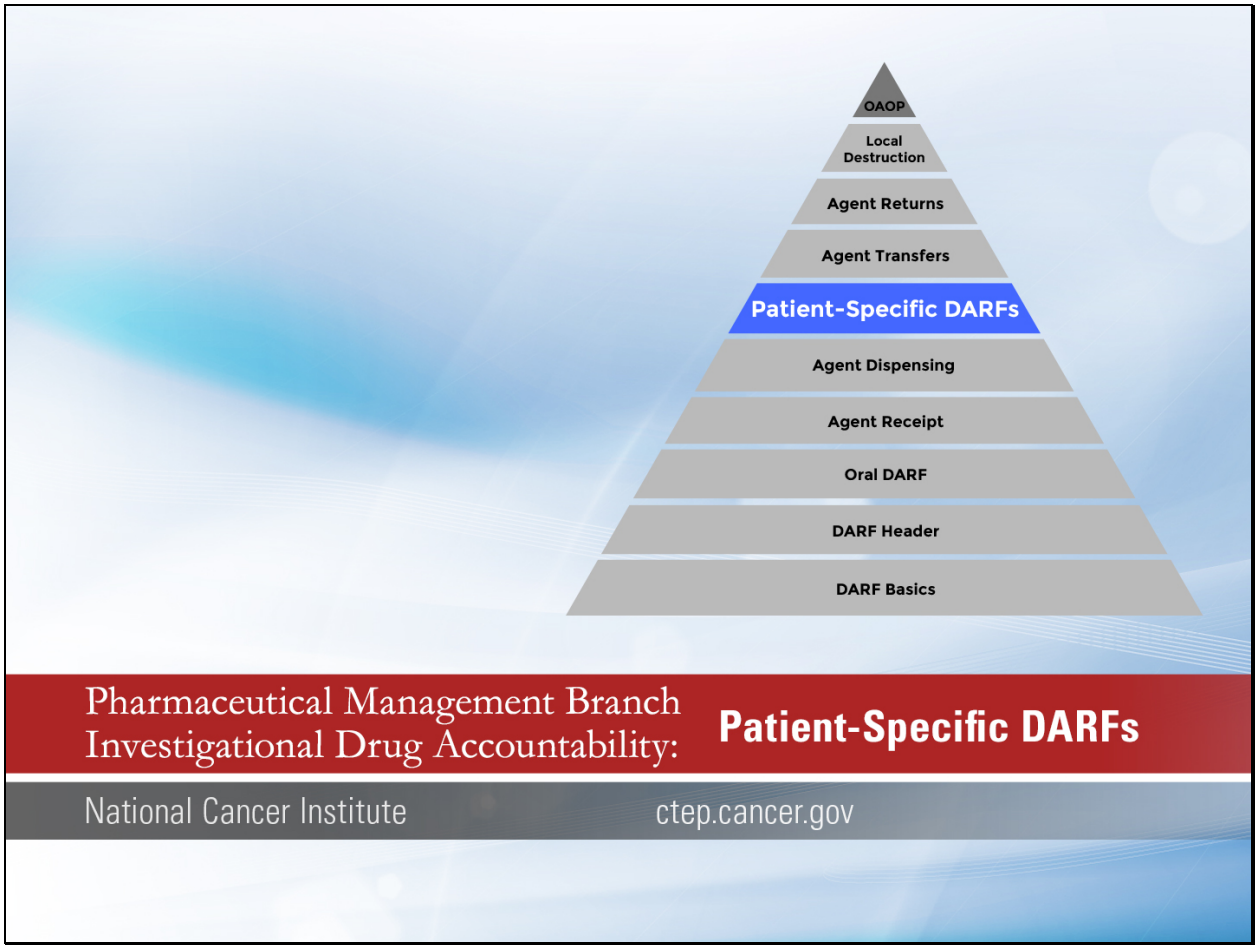
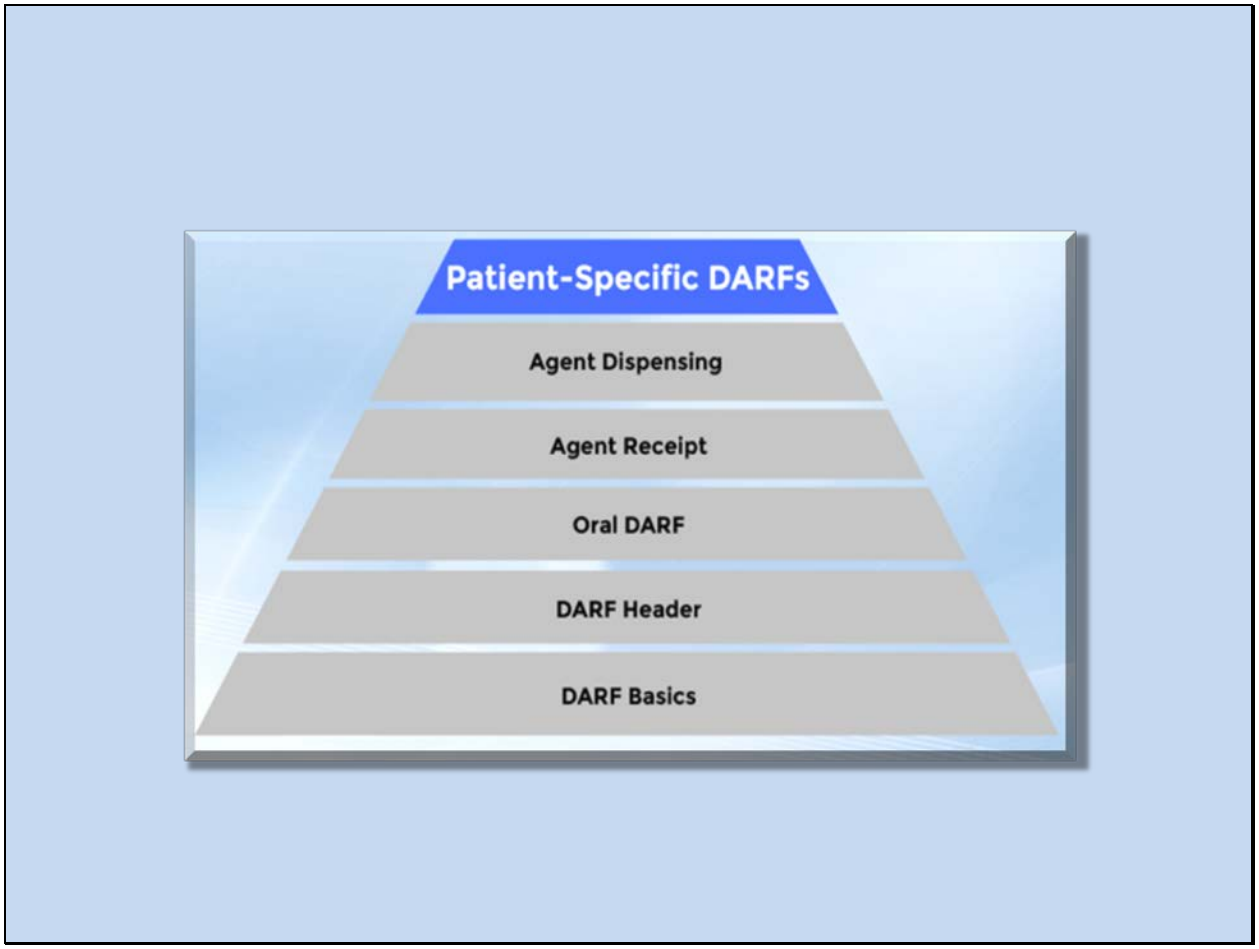
Slide 1



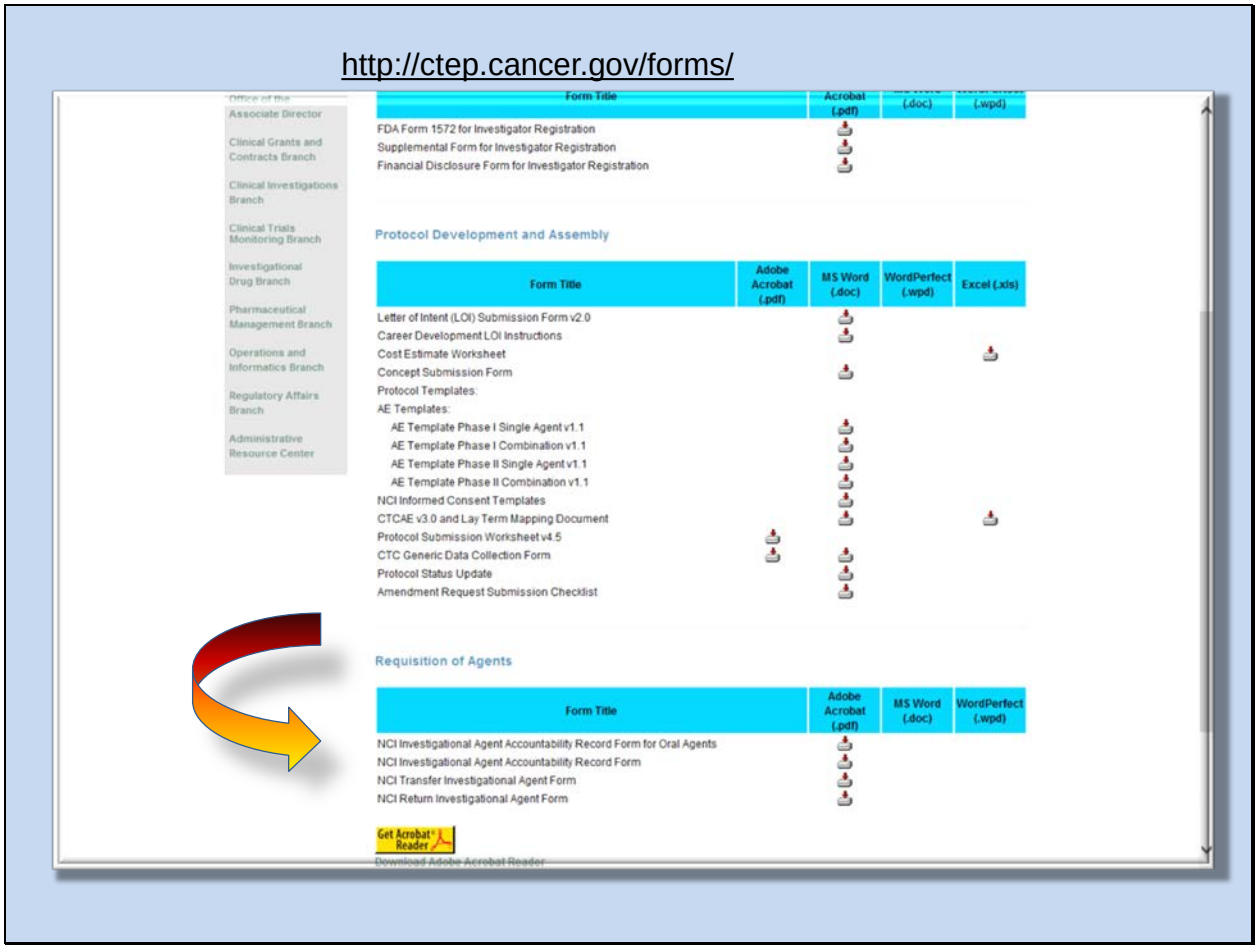
Welcome to this video tutorial on Patient-Specific DARFs in the PMB Investigational Drug Accountability series. This video will review how to manage your DARF when using it for a patient-specific or blinded study. For the purposes of this video, the term blinded and patient-specific will be used interchangeably. Any references to the Investigational Agent Accountability Record in this presentation apply exclusively to the NCI DARF.

Slide 2



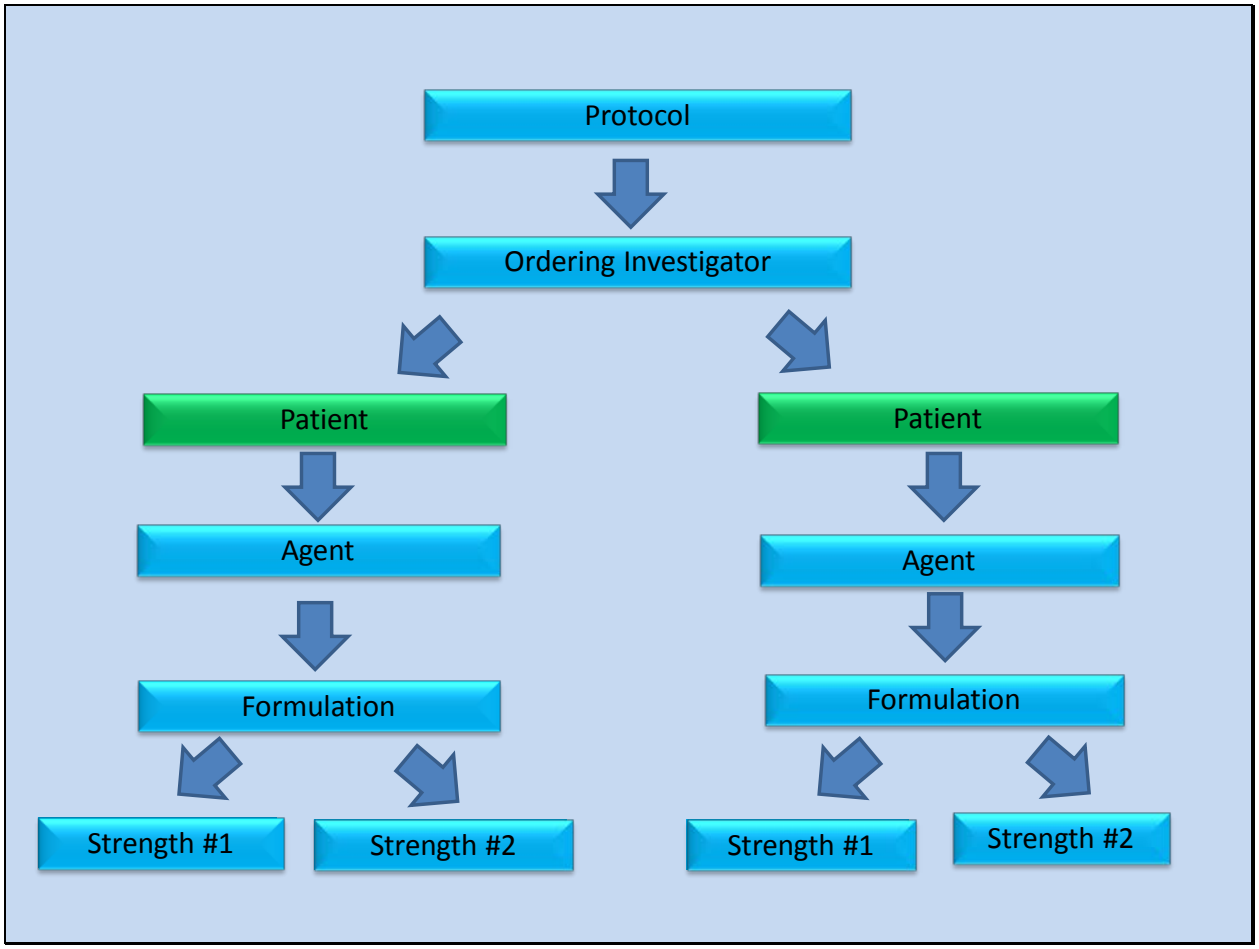
Much of the information in this presentation will build off of previously released videos in the Investigational Drug Accountability series. Please consider viewing the other videos in this series before viewing the patient-specific DARF video. From the earlier videos, you already know that DARFs must be maintained to track the disposition of all study-supplied agents for NCI clinical trials.

Slide 3



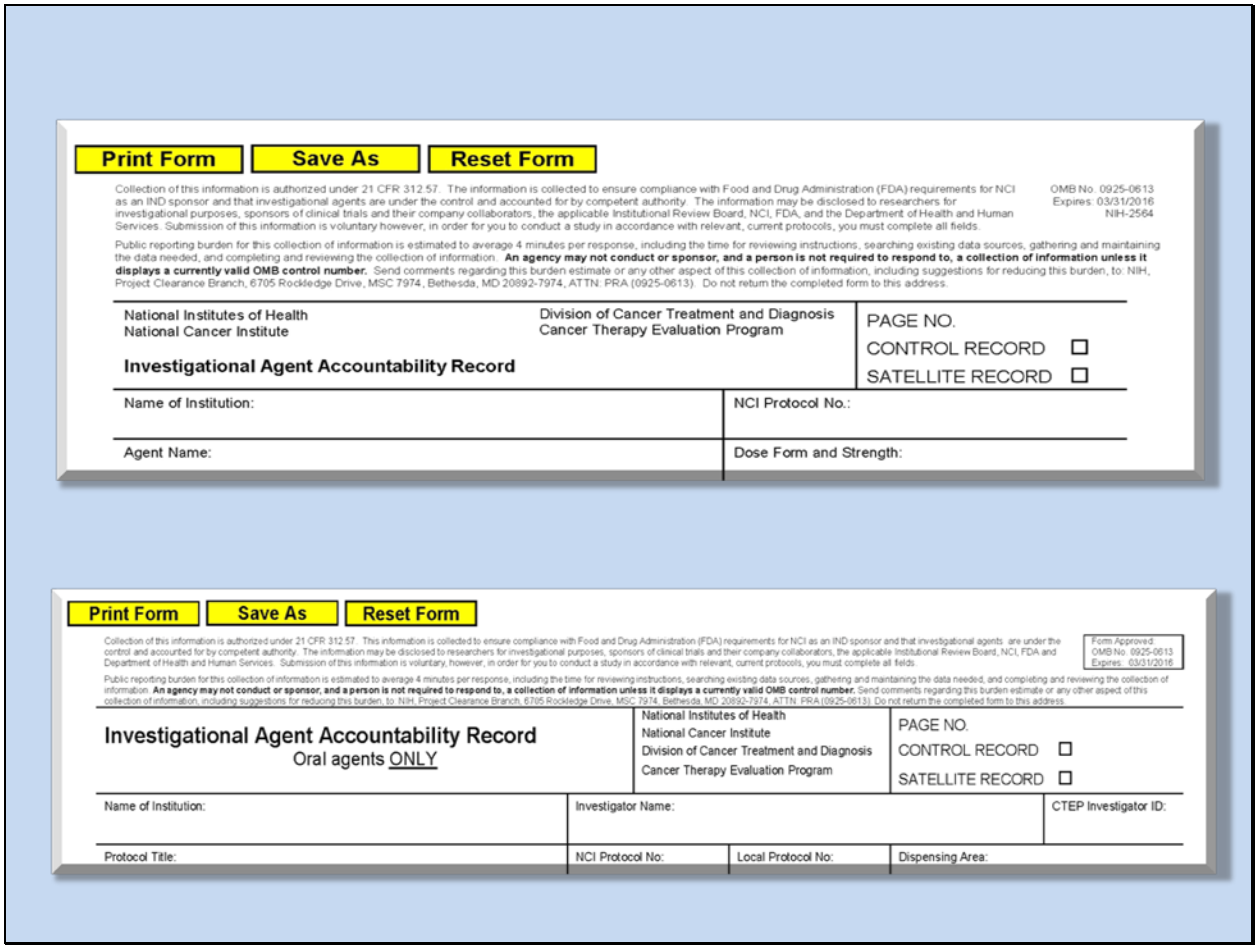
As a reminder, you can find the DARFs and other forms on the CTEP website listed here.

Slide 4



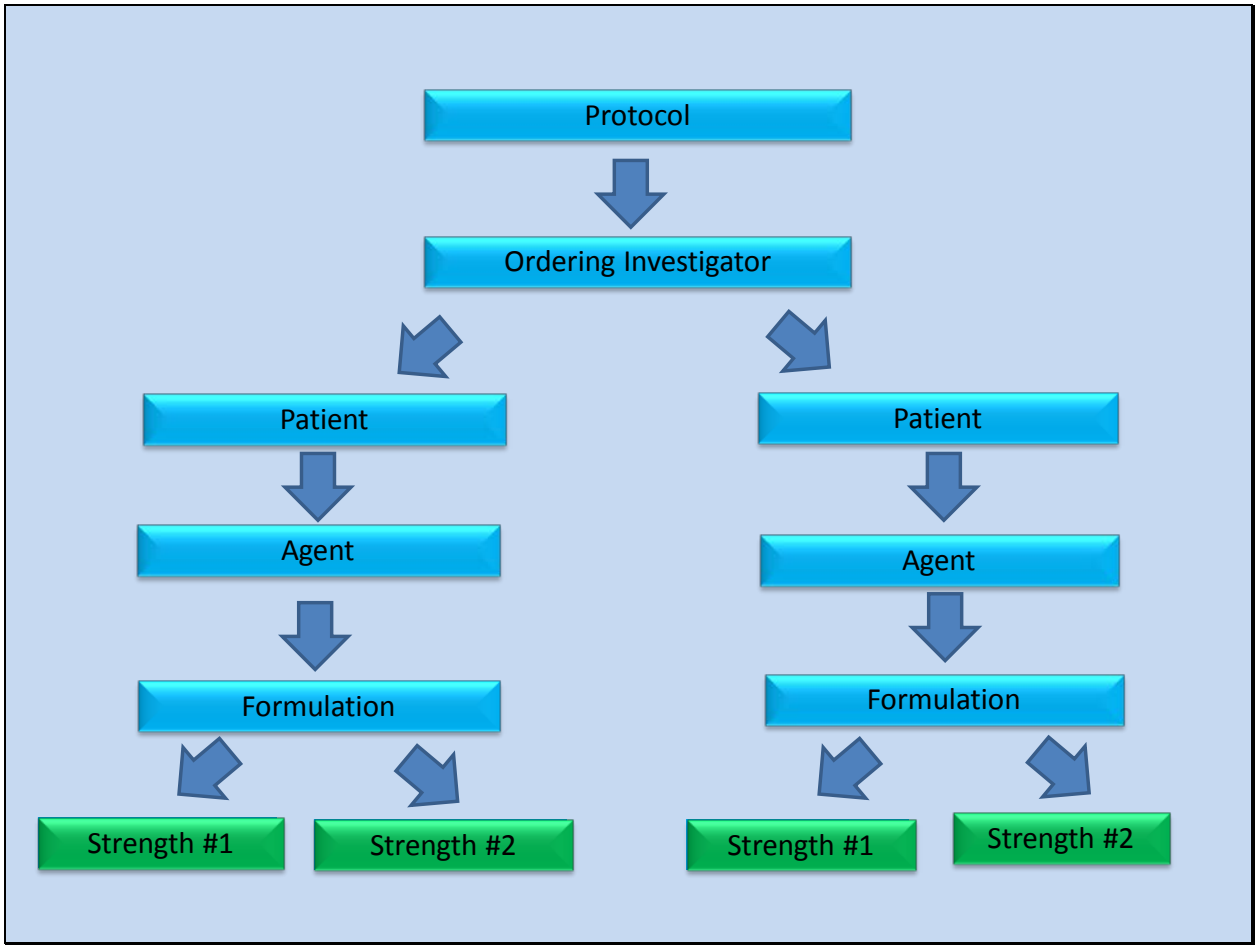
Before deciding whether a patient-specific DARF is required, you will need to determine whether the agent supplies are provided on a patient-specific basis. For agents that PMB distributes, most of these studies will be placebo-controlled blinded studies, which should be easily identifiable from the protocol title. This information is also clearly defined in the pharmaceutical section of the protocol under "Agent Ordering and Accountability."

Slide 5



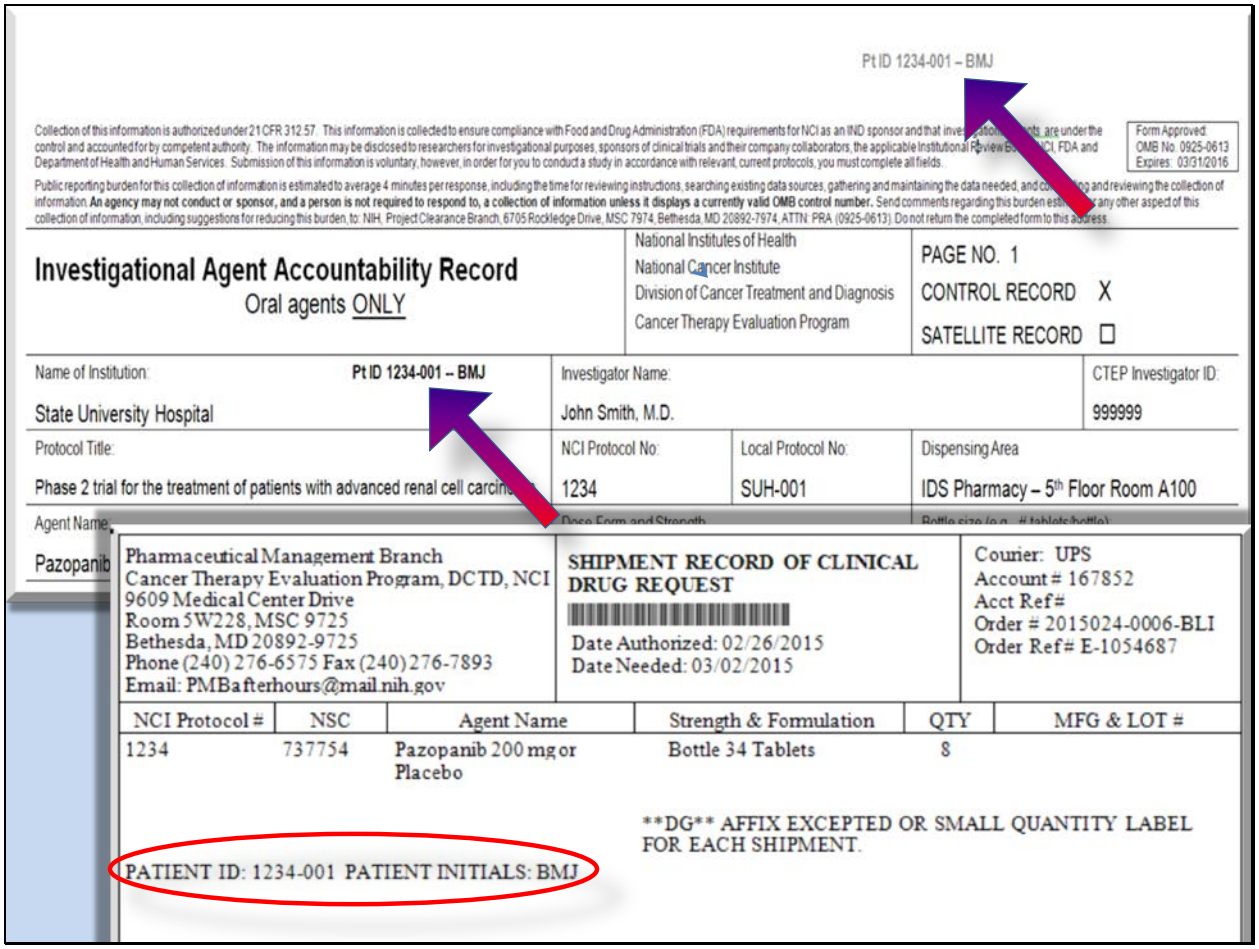
Once you have determined that the protocol provides patient-specific supplies you can create your DARFs. The agent's route of administration will determine which DARF to use.

Slide 6



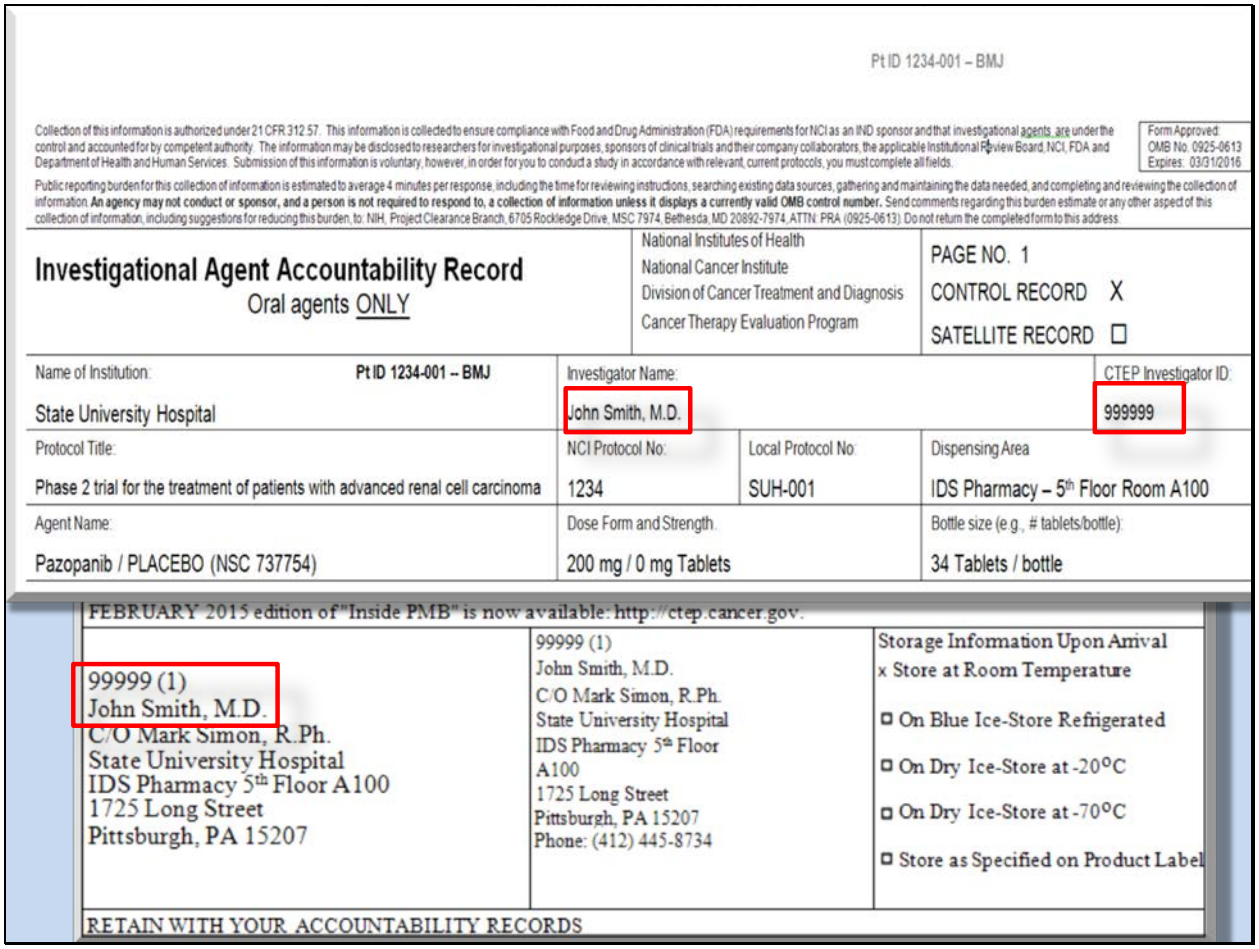
While protocol-specific DARFs allow you to record multiple patients on the same form, a patient-specific DARF is limited to a single patient. A separate DARF is required for each agent and each strength provided by PMB for the patient. In this example, you will receive 2 different strengths of the agent, which requires 2 unique DARFs for each patient. If you only receive a single strength with the initial shipment, you can start with a single DARF. If additional strengths are later required to accommodate a dose adjustment, additional DARFs can be created at that time.

Slide 7



Here is an example of a completed patient-specific Oral DARF header. Please refer to the DARF headers video for instructions on how to complete the basic elements of the header for each form. To make the DARF patient-specific, you need to insert the patient identifier into the header. The identifier should include the patient ID assigned at randomization, along with the patient initials. The exact location is not important as long as the information is clear and does not obstruct the other fields in the header.

Slide 8



Pt ID 1234-001 – BMJ

Collection of this information is authorized under 21 CFR 312.57. This 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 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.

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

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 and maintaining 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 information unless it 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 burden, to: NIH, 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.

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. 1
CONTROL RECORD X
SATELLITE RECORD ☐

Name of Institution:	Investigator Name:	CTEP Investigator ID:
State University Hospital (Pt ID 1234-001 – BMJ)	John Smith, M.D.	999999

Protocol Title:	NCI Protocol No:	Local Protocol No:	Dispensing Area
Phase 2 trial for the treatment of patients with advanced renal cell carcinoma	1234	SUH-001	IDS Pharmacy – 5th Floor Room A100

Agent Name:	Dose Form and Strength:	Bottle size (e.g., # tablets/bottle):
Pazopanib / PLACEBO (NSC 737754)	200 mg / 0 mg Tablets	34 Tablets / bottle

FEBRUARY 2015 edition of "Inside PMB" is now available: http://ctep.cancer.gov.

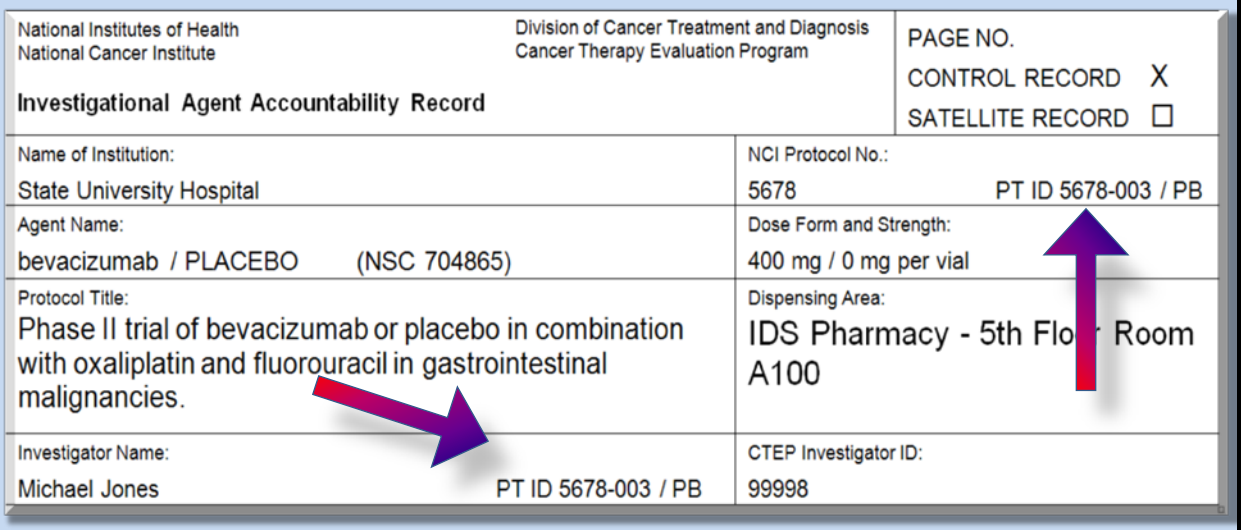
99999 (1) John Smith, M.D. C/O Mark Simon, R.Ph. State University Hospital IDS Pharmacy 5th Floor A100 1725 Long Street Pittsburgh, PA 15207	99999 (1) John Smith, M.D. C/O Mark Simon, R.Ph. State University Hospital IDS Pharmacy 5th Floor A100 1725 Long Street Pittsburgh, PA 15207 Phone: (412) 445-8734	Storage Information Upon Arrival x Store at Room Temperature ☐ On Blue Ice-Store Refrigerated ☐ On Dry Ice-Store at -20°C ☐ On Dry Ice-Store at -70°C ☐ Store as Specified on Product Label

RETAIN WITH YOUR ACCOUNTABILITY RECORDS

The investigator listed on the Shipping Receipt must be the investigator listed on the patient-specific DARF. Subsequent orders are submitted under this "responsible" investigator unless a patient transfer has been approved by the lead organization and a copy of the approval provided to PMB.

Slide 9

Original DARF patient-specific header



National Institutes of Health
National Cancer Institute

Division of Cancer Treatment and Diagnosis
Cancer Therapy Evaluation Program

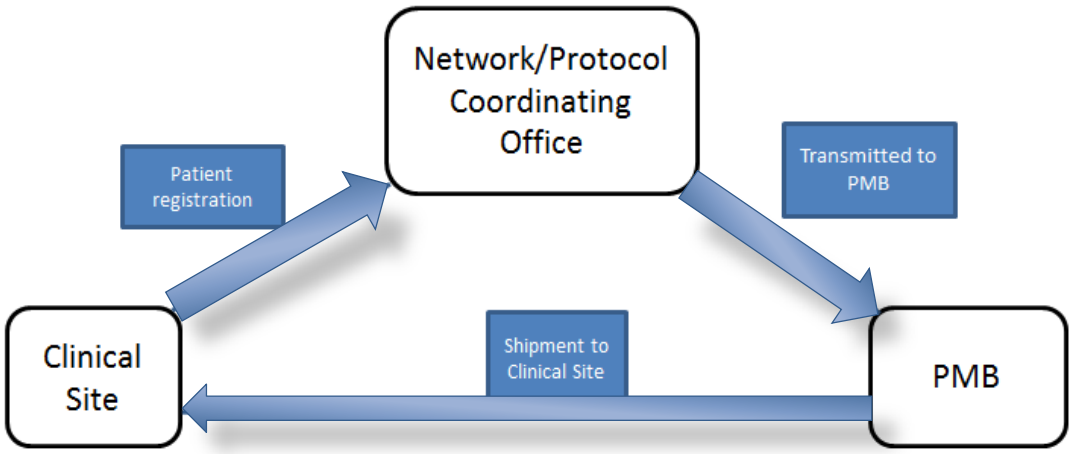
Investigational Agent Accountability Record

PAGE NO.
CONTROL RECORD X
SATELLITE RECORD ☐

Name of Institution: State University Hospital	NCI Protocol No.: 5678 PT ID 5678-003 / PB
Agent Name: bevacizumab / PLACEBO (NSC 704865)	Dose Form and Strength: 400 mg / 0 mg per vial
Protocol Title: Phase II trial of bevacizumab or placebo in combination with oxaliplatin and fluorouracil in gastrointestinal malignancies.	Dispensing Area: IDS Pharmacy - 5th Flo[illegible] Room A100
Investigator Name: Michael Jones PT ID 5678-003 / PB	CTEP Investigator ID: 99998

You can see on this example of the completed Original DARF header, that the patient ID and initials have been included in a different spot than on the Oral DARF. Again, it is not important where the information is in the header as long as it is clearly noted.

Slide 10



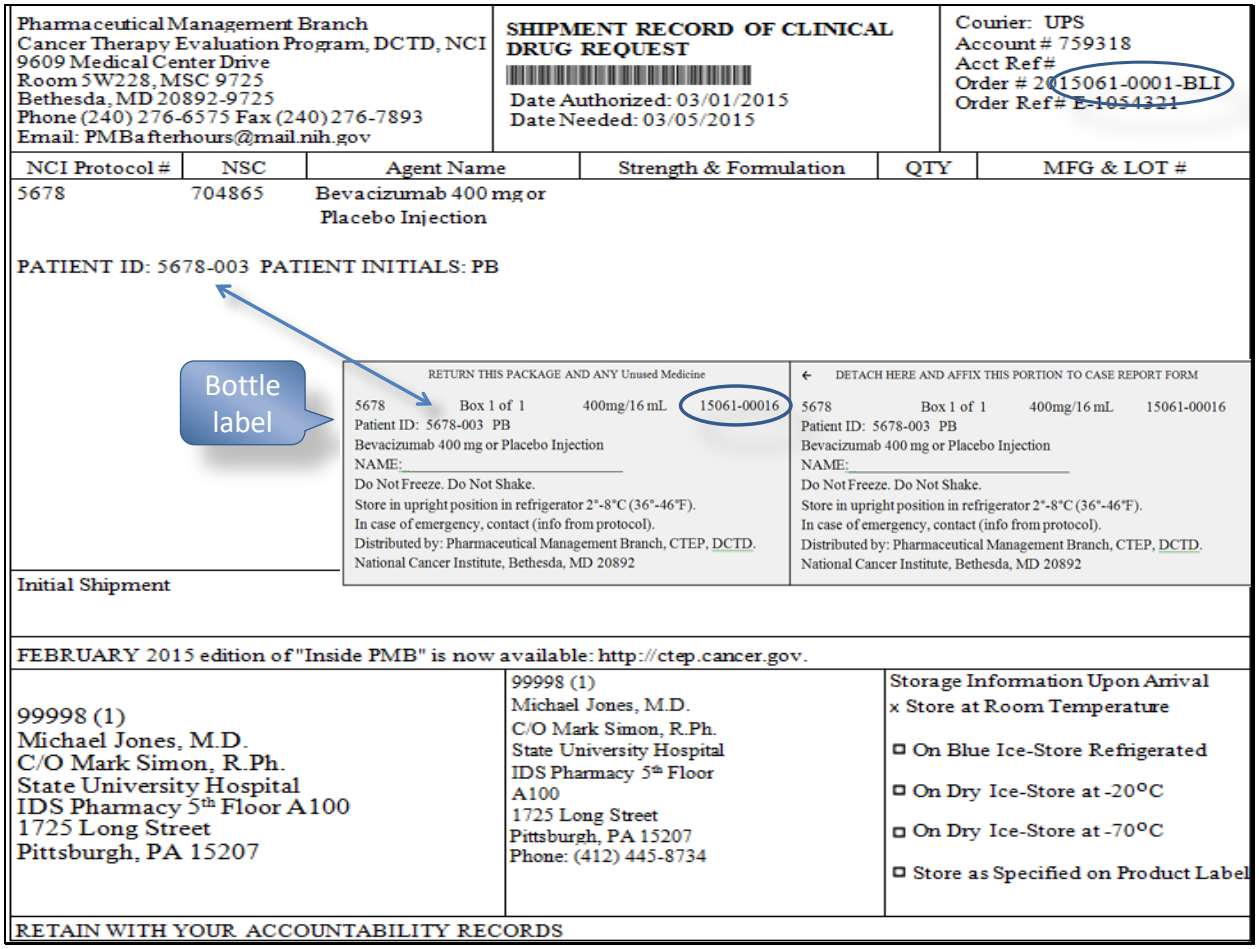
PMB Blinded Order Shipment Schedule (Express Courier)

Patient Randomized with NCTN	Initial e-Order Transmitted by NCTN	Initial e-Order Received and Approved by PMB	Initial Order Shipped By PMB	Initial Order Received at Site *
Monday	Monday	Tuesday	Wednesday	Thursday
Tuesday	Tuesday	Wednesday	Thursday	Friday
Wednesday	Wednesday	Thursday	Monday	Tuesday
Thursday	Thursday	Friday	Monday	Tuesday
Friday	Friday	Monday	Tuesday	Wednesday

* Shipments sent by **Federal Express**, arrival times are approximate.

Let's move onto documenting transactions such as receipt, dispensing and returns. For patient specific studies in which PMB distributes the agent, the first order is not entered in OAOP. When the patient is registered, the coordinating office transmits an electronic order notifying PMB that a patient was randomized and to which arm they were assigned. The PMB will prepare the shipment and send it to the site. Because patient-specific labeling is added to these supplies, the orders take a few extra days to arrive at your location. Keep in mind that next day delivery is not available for patient-specific orders. For the initial shipment, the Shipping Designee linked to the responsible investigator will receive an email notifying them of the impending shipment. This may be the first time you are notified of a new patient on the protocol. If that's the case, you should obtain and review a current copy of the protocol for details on the initial and subsequent orders for this patient.

Slide 11



Pharmaceutical Management Branch
Cancer Therapy Evaluation Program, DCTD, NCI
9609 Medical Center Drive
Room 5W228, MSC 9725
Bethesda, MD 20892-9725
Phone (240) 276-6575 Fax (240) 276-7893
Email: PMBafterhours@mail.nih.gov

SHIPMENT RECORD OF CLINICAL DRUG REQUEST

Date Authorized: 03/01/2015
Date Needed: 03/05/2015

Courier: UPS
Account # 759318
Acct Ref #
Order # 215061-0001-BLI
Order Ref # ~~E-1054321~~

NCI Protocol #	NSC	Agent Name	Strength & Formulation	QTY	MFG & LOT #
5678	704865	Bevacizumab 400 mg or Placebo Injection			

PATIENT ID: 5678-003 PATIENT INITIALS: PB

Bottle label

RETURN THIS PACKAGE AND ANY Unused Medicine
5678 Box 1 of 1 400mg/16 mL 15061-00016
Patient ID: 5678-003 PB
Bevacizumab 400 mg or Placebo Injection
NAME:
Do Not Freeze. Do Not Shake.
Store in upright position in refrigerator 2°-8°C (36°-46°F).
In case of emergency, contact (info from protocol).
Distributed by: Pharmaceutical Management Branch, CTEP, DCTD.
National Cancer Institute, Bethesda, MD 20892

← DETACH HERE AND AFFIX THIS PORTION TO CASE REPORT FORM
5678 Box 1 of 1 400mg/16 mL 15061-00016
Patient ID: 5678-003 PB
Bevacizumab 400 mg or Placebo Injection
NAME:
Do Not Freeze. Do Not Shake.
Store in upright position in refrigerator 2°-8°C (36°-46°F).
In case of emergency, contact (info from protocol).
Distributed by: Pharmaceutical Management Branch, CTEP, DCTD.
National Cancer Institute, Bethesda, MD 20892

Initial Shipment

FEBRUARY 2015 edition of "Inside PMB" is now available: http://ctep.cancer.gov.

99998 (1)
Michael Jones, M.D.
C/O Mark Simon, R.Ph.
State University Hospital
IDS Pharmacy 5th Floor A100
1725 Long Street
Pittsburgh, PA 15207

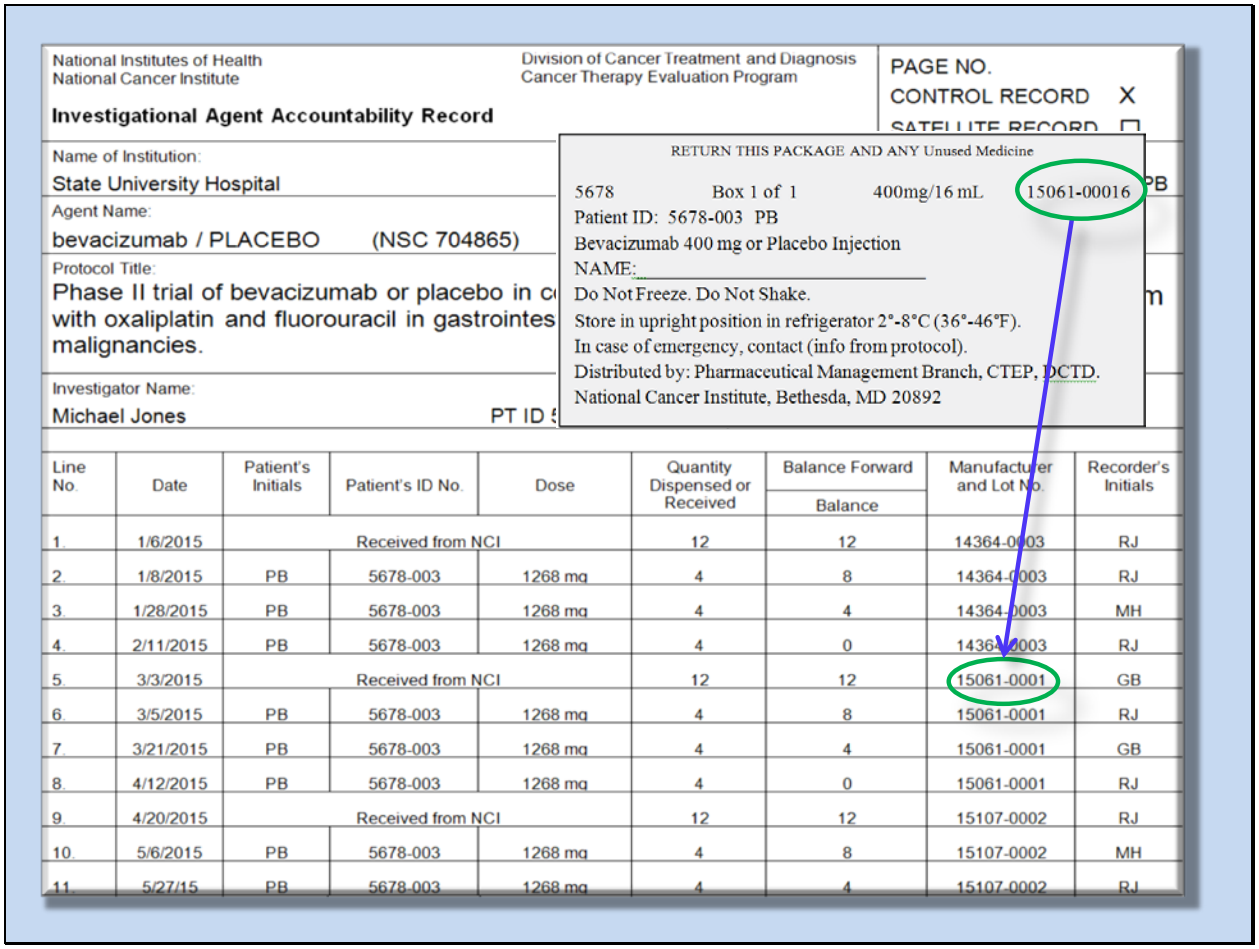
99998 (1)
Michael Jones, M.D.
C/O Mark Simon, R.Ph.
State University Hospital
IDS Pharmacy 5th Floor
A100
1725 Long Street
Pittsburgh, PA 15207
Phone: (412) 445-8734

Storage Information Upon Arrival
x Store at Room Temperature
☐ On Blue Ice-Store Refrigerated
☐ On Dry Ice-Store at -20°C
☐ On Dry Ice-Store at -70°C
☐ Store as Specified on Product Label

RETAIN WITH YOUR ACCOUNTABILITY RECORDS

When you receive the shipment, please review the Shipping Receipt carefully. You will notice that the patient-specific shipping receipt from PMB looks a little different than the open label supply receipt you may be used to. The first difference is the addition of the patient ID and patient initials below the protocol and agent name. Also notice that the receipt does not have a lot identifier listed in the lot number column. Because the lot identifier is a potential source of unblinding, it will not be printed on the shipping receipt. When you receive the patient specific supply for your patient, record the receipt on the DARF that you created earlier. Verify that the patient ID on the bottle labels matches the patient ID from the Shipping Receipt. Notice that the supplies that were received match the patient ID from the shipping receipt. However, there is no lot number on the bottles or Shipping Receipt. So, what lot identifier should you record on the DARF?

Slide 12



National Institutes of Health
National Cancer Institute

Division of Cancer Treatment and Diagnosis
Cancer Therapy Evaluation Program

PAGE NO.
CONTROL RECORD X
SATELLITE RECORD ☐

Investigational Agent Accountability Record

Name of Institution:
State University Hospital

Agent Name:
bevacizumab / PLACEBO (NSC 704865)

Protocol Title:
Phase II trial of bevacizumab or placebo in c
with oxaliplatin and fluorouracil in gastrointes
malignancies.

Investigator Name:
Michael Jones PT ID

RETURN THIS PACKAGE AND ANY Unused Medicine

5678 Box 1 of 1 400mg/16 mL 15061-00016
Patient ID: 5678-003 PB
Bevacizumab 400 mg or Placebo Injection
NAME:
Do Not Freeze. Do Not Shake.
Store in upright position in refrigerator 2°-8°C (36°-46°F).
In case of emergency, contact (info from protocol).
Distributed by: Pharmaceutical Management Branch, CTEP, DCTD.
National Cancer Institute, Bethesda, MD 20892

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.	1/6/2015	Received from NCI			12	12	14364-0003	RJ
2.	1/8/2015	PB	5678-003	1268 mg	4	8	14364-0003	RJ
3.	1/28/2015	PB	5678-003	1268 mg	4	4	14364-0003	MH
4.	2/11/2015	PB	5678-003	1268 mg	4	0	14364-0003	RJ
5.	3/3/2015	Received from NCI			12	12	15061-0001	GB
6.	3/5/2015	PB	5678-003	1268 mg	4	8	15061-0001	RJ
7.	3/21/2015	PB	5678-003	1268 mg	4	4	15061-0001	GB
8.	4/12/2015	PB	5678-003	1268 mg	4	0	15061-0001	RJ
9.	4/20/2015	Received from NCI			12	12	15107-0002	RJ
10.	5/6/2015	PB	5678-003	1268 mg	4	8	15107-0002	MH
11.	5/27/15	PB	5678-003	1268 mg	4	4	15107-0002	RJ

The Julian Date and order number in the upper right hand corner of this label are used as the lot identifier. The Julian Date is a code for the exact day of the year and the order number is the sequence order number processed on that specific day. This is a unique identifier to this patient supply. Refer to the Agent Receipt video for more information.

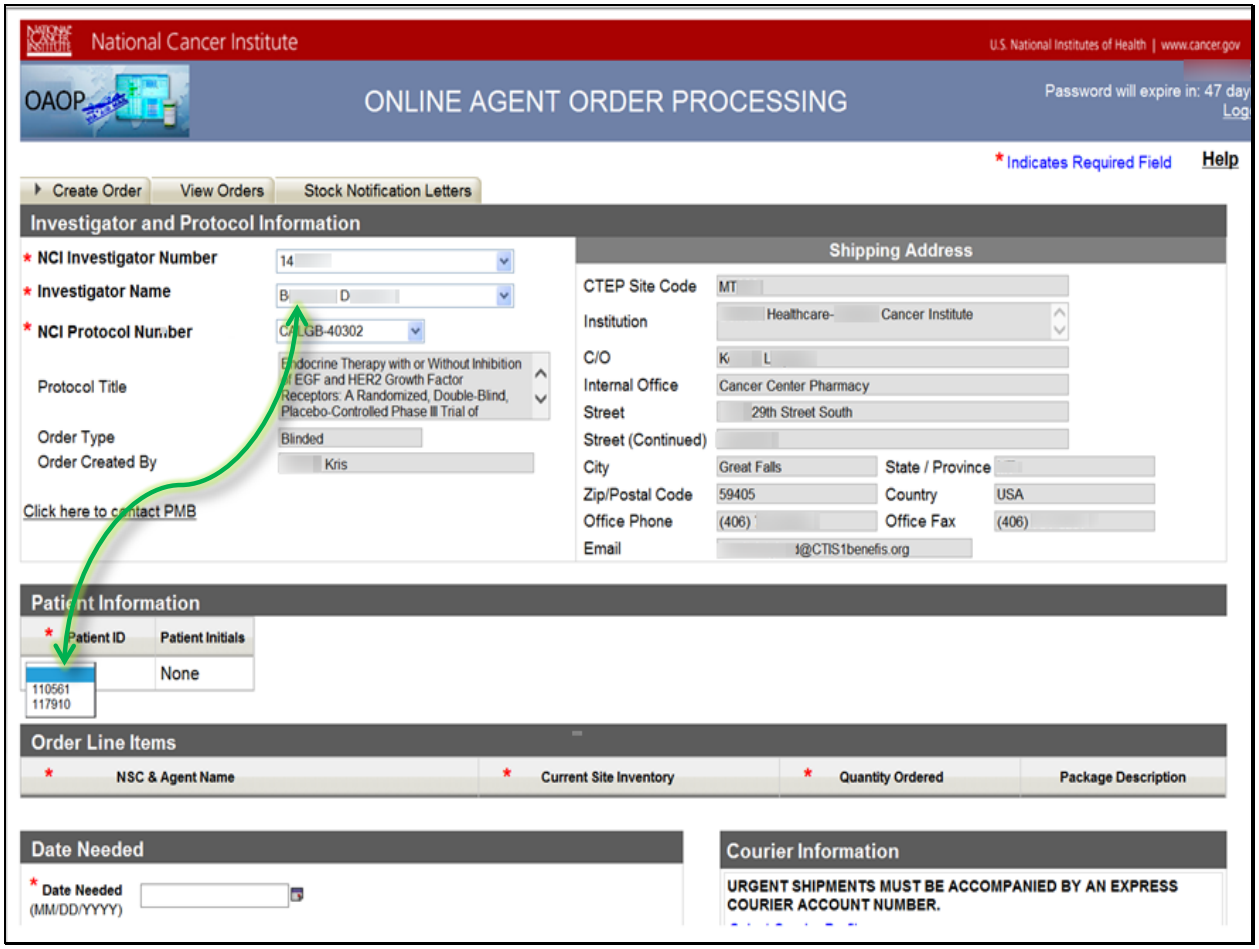
Slide 13

Once the supplies are checked in, make sure that the supplies are stored in a way that separates them from other studies and other patients on the same study. The supplies should not be removed from their original packaging (which contains the Julian Date) when stored at the site. For example, many of the vials that we distribute do not have space for a full label to be applied. In these cases, we package the supplies in a box with a full label on the outside of the box. The vials contained in the box only contain the patient ID number. Storing them in the original shipping box will ensure the supplies are connected to the appropriate Julian Date and shipment.

Slide 14

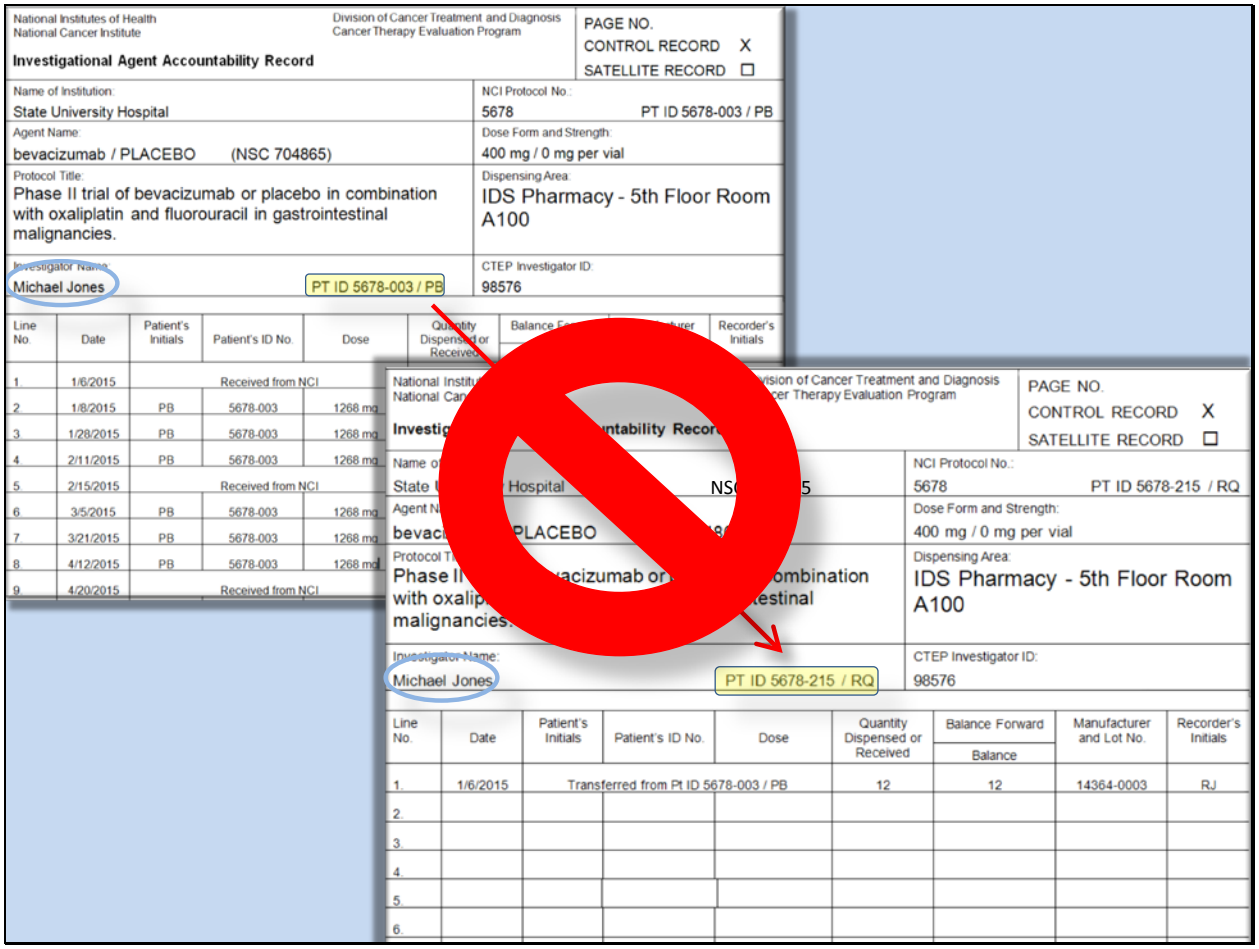
Now that you have stored your agents properly, it's time to dispense to the patient. This is the easy part. You document the dispensing the same way as on the open label record, but the DARF will only ever contain one patient ID.

Slide 15



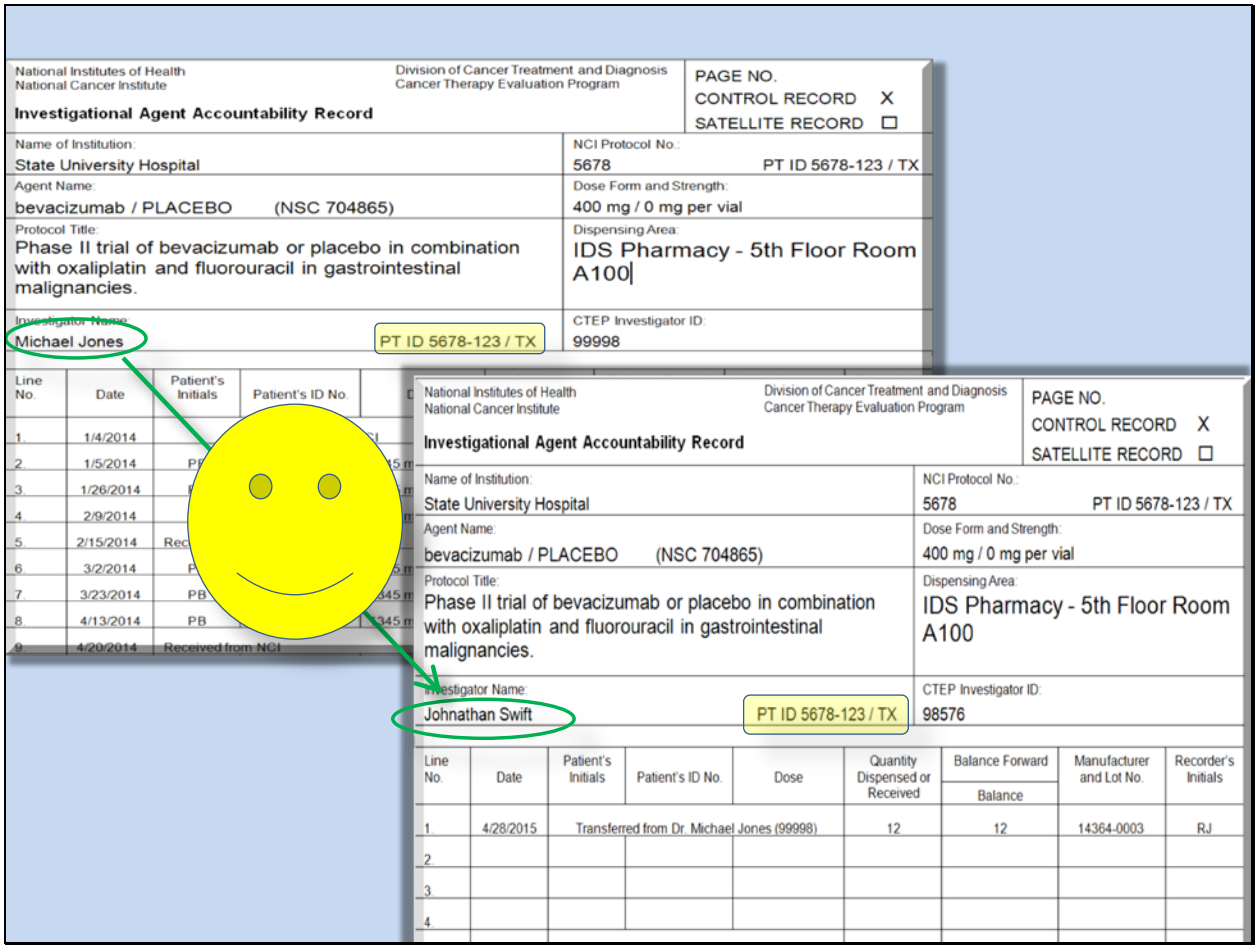
When it is time to reorder supplies, please refer to the protocol for appropriate instruction. Specific instructions on the timing of reorders are stated in the Pharmaceutical Section of the protocol. Most reorders need to be entered by the site using OAOP. Because there is a unique link between the investigator listed on the Shipping Receipt and the patient ID, you need to order under the same investigator that is noted on the initial shipping receipt. Unless the patient has been transferred to a different investigator through direct discussion with the coordinating office and PMB is notified, the patient ID will only display under this investigator in OAOP. You will not be able to see the patient ID to order supplies under a different investigator or if you are not a designee of the investigator listed on the shipping receipt.

Slide 16



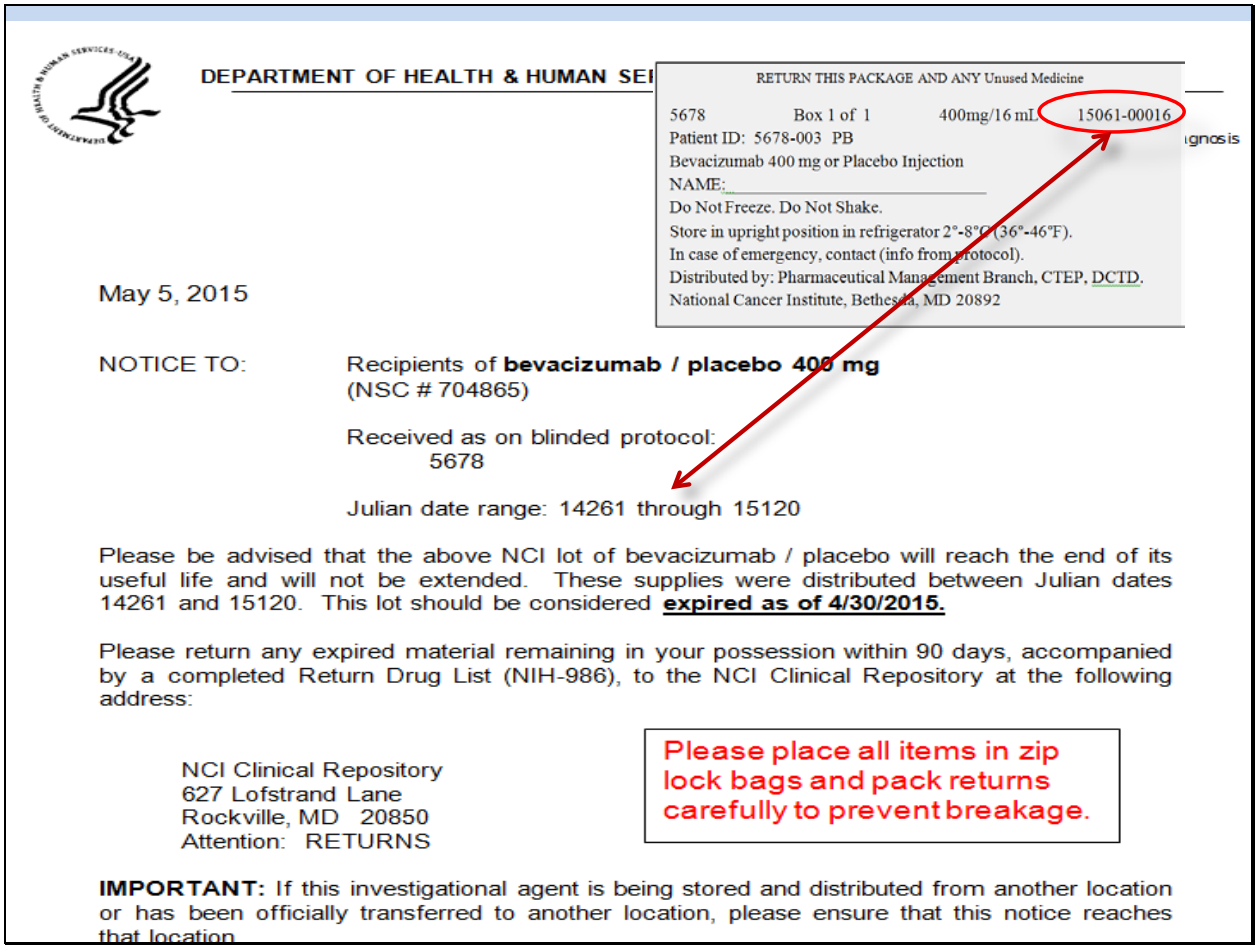
Unlike open-label supplies, patient-specific supplies cannot be transferred to other patients.

Slide 17



The only exception to transferring patient-specific supplies is if the patient changes responsible investigators. In certain situations, the agent supply may be transferred to the new investigator after the investigator transfer notification has been received and processed by PMB. If this happens, you need to submit the PMB agent transfer form found on the PMB website. Once the patient has been transferred to a new investigator, you also need to create a new DARF for that patient to reflect the updated investigator.

Slide 18



DEPARTMENT OF HEALTH & HUMAN SE

RETURN THIS PACKAGE AND ANY Unused Medicine

5678 Box 1 of 1 400mg/16 mL 15061-00016

Patient ID: 5678-003 PB

Bevacizumab 400 mg or Placebo Injection

NAME:

Do Not Freeze. Do Not Shake.

Store in upright position in refrigerator 2°-8°C (36°-46°F).

In case of emergency, contact (info from protocol).

Distributed by: Pharmaceutical Management Branch, CTEP, DCTD.

National Cancer Institute, Bethesda, MD 20892

May 5, 2015

NOTICE TO: Recipients of **bevacizumab / placebo 400 mg** (NSC # 704865)

Received as on blinded protocol: 5678

Julian date range: 14261 through 15120

Please be advised that the above NCI lot of bevacizumab / placebo will reach the end of its useful life and will not be extended. These supplies were distributed between Julian dates 14261 and 15120. This lot should be considered **expired as of 4/30/2015.**

Please return any expired material remaining in your possession within 90 days, accompanied by a completed Return Drug List (NIH-986), to the NCI Clinical Repository at the following address:

NCI Clinical Repository
627 Lofstrand Lane
Rockville, MD 20850
Attention: RETURNS

Please place all items in zip lock bags and pack returns carefully to prevent breakage.

IMPORTANT: If this investigational agent is being stored and distributed from another location or has been officially transferred to another location, please ensure that this notice reaches that location.

Alright, let's move onto stock recovery of a patient-specific supply. This is where things may get a little confusing. In the event of a stock recovery notification, refer to the Julian Date portion of the lot identifier you pulled from the patient label. This is the same number that is entered in the Lot Number field on your patient-specific DARF. Using the Julian date from our previous bevacizumab or placebo example, 15061, this stock recovery letter identifies a date range during which the supplies to be recovered were distributed. In this example, the supplies distributed between 14261 and 15120 should be returned. Since 15061 falls within that date range, the supply needs to be returned or destroyed as per the stock recovery notification. Using the Julian Date for stock recovery notifications allows us to recover both the active and placebo supplies, thus ensuring that the blinding is maintained.

Slide 19

Return of Patient-Specific Supplies

National Institutes of Health
National Cancer Institute

Division of Cancer Treatment and Diagnosis
Cancer Therapy Evaluation Program

Investigational Agent Accountability Record

PAGE NO.
CONTROL RECORD X
SATELLITE RECORD ☐

Name of Institution: State University Hospital

NCI Protocol No.: 5678 PT ID 5678-123 / TX

Agent Name: bevacizumab / PLACEBO (NSC 704865)

Dose Form and Strength: 400 mg / 0 mg per vial

Protocol Title: Phase II trial of bevacizumab or placebo in combination with oxaliplatin and fluorouracil in gastrointestinal malignancies.

Dispensing Area: IDS Pharmacy - 5th Floor Room A100

Investigator Name: Johnathan Swift PT ID 5678-123 / TX

CTEP Investigator ID: 98576

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.	1/4/2015	Received from NCI			12	12	14364-0003	RJ
2.	1/5/2015	PB	5678-003	1345 mg	4	8	14364-0003	RJ
3.	1/26/2015	PB	5678-003	1345 mg	4	4	14364-0003	MH
4.	2/9/2015	PB	5678-003	1345 mg	4	0	14364-0003	RJ
5.	2/15/2015	Received from NCI			12	12	15041-0009	GB
6.	3/2/2015	PB	5678-003	1345 mg	4	8	15041-0009	RJ
7.	3/23/2015	PB	5678-003	1345 mg	4	4	15041-0009	GB
8.	4/13/2015	PB	5678-003	1345 mg	4	0	15041-0009	RJ
9.	4/20/2015	Received from NCI			12	12	15107-0002	RJ
10.	5/4/2015	PB	5678-003	1345 mg	4	8	15107-0002	MH
11.	5/25/15	PB	5678-003	1345 mg	4	4	15107-0002	RJ
12.	6/2/2015	Pt off study – returned to NCI			4	0	15107-0002	RJ
13.								

Another reason for returning patient-specific supplies is when you become aware that the patient is no longer receiving protocol treatment. Note that this reason for return is independent of receiving any correspondence from PMB such as a stock recovery notification.

Slide 20

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 X
SATELLITE RECORD ☐

Name of Institution:	Investigator Name:		CTEP Investigator ID:
State University Hospital	Michael Jones		99998
Protocol Title:	**NCI Protocol No:**	**Local Protocol No:**	**Dispensing Area**
Phase II trial of pazopanib or placebo in combination with paclitaxel in metastatic peritoneal cancer.	1234	SUH-075	IDS Pharmacy - 5th Floor Room A100
Agent Name:	**Dose Form and Strength.**		**Bottle size (e.g., # tablets/bottle):**
Pazopanib/placebo (NSC 757754)	200 mg / placebo		34 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.	1/12/2014	Received from NCI			8 bottles	8	14008-0006	RPH				
2.	1/16/2014	B,MJ	1234-001	800 mg	4 bottles	4	14008-0006	RPH		2/14/14	8 tablets	RPH
3.	2/14/2014	B,MJ	1234-001	800 mg	4 bottles	0	14008-0006	RPH				
4.	2/22/2014	Received from NCI			8 bottles	8	14050-0002	RPH				
5.	3/16/2014	B,MJ	1234-001	800 mg	4 bottles	4	14050-0002	KHU				
6.	4/15/2014	B,MJ	1234-001	800 mg	4 bottles	0	14050-0002	RPH		5/13/14	6 tablets	FKP
	4/21/2014	Received from NCI			8 bottles	8	14108-0015	MOP				
7.	5/13/2014	B,MJ	1234-001	800 mg	4 bottles	4	14108-0015	FKP		6/15/14	8 tablets	KHU
8.	6/15/2014	B,MJ	1234-001	800 mg	4 bottles	0	14108-0015	KHU				
9.	6/24/2014	Received from NCI			8 bottles	8	14170-0075	KHU				
10.	7/14/2014	B,MJ	1234-001	800 mg	4 bottles	4	14170-0075	RPH				
11.	8/16/2014	B,MJ	1234-001	800 mg	4 bottles	0	14170-0075	RPH				

When a patient returns unused study agent as shown in this example, record the returns on the patient-specific Oral DARF, just like on the protocol-specific DARF. You can see a trend here, as most of the documentation procedures are the same as for the protocol-specific DARF once you have properly set up the patient-specific DARF. Refer to other videos in this series for more on dispensing and returns.

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	Patient-Specific Accountability	Protocol-Specific Accountability
DARF header	• Separate DARFs prepared for each patient, agent, formulation and strength	• DARFs prepared for each ordering investigator, agent, formulation and strength used on the protocol
Ordering (PMB supplied agents)	• Initial order processed automatically after patient assignment • Future orders placed in OAOP by site are specific to original "Drug Shipment" investigator	• All orders placed in OAOP by site • All registered and eligible investigators can participate
Shipping receipt	• Allow at least 2 days for processing • Patient initials on bottle matches with shipping receipt • Julian date used as lot identifier on DARF	• Expedited ordering/shipping available with express courier account number • Lot identifier on bottle matches with shipping receipt
Dispensing	• Supplies can only be used for a specific patient	• Supplies can be used for any eligible patient enrolled on that study
Agent transferring	• No agent transfers allowed, only treating investigator "transfers"	• Transfer requests are acceptable
Returns	• Stock notifications made using Julian date range • In-date supplies returned when patient comes off study	• Stock notifications made using lot identifier • In-date supplies used for multiple patients on same study

Please keep in mind that patient-specific agent accountability presents different issues than protocol-specific supplies. Refer to the table in this slide for similarities and differences between patient-specific and protocol-specific supplies. PMB staff is always available to answer questions or clarify issues unique to patient-specific accountability. Feel free to contact us by phone or email to address your questions.

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Thank you for watching this video tutorial. Additional PMB Investigational Drug Accountability videos are available through our YouTube Playlist.
Please note that the video and any items displayed within the videos are subject to change. Check back periodically for updates.
Questions can be directed to the Pharmaceutical Management Branch, CTEP, NCI by phone Monday through Friday from 8:30am to 4:30pm Eastern Time or by email any time.

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