Mastering Clinical Research
April 19, 2017
7:30 am

New Question and Answer Response System Log In Directions

Use the following link to access pre and post test questions:
http://www.socrative.com/

Click three bars in top right corner and Select Student Log In
Enter Room Name: PRESLEY4685
Enter your name:
Wait for quiz to begin
Answer questions and click submit

After the pre-test, you will need to re-enter your name for the post-test.
Mastering Clinical Research

Pre-Test Questions
SOP Updates

Tatiana Kurilo, MPH, CCRC
Quality Management and Education
Outline

• Pharmacy Orders Audit
• Obtaining Informed Consent for Greater than Minimal Risk Interventional Clinical Trials
• Study Drug Orders for IDS study drugs
• Non-IDS Study Drugs Pharmacy Orders
QM Internal Pharmacy Orders Audit Purpose:

• To perform a random QA check on the Pharmacy Orders created in 2016 calendar year for the Winship cancer-related clinical trials

• According to the CAPA implemented in March 2015, all pharmacy orders going forward must have a box with all protocol specific labs and the check box by each of the lab value

• The oncology nurse in the infusion area or CRC/CRN must review all required labs on the research orders and check in Powerchart to see if the protocol specific labs are being processed

• If not processed or pending, treatment is not given until the labs have been added and are pending
QM Pharmacy Orders Audit Scope:

• Pharmacy Orders have the section with the protocol specific labs listed with a box for the checkmark by each lab value

• The oncology nurse in the infusion area or CRC/CRN checked each box

• The oncology nurse in the infusion area or CRC/CRN initialed and dated each verified lab parameter

• If the boxes weren’t checked, were the protocol specific labs drawn and processed?

• If the deviation was noted, was it captured in Oncore?

• Pharmacy Orders compliance with the Winship CTO pregnancy test verification policy
QM Pharmacy Orders Audit Findings:

During the November 2016 – January 2017 Pharmacy Audit, eleven (11) teams were reviewed which included eighteen (18) different protocols.

Out of the 24 cases that were reviewed, the following results were found:

- Non-Compliance was noted on 10 cases where the Pharmacy Orders did not have the section with the protocol specific labs listed with a box for the checkmark by each lab.
- Non-Compliance was noted on 10 cases where the box for labs were not checked or verified.
- Non-Compliance was noted on 6 cases where the initials oncology nurse in the infusion area or CRC/CRN and date were missing.
- In the cases where labs were not verified, there were 4 cases where the protocol specific labs were not drawn.
- 10 deviations are not captured in Oncore.
- Pregnancy test verification policy non-compliancy noted in 14 cases.
QM Actions

• QM Team conducted a training session on the Winship CTO Pharmacy Orders policy for CRC/CRNS

• Cabell Pietras conducted a training on the Winship CTO Pharmacy Orders policy for Winship oncology nurses who work in the infusion area

• QM Team will perform another Pharmacy Orders Audit on randomly selected cases from each Winship Clinical Trials Working Group in May 2017
**Cycle 1 orders**

This Order Is Not Valid Unless This Section Has Been Completed:

Have dosage adjustments, as specified per study protocol guidelines, been made on any medications listed on this order?

☐ NO

Diagnosis: Multiple Myeloma

1 Cycle = 28 Days

<table>
<thead>
<tr>
<th>Cycle</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 8</th>
<th>Day 15</th>
<th>Day 16</th>
<th>Day 22</th>
</tr>
</thead>
<tbody>
<tr>
<td>#1</td>
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</tbody>
</table>

Date and Time Order Written

Age

Measured Height (cm)

Measured Weight (kg)

SBA (m²)

max of 2.2 m²

1 Labs:

On CD1 administer study drug if:

a. ANC: > 1000 (if BMEl ≥ 50% plasma cells, then ANC ≥ 1000)
b. Platelets: > 75,000 (if BMEl ≥ 50% plasma cells, then plt ≥ 50,000)
c. AST/ALT: ≤ 3X ULN
d. T. Bil: ≤ 1.5 mg/dL

Serum creatinine ≤ 2.5 mg/dL or creatinine clearance ≥ 30 mL/min

Is patient of child bearing potential? ☐ Yes ☐ No
c. Proceed to treat if judged by investigator to be in best interest of patient

t. If pregnancy test confirmed to be negative Yes ☐ No ☐

Confirmed by MDRN/CRC Initial Date

If metastatic, required on Days 1 and 15.

On CD15 administer study drug if:

a. ANC: ≥ 1000 if ≥ 50% plasma cells in BMEx
b. Platelets: ≥ 50,000 if ≥ 50% plasma cells in BMEx

*If ≤ 50% plasma cells in BMEx, may proceed to treat if judged by investigator to be in best interest of patient

c. AST/ALT: ≤ 5 X ULN
d. T. Bil: ≤ 3 X ULN

Creatinine: < 3 X ULN

2 Nursing Considerations: Perform as outlined in table below

Note: BOI = Beginning of Infusion
EOI = End of Infusion

<table>
<thead>
<tr>
<th>Cycle Day 1</th>
<th>Tasks to be Performed</th>
<th>Date/Time Performed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**All information provided and calculations have been independently confirmed by the following licensed healthcare providers**

Printed by Licensed Medical Professional Name

Date: ____________________________

Physician Name

Date: ____________________________
If No Language Imbedded- Please use

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**EMORY HEALTHCARE**
**EMORY HOSPITALS AND WINSHIP CANCER INSTITUTE**
**PHYSICIAN’S ORDERS**

**Allergies/Sensitivities**: NKA

**Protocol #**: ARRAY520215

**Investigational Protocol**: A Multicenter Phase 2 Study of Single-agent Filanesib (ARRAY-520) in Patients With Advanced Multiple Myeloma

**Primary Investigator**: Sagar Lonial, MD

**Research Coordinator**: [Red preprinted label]

**Status**: [Red preprinted label]

**Cycle 1 orders**

**Diagnosis**: Multiple Myeloma

**Day**: 1

**Cycle**: 1

**Cycle Duration**: 28 Days

**Date and Time Order Written**: 03/27/2015 9:00 AM

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**Lab Tests**

- ANC: 5 x 10^9/L
- Platelets: > 75,000
- BMBx: > 50% plasma cells
- ASTALT ≤ 5 x 10^9/L
- T Bil: ≤ 1.5 mg/dL
- Creatinine: ≤ 1.5 mg/dL

**Nursing Considerations**

- Perform as outlined in table below

---

**Cycle 1 Day 1**

**Tasks to be Performed**

- Verify study drug received and infused
- Infusion sites for IV and subcutaneous

---

**Additional Instructions**

- All information provided and calculations have been independently confirmed by the following licensed healthcare providers:
  - [Red preprinted label]

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**Approval**

- [Red preprinted label]
2.1 Obtaining Informed Consent for Greater

- The reconsent procedure is the same as the initial consent procedure
- FOR RECONSENT ONLY: If the changes to the trial do not change the risk, then reconsent can be obtained by a designated licensed professional such as, NP, PA, CRN, RN, LCSW, or a physician-investigator (delegated this task on the DOA log and, when required, listed on 1572)
- The MD-investigator or other licensed professional obtaining initial consent or reconsent shall document in the subject's research record the facts of provision of the fully signed informed consent document to the subject
6.2 Study Drug Orders for IDS Study Drugs

• A drug order set and if applicable a nursing consideration order set will be created for each protocol, per protocol requirements, and will include all safety labs and required research labs
• The working group CRC will work with the Research Order Committee to develop the order set templates and obtain approval for them prior to use
• CRCs may have input for this process but changes must be approved by the Research Order Committee
6.2 Study Drug Orders for IDS Study Drugs

- Protocol amendments that affect study drug orders or nursing consideration orders will be submitted after PI assessment and prior to IRB approval to the Research Order Committee for review and approval.

- The study PI will review and provide final approval of both study drug and nursing consideration order sets.
6.2 Study Drug Orders for IDS Study Drugs

• All preprinted orders and prescriptions for study drug and nursing consideration order sets will have two signatures:
  1. The signature of the PI or sub-investigator (delegated this task on the DOA log and when required on the Form 1572) indicates that the order or prescription has been reviewed carefully for protocol compliance with dose, route of administration, time, and duration of therapy
  2. The signature of another licensed staff member, such as, Pharm. D., MD -investigator, CRN, and APP (does not have to be delegated this task on the DOA log or listed on the Form 1572) indicates that each has reviewed the orders for accuracy and verified that the calculations (e.g. BSA and dosing) are correct
6.2 Study Drug Orders for IDS Study Drugs

• Oncology nurses in the infusion area will sign the drug order set on page one which signifies they have reviewed all pages of the order set as well as confirmed all dose calculations.

• If applicable, oncology nurses in the infusion area will sign the Nursing Considerations Order set on the last page of the document.
6.2 Study Drug Orders for IDS Study Drugs

- A copy of the ERMS registration, the signed signature page of the Informed Consent Form and the signature page verifying eligibility by the investigator will accompany the initial orders to pharmacy.
- For multi-step registration/randomization studies, the registration/randomization confirmation for the final step will accompany the orders.
6.2 Study Drug Order for IDS Study Drugs

- The PI, sub-investigator or licensed professional who is delegated this task on the DOA log and when required on Form 1572 for this study will review and evaluate laboratory values in real time, which may result in a change of dose prior to the dispensing of study drug and document review & any changes in subject’s medical or research record.
6.2 Study Drug Order for IDS Study Drugs

- On Day 1 of each cycle, prior to study drug administration, the oncology nurse in the infusion area, investigator or CRC/CRN will review safety and required research labs on the research orders and check in Powerchart to see if there are results for each safety lab and if required research labs have been obtained (when appropriate)

- The CRC/CRN, investigator or oncology nurse will initial and date the study drug orders indicating that safety lab results have been verified and required research labs have been obtained

- For all subsequent visits, the oncology nurse is responsible for ensuring that safety lab results are available and required research labs have been obtained and will check off each lab on the study drug orders

- If results are not available for the required safety labs and/or required research labs aren’t pending, study drug will not be given to the subject
6.2 Study Drug Orders for IDS Study Drugs

• Prior to administration of study drug, the oncology nurse in the infusion area or an investigator will review required safety labs to confirm results are within the specified study parameters prior to administering study drug.

• If any of the safety labs are outside of the study parameters, the oncology nurse will not administer the study drug and will notify the investigator.
6.2 Study Drug Orders for IDS Study Drugs

• For self-administered study drugs, IDS will dispense the exact amount of drug to complete the cycle (no excess).

• In the event that a subject would need more study drug to complete the cycle, IDS will ship the study drug overnight to the subject’s home at the request of the PI or CRC/CRN. This request is to be submitted in writing with the subject’s current mailing address. IDS will notify the CRC/CRN of the air bill # for tracking purposes.

• Any exceptions to this policy must be approved by the PI and one of the following: the Associate Director of Clinical Research, the Medical Director of Phase I Unit, the Director of Clinical Trials, or the Assistant Director of Clinical Research Staff.
6.2 Study Drug Orders for IDS Study Drugs

- All study drug which is self-administered will be documented on the Dosing and Compliance Log or an equivalent protocol specific form including the study drug dispensed or prescription provided, the quantity provided or prescribed, the date the subject started taking the study drug, the date the subject stopped taking the study drug, and the quantity and date of drug return.
6.2 Study Drug Orders for IDS Study Drugs

- Licensed healthcare professionals are the only ones who can provide the subject education regarding the study drug.
- Any drug given to a subject will be administered by a licensed healthcare professional and documented in the subject’s medical record.
- Any drug dispensed by IDS may be transported and delivered to the subject by an unlicensed healthcare professional. The study team member delivering study drug to the subject will check the subject's identity, protocol name, study number, the name or number of the drug, dose, route, and frequency prior to delivering the drug.
6.3 Non-IDS Study Drug Pharmacy Orders

All preprinted orders and prescriptions for study drug that is being dispensed to a clinical trials subject through any Emory Pharmacy will have **TWO signatures** (written or electronic):

1. Investigator or sub-investigator (delegated this task on the DOA log) ordering the study drug will sign and print name and date signed

2. Another licensed staff member, such as, Pharm. D., physician-investigator, CRN, and APP (does not have to be on the DOA log), will sign and print name and date signed, indicating that each has reviewed the orders for accuracy and verified that the calculations (e.g. BSA and dosing) are correct
Important Reminders

• All SOPs are available:
  – In the CTO
  – At each Winship site
  – On the Winship intranet under Clinical Trials
    https://apps.winship.emory.edu/intranet/clinicaltrials/index.php

• The Monthly Protocol Card is now available on
  the Winship Cancer Institute Website
Questions?
Dosing and Compliance Log

Michal Hananel
Clinical Trials Monitors for DSMC, Manager
Dosing and Compliance Form

Protocol #: ____________________  Subject #: ____________________

STUDY DRUG DELIVERY COMPLETED FOR CYCLE

Drug Delivered: ____________________  Date Delivered: ______/____/____

Quantity Per Bottle: ______  Number of Bottles: ______
(per label on bottle)  (i.e. 30)

Total Quantity Delivered: ______
(i.e. 180)

Total Daily Dose: ______  Dose Form: ______
(i.e. 200mg, 1 vial, etc.)

Dosing Regimen: ______  Cycle Start Date: ______/____/____ am/pm
(i.e. take 2 pills twice a day by mouth)

Delivered by: ____________________

STUDY DRUG AND DIARY RETURN

Date Study: ______/____/____  Dosing Start Date: ______/____/____ am/pm

Drug Returned: ______  Dosing End Date: ______/____/____ am/pm

Number of Bottles (or blister packs, syringes, etc.) Returned: ______

A) Total # of Pills that should be taken
   [ ]    [ ]    [ ]

B) Total # of Pills Remaining
   [ ]    [ ]    [ ]

C) Total # of Pills Actually Taken
   [ ]    [ ]    [ ]

OR:

D) Total Vials/Syringes that should be used
   [ ]    [ ]    [ ]

E) Total Vials/Syringes Remaining
   [ ]    [ ]    [ ]

F) Total Vials/Syringes Actually used
   [ ]    [ ]    [ ]

Was study drug diary returned?  Yes [ ]  No [ ]  N/A [ ]

If dosing non-compliance is noted, was subject counseled on correct dosing procedure by a delegated, licensed professional?  Yes [ ]  No [ ]  N/A [ ]

If a compliance count is required, please indicate dosing percentage (pills x 100 - [a/b] x 100):

Comments (i.e. missed doses, dose adjustments, diary non-compliance, etc.):

____________________________________________________

CRC/CRN Signature: ____________________  Date: ______/____/____

Version 3.22.2014
# Dosing and Compliance Log

## Subject Dosing and Compliance Log

<table>
<thead>
<tr>
<th>Cycle #</th>
<th>Dose Modification Required? If so, enter new Total Daily Dose and Dosing Regimen</th>
<th># of Bottles/ Vials/ syringes Dispensed</th>
<th>Total Pill Quantity Delivered</th>
<th>Date &amp; Time Dispensed to Subject</th>
<th>Staff Initials Delivering IP</th>
<th>Dosing Start Date</th>
<th>Dosing End Date</th>
<th>Date Study Drug Returned</th>
<th>Total # of Pills/Vials Returned</th>
<th>Total # of Pills/Vials Returned That should have been taken</th>
<th>Total # of Pills/Vials Taken</th>
<th>Drug Diary Returned and Reviewed?</th>
<th>Reasons for IP Discrepancies</th>
<th>Staff Initials Performing IP Accountability/IP delivered by</th>
</tr>
</thead>
<tbody>
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</tr>
</tbody>
</table>
# Dosing and Compliance Log Example

## Subject Dosing and Compliance Log

<table>
<thead>
<tr>
<th>Cycle #</th>
<th>Dose Modification Required?</th>
<th>Protocol #: Winship1234-17</th>
<th>PI: Dr. Winship</th>
<th>Subject #: 001</th>
<th>Subject Initials: A-B</th>
<th>Initial Total Daily Dose: 200mg</th>
<th>Initial Dosing Regimen: PO DrugX 100mg BID</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cycle 1</td>
<td>No</td>
<td>1/2/17</td>
<td>Date &amp; Time Dispensed to Subject</td>
<td>C-D</td>
<td>1/2/17</td>
<td>1/29/17</td>
<td>1/30/17</td>
</tr>
<tr>
<td>Cycle 2</td>
<td>Yes 100mg QD</td>
<td>1/30/17</td>
<td>Date Study Drug Returned</td>
<td>E-F</td>
<td>1/30/17</td>
<td>2/26/17</td>
<td>2/27/17</td>
</tr>
</tbody>
</table>

Version 04/13/2017
Questions?
Standard Operating Procedures
8.1

Kim Nguyen, BS
Assistant Director, Regulatory Affairs
Purpose: To provide guidance to research personnel in managing study changes.

Scope: All investigators and staff involved in management of subject who participate in Winship cancer-related clinical research trials.
Procedure:

1. Regulatory specialists will monitor sponsor's communication for updates which include, but are not limited to Amendments, Investigator Brochure changes, Investigator Alerts, accrual status changes, and other announcements.

2. Study changes will be discussed at the Working Group meeting.

3. Regulatory specialists will submit study changes for IRB review and manage the IRB review process. IRB approval is expected to be obtained within 90 days of memorandum date announcing the Protocol Amendment, unless specified otherwise by the sponsor or contract.

4. The regulatory specialist will:
   
   A. Create an amendment workspace in eIRB and OnCore within 30 business days of the receipt of study change.

   B. Complete the Protocol Amendment Assessment Form for review and PI signature (see attached).

   C. Complete the Amendment request including all changes, e.g. consent, protocol, study status, for PI submission to the IRB within 10 business days of the amendment workspace being created. Regulatory specialist will follow-up with the PI if necessary.
D. Notify the IRB protocol analyst of the urgency of the amendment, if applicable.

E. The regulatory specialist will respond within 5 business days to requests from the IRB, conferring with the PI and/or sponsor for responses to requested information.

F. Review and update study personnel in elRB if applicable

5. If IRB approval not obtained within 60 days after receipt of the Amendment, the Assistant Director of Regulatory Affairs will be notified for further action.

6. Once IRB approval is obtained, the regulatory specialist will manage the implementation process. The regulatory specialist will:

   A. Review the IRB approval letter and approved documents for accuracy. Inaccuracies will be referred to the IRB for prompt correction via a logged comment and/or email to the IRB protocol analyst.

   B. Upload the IRB approval letter and approved documents to OnCore and promptly release.

   C. Notify the research team via e-mail that the amendment was approved and the approved documents are uploaded to OnCore. If this is an amended protocol, the regulatory specialist will initiate training via OnCore notification email
D. Notify the team if subjects need to be re-consented.
E. Update the regulatory team spreadsheet and provide an update during the Working Group meeting. Re-consenting and training requirements will be discussed.
F. Print and file the approved documents in regulatory binder, if applicable.
G. Send a copy of the IRB approval letter, approved consent, revocation letter and HIPAA authorization to sponsor, if applicable.
H. Verify and update study status and accrual in OnCore, if applicable.

7. When a new amendment is received prior to approval of an amendment already in review by the IRB, the regulatory specialist will log a comment in eIRB informing the IRB analyst of the new amendment. When multiple amendments are received at the same time, the regulatory specialist will bundle the amendment submission. The regulatory specialist will inform the IRB analyst that the eIRB amendment submission contains more than one amendment.

8. Regulatory specialists will review the completed Protocol Amendment Assessment Form and submit study changes for additional review as indicated and manage the review process.
   A. If changes are made that could affect the study budget, the protocol amendment will be sent to ocr@emory.edu for review.
B. If changes could affect the contract, all appropriate documents will be sent to the Research Administration Services (RAS) group for review.

C. If changes are made that could affect the drug or nursing consideration orders, the protocol amendment will be sent to the Research Order Committee for review.

6. Sponsor-Investigator Studies
   A. Changes, such as an amended protocol, the addition of a new investigator or a new protocol along with documents that are applicable will be sent to the FDA by regulatory specialists as required by regulations.
   B. Amendments involving an IND transfer or addition of a new investigator require completion of the appropriate S-I Responsibility Form by the Emory sponsor.

7. Multi-Site Studies
   A. Once IRB approval is obtained, the IRB approval letter, the approved amended protocol, and any other approved documents that are applicable will be sent to the sub-site.

Attachments: Protocol Amendment Assessment Form
PROTOCOL AMENDMENT ASSESSMENT FORM

Date Amendment Received: __________

Protocol #: ______________________

Protocol Title: ______________________

PI Name: ______________________

IRB #: ______________________

Protocol Amendment Number/Version Date: __________

As the Principal Investigator for this study, I have reviewed the changes to this amended protocol. The following items need to be addressed:

☐ No additional review required

☐ BUDGET review
Comment: ______________________

☐ PHARMACY ORDER changes
Comment: ______________________

☐ NURSING CONSIDERATIONS ORDER changes
Comment: ______________________

☐ CONTRACT review
Comment: ______________________

☐ INFORMED CONSENT changes
Comment: ______________________

☐ IND/IDE review (Emory S-I)
Comment: ______________________

☐ OTHER
Comment: ______________________

Principal Investigator Signature ______________________ Date __________

☐ Required Changes submitted
☐ No changes

Regulatory Specialist Signature ______________________ Date __________
Nguyen, Kim

From: Nguyen, Kim
Sent: Tuesday, April 18, 2017 10:57 AM
To: Nguyen, Kim
Subject: PROTOCOL AMENDMENT ASSESSMENT

Date Amendment Received: 
Protocol #: 
Protocol Title: 
PI Name: 
IRB #: 
Protocol Amendment Number/Version Date: 

As the Principal Investigator for this study, I have reviewed the changes to this amended protocol. The following items need to be addressed:

☐ NO ADDITIONAL REVIEW REQUIRED
☐ BUDGET review
Comment: 
☐ PHARMACY ORDER changes
Comment: 
☐ NURSING CONSIDERATIONS ORDER changes
Comment: 
☐ CONTRACT review
Comment: 
☐ INFORMED CONSENT changes
Comment: 
☐ IND/IDE review (Emory S-I)
Comment: 
☐ OTHER
Comment: 

Principal Investigator
Please confirm that you have reviewed and acknowledged the information listed above by checking this box: ☐

---------------------------------------------------------------

☐ Required Changes Submitted ☐ No changes

Regulatory Specialist
Please confirm that you have reviewed and acknowledged the information listed above by checking this box: ☐

Kim Nguyen
Winship CTO SOPs and Forms can be found on Winship Intranet:

https://apps.winship.emory.edu/intranet/clinicaltrials
Questions?