Use the following checklist to aid in identifying which documents can provide evidence that the Sponsor - Investigator has fulfilled his/her responsibilities as the holder of an Investigational New Drug (IND).

|  |  |
| --- | --- |
| **FDA REGULATIONS**  | **CORRESPONDING DOCUMENTS** |
| **SPONSOR RESPONSIBILITIES (312.50)*** *Sponsors are responsible for selecting qualified investigators and providing them with the information they need to conduct the investigation properly.*
* *Sponsors must ensure the investigation follows proper monitoring and is conducted in accordance with the investigational plan and protocol contained in IND*.
 |
| * **Protocol Amendments (312.30)**
* New protocol
* Changes to existing protocol
* New Investigator
 | * Original IND application (including 1571)
* FDA letter of no objection, if provided
 |
| * **Information Amendments (312.31)**
* Essential information not within the scope of a protocol amendment (e.g., new technical information, discontinuation of clinical investigation
 | * Amendments with 1571
 |
| * **IND Safety Reports (312.32)**
* Serious, related, unexpected or significant preclinical findings (written reports (e.g., MedWatch 3500A) to FDA, and all participating investigators if applicable, within 15 calendar days)
* Fatal or life-threatening reports (telephone or fax within 7 calendar days)
* Follow up information to a safety report (submitted as soon as possible)
 | * IND Safety reports with 1571
* Evidence of correspondence to other investigators
 |
| * **Annual Reports**
* Within 60 days of the anniversary date that the IND went into effect
 | * Annual reports (with 1571)
* Other correspondence with FDA (e.g., response to clinical hold, general correspondence)
 |
| * **Select Qualified Investigators and Monitors (312.53, 312.57(b)**
* Select PIs qualified by training and experience (multicenter trials only)
* Ship investigational product only to those investigators participating in the trial (multicenter trials only)
* Accurate records of financial disclosure according to 21 CFR 54
* Select monitors qualified by training and experience
 | * Signed FDA form 1572 (Investigator Agreement)
* Investigator CV and licensure
* IRB approval
* FDA for 3455 for PI and Sub-Investigators listed on FDA 1572
* For multicenter studies, Investigator information is required for each site
* 1572 and PI CV is provided to FDA
* Monitor of Study – PI
* CV and training experience of monitor
* Ensure monitor is trained on protocol
 |
| * **Ensure Ongoing Monitoring Investigations (312.56)**
* Ensure proper monitoring
* Ensure PI compliance or discontinue shipments of the investigational drug
* Review and evaluate drug safety and effectiveness
* Discontinue investigation within 5 working days when unreasonable and significant risk to subject are identified
* Ensure IRB and FDA approval to resume a terminated study
 | * Documentation of safety monitoring plan

Who will be reviewing safety data?* PI
* DSMB
* Medical Monitor
* Other: \_\_\_\_\_\_\_
* Reports/meeting minutes from DSMB or Medical Monitor
* Documentation of data monitoring plan
* Research team has been trained on data collection sheets and or CRFs
* Correspondence with monitor
* Documentation of monitoring (monitoring log)
* Notify all investigators, IRB, and FDA if investigation is discontinued
* IRB approval prior to resuming a terminated study
 |
| * **Informing Investigators (312.55)**
* Provide all clinical investigations with Investigators brochure
* Inform investigators of new observations discovered by or reported to the sponsor on the investigational product
 | * Current Investigators Brochure

For Multicenter study* Documentation that all sites have received Investigators Brochure
* Documentation of communication with investigators regarding new observations or adverse events
 |

|  |  |
| --- | --- |
| **FDA REGULATIONS**  | **CORRESPONDING DOCUMENTS**  |
| **INVESTIGATOR RESPONSIBILITIES (312.60)*** An investigator is responsible for ensuring the investigation is conducted according to the signed investigator statement, the investigational plan, and applicable regulations; for protecting the rights, safety and welfare under the investigators care and control of drugs under the investigation.
 |
| * **Assure IRB Review and Approval (312.66)**
 | IRB documentation* Initial review
* Continuing review
* Amendments
* Adverse event reporting
* Unanticipated events
* Protocol deviations
* Current Investigator Brochure
* Other IRB correspondence
 |
| * **Maintain Adequate and Accurate Case Histories on Each Subject’s Participation in the Trial (312.62(b)**
 | * Informed consents for all subjects
* Documentation that informed consent was obtained prior to study procedures
* Documentation that subject was given a copy of signed and dated consent form
* Subject eligibility documented
* Source data
* Progress notes
* CRFs
* Concomitant medications recorded
* Signature/date of staff obtaining data
 |
| * **Conduct Study According to Signed Investigators Statement, Protocol and Applicable Regulations (312.60)**
 | * Report violations/deviations to IRB
* Promptly report to IRB any “on site” adverse events/unanticipated adverse device effects in accordance to institutional requirements
* Obtain informed consent in accordance with provisions in 21 CFR 50
 |
| * **Personally Conduct and Supervise the Investigation**
* Appropriate delegation
* Adequate training
* Adequate supervision
 | * Delegation log
* Staff training log
* Routine research team meeting to review trial progress, adverse events, protocol changes
* Meeting minutes
* Routine meetings with study monitor
* Procedures for internal review of data
 |
| * **Protect the Rights, Safety, and Welfare of Study Subjects (312.60)**
 | * Adhere to protocol
* Provide reasonable medical care of adverse events
* Inform subject when medical care is needed for conditions unrelated to research
* Investigator is available to subjects during conduct of study
* Appropriate delegation to Co-Investigator if PI is not available
 |
| * **The Investigator is Responsible for Providing Sponsor with Reports (312.64)**
 | * The Investigator has provided sponsor with pertinent correspondence (e.g., enrollment numbers, adverse events, financial information and any changes in financial information)
* N/A Single center study
 |
| **DRUG ACCOUNTABILITY** |
| * **The Sponsor is Responsible for Record of Drug Disposition (312.57, 312.59)**
* Maintain adequate record of receipt and shipment of investigational drug
* Assure return of all unused investigational drug from individual investigators participating in trial or authorize alternative disposition of unused product
* Maintain written records of any disposition of the drug
 | *Drug* Receipt:* *Drug received from Industry:*

 Drug accountability log includes:* Receipt date
* Quantity
* Lot #
* Return / Disposition
* Method of disposal
* *Drug manufactured onsite*

*Drug Shipment:** *Single center study – no drug shipment*
* *Drug shipped to multiple sites:*
	+ *Drug accountability log includes:*
	+ *Date*
	+ *Destination*
	+ *Who shipped?*
	+ *Quantity*
	+ *Lot #*
	+ *Return/disposition*
	+ *Method of disposal*
 |
| * **The Investigator is Required to Maintain Adequate Records of the Disposition of the Drug (312.62)**
 | Drug dispensing record including:* Research pharmacy will manage drug
* Date
* Lot #
* Quantity
* ID of subject administered/implanted
* Disposition/record of return
* ID of person dispensing
* Return of drug, count and reason
 |
| * **The Investigator is Responsible to Ensure Control of Investigational Drug (312.61)**
* Drug will be administered only to those subjects enrolled in the clinical study and under investigator or designee’s supervision
 | * Enrollment log/Randomization log
* Delegation of Authority log
 |
| **RECORD RETENTION (312.57(c), 312.62(c)** |
| * **Sponsor and Investigator:**
* Retain records for 2 years after marketing or 2 years after investigation use is discontinued and FDA is notified
 | * Records are on file
 |
| **FDA INSPECTION (312.58, 312.68)** |
| * **Sponsor and Investigator:**
* **I**nspection of Investigator’s records and reports
 | * Upon request, permit FDA officer to access, copy and verify any records or reports made by the investigator
 |