Review of Accountability of Investigational Agents

Hether Seifert, MSM, BS

Alliance Group Meeting, 11/2014

Pop Quiz – Warm up!

- What is the appropriate way to fix a mistake that is made on a research document?
- When an PMB supplied IND is needed at a satellite location, how does the IND get from the main location, to the satellite location?
- When is a patient specific DARF required?

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Ask your Neighbor:

“In your pharmacy”,

- How are your INDs stored?
- How are your INDs secured?
- What is the process for temperature monitoring, recording and reviewing?
- How do you ensure the drug counts between the DARF and shelf supply are consistent? – How is it documented?
- What do you do for Double-Blinded studies?

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Lets Discuss!

- How are NCI supplied investigation products required to be tracked?

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Collection of this information is authorized under 21 CFR 312.57. The information is collected to ensure compliance with Food and Drug Administration (FDA) requirements for NCI as an IND sponsor and that investigational agents are under the control and accounted for by competent authority. The information may be disclosed to researchers for investigational purposes, sponsors of clinical trials and their company collaborators, the applicable Institutional Review Board, NCI, FDA, and the Department of Health and Human Services. Submission of this information is voluntary however, in order for you to conduct a study in accordance with relevant, current protocols, you must complete all fields.

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Public reporting burden for this collection of information is estimated to average 4 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering the data needed, and completing and reviewing the collection of information. **An agency may not conduct or sponsor, and a person is not required to respond to, a collection of informat displays a currently valid OMB control number.** Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this bu Project Clearance Branch, 6705 Rockledge Drive, MSC 7974, Bethesda, MD 20892-7974, ATTN: PRA (0925-0613). Do not return the completed form to this address.

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Division of Cancer Treatment and Diagnosis
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PAGE NO.

CONTROL RECORD ☐

SATELLITE RECORD ☐

Investigational Agent Accountability Record

Name of Institution:	NCI Protocol No.:
Agent Name:	Dose Form and Strength:
Protocol Title:	Dispensing Area:
Investigator Name:	CTEP Investigator ID:

Line No.	Date	Patient's Initials	Patient's ID No.	Dose	Quantity Dispensed or Received	Balance Forward / Balance	Manufacturer and Lot No.	Recor Initi
1.								

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Form Approved:
OMB No. 0925-0613
Expires: 03/31/2016

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Investigational Agent Accountability Record

Oral agents ONLY

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Name of Institution:	Investigator Name:	CTEP Investigator ID:

Protocol Title:	NCI Protocol No:	Local Protocol No:	Dispensing Area:

Agent Name:	Dose Form and Strength:	Bottle size (e.g., # tablets/bottle):

Line No.	Date	Patient's Initials	Patient's ID No.	Dose	Quantity Dispensed or Received	Balance Forward / Balance	Manufacturer and Lot No.	Recorder's Initials	Expiration Date (if available)	Date Patient Returned	Quantity Patient Returned	Recorder's Initials
1.												
2.												
3.												
4.												

DARF – Headers

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PAGE NO. 1

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Investigational Agent Accountability Record

Name of Institution: Southeast Cancer Control Consortium	NCI Protocol No.: CALGB 40503
Agent Name: Bevacizumab/Placebo NSC 704865 Refrigerate	Dose Form and Strength: 100 mg vial (2.5mg/ml - 4 ml vial)
Protocol Title: Endocrine Therapy in Combination with anti-VEGF Therapy: A Randomized, Double-Blind, Placebo-Controlled Phase III Trial of Endocrine Therapy Alone or Endocrine Therapy Plus Bevacizumab For Women with Hormone Receptor- Positive Advanced Breast Cancer	Dispensing Area: Main Pharmacy supplied by Genentech and provided by NCI
Investigator Name: James N. Atkins	NCI Investigator No.: 01234

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Oral DARF General Instructions

- Completing and Using the form
  - Per protocol specifications (by bottle or tablet)
  - Not in protocol? Just be consistent
  - Don’t for get the header information

http://ctep.cancer.gov/branches/pmb/faq/docs/accounting_for_oral_agents.pdf

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Oral DARF – Documenting Returns

Using the Return Portion

- Document the return on the correct form
- Correct dispensing row
- Date and quantity (number of caps or tabs)
- If dispensing didn't occur on the ORAL DARF do not document it on the ORAL DARF

http://ctep.cancer.gov/branches/pmb/faq/docs/patient_returns_of_oral_clinical_supplies.pdf

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Exercise: ORAL DARF Completion

- How to use the Oral DARF -general

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CONTROL RECORD ☒
SATELLITE RECORD ☐

Name of Institution:	Investigator Name:	CTEP Investigator ID:
Southeast Consortium for Cancer Clinical Trials	Hether Seifert	01234

Protocol Title:	NCI Protocol No:	Local Protocol No:	Dispensing Area:
Study of Oral DARF completion and oral IND returns	HE123456	HE123456	Main Pharmacy

Agent Name:	Dose Form and Strength:	Bottle size (e.g., # tablets/bottle):
M&Ms	1 piece	50/packet

bottle pieces

Line No.	Date	Patient's Initials	Patient's ID No.	Dose	Quantity Dispensed or Received	Balance Forward / Balance	Manufacturer and Lot No.	Recorder's Initials	Expiration Date (if available)	Date Patient Returned	Quantity Patient Returned	Recorder's Initials
1.	9/17/14	received from NCI			15 packets	15	ME2078	MAS				
2.	9/29/14	JD	127623	3	-1	14	ME2078	MAS				
3.	10/2/14	MW	123762	5	-1	13	ME2078	MAS				
4.	10/30/14	transfer	to Little		-5	8	ME2078	MAS				
5.	11/3/14	JD	127623	3	-1	7	ME2078	MAS	N/A	11/17/14	35	MAS
6.	11/4/14	Inventory				7	ME2078	MAS				
7.												

Be the Auditor!

- Find as many mistakes as you can…..

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Name of institution: Southeast Consortium for Cancer Clinical Trials

Investigator Name: Hether Seifert

CTEP Investigator ID: 01234

Protocol Title: Study of Oral DARF completion and oral IND returns

NCI Protocol No: HE123456

Local Protocol No: HE123456

Dispensing Area: Main Pharmacy

Agent Name: M&Ms

Dose Form and Strength: 1 piece

Bottle size (e.g., # tablets/bottle): 50/packet

Line No.	Date	Patient's Initials	Patient's ID No.	Dose	Quantity Dispensed or Received	Balance Forward / Balance	Manufacturer and Lot No.	Recorder's Initials	Expiration Date (if available)	Date Patient Returned	Quantity Patient Returned	Recorder's Initials
1.	9/13/14	DD		2	2	2	ME1273					
2.	9/20/14	Received			10	12	ME2173	MAS				
3.	9/17/14	JD	Z-428-567	4	1	11	ME1273	MAS				
4.	9/30/14	DD	Z-473-206	2	-100	-111		MAS				
5.	10/3/14	Returned by mas			+50	-61	ME1285	MAS				
6.	10/5/13	JD	Z-428567	4	1	8	ME1285	MAS				
7.	10/7/14	Inventory				9	ME1273	MAS				
8.	10/15/14	SLO	202-127			495	T45650	KEL	N/A	10/15/14	45	MAS
9.	10/15/14											
10.												

What did you find??????

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Investigator Name: Hether Seifert

CTEP Investigator ID: 01234

Protocol Title: Study of Oral DARF completion and oral IND returns

NCI Protocol No: HE123456

Local Protocol No: HE123456

Dispensing Area: Main Pharmacy

Agent Name: M&Ms

Dose Form and Strength: 1 piece

Bottle size (e.g., # tablets/bottle): 50/packet

Line No.	Date	Patient's Initials	Patient's ID No.	Dose	Quantity Dispensed or Received	Balance Forward / Balance	Manufacturer and Lot No.	Recorder's Initials	Expiration Date (if available)	Date Patient Returned	Quantity Patient Returned	Recorder's Initials
1.	9/13/14	DD		2	2	2	ME1273					
2.	9/20/14	Received			10	12	ME2173	MAS				
3.	9/17/14	JD	Z-428-567	4	1	11	ME1273	MAS				
4.	9/30/14	DD	Z-473-206	2	-100	-111		MAS				
5.	10/3/14	Returned by mas			+50	-61	ME1285	MAS				
6.	10/5/13	JD	Z-428567	4	1	8	ME1285	MAS				
7.	10/7/14	Inventory				9	ME1273	MAS				
8.	10/15/14	SLO	202-127			495	T45650	KEL	N/A	10/15/14	45	MAS
9.	10/15/14											
10.												

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Southeast Consortium for Cancer Clinical Trials	Hether Seifert	01234

Protocol Title:	NCI Protocol No:	Local Protocol No:	Dispensing Area:
Study of Oral DARF completion and oral IND returns	HE123456	HE123456	Main Pharmacy

Agent Name:	Dose Form and Strength:	Bottle size (e.g., # tablets/bottle):
M&Ms	1 piece	50/packet

Line No.	Date	Patient's Initials	Patient's ID No.	Dose	Quantity Dispensed or Received	Balance Forward / Balance	Manufacturer and Lot No.	Recorder's Initials	Expiration Date (if available)	Date Patient Returned	Quantity Patient Returned	Recorder's Initials
1.	9/13/14	DD		2	02	2	ME1273					
2.	9/20/14	Received			10	12	ME2173	MAS				
3.	9/17/14	JD	Z-428-562	4	01	11	ME1273	MAS				
4.	9/30/14	DD	Z-473-2016	2	-100	-111		MAS				
5.	10/3/14	Returned by mail			+50 ?	-61 ?	ME1285	MAS				
6.	10/5/13	JD	Z-428562	4	1	8	ME1285	MAS				
7.	10/7/14	Inventory		—	—	9	ME1273	MAS				
8.	10/15/14	SLD	202-127			495	T45650	KEL	N/A	10/15/14	45	MAS
9.	10/15/14											

Most Common Non-compliance – DARF

- If there is a space/box/line for something, it needs to be filled in/checked with the correct study information
  - Protocol titles
  - Agent Name
  - Dispensing location
  - Control or Satellite location (check boxes)
  - Page numbers
  - Dose form/strength
  - Manufacturer lot number (use Julian date if not provided)

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It’s Pharmacy!

- Security and Storage
  - temperature
- IND – Order, Receipt, Transfer, Return and Destroy
- Documents

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Guidelines and Regulations

- **Storage**
  - ICH guideline 4.6.4, 5.13.2, and 5.14.3
  - 21 CFR 312.69

- **Supply and Handling**
  - ICH Guideline 5.13.3 and 5.14
  - 21 CFR 312.59
- **Accountability**
  - ICH Guideline 4.6
  - 21 CFR 312.57 (a) and 312.62 (a)

- **Dispensing**
  - ICH Guideline 4.6.6
  - 21 CFR 312.61
- Guidelines For Auditing of Clinical Trials for Cooperative Groups (1/113)

Resources

- CTMB web site:
  - http://ctep.cancer.gov/branches/ctmb/clinicalTrials/docs/ctmb_audit_guidelines.pdf
- PMB web site:
  - http://ctep.cancer.gov/branches/pmb/
  - Drug Accountability Record Form (current version):
  - http://ctep.cancer.gov/forms/docs/agent_accountability.pdf
  - Oral Darf: http://ctep.cancer.gov/forms/docs/oral_agent_accountability.pdf

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Conclusion

THANK YOU!

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Mayo Clinic Cancer Center

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