Guidance: PI-Initiated, Externally-Sponsored Trials

Scope: This guidance covers protocols under an external sponsor where the principal investigator is responsible for the concept, design, and conduct of the protocol. In general, DF/HCC coordinates the trial and retains the rights to use the data for research, education and publication, but the sponsor holds the IND/IDE (where required) and retains regulatory responsibility for the research. This guidance does not apply to an Investigator-Sponsored Trial (IST), where the principal investigator initiates the research and is the regulatory sponsor.

DF/HCC Investigators must clearly understand their responsibilities as an Investigator and the responsibilities that remain with the sponsor. The following guidelines should be followed:

Sponsor Responsibilities

☐ **The IND/IDE holder, or party who requests and receives Exemption, is the sponsor.**

☐ **The sponsor may transfer some responsibilities to the DF/HCC investigator.**
Per 21 CFR 312.52, a sponsor may transfer some or all of their responsibilities. Provided the conditions within this guidance are met, the DF/HCC may choose to accept responsibility for:

- Electronic Case Report Form (eCRF) development
- Data collection, hosting, and storage

However, the DF/HCC will not accept responsibility for any of the following:

- Maintaining a third-party's IND/IDE with the FDA or communicating with the FDA regarding said IND/IDE.
- Monitoring activities or oversight of trial conduct.
- Clinicaltrials.gov or CTRP registration, unless otherwise designated in accordance with FDAAA 801 and approved by the Office of Data Quality.

Study Documents

☐ **Ensure all study documents clearly and consistently identify the sponsor.**
The protocol, informed consent document, front sheet and other study documents must clearly indicate who is the sponsor for the trial.

☐ **Responsibilities transferred to the DF/HCC investigator must be clearly listed in the protocol.**
Per 21 CFR 312.52 any responsibility not specifically transferred in writing remains with the sponsor. The DF/HCC requires that any transferred responsibilities be clearly laid out in the protocol or an appendix (see below).

Data Management

☐ **Determine whether DF/HCC will be responsible for ongoing data management.**
The DF/HCC does not routinely provide data management for trials with an external sponsor. If the sponsor requests that DF/HCC manage the data, the DF/HCC investigator should contact the Office of Data Quality and the Clinical Trials Research Informatics Office for guidance prior to protocol submission.

☐ **DF/HCC can only provide a maximum of 2 data transfers per year to the sponsor.**
The DF/HCC does not have the resources to support more frequent transfers of data to an outside party. The sponsor must notify the DF/HCC Clinical Trials Research Informatics Office (CTRIO) and the DF/HCC Office of Data Quality in advance of CRF development if they need to request certain transfer specifications.

☐ **DF/HCC requires reimbursement from the sponsor for data management resources.**
Below is an outline of common data management activities. Resource time estimates are approximate, and may vary widely due to protocol complexity. The sponsor is expected to reimburse these costs at a standard hourly rate.

DF/HCC Data Management: Reimbursable Activities	
Description	**Expected Hours**

Initial CRF Development: • Programming CRF data collection forms • Validation and testing	60-80
CRF Development – Change Requests: • Editing CRF data collection forms • Validation and testing	10-40
Data Transfer Programming and Validation: • Program data transfer specifications • Set up secure data transfer link	20 - 40
Data Transfer – Change Request: • Make changes to transfer specifications • Update programming	15-30
Data Transfer: • Time to initiate and complete each data transfer	5 - 10

Transfer of Obligations

The Sponsor and investigator must establish written agreement of obligations and responsibilities, including any responsibilities transferred to the DF/HCC Investigator. This must be incorporated into the protocol document, or attached as an appendix. Changes to the below require a renegotiation of the contract and budget.

21 CFR Sponsor Responsibilities

Ensuring proper monitoring of the investigation(s), ensuring that the investigation(s) is conducted in accordance with the general investigational plan protocols, as referenced in 21 CFR 312.50; Selecting monitors, as referenced in 21 CFR 312.53(d); Monitoring all clinical investigations, as referenced in 21 CFR 312.56(a);	Sponsor
Maintaining an effective IND (and/or IDE, where applicable) with respect to the investigations, as referenced in 21 CFR 312 (and/or 21 CFR 812); Submitting to the FDA annual reports on the progress of the investigation; Upon written request by FDA, submitting records or reports (or copies of them) relating to the clinical investigation to FDA; Submission of amendments to the IND/IDE(includes new protocol, changes in protocol, and the addition of any new investigator's information); Notifying the FDA of the termination of the study;	Sponsor
Ensuring that Food and Drug Administration (FDA) and all participating investigators are promptly informed of significant new adverse effects or risks with respect to the drug, as referenced in 21 CFR 312.50. Providing an investigator brochure, as referenced in 21 CFR 312.55(a); Informing investigators of new observations discovered by or reported to the sponsor, particularly with respect to adverse effects and safe use, as referenced in 21 CFR 312.55(b); Reviewing and evaluating the evidence relating to the safety and effectiveness of the investigational test article as such evidence is obtained from the investigator, as referenced in 21 CFR 312.56(c); Reporting information relevant to the safety of the test article to the FDA, as referenced in 21 CFR 312.56(c); Submission of written IND safety reports to FDA and all participating investigators, as referenced in 21 CFR 312.32.	Sponsor
Selecting qualified investigators, as referenced in 21 CFR 312.53(a); Qualifying the investigators by obtaining required information and commitments, as referenced in 21 CFR 312.53(c); Maintaining complete and accurate records showing any financial interest as described in 21 CFR 54.4, paid to clinical investigators by the sponsor of the covered study, and all other financial interests of investigators concerning part 54, as referenced in 21 CFR 312.57 (b);	Sponsor
Controlling the shipment of investigational test article, as referenced in 21 CFR 312.53(b); Maintaining adequate records showing receipt, shipment, or other disposition of the	Sponsor

investigational test article, as referenced in 21 CFR 312.57(a); Assuring the disposition of all outstanding stocks of the investigational test article as referenced in 21 CFR 312.56(d), and as required by 21 CFR 312.59; Assuring return of unused investigational test article from each investigator whose participation in the clinical study is discontinued or terminated, as referenced in 21 CFR 312.59; Authorizing alternative disposition of unused supplies of investigational test article, provided this alternative disposition does not expose humans to risks from the test article, as referenced in 21 CFR 312.59; Maintaining written records of test article disposition in accordance with 21 CFR 312.57, as referenced in 21 CFR 312.59.	
Retaining adequate records under 21 CFR 312, Subpart D, for two years after a marketing application is approved for the test article; or, if an application is not approved for the test article, until two years after shipment and delivery of the test article for investigational use is discontinued and FDA has been notified, as referenced in 21 CFR 312.57(c);	Sponsor
Upon request from any properly authorized officer or employee of FDA, permitting at reasonable times, access to, copying of, and verification of records and reports relating to the clinical investigation, as referenced in 21 CFR 312.58(a);	Both

Other Responsibilities

Protocol registration and maintenance of registration records (e.g., Clinicaltrials.gov and/or CTRP), including posting of accrual, amendments, and study results (when required).	Sponsor
Design and maintain electronic Case Report Forms (“CRFs”) for the collection of study data.	DF/HCC
Review and approve CRF design, and retain overall responsibility for CRF design and data collection (e.g., required data points, format).	Sponsor
Periodically, up to a maximum of 3 times per year, release to Sponsor study data captured in the CRFs in the form of raw data tables, which should include, in a de-identified manner, all information obtained in the CRFs. Data will only be released after any required monitoring activities have been completed, according to the protocol and data safety monitoring plan.	DF/HCC
Conduct of quality checks on data following transfer/release to the Sponsor, all subsequent manipulation of the data, including: formatting/re-formatting, analysis, generation of data listings, creation of figures and/or tables, etc. Responsibility for formatting or re-formatting the data so as to be acceptable for submission to the FDA or other regulatory agencies.	Sponsor
All other sponsor responsibilities under 21 CFR Part 312 and/or 21 CFR Part 812 and other applicable regulations not specifically noted.	Sponsor