A CHIM Site's Experience with an FDA Inspection

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Overview

Prep — Call — Inspection — Follow Up

100% Preparation

- You may expect an inspection
  - Pre-approval following submission of a new product application
  - Routine
  - For Cause
- Always be ready
  - FDA Resources
    - Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors
    - Audit Preparation Resource and Checklist
  - Your Site
    - Have a clear and comprehensive QC plan
    - Have a clear and comprehensive data management plan
    - Maintain quality records, document all communications (email organization)

General Prep

- Unit SOPs
- Travel plans
  - Who? When?
  - How will they get back if needed
- Chain of notification at your institution
- General inspection training for all team members

Items of interest to the auditor

- PI is versed in every aspect of the trials
- Delegation logs (who performed different aspects of the study)
- Training of all staff appropriate for delegated tasks
- Protocol compliance, including deviations and amendments
- 100% clean consenting process
- Data recording: accurate, timely, clear corrections
- IRB communications
- Vaccine accountability
- Record retention
- Monitoring communications
- Volunteer compensation

Common Indications of Fraud

- Study staff exhibiting lack of knowledge about the study, seeming lack of equipment or resources when compared to audited work
- Lack of any errors or corrections on CRFs
- Participants who are perfectly compliant with study visits and evaluations
- 100% of all participants who were screened, enrolled and completed the study
- Inconsistent sources of data
- Lack of variation in handwriting, ink, or writing style
- Study staff that are guarded or suspicious

Pre-Inspection: Documents

- Study
  - Protocol, all versions
  - Manual of Procedures, all versions
  - Pharmacy and Lab manuals, all versions
- Regulatory and Admin
  - 1572
  - Delegation/Signature Log
  - Institutional Review Board
  - Notes to File
  - Training Logs
  - Recruitment methods, screening and enrollment logs
- Communication
  - All emails

Pre-Inspection: Documents

- Subject Binders
  - Signed ICF
  - Screening docs – Demographics, Med Hx
  - Enrollment docs
  - Dosing docs
  - Study days
  - Cumulative AEs
  - Concomitant Meds
  - Labs

Pre-Inspection: Documents

- CRFs
  - Process
  - Personnel responsible
  - Data
- IP management
  - IB
  - Shipping, receiving, storage, chain of custody
- Other
  - Financial disclosures
  - Data management plan, security
  - List of PI's concurrently active protocols
  - Facility maps

Pre-Inspection: Tasks

Audit Preparation Task Item	Point Person	Timelines							
		10-Nov	17-Nov	24-Nov	1-Dec	Audit Ready ?	2-Dec	3-Dec	4-Dec
Clinic								AUDIT	
Screening and enrollment logs clean and ready		X							
Preparation of Informed Consent documents		X							
Regulatory Binder preparation				X					
All subject binders compiled and QC'ed and LTFU doc			X						
Protocol deviations summarized		X							
AE and concommitant meds summaries			X						
Staff roster and delegation log				X					
Location and schemata of Baird 7			X						
Training log for CliniTek			X						
Screening and enrollment logs clean and ready				X					
Preparation of Informed Consent documents		X							
Regulatory Binder preparation			X						
All subject binders compiled and QC'ed			X						
Protocol deviations summarized		X							
AE and concommitant meds summaries			X						
Staff roster and delegation log				X					
CRC equipment records (calibration, centrifuge, etc)			X						
Clinic staff training records and credentials				X					
Review of all regulatory and subject binders		X							
FAHC clinical lab information and CLIA cert			X						
Clinical facility prep for tour				X	X				
Overall study calendars		X							
Pharmacy									
Site blinding plan prepped									
Vaccine randomization documentation prepped									
Vaccine administration documentation prepped									
Site blinding plan prepped									
Vaccine randomization documentation prepped									
Vaccine administration documentation prepped									
Pharmacy delegation log									

Lab
Product receipt and storage documentation (challenge, buffer, sterile water, Na Bicarb, vaccine)
Challenge randomization documentation prepped
Site blinding plan documentation
Challenge preparation and transport documentation
Vaccine transport documentation
Lab data: stool worksheets, requisitions, CRFs
Shipment of stool in RNA later
Specimen shipping logs
Vaccine and challenge strain destruction/return documentation
VTC stool scale logs
Vaccine receipt and storage documentation
Site blinding plan documentation
Vaccine preparation and transport documentation
Specimen shipping logs
Vaccine destruction/return documentation
IBC documentation
Equipment maintenance logs
Lab staff training records and credentials
Lab facility prep for tour
VTC Unit and Admin
Finalize audit agenda
Confirm auditor's work space
Summary of all VTC studies
Consolidate VTC unit SOPs to those used during trials
VTC QMP
Cross-check unit SOPs with PaxVax MOP
Institutional Name Change
Team Meeting

Important Dates

Date of Initial IRB approval of protocol	7/12/2013
Dates of amendments to protocol if any	8/8/2013
	8/16/2013
	8/21/2013
	10/16/2013
	12/6/2013
Date of IRB approval of informed consent	7/12/2013
Date Form FDA 1572 was signed by Clinical Investigator	1/23/2014
Date first subject was screened	8/1/2013
Date first subject signed informed consent document	8/1/2013
Date test article was first administered	9/27/2013
Dates of last follow up visit for study subjects	
R-xx-zzz	6/5/2014

- Know what your monitors are doing at each visit – are they monitoring all charts, just a select percentage?

Screening #	subject #	Cohort	Treatment	Internal QC	Monitor Status	Date of monitoring
S-xx-aaa	R-xx-aaa	1	C	complete thru discharge	Pending	24-Apr-14
S-xx-bbb	R-xx-bbb	1	C	complete thru discharge	Pending	24-Apr-14
S-xx-ccc	R-xx-ccc	1	vax only	complete thru discharge	Pending	24-Apr-14
S-xx-ddd	R-xx-ddd	1	C	complete thru discharge	Pending	24-Apr-14
S-xx-eee	R-xx-eee	1	C	complete thru discharge	Pending	24-Apr-14
S-xx-fff	R-xx-fff	1	C	complete thru discharge	Pending	24-Apr-14
S-xx-ggg	R-xx-ggg	1	C	complete thru discharge	Pending	24-Apr-14
S-xx-hhh	R-xx-hhh	1	C	complete thru discharge	Pending	24-Apr-14
S-xx-iii	R-xx-iii	1	C	complete thru discharge	Pending	24-Apr-14
S-xx-jjj	R-xx-jjj	1	C	complete thru discharge	Pending	25-Apr-14

Staff Training

- How to interact with the inspector, what the inspector is looking for
- Review of the study being inspected
  - Study design
  - Source docs
- On inspection schedule, personnel responsible
- Notify study personnel not still with your group

Role	Responsibilities	Primary	Back-Up 1	Back-Up 2
Greeter	Meet at ACC, greet, credential, bring to MedEd 201	CEL	BK	RC
Investigator	Primary responsibility for the study	CEL	BK	CR
Liaison	Primary point of contact with Inspector: answer questions, relay material, coordinate with IC	CJL	RC	MC
Recorder	Always accompany Liaison, take notes throughout	DD	MCW	MB
Escort	Sit outside Inspector's room; assist Liaison, Inspector	NG	DC	SW
Lab	Respond to lab-specific questions	MC	ES	BM
Clinic/CRC	Respond to CRC-specific questions	JB	CR	KL
Pharmacy	Respond to Pharmacy-specific questions	SZ	MD	DM
Incident Command	Coordinates Hub	RC	MB	MCW
Hub Admin	Admin support for IC, maintains documentation on all requested material	MB	BM	SW
Courier	Photocopying, printing,	SW	DB	MM
Room Prep	Preps Inspector's room	MB		

Pre-Inspection: Activities

- Mock audit
  - Sponsor
  - Objective party with expertise
- Contact list
- Short presentation for inspector about site and study

On Inspection

- Institution-wide notifications
- Room prep – Inspector's, team
- Ask for ID when inspector arrives
- Record keeping / minutes
- List of what got copied
- Limit documents, speech, space to only what is asked for; keep it simple

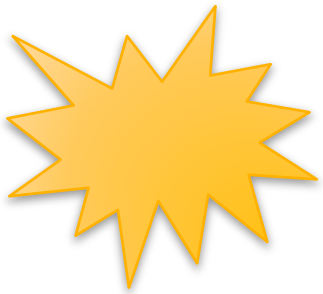
Document Requested by Auditor	Original Distributed?	Original Returned?	Copied for Inspector?
Dr. Caroline Lyon's CV (version 17May2013)	Y	Y	N
Cohort 1: Lab Challenge Day 11 Worksheet	Y	Y	Y
Cohort 1: Challenge Inoculum Prep	Y	Y	Y
Regulatory Binders (vol 1-3)	Y	Y	N
Delegation of Authority Form	Y	Y	Y
Screening and Enrollment Logs (14Nov2014)	Y	Y	Y
1572 Caroline Lyon	Y	Y	Y
1572 XXX	Y	Y	Y
Dr. Lyon's introduction presentation	N	NA	Y
IRB Clarification Memo (xxx OFFICIAL_24Jun2013)	Y	Y	Y
Approval memorandum (12Jul2013)			
Protection of Human Subjects Assurance (approved 12Jul2013; expires 18Jun2014)			
HIPAA Authorization Review memo (12Jul2013)			
Amendment form for recruitment materials (approved 12Jul2013), with attachment 'UVM Center Demonstrates Global Health Commitment with Launch of Oral Cholera Vaccine Study'			
Amendment form for ICF and HIPAA revisions, subject information and additional recruitment material (approved 17Jul2013)			

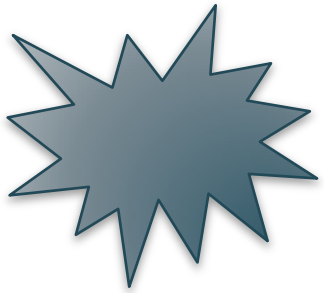
General Terms

- FDA 482 – notice of inspection
- FDA 483 - inspectional observations
- Warning Letter – possible issues that may be followed up on
- CAPA – Corrective and Preventive Action

Follow Up

Post FDA Audit Inspection Files	file name	hard copy location	electronic file location	date of document	comments
· Maintain a File for each Inspection					
· Form FDA 482, Notice of Inspection					
· Duplicates of copies provided to Inspector to take off-site					
· Form FDA 484, Receipt for Sample					
· FDA Letter No Inspectional Findings					
· Form FDA 483, Inspectional Findings					
· Your own report of the inspection Internal notes on the inspection					
· FDA Establishment Inspection Report (EIR)					
· Response to Form FDA 483 Subsequent documentation, e.g. Warning Letter and your response.					



PARTY