Policy on Minimum Standards for Partnerships with International Clinical Research Organizations (CROs)

Purpose

This policy defines the vetting process whereby the DSMC and CCCROC will approve the proposed use of international CROs to monitor/audit non-US sites for Multicenter and Consortium Investigator-initiated trials conducted at the UCSF HDFCCC.

Background

All HDFCCC Multicenter and Consortium Investigator-Initiated trials in which the Study Chair (UCSF PI) is proposing to open non-US subsites must always utilize/contract with an international Clinical Research Organization (CRO) to provide monitoring/auditing services for the review of these non-US subsite(s). The UCSF HDFCCC Data and Safety Monitoring Committee (DSMC) will not be responsible for providing monitoring/auditing services for non-US subsites; however, the DSMC will act as the DSMB for the trial. Thus, the contracted international CRO will be required to submit all Monitoring Visit Reports (MVRs) to the UCSF DSMC for safety review, dose escalation approvals, and DSMB Reports. The UCSF DSMC and Cancer Center Clinical Research Oversight Committee (CCCROC) must review and approve each contracted international CRO prior to utilization of this CRO by the Study Chair for each non-US subsite.

References

- Helen Diller Family Comprehensive Cancer Center Data and Safety Monitoring Plan (DSMP), version 06Dec2017.
- 21 CFR 312.50.
- 21 CFR 812.40.

Procedure

As per decision from CCCROC on 12Oct2018, the UCSF DSMC will not be required to provide monitoring/auditing for non-US subsites for Multicenter and Consortium Investigator-Initiated Trials conducted in the HDFCCC. The Study Chair will be required to select/contract with an International CRO in order to conduct the monitoring/auditing oversight of each of the non-US subsites in these trials. The HDFCCC DSMC must be able to review the proposed international CRO’s Monitoring/Auditing Standard Operating Procedures (SOPs) and conduct a brief teleconference with a CRO’s representative in order to determine if the CRO will be able to comply with the minimum HDFCCC DSMC and CCCROC requirements to adequately review this trial. The minimum requirements for an international CRO to be able to be selected as the monitoring/auditing entity for the trial at the international site(s) will include the following:

- Must have Standard Operating Procedures (SOPs) that are in alignment with the minimum requirements of the HDFCCC DSMP.
University of California, San Francisco  
Helen Diller Family Comprehensive Cancer Center  
Policy and Procedure

Policy on Minimum Standards for Partnerships with International Clinical Research Organizations (CROs)  
(Version 07Dec2018)

- Must follow the HDFCCC DSMP for each of the trials, including:
  - monthly monitoring of all enrolled patients through the Dose Limiting Toxicity (DLT) period for therapeutic Phase I trials
  - twice yearly auditing of all patient data for twenty percent of the enrolled patients for therapeutic Phase II and III trials
  - yearly auditing of all patient data for twenty percent of the enrolled patients for non-therapeutic Phase III trials.

- Must provide monitoring of all enrolled patients in a dosing cohort and provide written monitoring visit reports to the HDFCCC DSMC prior to review and approval of the dose escalation request by the UCSF Study Chair for the trial.

- Must provide the HDFCCC DSMC with the Monitoring Visit Reports (MVRs) within three business days after completion of the monitoring visits for Phase I trials with Dose Escalations and five business days for Phase II/III trials.

- Must follow the communication plan of the protocol and DSMP, which requires that noncompliance issues of the non-US subsites are communicated to the Study Chair and the HDFCCC DSMC within two business days of awareness of this issue.

- Must be able to perform either on-site or remote monitoring/auditing of the source documents when conducting these oversight visits.

Once the CRO has been reviewed, vetted, and approved by the HDFCCC DSMC Manager and Chair via the signed DSMC and CCCROC CRO International Site Approval Form (Appendix 1), then CCCROC Leadership must perform a final review and provide final approval via signature on this document from the Deputy Director and Co-Director of CCCROC. The final signed document will then be submitted to the Study Chair signifying approval of the proposed contracted CRO(s) for the monitoring/auditing of each of the non-US sites.

Alternate Procedures

There are no alternate procedures to this policy. FOR IRB POLICIES ALWAYS CHECK THE UCSF HRPP WEBSITE FOR FORMS AND GUIDANCE.

https://irb.ucsf.edu/

Summary of Changes

<table>
<thead>
<tr>
<th>Version Number (Date)</th>
<th>List of Changes</th>
<th>Training Required (yes/no)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (19Nov2018)</td>
<td>N/A – original version</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Policy Approval

The personnel approved this policy document on the following dates:
Policy on Minimum Standards for Partnerships with International Clinical Research Organizations (CROs)
(Version 07Dec2018)
Appendix 1: UCSF HDFCCC DSMC and CCCROC International Site Approval Form

<table>
<thead>
<tr>
<th>CRO Minimum Requirement</th>
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<tbody>
<tr>
<td>a. Must have Standard Operating Procedures (SOP) that are in alignment with the minimum requirements of the HDFCCC DSMC.</td>
<td>a. □ Yes □ No</td>
</tr>
<tr>
<td>b. Must follow the HDFCCC DSMC for each of the trials, including:</td>
<td>b. □ Yes □ No</td>
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<tr>
<td>a. monthly monitoring of all enrolled patients through the Dose Limiting Toxicity (DLT) period for therapeutic Phase I trials</td>
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<tr>
<td>b. twice yearly auditing of all patient data for twenty percent of the enrolled patients for therapeutic Phase II and III trials</td>
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<tr>
<td>c. yearly auditing of all patient data for twenty percent of the enrolled patients for non-therapeutic Phase III trials</td>
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<tr>
<td>c. Must provide monitoring of all enrolled patients in a dosing cohort and provide written monitoring visit reports to the HDFCCC DSMC prior to review and approval of the dose escalation request by the UCSF study chair for the trial.</td>
<td>c. □ Yes □ No □ N/A</td>
</tr>
<tr>
<td>d. Must provide the HDFCCC DSMC with the Monitoring Visit Reports (MVRs) within three business days after completion of the monitoring visits for Phase 1 trials with Dose Escalations and five business days for Phase II/III trials</td>
<td>d. □ Yes □ No</td>
</tr>
<tr>
<td>e. Must follow the communication plan of the protocol and DSMC, which requires that non-compliance issues of the foreign subsites are communicated to the Study Chair and the HDFCCC DSMC within two business days of awareness of this issue.</td>
<td>e. □ Yes □ No</td>
</tr>
<tr>
<td>f. Must have the ability to perform either on-site or remote monitoring/auditing of the source documents when conducting these oversight visits.</td>
<td>f. □ Yes □ No</td>
</tr>
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</table>
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UCSF Helen Diller Family Comprehensive Cancer Center
DSMC and CCCROC International Site CRO Approval Form

Comments:

☐ CRO met minimum requirements as determined by the HDFCCC DSMC and CCCROC.
☐ CRO did not meet minimal requirements as determined by the HDFCCC DSMC and CCCROC.

John F. McAdams, MS (DSMC Manager)  Date

Thierry Jahan, MD (Chair, DSMC)  Date

Eric Small, MD (Chair, CCCROC)  Date

Mary Feng, MD (Vice Chair, CCCROC)  Date

DSMC and CCCROC International Site CRO Approval Form
Version 1.0, 05Dec2018