Pharmacist Considerations for Investigational Drug Studies

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KENTUCKY HEMATOLOGY/ONCOLOGY
PHARMACY SYMPOSIUM 2020

Disclosures

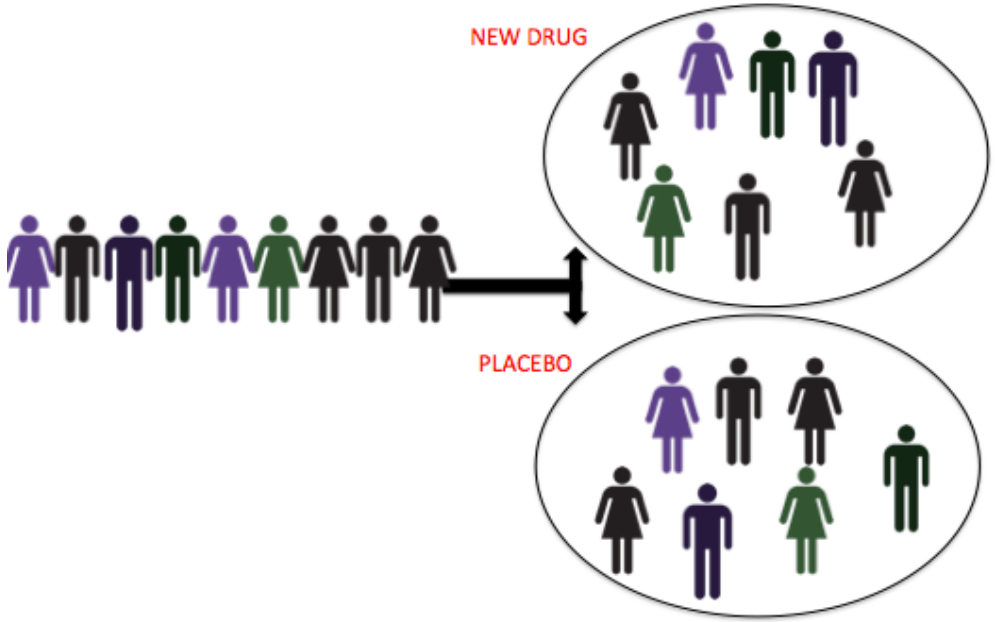
I have no actual or potential conflicts of interest to disclose.

Learning Objectives

- Describe the roles and responsibilities of an investigational research pharmacist
- Discuss proper handling of investigational medications
- Recognize the importance of site-specific Standard Operating Procedures (SOPs) regarding investigational medications
- Identify common pharmacy related protocol deviations

Why Do We Have Investigational Research Pharmacists?

- Oversee proper handling, storage, and blinding of investigational drugs
- Source of knowledge for study drugs (Phases 1, 2 and 3)
- Provide added support to research team including:
  - Randomization
  - Drug accountability and disposition
  - Blinding/Unblinding



Compliance

- Ensure compliance with all federal (FDA, NIH, NCI), state, The Joint Commission, and IRB regulations concerning investigational medications
- Ensure compliance with all site-specific administrative, nursing, and pharmacy policies
- Implementation of research medication-specific policies compliant with USP 795 and 797, as well as creation of policies pertaining to USP 800 guidelines regarding research-specific medications

NIH = National Institutes of Health, NCI = National Cancer Institute, IRB = Institutional Review Board, USP = United States Pharmacopeia

Research and Development Activities

- Initial protocol review
- Assess the pharmacy's ability to accommodate the protocol
- Site qualification, initiation, and monitor visits
- Act as unblinded personnel (will break blind if necessary)
- Randomization
- Preparation of dosage forms
- Quality control

Basic IDS Activities

- Order investigational product (IP)
- Maintain inventory
- Process returns
- Assure appropriate storage of IP
- Prepare and package IP
- Compound, deliver, and dispense IP
- Provision of drug information
- Maintain proper medication records

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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NIH-2

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National Institutes of Health
National Cancer Institute

Division of Cancer Treatment and Diagnosis
Cancer Therapy Evaluation Program

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.	Recorder's Initials
1.								
2.								
3.								
4.								
5.								
6.								
7.								
8.								
9.								
10.								
11.								

Designated Staff and Locations

- Specific access for staff that receive and dispense investigational supply
- Investigational drug supply should be separated from commercial supply

FDA Requirements for Investigational Drug Storage

- FDA Code of Federal Regulations Title 21 Part 312
- Secure location with limited access
- Storage conditions comply with study protocol or instructions on the label of the drug
- Responsibilities of the Investigator:
  - Administer drug only to subjects under personal supervision of primary investigator (PI) or sub-investigator
  - Access to the drug is limited and not supplied to those not authorized to receive it

TRUE OR FALSE

Investigational drugs that are FDA approved can be stored next to the same commercially available drug in order to save space.

FALSE

Investigational drug supply should be separated from commercial supply.

Standard Operating Procedures (SOPs)

- Implementation of investigational drug-specific SOPs
  - Receipt, inventory, safe handling and compounding, storage and security, transport and transfer of inventory, protocol review and training, return and disposal, and monitor/auditor visits.
- Transparency with sponsors/investigators
- Clear responsibilities of everyone involved in investigational drug dispersion
- Staff turnover issues

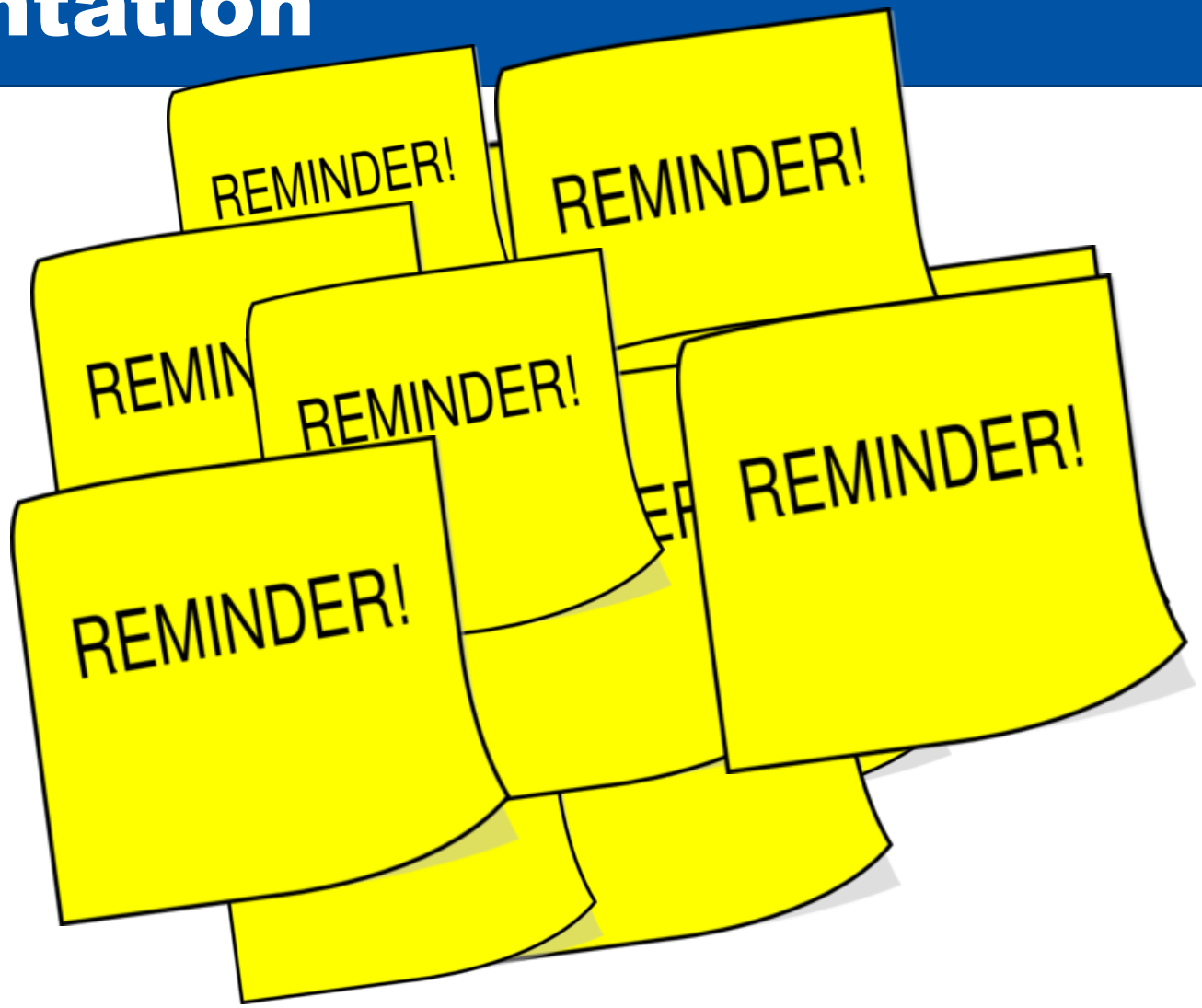
UK IDS is available to facilitate SOP creation

"When In Doubt DON'T Throw It Out"

- Treat study drugs/documentation as controlled medications
  - Keep any files that you are unsure of their importance, expiration, or purpose
  - Consult UK IDS if needed
- Make sure to follow protocol-specific instructions regarding destruction and proceeding documentation
- Maintain drug accountability records for at minimum the time required by site- or protocol-specific recommendations.

Real-Time Documentation

- Stay up-to-date on record-keeping by documenting in real-time
- Incomplete or incorrect documentation can lead to protocol deviations.

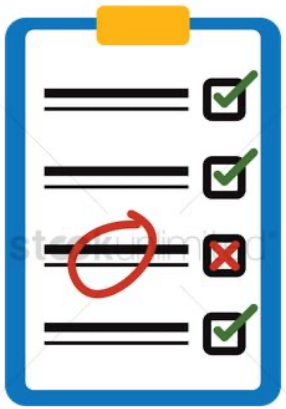


Common DARF Non-Compliance Issues

DARFs not filled out correctly or do not contain all the information in the header that is required

DARFs not maintained in real-time

Paper DARFs: corrections not lined out, initialed and dated (no scribble marks or black-out marks)



Study supplied agent dispensed to a registered study patient, yet not recorded appropriately on DARF

Single DARF used for multiple patients/study participants on study when patient-specific DARF should be maintained

Lack of documentation on DARF of study-supplied agent transactions and local destruction

Participant return of oral study supplied agents not documented on Oral DARF or recorded inaccurately

One DARF used for multiple agent strengths, dosage forms, or ordering investigators (new DARFs are required for new PIs)

One DARF used for a protocol using multiple study agents

Examples of DARF Non-Compliance

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Investigational Agent Accountability Record
Oral agents ONLY

National Institutes of Health
National Cancer Institute
Division of Cancer Treatment and Diagnosis
Cancer Therapy Evaluation Program

PAGE NO.
CONTROL RECORD ☒
SATELLITE RECORD ☐

Name of Institution:	Investigator Name:	CTEP Investigator ID:
University of Kentucky	John Doe, MD	

Protocol Title:	NCI Protocol No:	Local Protocol No:	Dispensing Area:
Oral Acetaminophen for Post-Surgical Pain	5345123	XYZ-123	Investigational Drug Service Pharmacy

Agent Name:	Dose Form and Strength:	Bottle size (e.g., # tablets/bottle):
Acetaminophen	Oral - 500mg	20 tablets/bottle

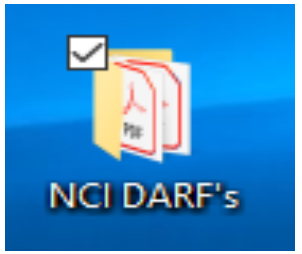
Line No.	Date	Patient's Initials	Patient's ID No.	Dose	Quantity Dispensed or Received	Balance Forward / Balance	Manufacturer and Lot No.	Recorder's Initials	Expiration Date (if available)	Date Patient Returned	Quantity Patient Returned	Recorder's Initials
1.	08/01/2020	DBL	12345678-90	500mg	1 bottle	-1 / 8	Johnson & Johnson 432-05	SL	11/20	8/30/20	0	SL
2.	09/01/2020	DBL	12345678-90	500mg	1 bottle	-1 / 7	Johnson & Johnson 432-05	SL	11/20	9/30/20	3 tablets	SL
3.	10/01/2020	DBL	12345678-90	500mg	1 bottle	-1 / 6	Johnson & Johnson 432-05	SL	11/20	10/30/20	6 tablets	SL
4.	11/01/2020	DBL	12345678-90	500mg	1 bottle	-1 / 5	Johnson & Johnson 488-05	SL	11/20	11/30/20	2 tablets	SL
5.	12/01/2020	DBL	12345678-90	1000mg	1 IV	-1 / 4	Johnson & Johnson 488-05	SL	11/20			
6.												
7.												

DARFs not filled out correctly or do not contain all the information in the header that is required

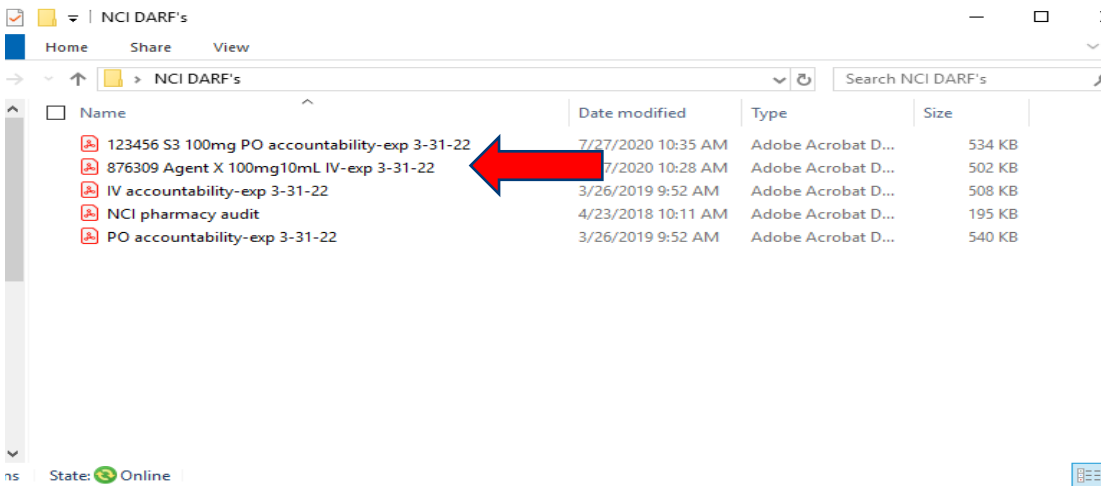
One DARF used for multiple agent strengths, dosage forms, or ordering investigators

NCI Drug Accountability Record Template

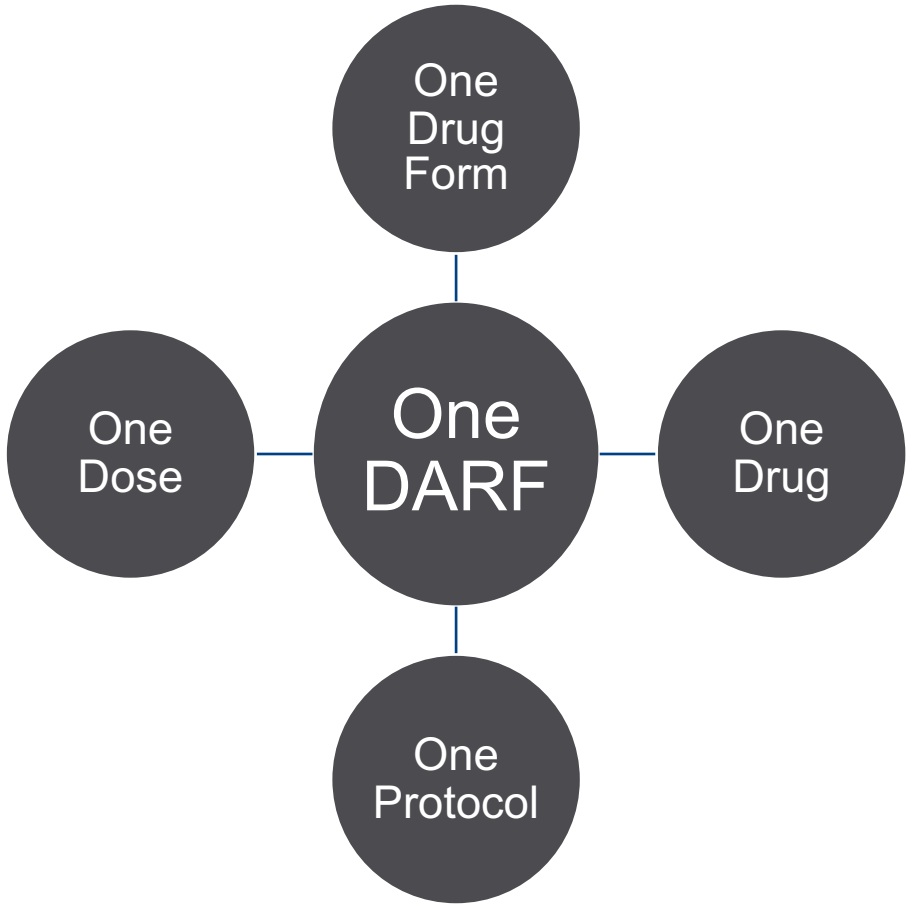
- Create a shared folder for drug accountability forms
  - Share access with other investigational pharmacists/technicians



- Develop generic oral and IV drug accountability form templates for easier implementation of new/expired research medication disposition documentation
  - Suggested format for name: “Study Name/Code – Agent – Strength – DARF Expiration Date”



DARF Assistance



- NIH/NCI Investigational Drug Accountability Training Videos
  - https://ctep.cancer.gov/branches/pmb/drug_training_videos.htm

- Maintaining in-date DARFs – NCI/CTEP sends out automated reminders.

TRUE OR FALSE

Single Drug Accountability Record Forms (DARFs) can only be used for one drug, for one strength, for one dosage form, for one study.

TRUE

Other Non-Compliance Examples

- Quantities not accounted for in physical inventory; quantity does not match DARF
  - Treat everything as a control
  - Ramifications of inaccurate documentation – protocol deviations/audits/CAPA

- Unused/un-dispensed NCI-supplied study agent is not returned or not transferred to an appropriate NCI protocol or not destroyed within 90 days of notification from NCI;

- NCI-supplied study agent is locally destroyed without NCI authorization or not locally destroyed per local institution's destruction policy

Other Non-Compliance Examples (cont.)

- Pharmacy does not have procedures in place to ensure person prescribing or cosigning prescriptions for study-supplied agent is an authorized prescriber
  - Verify active prescriber authorization via the CTSU website: https://www.ctsu.org/Public/Default.aspx

- Participant given commercial supply instead of the study supplied agent
  - Cannot replace research provided medications with commercial supply

TRUE OR FALSE

If a drug is commercially available and is used by mistake for a study specific dose, the pharmacy can restock their inventory with the study supplied drug.

QUESTIONS?

General IDS Email: IDS@uky.edu