at least 30 calendar days prior to submission to the IRB.
- 5.2 The continuing review form should include the following information:

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- 5.2.1.1** Study objectives
  - 5.2.1.2** Accrual goals and current enrollment status
  - 5.2.1.3** Enrolled patient status, including Off-Treatment and Off-Study reasons
  - 5.2.1.4** Reconciliation of SAE reports and Deviation reports submitted to the IRB and the DSTC
  - 5.2.1.5** Clinical responses—only those that have been previously confirmed by the DSTC
- 5.3** Continuing reviews will be submitted to the DSTC coordinator prior to the twice monthly DSTC meetings and will be reviewed at the committee’s next scheduled meeting.
  - 5.3.1** Approval, disapproval, or questions from the committee will be communicated within 7 calendar days to the PI, the regulatory specialist, and any involved parties to await reply. A reply from the PI, if applicable, is requested within 14 calendar days. A lack of response from the PI will result in an escalation of the issue to the Associate Director for Clinical Research and the CTO Medical Director for the Case CCC. (Refer to Case CCC SOP: DSTC/DSM-7.3.0: *Data Safety and Toxicity Committee Reporting and Communicating Action Items*)
    - 5.3.1.1** All results will be entered in OnCore into the Review section under DSMC Action History by each institution’s coordinator.
- 5.4** In rare circumstances, the DSTC can review CRs and render its decision via email between twice monthly meetings. If a CR is submitted less than 30 days before IRB submission, prior approval from the DSTC Chair must first be obtained by the PI.
- 5.5** Reasons for protocol suspension, closure to accrual or termination may include, but are not limited to, the following:
  - 5.5.1** accrual goal met;
  - 5.5.2** stopping rules activated due to:
    - 5.5.2.1** the dose escalation has reached the dose limiting toxicity or the maximum tolerated dose, as indicated by the protocol,
    - 5.5.2.2** excessive toxicity and/or,
    - 5.5.2.3** interim analysis of two-stage design indicates a response above or below the margins outlined in the trial;
  - 5.5.3** deviation rate deficient and/or correction action not effective;
  - 5.5.4** DSTC has concerns about protocol conduct or ability of the PI to continue to meet local or federal regulations.

**6.0 References**

Case CCC Data and Safety Monitoring Plan.

**7.0 Appendices**

None

**Case Comprehensive Cancer Center  
Standard Operation Procedures for Clinical Research**

**SOP #: DSTC/DSM - 7.2.0 Version #: 1.0**

**Approved by:**

Name: Robert Dreicer, MD

Position: Deputy Associate Director of Clinical Research; Director of Clinical Trials

Signature:



Date:

9/15/14

**Case Comprehensive Cancer Center  
Standard Operation Procedures for Clinical Research**

**Title: Data Safety and Toxicity Committee Reporting and Communicating Action Items**  
**SOP #: DSTC/DSM-7.3.0**  
**Version #: 1.0**

<b>Original Approval Date:</b>	<b>September 2, 2014</b>
<b>Effective Date:</b>	<b>November 2, 2014</b>
<b>Revision Dates:</b>	

**1.0 Standard Operating Procedure Statement / Purpose / Background**

To document the process for reporting and communicating Data Safety and Toxicity Committee action items to all necessary parties, including the PI, IRB, PRMC, Associate Director for Clinical Research, and CTO Medical Director.

**2.0 Scope**

The DSTC is an independent committee that communicates its actions, such as immediate administrative hold, suspension of enrollment, or study termination to the PI, IRB, PRMC, Associate Director for Clinical Research, and CTO Medical Director.

**3.0 Responsibility**

It is the responsibility of the DSTC chair to report and communicate the committee's actions to all applicable parties. It is the PI responsibility (with support of the CTU or CRO) to communicate the DSTC actions to the study sponsor and other oversight agencies, as applicable and /or as dictated by a particular protocol.

**4.0 Definitions**

- 4.1 Case CCC: Case Comprehensive Cancer Center
- 4.2 CCF: Cleveland Clinic Foundation
- 4.3 CRO: Clinical Research Office
- 4.4 CTO: Clinical Trials Office
- 4.5 CTU: Clinical Trials Unit
- 4.6 DSTC: Data Safety and Toxicity Committee
- 4.7 IRB: Institutional Review Board
- 4.8 PI: Primary Investigator
- 4.9 PRMC: Protocol Review and Monitoring Committee
- 4.10 SCC: Seidman Cancer Center
- 4.11 TCI: Taussig Cancer Institute
- 4.12 UH: University Hospitals

**5.0 Procedures**

- 5.1 Action items identified at DSTC meetings—including but not limited to: administrative hold, suspension of enrollment, or study termination—will be detailed within the meeting minutes and individual notice will be sent to involved parties.

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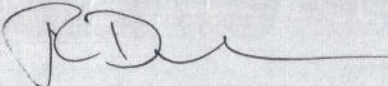
- 5.1.1 Meeting minutes will be sent to the PRMC, Associate Director for Clinical Research, CTO Medical Director, UH SCC CTU Medical Director, CCF TCI CTU Medical Director, and Administrative Director of the CRO within 7 calendar days.
- 5.1.2 Any issues requiring immediate action will be communicated to the PI, respective IRB, PRMC, Associate Director for Clinical Research, CTO Medical Director, the respective institution's CTU Medical Director, Administrative Director of the CRO, and the respective institution's CTU Administrative Director. Notifications will be sent by the DSTC Chair.
  - 5.1.2.1 The PI is responsible for providing a response to the DSTC chair and, if applicable, a corrective action plan within 14 calendar days.
  - 5.1.2.2 The PI is also responsible for communicating the above actions to the study sponsor and other agencies, as applicable.
- 5.2 Following communication of action items, protocols cannot be re-opened without resolution and written approval by the DSTC.
- 5.3 If response or corrective action plan is not provided by the PI within 14 calendar days, the DSTC will escalate the issue to the Associate Director for Clinical Research and the CTO Medical Director.

**6.0 References**

Case CCC Data and Safety Monitoring Plan.

**7.0 Appendices**

None

<b>SOP #: DSCT/DSM-7.3.0 Version #: 1.0</b>	
<b>Approved by:</b>	
Name: Robert Dreicer, MD	
Position: Deputy Associate Director of Clinical Research; Director of Clinical Trials	
Signature: 	Date: 9/15/14

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**SECTION 8: AUDITING AND MONITORING  
[QUALITY ASSURANCE] (QA)**

**Case Comprehensive Cancer Center  
Standard Operation Procedures for Clinical Research**

**Title: Monitoring Investigator-Initiated Clinical Trials**  
**SOP #: QA-8.1.0**  
**Version #: 3.0**

<b>Original Approval Date:</b>	<b>May 5, 2011</b>
<b>Effective Date:</b>	<b>July 3, 2011</b>
<b>Revision Dates:</b>	<b>September 4, 2012</b> <b>May 5, 2015</b>

**1.0 Standard Operating Procedure Statement / Purpose / Background**

Case Comprehensive Cancer Center (Case CCC) monitoring of clinical investigations SOP establishes the monitoring procedure to assure the quality of the clinical investigation and verification expectations of each person involved in the monitoring process. Proper monitoring is necessary to assure:

- Adequate protection of the rights of human subjects,
- Safety of all subjects involved in clinical investigations,
- The reported data is accurate, complete, and verifiable from source documents,
- Facilities used in the clinical investigation are acceptable, and
- The conduct of the trial is being conducted in compliance with the approved protocol, Standard Operating Procedures, Good Clinical Practice (GCP), and applicable regulatory requirements.

**2.0 Scope**

Monitoring will be required for all investigator-initiated clinical trials being conducted under an Investigational New Drug Application (IND) and not already monitored via a Good Clinical Practice (GCP) compliant monitoring plan. Other studies may be monitored at the discretion of the Associate Director for Clinical Research, Case Comprehensive Cancer Center or the research administrator at each Clinical Trial Unit. Monitoring will not be directed toward clinical trials monitored by industry sponsors (or contract research organizations). In compliance with GCP and applicable regulatory requirements, quality assurance personnel or designated clinical research personnel will perform independent site monitoring to verify regulatory compliance and data accuracy through periodic visits. The monitor will compare the practices and procedures of the investigator with the commitments made in the protocol and applicable regulatory applications.

**3.0 Responsibility**

Quality assurance team or research manager

**4.0 Definitions: None.**



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**5.0 Procedure**

**5.1 Selection and Responsibility of a Monitor**

- 5.1.1** The Sponsor-Investigator or Principal Investigator (PI) will delegate quality assurance personnel and/or clinical research personnel to monitor the progress of the clinical investigations in accordance with the monitoring plan.
  - 5.1.1.1** Sponsor-Investigators holding an Investigational New Drug Application (IND) or Investigational Device Exemption (IDE) who do not use institutional monitors must choose a GCP-compliant monitoring service and transfer the monitoring obligation.
- 5.1.2** Monitors must be appropriately trained and qualified to monitor the progress of a clinical investigation. At a minimum monitors must meet the following requirements:
  - 5.1.2.1** Experience in a clinical research environment and completion of monitoring training and/or hands-on monitoring or auditing clinical investigations experience documented on the Monitor Training Checklist attached as Appendix I. Qualifications of monitors can be reviewed by the Case CCC office.
  - 5.1.2.2** Documented training on the investigational product(s), the protocol, the informed consent form, and any other study related documents.
    - 5.1.2.2.1** Protocol specific training should be received from the Sponsor-Investigator or PI and documented on the study training and delegation log.
- 5.1.3** Monitors should be considered an extension of the study team to identify problems affecting the conduct and quality of data collected. Monitors are to be impartial but supportive.

**5.2 Monitoring Plan Development**

- 5.2.1** The monitoring plan will be developed for each clinical investigation to be monitored utilizing the Monitoring Plan Template in Appendix II upon receipt of the final protocol.
  - 5.2.1.1** The plan will outline the data to be monitored and frequency of the visits.
  - 5.2.1.2** The template provided includes the minimum requirements to conduct monitoring.
- 5.2.2** Clinical Investigations Conducted at Multiple Sites
  - 5.2.2.1** For clinical investigations conducted jointly within Case CCC, the lead site of the clinical investigation will lead the monitoring efforts.
    - 5.2.2.1.1** Monitors at the lead site will develop the monitoring plan and provide to the other site prior to opening the study to accrual.
    - 5.2.2.1.2** Monitors will be responsible for monitoring the clinical investigation at their designated site and providing monitoring reports to the quality

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assurance monitor or designee of the lead site to be shared with the Sponsor-Investigator.

**5.2.2.1.3** In instances where monitors are not available to conduct the required visits, a request to the administration staff at either site is required to accommodate required monitoring.

- 5.2.3** For clinical investigations conducted at affiliated sites outside the Case CCC, the monitoring plan will outline specific monitoring procedures.
- 5.2.4** The monitoring plan will be finalized and signed by the Sponsor-Investigator or PI prior to opening the clinical investigation to accrual.

**5.3 Monitoring Visits**

- 5.3.1** Monitors will notify the PI and study team in writing to confirm the plan prior to the monitoring visit.
- 5.3.2** Monitors will prepare for the monitoring visit by reviewing previous monitoring reports, current study documentation and requirements outlined in the monitoring plan.
- 5.3.3** Monitors will perform tasks at the visits according to the monitoring plan. The monitor will assure that the investigator's obligations are being fulfilled.
  - 5.3.3.1** Monitors will complete the Monitoring Visit Log for each visit attached as Appendix III.
- 5.3.4** After each monitoring visit, the monitor may debrief the PI and/or designated personnel to identify successful achievement and highlight areas which need improvement.
- 5.3.5** The monitor will notify the Sponsor-Investigator or PI and other required personnel per institutional procedure of any findings suggestive of intentional misrepresentation of data and/or non-compliance with regulatory requirements for any of the components of the monitoring visit immediately. This will be documented in the site visit report.
- 5.3.6** Monitoring visits are conducted until study participant follow-up is complete and a final close-out visit and report is completed.

**5.4 Record of Monitoring Visits**

- 5.4.1** The monitor will maintain a record of the findings, conclusions and actions taken to correct deficiencies for each on-site visit utilizing the Monitoring Visit Letter template and the Monitoring Visit Regulatory Binder Report template attached as Appendix IV and Appendix V, respectively.
- 5.4.2** Monitoring Visit Regulatory Binder Reports are to be filed in the regulatory binder/file. The Monitoring Visit Letter and any additional detailed reports, checklists or tools used during the visit will be filed in internal quality assurance files and provided to the Sponsor-Investigator if applicable.
- 5.4.3** Dissemination of report findings
  - 5.4.3.1** The Monitor Visit Letter, the Monitoring Visit Regulatory Binder Report, and any other detailed

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tools (if applicable) will be provided to the Sponsor-Investigator (if applicable), PI and designated personnel as defined by the study specific monitoring plan and as required to meet institutional policy.

**5.4.3.1.1** For joint trials, the monitor will provide the Monitor Visit Letter, the Monitoring Visit Regulatory Binder Report, and any other detailed tools (if applicable) to the quality assurance monitor or designee of the lead site.

**5.4.3.1.2** The Sponsor-Investigator will review the report and provide recommendations, if applicable.

**5.4.3.2** The PI and designated personnel will review the report and ensure that all delegated personnel understand the findings.

### **5.5 Investigator Compliance**

**5.5.1** In response to findings, the PI and/or designee will provide the site's plan to resolve any action items including the action to be taken, the person responsible for the action and the timeframe for completion to document resolution of all identified issues if applicable.

**5.5.1.1** The Sponsor-Investigator, if applicable, will review and discuss responses.

**5.5.2** The monitor is responsible for confirming and documenting resolution of all findings from previous visits.

### **6.0 References**

- 21 Part 312.53 Selecting Investigators and Monitors
- 21 Part 312.56 Review of Ongoing Investigations
- 21 Part 812.43 Selecting Investigators and Monitors
- 21 Part 812.46 Review of Ongoing Investigations: FDA Guidelines for Monitoring of Clinical Investigations (January 1988)
- ICH E6, 4.1 Investigator's Qualifications and Agreement
- ICH E6, 5.5 Trial Management, Data Handling and Record Keeping
- ICH E6, 5.18 Monitoring

■ Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors: FDA Inspections of Clinical Investigators (June 2010)  
<http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126553.pdf>

### **7.0 Appendices**

- Appendix I: Monitoring Training Checklist
- Appendix II: Monitoring Plan Template
- Appendix III: Monitoring Visit Log Template
- Appendix IV: Monitoring Visit Letter Template
- Appendix V: Monitoring Visit Regulatory Binder Report Template

**Case Comprehensive Cancer Center  
Standard Operation Procedures for Clinical Research**

**SOP #: QA-8.1.0; Version #: 3.0**

**Approved by:**

Name: Mikkael Sekeres, MD

Position: Deputy Associate Director of Clinical Research; Director of Clinical Trial

Signature:



Date:

5/13/15

## Appendix I

### Monitoring Training Checklist

This checklist with appropriate documentation will be maintained in departmental files. The designated management personnel will verify that the information on this form is complete and that the staff is prepared to monitor.

**Name of Monitor:** \_\_\_\_\_

**Date of Hire:** \_\_\_\_\_

Requirements	
Document Name	Yes or No
Current Curriculum Vitae that demonstrates two or more years of clinical research experience	
Copy of quality assurance course (including certificate of completion, agenda) on file	
Documentation of at least two site monitoring training visits with a trained and more experienced site monitor or minimum of six months hands-on monitoring experience/assessment of regulatory compliance	
Review of Institutional Policy	
Review of CCCC Monitoring of Clinical Investigations SOP	
Review of CCCC Clinical Trials Manual of Operations	
Review of ICH E6 Good Clinical Practice Guidelines	
Review of Federal Code of Regulations Title 21 Part 11, 50, 54, 56, 312, 812 Guidelines for Monitoring of Clinical Investigations (January 1988)	

**Monitor Signature:** \_\_\_\_\_ **Date:** \_\_\_\_\_

---

## Monitoring Plan Template

<b>Study Title:</b>	
<b>PRMC # and/or IRB #:</b>	
<b>Sponsor Investigator:</b>	

**Sponsor-Investigator Signature:** \_\_\_\_\_ **Date:** \_\_\_\_\_

## Abbreviations

AE	Adverse Event
CFR	Code of Federal Regulations
eCRF	Electronic Case Report Form
DSTC	Data Safety Toxicity Committee
FDA	Food and Drug Administration
GCP	Good Clinical Practice
ICF	Informed Consent Form
ICH-GCP	International Conference on Harmonization -Good Clinical Practice
IND	Investigational New Drug
IDE	Investigational Device Exemption
IRB	Institutional Review Board
PI	Principal Investigator
SAE	Serious Adverse Event
SD	Source Documents
SDV	Source Data Verification
SOP	Standard Operating Procedures

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## 1.0 Introduction

This Monitoring Plan should be used as a guide to monitor the progress of clinical trial, [PRMC # and/or IRB #]. The following is a list of the **minimum** criteria and does not replace an understanding of, or adherence to, the requirements contained in the approved protocol, any possible amendment(s) or numbered memo(s). Monitors will ensure that the clinical trial is conducted, recorded and reported in accordance with the protocol, Code of Federal Regulations (CFR), International Conference on Harmonization-Good Clinical Practice (ICH-GCP), IRB Policies and Procedures, any applicable local regulations, and Case Comprehensive Cancer Center (CCCC) /Institute / Enterprise SOPs, as well as the Sponsor-Investigator's Standard Operating Procedures (SOP). In the event of a conflict between this document and an SOP, this document supersedes the SOP.

## 2.0 Monitoring Scope

### 2.1 Monitor Primary Responsibilities

Monitors will review clinical data that affect clinical trial endpoints defined in the protocol. The monitor will compare the practices and procedures of the investigator with the protocol and regulatory applications. The primary responsibilities of the monitor include the following:

- Verify investigators have adequate qualifications to safely and properly conduct the trial.
- Verify that facilities remain compliant throughout the trial.
- Verify storage, dispensing, instructions for use, and disposition of the investigational agent complies with regulatory requirements.
- Verify the site follows the approved protocol and deviations are filed for noncompliance as applicable.
- Verify that written consent was obtained before subjects' participation and consent process was completed and documented.
- Verify that delegated personnel are informed about the trial and no unauthorized individuals have been delegated responsibilities.
- Verify that only eligible subjects are enrolled.
- Verify trial records are accurate, complete, and current.
- Check the accuracy and completeness of electronic Case Report Form (eCRF) entries, source documents (SD), and other trial-related records against each other.
- Inform the investigator(s) of any eCRF errors and ensure corrections are made, dated and explained and initialed by the investigator or designee as applicable.
- Determine whether all adverse events (AEs) and serious adverse events (SAEs) are reported.
- Determine all regulatory documents are maintained.

- Verify all study-related correspondence with the Food and Drug Administration (FDA) related to the IND / IDE (as applicable), Institutional Review Board (IRB), and Data Safety Toxicity Committee (DSTC).
- Communicate deviations from the protocol, GCPs or regulatory requirements to the investigator and discuss appropriate action to prevent recurrence of the deviations.

At the end of each monitoring visit, the monitor will meet with the PI and/or delegated personnel to review findings and discuss follow up of the visit.

## **2.2 Data Monitoring**

Source Data Verification (SDV) is the process of comparing data recorded on the eCRF to the data contained in the SDs. SDs are defined as any original records or data related to the study or to subject treatment or medical history. SDs may include but not be limited to subject medical history, current hospitalization examinations, chart notes, lab reports, x-rays and electrocardiograms (ECGs). The subject's record will be screened for relevant data that is not captured in the eCRF (e.g. verifying that no AEs and /or other endpoints are missed).

Verification of the following will be conducted at 100% SDV for all patients:

- Initial study consent and the consent process for 100% of enrolled and screened patients;
- Study eligibility for 100% of enrolled patients;
- SAE/AE reporting for 100% of enrolled patients;
- Study drug dosing for 100% of enrolled patients (as applicable).

An excessive number of eCRF discrepancies at the site will prompt review of additional subjects and/or data in addition to those planned.

## **2.3 Monitoring Visit Reports**

The monitor will complete a monitoring visit letter and monitor visit regulatory binder report for each visit and send to the Sponsor-Investigator and to the PI (if not the same) and/or designated personnel within 10 business days of the conclusion of the monitoring visit. A copy of every monitoring visit letter, monitoring visit regulatory binder report and site specific documentation will be retained by the monitor. The monitor will notify the Sponsor within three business days of the visit of any critical site issues noted during the visit.

The monitoring visit report and cover letter will describe the progress of the study, findings of the visits, unresolved issues and follow-up

required. Follow-up items will be checked and documented at the next monitoring visit as applicable. The monitoring visit report will include, but not limited to, the following:

- Summary of data and regulatory documents that were reviewed;
- Statement that regulatory, pharmacy and data were acceptable, acceptable with follow-up required, unacceptable or not reviewed;
- Statement concerning significant findings such as under-reporting of adverse events;

### **3.0 Initiation Visit**

#### **3.1 Purpose and Scope**

The purpose of the initiation visit is to conduct and document the training of the PI and delegated personnel in the written approved protocol, verify that the PI and delegated personnel clearly understand and accept their obligations in undertaking the clinical trial, understand all required data, eCRF completion and associated activities necessary to conduct [PRMC # and/or IRB #] in accordance with the federal regulations and ICH-GCP.

The Initiation Visit will occur after IRB approval, but prior to opening the trial to accrual.

#### **3.2 Initiation Visit Monitoring Activities**

Monitoring activities will include, but not be limited to, discussions related to PI and delegated personnel responsibilities during the conduct of the trial, inclusion/exclusion criteria, definitions of AE/SAE, AE/SAE reporting procedures, regulatory obligations, appropriate use of the investigational drug/device, [study drug/device], and its accountability and destruction/return, the informed consent process, and CRF completion instructions. A tour of the facility may also be requested to ensure it is adequate to conduct the study. This may include, but not be limited to, the emergency department, study drug/device storage area, monitoring areas; CRF and study supply storage areas. Prior to opening this study to accrual the monitor will perform the following tasks:

Regulatory specific study start up monitoring (all regulatory documents will be reviewed to ensure the study start-up documentation meets the following minimal requirements):

- PRMC Approval
- IRB Approval
- FDA submission (may proceed or 30 day period without notification from the FDA)
- Regulatory File Review

#### Regulatory ONCORE specifics

- Verify current protocol, IRB approval letter, and consent are uploaded into the documents / information tab
- Verify Status / Institution tabs are updated
- Verify that the Details, Management, Sponsor, IND/IDE tabs (PC Console) are correct and updated
- Verify that correct approved consent information has been entered in the IRB Reviews section

### **4.0 Interim Monitoring Visits**

#### **4.1 Purpose, Frequency and Scope**

The primary goal of the interim monitoring visit is to assure the study is conducted in compliance with the currently approved protocol, federal regulations, ICH-GCP, ensure subject safety, and validate clinical data against source documents. The monitor will review previous monitoring reports to identify any unresolved issues and discuss with the team during the interim visit.

The first interim monitoring visit will occur as soon as possible after the first subject is enrolled. Thereafter interim monitoring visits will occur every 4-6 weeks during the conduct of the trial.

Additional monitoring visits could be triggered by sponsor-investigator request, unexpected enrollment rates, unacceptable number of queries and/or protocol violations or non-compliance with GCPs, and/or complexity of the trial. These visits are to occur within 10 business days of notification to the monitor.

#### **4.2 Interim Monitoring Activities**

The following minimum activities will be completed during interim monitoring visits:

- Data monitoring to occur as outlined in Section 2.2;
- Verify protocol compliance and note any issues for follow-up with the site;
- Verify appropriate drug/device accountability; drug/device storage and handling including review of the drug accountability forms and temperature log completion as outlined in Section 6.0;
- Review the Subject Identification, Enrollment and Screening Logs; and
- Facilitate data query resolution.

### **Informed Consent Form Process**

- Verify that the appropriate IRB has approved the Informed Consent Form (ICF) document in use;
- Verify that the most recently approved ICF as approved by the IRB was signed and dated by the subject or legal representative, witness and by the PI prior to any study procedure being performed;
- Verify all original signed ICFs are filed at the study site and that they are available for review;
- Review documentation that all subjects consented have received a copy of the ICF;
- Verify that the informed consent process is documented in the SDs and in the study database.

### **Inclusion/Exclusion Criteria**

- Verify that all subjects are eligible to participate in the trial based on the protocol's inclusion and exclusion criteria;
- Assigned number will be confirmed for all subjects.

### **Regulatory Documents**

In addition to monitoring subject data, the monitor will review the regulatory documents for any additions or revisions since the last visit including but not limited to the following:

- Verify that any staff changes are reflected on a revised Form FDA 1572/Investigator Agreement, and the Signature and Delegation log are submitted to the IRB;
- Verify any changes or amendments to the protocol and/or to the informed consent, any SAEs / deviations are reported to the Sponsor-Investigator, IRB, FDA (SAEs only – if applicable), and DSTC and follow-up occurred;
- Verify that the site submits required continuing reviews and reports to the IRB/DSTC, and confirms that IRB approval is current;
- Verify the site submits annual report to the FDA (if applicable)
- Verify that all training has occurred and training log has been signed for delegated personnel;
- Review of site regulatory files and IRB/FDA communication;

## **5.0 Electronic Case Report Form Completion and Retrieval**

The data for [PRMC # and/or IRB #] will be captured in ONCORE, the Case Comprehensive Cancer Center's oncology database. The CRF pages for [PRMC # and/or IRB #] are created and maintained in ONCORE, therefore there are no paper CRF forms. All data will be held in ONCORE and all source documentation will be managed and stored by the research team. The delegated personnel responsible for entering data are required to enter the data per institutional requirements.

eCRF completion timelines will be reviewed according to the institutional requirements.

eCRF review will include review for completeness and consistency with source documents. eCRFs should be completed on all subjects that have been screened and enrolled.

## **6.0 Investigational Agent Accountability**

The monitor will perform accountability of the investigational agent at each monitoring visit. Verification of the investigational agent includes documenting any discrepancies between the total amounts [study drug/device] shipped to the study site with the total amount of [study drug/device] dispensed to subjects along with unused [study drug/device]. The monitor will verify that correct study drug/device was administered by comparing the medical record against pharmacy documentation.

The monitor will perform the following checks and verifications:

- Confirm all [study drug/device] was used for each subject and verify dispensed dates;
- Check for site pharmacy personnel changes. If changes occur, ensure new personnel will have access to receive the study drug/device during the trial;
- Verify that the drug number administered to the subject matches the number assigned for all subjects enrolled;
- Review the temperature log. Ensure the temperature is maintained and current.
- Ensure that receipt of drug shipments has been acknowledged by the Investigational Pharmacy on Record;
- Verify that the test article is stored in a securely locked area.

The site staff should not destroy/return study drug/device until the monitor has checked the dispensing records for all subjects against the appropriate documentation (if applicable).

## **7.0 Close-Out Visit**

### **7.1 Frequency and Scope**

A close-out visit should occur prior to the termination of the study with the IRB.

### **7.2 Close-Out Visit Activities**

The monitor will perform the following tasks during the study close-out visit:

- At the end of the study, the monitor will verify submission of a final report to IRB and FDA (if applicable) and proper close out procedures have been followed;

- Facilitate the resolution of outstanding observations/queries;
- Perform final [study drug/device] accountability and verify that the [study drug/device] destruction form was completed;
- Review regulatory documents;
- Review record retention and regulatory responsibilities with the PI and delegated personnel;
- Verify all outstanding items from the previous visits have been addressed.

The monitor will remind the PI of his/her obligations regarding study record maintenance and storage according to the applicable FDA and any applicable local regulations.

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## Monitoring Visit Log

Date	Type of visit	Name of study monitor	Signature of study monitor	Name of representative of study personnel	Signature of representative of study personnel



## Appendix IV

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### Monitoring Visit Letter Template

[Insert Current Date]

**Sponsor-Investigator:** [Enter Sponsor-Investigator name]

**Type of Visit:** [Enter type of monitoring visit; initiation, interim or close-out]

**PRMC # and/or IRB #:** [Enter PRMC and/or IRB number]

**IND or IDE #:** [Enter IND / IDE number]

**Protocol Title:** [Enter full protocol title]

Dear [Insert PI name],

On [insert dates of monitoring visit], I conducted a [insert type of monitoring visit] monitoring visit on the above referenced project. Attached is the monitoring visit regulatory binder report for [study number], which should be filed in the regulatory binder in lieu of this letter. The purpose of my review of this area was to determine compliance with the protocol, federal regulations, IRB policies and procedures, ICH-GCP requirements and Case CCC/ institutional / Enterprise SOPs. The results and areas reviewed during my visit are as follows:

#### **Regulatory Documents**

The documents reviewed included: [list documents reviewed if a detailed report is not attached].

My review confirmed that you [are complying or have complied (if close-out)] with all required review requirements. Therefore this study has earned an acceptable rating for this section.

**OR**

My review confirmed that you are complying or have complied (if close-out) with all required review requirements with the following exception(s):

#### **Finding/Concern**

[State nature of finding/concern and the corrective/recommended action if required]

Due to these findings, this study has earned an [acceptable with follow-up or unacceptable] for this section.

#### **Investigational Agent Accountability and Pharmacy Operations**

The documents reviewed included: [list documents reviewed if a detailed report is not attached].

My review confirmed that you [are complying or have complied (if close-out)] with all required review requirements. Therefore this study has earned an acceptable rating for this section.

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**OR**

My review confirmed that you are complying or have complied (if close-out) with all required review requirements with the following exception(s):

### **Finding/Concern**

[State nature of finding/concern and the corrective/recommended action if required]

Due to these findings, this study has earned an [acceptable with follow-up or unacceptable] for this section.

### **Subject Records Review**

The target accrual rate for this study is [enter the target accrual rate as provided to IRB] subjects. At the time of this visit, [enter the current accrual rate] subjects were enrolled onto the study. The subjects and documents reviewed include: [list subject numbers and documents reviewed].

My review confirmed that you [are complying or have complied (if close-out)] with all required review requirements. Therefore this study has earned an acceptable rating for this section.

**OR**

My review confirmed that you are complying or have complied (if close-out) with all required review requirements with the following exception(s).

### **Finding/Concern**

[State nature of finding/concern and the corrective/recommended action if required]

Due to these findings, this study has earned an [acceptable with follow-up or unacceptable] for this section.

### **Summary**

Based on my monitoring review, [PRMC # and/or IRB #] is proceeding in a timely manner and is being administered in compliance with applicable requirements. I will schedule a [insert type of visit] for [insert date or timeframe known for next visit].

**OR**

Based on my monitoring review, [PRMC # and/or IRB #] is proceeding in a timely manner and is being administered in compliance with applicable requirements, with the exception of the areas previously noted. I will schedule a [insert type of visit] for [insert date or timeframe known for next visit]. You are reminded that the findings listed above must be addressed by [insert date].

**OR**

Based on my monitoring review, [PRMC # and/or IRB #] was administered in compliance with applicable requirements. The project is hereby closed pending receipt

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and approval of the outstanding findings identified above. These findings must be addressed by [insert date] in order to close the study with the IRB.

Thank you for your assistance and cooperation extended to me during the visit. Should you have any questions or require additional information, please feel free to contact me at [enter monitor's phone number].

Sincerely,

[Name, Title of Monitor and Site Name]

Cc: [enter as appropriate; should include Sponsor-Investigator and/or designated personnel, Quality Assurance Manager, Manager of Research Personnel]

**Monitoring Visit Regulatory Binder Report Template**

<b>I. General Information</b>	
<b>Sponsor-Investigator</b>	
<b>Lead Clinical Site</b>	<input type="checkbox"/> UH <input type="checkbox"/> CC <input type="checkbox"/> Other _____
<b>Investigator</b>	
<b>Site Monitored</b>	<input type="checkbox"/> UH <input type="checkbox"/> CC <input type="checkbox"/> Other _____
<b>Protocol Title</b>	
<b>IND or IDE #</b>	
<b>Protocol Target Accrual</b>	Enrollment to Date _____
<b>Visit Conducted By</b>	
<b>Date(s) of Visit</b>	___/___/___ to ___/___/___
<b>Type of Visit (check all that apply)</b>	<input type="checkbox"/> Study Initiation <input type="checkbox"/> Unscheduled <input type="checkbox"/> Interim Monitoring <input type="checkbox"/> Close Out
<b>Study Status</b>	<input type="checkbox"/> Open to Accrual <input type="checkbox"/> Suspended <input type="checkbox"/> Closed to Accrual <input type="checkbox"/> Terminated
<b>Summary of Documents Reviewed</b>	
<b>Date of Next Visit:</b>	

**Instructions:** For the following categories, indicate the assessment for each of the three components of the monitoring visit.

<b>II. Assessing Regulatory Documents, IRB and Informed Consent Findings</b>		
Check one that applies	Rating	Explanation of Rating
<input type="checkbox"/>	<b>Acceptable</b>	No deficiencies identified. Few minor deficiencies identified. Major deficiencies identified during the site visit that were addressed and/or corrected prior to the site visit for which documentation exists and no further action is required.
<input type="checkbox"/>	<b>Acceptable, Follow-up</b>	Multiple minor deficiencies identified. Major deficiencies identified during the site visit, but not corrected and/or addressed prior to the site visit.
<input type="checkbox"/>	<b>Unacceptable</b>	Multiple major deficiencies identified. A single major flagrant deficiency found. Excessive number of minor deficiencies found.
<input type="checkbox"/>		Not reviewed
<b>Additional Comments:</b>		

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<b>III. Assessing the Accountability of Investigational Agent and Pharmacy Operations</b>		
<b>Check one that applies</b>	<b>Rating</b>	<b>Explanation of Rating</b>
<input type="checkbox"/>	<b>Acceptable</b>	Compliance found for security, drug accountability record forms completed correctly, protocol and drug-specific usage and/or return of study drug. Noncompliant items identified during the site visit that were addressed and/or corrected prior to the site visit for which documentation exists and no further action is required.
<input type="checkbox"/>	<b>Acceptable, Follow-up</b>	Category found noncompliant during the site visit which was not corrected and/or addressed prior to the site visit.
<input type="checkbox"/>	<b>Unacceptable</b>	Inability to track the disposition of the supplied investigational agent. Multiple noncompliant categories identified.
<input type="checkbox"/>		Not reviewed
<b>Additional Comments:</b>		

<b>IV. Review of Subject Records</b>		
<b>Check one that applies</b>	<b>Rating</b>	<b>Explanation of Rating</b>
<input type="checkbox"/>	<b>Acceptable</b>	No deficiencies identified. Few minor deficiencies identified. Major deficiencies identified during the site visit that were addressed and/or corrected prior to the site visit for which documentation exists and no further action is required.
<input type="checkbox"/>	<b>Acceptable, Follow-up</b>	Multiple minor deficiencies identified. Major deficiencies identified during the site visit, but not corrected and/or addressed prior to the site visit.
<input type="checkbox"/>	<b>Unacceptable</b>	Multiple major deficiencies identified. A single major flagrant deficiency found. Excessive number of minor deficiencies found.
<input type="checkbox"/>		Not reviewed
<b>Additional Comments:</b>		

**Action Items Identified:**

**Additional Comments/General Impressions of Site Performance/ Recommendations:**

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**Prepared by:** \_\_\_\_\_ **Title:** \_\_\_\_\_

**Signature:** \_\_\_\_\_ **Date:** \_\_\_\_\_

**Case Comprehensive Cancer Center  
Standard Operation Procedures for Clinical Research**

**SECTION 9: REGULATORY AFFAIRS (RA)**

**Case Comprehensive Cancer Center  
Standard Operation Procedures for Clinical Research**

**Title: Statement of Investigator (Form FDA 1572)**  
**SOP #: RA-9.1.0**  
**Version #: 2.0**

<b>Original Approval Date:</b>	<b>May 3, 2011</b>
<b>Effective Date:</b>	<b>July 3, 2011</b>
<b>Revision Dates:</b>	<b>October 4, 2016</b>

**1.0 Standard Operating Procedure Statement/ Purpose/Background**

To assist in accurate completion of a protocol specific FDA Form 1572 required for studies being conducted by the investigator for pharmaceutical or governmental agencies.

**2.0 Scope**

- 2.1** All FDA regulated studies conducted under the Investigational New Drug Application (IND) and managed within the Case Comprehensive Cancer Center (Case CCC) require Form FDA 1572.
- 2.2** National Cancer Institute (NCI) cooperative group studies: NCI does not require the Form FDA 1572 for each protocol. NCI guidelines for registration of all investigators, which include an annual 1572 (among other documents) per investigator, must be followed. Industry sponsors may also require a 1572 for select NCI trials.

**3.0 Responsibility**

Principal Investigator; Regulatory Coordinator; Study Coordinator; Research Nurse.

**4.0 Definitions:** None

**5.0 Procedure**

**5.1 Definition and Responsibilities**

- 5.1.1** The FDA Form 1572 is the Investigators ‘Statement’ and ‘Agreement’ to follow the protocol and the federal regulations.
- 5.1.2** The Principal Investigator (PI) is responsible for the contents of the 1572 and the subsequent study.
- 5.1.3** The PI or designee completes the form and files in the trial master file.
- 5.1.4** Each Case CCC Institution must complete separate 1572 forms. For investigator-initiated studies, the designated lead Institution must maintain copies of 1572s from all participating sites.

**5.2 Form Location**

- 5.2.1** The current version of FDA Form 1572 is located on the FDA website at: <http://www.fda.gov/opacom/morechoices/fdaforms/cder.html>

**5.3 Initial Form Completion**



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- 5.3.1** Section 1: The investigator is the individual at the site who both initiates and conducts the clinical trial and under whose immediate direction the investigational drug is being administered or dispensed.
  - 5.3.2** Section 2: The box marked curriculum vitae (CV) must be checked.
    - 5.3.2.1** A copy of the principal investigator's CV must be on file.
  - 5.3.3** Section 3: The address to which written correspondence from the FDA should be directed.
  - 5.3.4** Section 4: List all clinical labs that will be utilized for the study, including central and sponsor laboratories as applicable.
    - 5.3.4.1** For example, include a lab within the Case CCC Institutions if they provide results for the study. Not required to be added if the lab is only preparing send-outs to an external laboratory.
  - 5.3.5** Section 5: List the IRB address as appropriate
  - 5.3.6** Section 6: List all sub-investigators for the study.
    - 5.3.6.1** A sub-investigator is defined as anyone who makes a direct and significant contribution to the data.
    - 5.3.6.2** If a research staff is performing a critical study function and collecting and evaluating study data the staff should be listed as a sub-investigator. If the research staff is only transcribing study data and maintaining study files (e.g. data or regulatory coordinator), the staff does not need to be listed.
    - 5.3.6.3** Hospital staff, including nurses, residents, or fellows and office staff who provide ancillary or intermittent care but who do not make a direct and significant contribution to the data do not need to be listed individually.
    - 5.3.6.4** Any other member of the study team who would makes clinical decisions during the study. If a question arises as to if an individual is to be included in this section, please contact the respective research manager.
      - 5.3.6.4.1** Back-up nurses and/or physicians do not need to be added if he/she provides intermittent care and does not make a direct and significant contribution to the data.
    - 5.3.6.5** Statistician is only listed if he/she is listed on the study as an investigator.
    - 5.3.6.6** Pharmacist is only listed if he/she is one of the study investigators or randomizes patients.
  - 5.3.7** Section 7: List the full study title
    - 5.3.7.1** If multiple studies are included under one IND, all studies associated with that IND should be included.
  - 5.3.8** Section 8: Check one or both boxes which applies (Phase 1, 2 or 3) dependent upon the clinical phase of the study.
  - 5.3.9** Section 10: Obtain principal investigator signature and date.
  - 5.3.10** The original form should be double sided prior to obtaining the principal investigator's signature. If the 1572 is comprised of multiple pages, the pages should be stapled so that there is no question about what document(s) the investigator signed.
- 5.4** Subsequent Form Completion

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**5.4.1** The 1572 form needs to be updated for any of the following changes (\*needs to be submitted to the FDA within 30 days):

- 5.4.1.1** PI\*
- 5.4.1.2** A new study is being added to the IND within the same research team\*
- 5.4.1.3** Sub-investigator
- 5.4.1.4** Name and/or address of the research site, local laboratory and/or IRB
- 5.4.1.5** Any information supplied by the sponsor (e.g. change in protocol title, supporting labs, etc.)


**5.5 Form Retention**

- 5.5.1** The original 1572 forms are kept in the study master file of each institution.
- 5.5.2** Copies are sent to the sponsor or government agency (as applicable).
- 5.5.3** Copies of the 1572 forms are filed in the study regulatory binder of the lead institution.

**6.0 References**

- Information Sheet Guidance for Sponsors, Clinical Investigators, and IRBs: Frequently Asked Questions - Statement of Investigator (Form FDA 1572) (May 2010)  
<http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM214282.pdf>

**7.0 Appendices: None**

<b>SOP #: RA-9.1.0; Version #: 2.0</b>	
<b>Approved by:</b>	
Name: Mikkael Sekeres, MD	
Position: Deputy Associate Director of Clinical Research; Director of Clinical Trials	
Signature: 	Date: 11-07-16

**Case Comprehensive Cancer Center  
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**Title: Regulatory Documentation Management**  
**SOP #: RA-9.2.0**  
**Version #: 2.0**

Original Approval Date:	July 5, 2011
Effective Date:	August 5, 2011
Revisions Dates:	September 4, 2012

### **1.0 Standard Operating Procedure Statement / Purpose / Background**

To provide standardized components for all regulatory files/binders for Case Comprehensive Cancer Center investigator-initiated and cooperative group studies, so that they are complete, easy to follow, and contain all necessary documents.

### **2.0 Scope**

All cancer-related investigator-initiated and cooperative group research studies.

### **3.0 Responsibility**

All department and division personnel responsible for maintaining regulatory documents will utilize this procedure as applicable.

### **4.0 Definitions: None**

### **5.0 Procedure**

#### **5.1 Regulatory File/Binder Creation**

**5.1.1** Prior to study initiation, the assigned research personnel will create a regulatory file/binder organized into sections per Section 5.2

**5.1.2** If the trial is activated at regional sites, each institution will adhere to its own regulatory documentation practice.

#### **5.2 Regulatory File/Binder Components**

##### **5.2.2 Protocol Section**

**5.2.2.1** File all IRB approved versions of the protocol in reverse chronological order.

##### **5.2.3 Delegation of Responsibility and Study Training Log Section**

**5.2.3.1** File all Delegation of Responsibility and Study Training logs listing all personnel involved in the study with their assigned and authorized responsibilities.

##### **5.2.4 Protocol Review and Monitoring Committee (PRMC) and Institutional Review Board (IRB) Correspondence.**

**5.2.4.1** File all PRMC and IRB correspondence in reverse chronological order.

**5.2.4.2** This section should begin with the initial new review PRMC and subsequently IRB submission.

**5.2.4.3** IRB approved consent will also be included in this section.

**5.2.4.4** Deviations

##### **5.2.5 Screening and Enrollment Section.**

**5.2.5.1** Screening (consented subjects) and enrollment log will be maintained in OnCore.

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- 5.2.5.2** Accrual report should be printed prior to an external monitoring/audit visit.
- 5.2.6** Drug Accountability Log Section.
  - 5.2.6.1** The original drug accountability log is maintained by the Research/Investigational Pharmacy.
- 5.2.7** Financial Disclosures / 1572 Section (IND studies only).
  - 5.2.7.1** 1572 and Financial disclosures for all investigators listed on the delegation of responsibility and training log for the trial must be filed in this section.
- 5.2.8** Sub-Investigator Qualification Documentation (IND studies only)
  - 5.2.8.1** Review and File the current FDA Debarment List (Drug Product Applications).
  - 5.2.8.2** Complete and File the Investigator Qualification Checklist.
- 5.2.9** FDA Correspondence.
  - 5.2.9.1** File all FDA Correspondence in reverse chronological order, the most recent correspondence on top.
- 5.2.10** Industry supporter / supplier Correspondence.
  - 5.2.10.1** File all drug / device supplier / supporter correspondence in reverse chronological order.
- 5.2.11** Monitoring Documentation (as applicable).
  - 5.2.11.1** This should include all monitoring reports and the monitor visit log.
- 5.2.12** General Correspondence.
  - 5.2.12.1** The general correspondence section should contain relevant communications not captured in the sections outlined above.
  - 5.2.12.2** Material should be filed by date.
- 5.2.13** Miscellaneous Section.
  - 5.2.13.1** All other original documents that do not fit into the above listed sections should be maintained under this section.
  - 5.2.13.2** All documents should be filed in reverse chronological order.
- 5.2.14** Documents that may be located centrally.
  - 5.2.14.1** IRB membership list.
  - 5.2.14.2** Federal Wide Assurance letter.
  - 5.2.14.3** Investigator Brochure.
  - 5.2.14.4** Curriculum Vitae (CV) and Medical License for all Clinical Laboratory Directors.
  - 5.2.14.5** CLIA/Certification of Anatomic Pathology (CAP) certificates.
  - 5.2.14.6** Lab normal value(s)/ranges for medical/laboratory/technical procedure(s) and or test(s) of all participating sites and/or central laboratories.
  - 5.2.14.7** Curriculum Vitae (CV) and Medical License for all Investigators.

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**5.2.15** Serious Adverse Events (SAEs).

**5.2.16** It is acceptable to collect and store some regulatory documents electronically per your Institutional policy.

**5.3** Regulatory File/Binder Maintenance.

**5.3.1** Upon receipt of any revised or updated documents, documents should be filed appropriately.

**5.4** Items NOT to be Included in the regulatory binder

**5.4.1** The following information should not be included in the Regulatory File/Binder: 1) financial information (budgets, contacts, agreements; 2) internal audits; 3) identifiable patient information; and 4) signed informed consent forms.

**6.0 References**

- Case Comprehensive Cancer Center Clinical Trials Operation Manual
- International Conference on Harmonisation Guidelines E6 Section 8.2
- 21 CFR Part 50; 56; 312; 812

**7.0 Appendices:** None

**Approved by:**

Name: Robert Dreicer, MD

Position: Deputy Associate Director for Clinical Research; Director of Clinical Trials

Signature:



Date:

10/1/12

**Case Comprehensive Cancer Center  
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**SECTION 10: PROTOCOL REVIEW AND  
MONITORING COMMITTEE (PRMC)**

**Case Comprehensive Cancer Center  
Standard Operation Procedures for Clinical Research**

**Title: Protocol Review and Monitoring Committee Initial Submission**  
**SOP #: PRMC-10.1.0**  
**Version #: 3.0**

<b>Original Approval Date:</b>	<b>July 5, 2011</b>
<b>Effective Date:</b>	<b>August 5, 2011</b>
<b>Revision Dates:</b>	<b>April 7, 2015</b> <b>April 24, 2017</b>

### **1.0 Standard Operating Procedure Statement / Purpose / Background**

A procedure documenting the process for submission to the Protocol Review and Monitoring Committee (PRMC) to assure that the process is consistent and efficient.

### **2.0 Scope**

The PRMC reviews all cancer protocols, including protocols sponsored by the national cooperative oncology groups and the pharmaceutical industry, conducted at the institutions affiliated with the Case Comprehensive Cancer Center.

Studies that are NCI Peer-reviewed, do not go to full board and are administratively approved. These include R01s and P01s, CTEP, cooperative group or others deemed by the Chairs.

Investigator initiated studies from other NCI-designated Cancer Centers that have undergone the scientific review by their Scientific Review Committee (SRC), do not go to full board. They are reviewed by the PRMC Chairs who may opt to have the study reviewed by the full board or other members of the PRMC committee.

Protocols containing research involving only retrospective chart reviews do not require review by the PRMC and can proceed straight to the IRB. IRB forms and contact info can be found on the IRB websites at the respective institutions.

### **3.0 Responsibility**

Principal Investigator; Regulatory Coordinator; Study Coordinator

### **4.0 Definitions: None**

### **5.0 Procedures**

**5.1** The PRMC submission is sent electronically via email to the PRMC manager and consists of the submission application including required attachments.

**5.1.1** **Studies sponsored by other NCI-designated cancer centers must include their SRC approval letter with submission to the PRMC.**

**5.1.2** No changes to investigators listed on the PRMC application can be made until the protocol is reviewed and approved by the PRMC, so as not to create a conflict of interest when assigning reviewers.

**5.1.3** Once a protocol is assigned to an agenda, amendments will not be accepted for PRMC review until after PRMC review and approval of

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an initial protocol. See the PRMC Amendment Submission SOP (PRMC-10.2.0) for specific protocol changes that require PRMC review.

- 5.2 Application and other documents can be found on the PRMC webpage at <http://cancer.case.edu/research/clinical-research-office/prmc/>
- 5.3 Submission deadlines and meeting dates are posted on the PRMC webpage. Meetings are held the 2<sup>nd</sup> and 4<sup>th</sup> Tuesdays of the month, except December which only has one meeting on the 3<sup>rd</sup> Tuesday.
- 5.4 Agenda is sent to the Principal Investigator (PI) with meeting logistics at least 10 days before meeting.
- 5.5 PRMC outcome memos are emailed within 2 days following the initial review. Trials can either be approved, approved with stipulations, not approved, or deferred.
  - 5.5.1 If a trial qualifies for administrative review (i.e. CTEP approved, cooperative group, and others as determined by chair) approval memos will be generated without the need for full board review.
  - 5.5.2 If a trial is approved with no issues during a full board review, approval memos will be generated within 2 business days.
  - 5.5.3 If a trial is considered “approved pending resolution of issues”, the PRMC manager will send the issues to the PI. The PI is responsible for sending the responses and any revisions to PRMC manager within 90 days of the initial review. The PRMC manager then corresponds with the original reviewers to determine if the revisions adequately address the issues. Approval memos are generated once the process is completed.
    - 5.5.3.1 Responses not returned within 90 days will have to be re-reviewed at a full board meeting.
  - 5.5.4 If a trial is considered “not approved,” the responses and protocol revisions will have to undergo an additional full board review by the PRMC. Same submission requirements and deadlines apply as an initial review.
  - 5.5.5 If a trial is considered “deferred” (due to lack representation at the PRMC meeting), it will automatically be postponed to the next available meeting.
- 5.6 After the final PRMC approval, the IRB application should be completed and PRMC approval memo included in the submission. Any responses from the PI and/or sponsor to issues raised by the PRMC should also be included in the IRB submission packet.

## **6.0 References**

<http://cancer.case.edu/research/clinical-research-office/prmc/>  
<http://www.uhhospitals.org/clinical-research/institutional-review-board>  
<http://cancercenters.cancer.gov/documents/PeerReviewFundingOrganizations508C.pdf>  
<https://grants.nih.gov/grants/guide/notice-files/NOT-CA-16-038.html>  
<https://www.cancer.gov/research/nci-role/cancer-centers/find>

## **7.0 Appendices: None**



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SOP #: PRMC-10.1.0; Version #: 3.0

Approved by:

Name: Mikkael Sekeres, MD

Position: Deputy Associate Director of Clinical Research; Director of Clinical Trials

Signature:



Date:

5.08.17

**Case Comprehensive Cancer Center  
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**Title: Protocol Review and Monitoring Committee Amendment Submission**  
**SOP #: PRMC-10.2.0**  
**Version #: 2.0**

<b>Original Approval Date:</b>	<b>July 5, 2011</b>
<b>Effective Date:</b>	<b>August 5, 2011</b>
<b>Revision Dates:</b>	<b>April 7, 2015</b> <b>June 21, 2017</b>

**1.0 Standard Operating Procedure Statement / Purpose / Background**

A procedure documenting the process for an amendment submission to the Protocol Review and Monitoring Committee (PRMC) to assure that the process is consistent and efficient.

**2.0 Scope**

Amendments may receive full or administrative review by the PRMC as determined by the Chair or designate. Amendments from NCI-approved national cooperative groups, NCI-designated cancer centers or reviewed by CTEP do not require PRMC review and can proceed straight to the IRB.

The PRMC reviews all amendments that include changes in the following areas:

- 2.1 Objectives or endpoints
- 2.2 Biostatistics
- 2.3 Sample collection
- 2.4 Treatment/dosing (includes changes to study calendar/time-points)
- 2.5 Eligibility

**3.0 Responsibility:** Principal Investigator; Regulatory Coordinator.

**4.0 Definitions:** None.

**5.0 Procedures**

- 5.1 PRMC amendment submission is sent electronically via email to the PRMC manager. Submission should include a revised tracked and clean protocol with a summary of changes table included within the protocol or as a separate document.
- 5.2 PRMC checklist containing outcome of review is emailed to study personnel within 10 business days. This checklist should be included with the IRB submission.

**6.0 References**

- <http://cancer.case.edu/research/clinical-research-office/prmc/>

**7.0 Appendices:** None.

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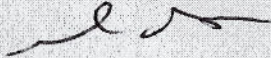
SOP #: PRMC-10.2.0; Version #: 2.0

Approved by:

Name: Mikkael Sekeres, MD

Position: Deputy Associate Director of Clinical Research; Director of Clinical Trials

Signature:



Date:

09-06-17

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**Title: Protocol Review and Monitoring Committee Accrual Monitoring**  
**SOP #: PRMC-10.3.0**  
**Version #: 3.0**

<b>Original Approval Date:</b>	<b>October 4, 2011</b>
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### **1.0 Standard Operating Procedure Statement / Purpose / Background**

A procedure documenting the process for accrual monitoring by the Protocol Review and Monitoring Committee (PRMC).

### **2.0 Scope**

The PRMC is responsible for monitoring accrual to interventional clinical trials and mandating closure of studies when low accrual affects the likelihood of successful and timely completion of the research.

### **3.0 Responsibility**

PRMC, Case CCC Clinical Research Leadership Committee, Principal Investigator (PI), Clinical Trials Units (CTU)

### **4.0 Definitions**

**4.1 Case CCC:** Case Comprehensive Cancer Center.

**4.2 OnCore<sup>®</sup> Clinical Trials Management System (referred to as OnCore):** database to track information from clinical trials conducted by the Case CCC.

**4.3 NCI:** National Cancer Institute

**4.4 UH:** University Hospitals

**4.5 CC:** Cleveland Clinic

### **5.0 Procedure**

**5.1** Reports will be run monthly to review accrual to trials. Accrual to interventional trials is reviewed every 6 months from study activation. Accrual to sponsored trials that have not accrued at least 1 patient in the previous 6 months will be reviewed. Investigator-initiated trials that have not accrued 50% of expected 6-month accrual will be reviewed.

**5.1.1** For sponsored joint trials (between UH and CC) whereas the open to accrual date is different, each site will be reviewed separately. Communication between the sites must occur if one side chooses to close voluntarily. If the PRMC decides the study should be closed at a particular site, the CTU must communicate with the other site so regulatory processes can be put in place.

**5.1.2** For investigator initiated trials joint (between UH and CC) the PRMC will monitor from the earliest open date. Decisions will be sent to the

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lead site and cc the non-lead site. Any decision made on closure should be communicated with the non-lead site by the CTU and PRMC.

- 5.1.3 Accrual analysis conducted by PRMC will utilize OnCore for patient enrollment information.
- 5.1.4 Rare Disease Trials: NCI guidelines regarding rare disease states that the PRMC can make exceptions for trials that fall under the definition of rare disease, this includes all pediatric trials. Adult rare disease studies will be monitored every yearly and pediatric studies will be monitored every 2 years from activation.
- 5.2 The PRMC will send a memo to the designated clinical site CTU representative. This document will contain the current status and accrual information. Response to questions as well as a justification of the accrual level, a corrective strategy to improve accrual, or voluntarily closing the study is required.
- 5.3 CTU representative is responsible for acquiring the response from both the CTU and PI. These responses will follow discussion between the PI and CTU. Completed memo is sent back to PRMC within 2 weeks.
- 5.4 PRMC will review the responses at the following PRMC meeting. Based on the response, the PRMC will recommend closure or continuation to further accrual.
  - 5.4.1 Decision to continue will be documented and sent to the CTU representative and PI.
  - 5.4.2 Trials recommended by PRMC to close will send second memo to the PI and “cc” the CTU representatives and Case CCC Clinical Research Leadership Committee. If the PI wishes to appeal the trial closure decision, a letter of explanation should be sent to the Case CCC Clinical Research Leadership Committee via the PRMC manager within 1 week of closure notification. The Case CCC Associate Director for Clinical Research will respond in writing of his/her decision regarding trial closure. This decision will be final.

**6.0 References**

- Case CCC Clinical Trials Operations Manual
- PRMC website: <http://cancer.case.edu/research/clinical-research-office/prmc/>

**7.0 Appendices:** None.

<b>SOP #: PRMC-10.3.0; Version #: 3.0</b>	
<b>Approved by:</b>	
Name: Mikkael Sekeres, MD	
Position: Deputy Associate Director of Clinical Research; Director of Clinical Trials	
Signature: 	Date: 09-06-17