

SECTION 18. DRUG DISTRIBUTION

18.1 Introduction

This Chapter of the manual describes the current system of drug distribution by patient ID and box number, and includes information on use of pill boxes.

18.2 Detailed Instructions For The New AASK Blinded Drug Distribution System

18.2.1 Dispensing Randomized Medication For An AASK Participant

Allocation takes place at three different areas within the system: the randomization form (Form 52), the visit form (Form 11), or from within the Drug Inventory menu Ad Hoc Drug Reservation option. The “Ad Hoc” option is for special cases when the patient does not have enough drug reserved for some unusual reason.

18.2.2 Allocation of Blinded Medication at the Randomization Visit

Allocation of randomized medication at randomization time occurs when the Form 52 is rekey verified. The allocation takes place behind the scenes and a “Blinded Drug Allocation” report is generated and e-mailed to the appropriate clinical center. This report can then be used to select a bottle pair of randomized medication to dispense to the patient at the FV0-0 visit.

When randomized medication is dispensed to the patient, the confirmation code of the bottles dispensed should be written on the blank lines provided on the report and the report should be attached to the Form 11. These confirmation codes will be necessary when the Form 11 is being entered at FV0-0. Thus, the Blinded Drug Allocation Report can be considered more of a “worksheet” than simply a report. If the Blinded Drug Allocation Report is lost, it may be re-generated from within the “Drug Inventory” menu.

18.2.3 Allocation/Dispensing of Blinded Medication During Follow-Up

Form 11 has been modified to handle maintaining the randomized drug inventory. Before attempting to enter a Form 11 into the computer at a visit where randomized drug was dispensed, it is imperative that the confirmation code of the bottles dispensed be available to data entry personnel. These confirmation codes should have been written onto the Blinded Drug Allocation Report and attached to the Form 11 (as explained above). If these confirmation codes are available, then proceed with entering and re-key verifying Form 11 as usual. If these confirmation codes are not available, they must be acquired or re-acquired before proceeding with Form 11.

When the <COMMIT> key is pressed upon successful re-key verification of Form 11, a new screen will appear entitled “Blinded Medication Dispense Form.” This is the screen where the confirmation codes are necessary. To complete this form, use the Blinded Drug Allocation Report and enter the confirmation codes for the appropriate dispensed medication. Confirmation codes are the only information that may be input into this

screen.

The system will check the confirmation code entered with the actual confirmation code for that bottle of randomized medication. If the code entered on the screen doesn't match the actual code, an error message will be displayed and the medication in error will not be considered dispensed. Typically, any errors like this will be because the cursor was accidentally on the wrong row or a typographical error occurred during key entry. If this is the case, clear the field in error and proceed to the correct row and enter the confirmation code.

If something goes wrong that can't be resolved at the Blinded Medication Dispense Form, press the <EXIT> key to leave the Blinded Medication Dispense Form and go back to the Visit form. Please note, however, that when this is done, the re-key verification of the Form 11 will be un-done, i.e., the Form 11 will not be considered re-key verified. At this point, please contact the appropriate sources to resolve the randomized medication error before attempting to re-key verify the Form 11 again. When the correct confirmation codes have been entered for the appropriate dose and number of bottle pairs, press <COMMIT>.

After successfully committing the data on the Blinded Medication Dispense Form to dispense the randomized medication, the next activity is allocating or reserving randomized medication for the patient's next protocol visit. This process is automatically performed when the <EXIT> key is pressed.

It should be noted that once the Form 11 and drug dispensing information have been successfully committed, subsequent attempts to change questions 6a and 6b may be blocked. For example, an attempt to change question 6a indicating that blinded drug was not dispensed after the form was entered and verified as indicating that drug was dispensed will not be allowed. Instead, a CC initiated change request will be necessary to make this change. A change to question 6a indicating that drug was dispensed after previously indicating that none was dispensed will cause the "Blinded Medication Dispense Form" to come up when the dose field is input.

18.2.4 Optional Features on the Blind Drug Inventory Menu

The Ad Hoc Drug Reserve screen is actually a pop-up box that will appear when the "Ad Hoc Drug Reserve" option from the Blind Drug Inventory menu is selected. The pop-up box will need three items of information.

Before describing the fields on the pop-up box, the concept of "early" versus "late" visits must be defined. Visits from FV2-0 and prior occur every month and are considered "early" visits for the purpose of drug reservation. Visits after FV2-0 are considered "late" visits for the purpose of drug reservation. The following paragraphs describe the information required by the Ad Hoc Drug Reservation pop-up box.

First, the PID of the patient for whom drug should be reserved or allocated should be entered. This is self-explanatory.

The next field to enter is preceded by the prompt “Allocate an Extra Pair?”. If you think an extra bottle pair will be required for the patient’s next visit, enter a “Y” (without the quotes) for this field.

The last field is preceded by the prompt “Early Visit” and is needed to inform the drug reservation program whether or not this is an “early” visit. For example, if the next time the patient is to come in and be dispensed blinded medication is to be FV3-0 or greater, then you should answer “N” to this question (i.e., not an early visit). Similarly, if the next time the patient is to come in and be dispensed blinded medication is to be FV2-0 or less, then answer “Y” to this question (i.e., it is an early visit).

After the “Early Visit” prompt has been answered, press <ENTER>. This will trigger the drug reservation program. The program will run behind the scenes, so after pressing <ENTER> you can immediately go on to other things. After a few minutes however, you will probably want to run another Blinded Drug Allocation Report to see the results of the Ad Hoc Drug Reservation process.

18.2.5 View Box Contents

Another feature of the new drug distribution system is the “View Box Contents” screen. This is a screen designed to allow you to see at a glance the contents of the boxes of blinded drug at your center. The screen is accessed via the “View Box Contents” option of the Blind Dug Inventory menu.

The <ENTER QUERY> and <EXECUTE QUERY> keys must be used on this screen. For example, to view the contents of a particular box, press <ENTER QUERY> upon entry to the screen. Then, enter your center number and the CC Box number and press <EXECUTE QUERY>. The box and its contents should appear on the screen. If you want to see all boxes at your center, just press the <EXECUTE QUERY> key when the screen comes up. Pressing the <DOWN> key will allow you to scroll through all of the boxes at your center one at a time.

18.3 Drug Distribution by Treatment ID and Box

Towards the end of February, all clinical centers will receive boxes containing blinded study drug for all currently randomized patients, as well as for additional patients projected to be randomized in the next few months. Each patient will use one box, which will be labelled with the patient's randomized treatment ID.

Each box will contain 6 rows each containing 6 bottles, for a total of 36 bottles of drugs. The order of the rows is as follows:

- Row 1. Low dose capsules
- Row 2. Low dose tablets

- Row 3. Medium dose capsules
- Row 4. Medium dose tablets
- Row 5. High dose capsules
- Row 6. High dose tablets

Each bottle should contain exactly 80 pills. New bottles should always be dispensed as pairs, with a new bottle of capsules dispensed along with a new bottle of the same dose of tablets, and a new bottle of tablets dispensed in conjunction with any new bottle of the same dose of capsules.

After any new bottles are dispensed, it is essential that this be indicated on Form 11. Form 11 has been revised to include a new item for the number of bottle pairs dispensed (you will indicate either 0, 1, or 2). The DCC uses the data from Form 11 to keep an inventory of remaining blinded drug at the Clinical Centers and to determine when patients require resupply of blinded drugs. Therefore, it is absolutely essential that all new bottles dispensed be correctly indicated on this form.

It is recommended that bottles be dispensed from left to right in the boxes. In this way, the number of remaining bottles can be determined at a glance. The DCC will maintain an inventory of the number of remaining bottles based on Form 11. However, as a precaution Clinical Centers should notify the DCC whenever no bottles remain in the box for one of the doses.

18.4 Use of Pill Boxes

18.4.1 Dispensing in Pill Boxes

At the annual meeting in January, the use of pill dispensers was discussed and encouraged for patients who have difficulty complying with their medications. Because the patient will be seen much more frequently for new medication supplies (weekly in the case of the 7 day dispensers), the instruction below will help clarify how Form 5 can be completed.

It is important to define what we mean by the term “dispense”. Up until now, it was clear that when medications are dispensed, it referred to a new or fresh bottle being pulled from the shelf or pharmacy. With the use of pill dispensers and more specifically, pill dispensers being filled by clinical center staff at the center (not filled by the patient at home), a different meaning of “dispense” emerges. Pills are being dispensed into another container from the original bottle of pills under these circumstances. When we refer to pills being dispensed on the Form 5 and the Form 11, we are referring to a full bottle of pills being dispensed. Thus, when completing Form 5 under the plan where the clinical center holds on to the medication for the patient and fills a pill dispenser as needed, please be careful that the column labelled “# of new pills dispensed” is > 0 only when a “new” or “fresh” bottle of medication is dispensed.

The Form 5 can be completed 2 different ways depending on how often you do the pill counts. Recall, that according to the protocol, “pill counts” are required at each “protocol” visit only. If you chose to count once per visit window, refer to Option #2. If

you chose to conduct a pill count every time the patient returns to have the pill dispenser refilled, refer to Option #1.

18.4.2 Option #1 for dispensing

When a fresh bottle of medications is opened, Form 11 will indicate that new drugs are dispensed and Form 5 will indicate that the content of the entire bottle was dispensed (even though the patient left the clinic with a fewer pills). At the next visit do a pill count with whatever the clinic has left in the bottle and whatever the patient brings back. Form 11 and Form 5 for this visit will indicate that no new drugs are dispensed (Even though at this visit the patient receives a fresh supply from the bottle). On Form 11 indicate drugs are dispensed ONLY when a fresh bottle is opened.

Example

- 1) At FV1-0, New bottle (containing 80 pills) was opened and 7 pills were given to the patient (dose = 1). Form 11 Q6A will be 1 (pills were dispensed) and col. k in Form 5 for FV1-0 will be 80.
- 2) At the next visit after 7 days (FV1-1) The patient comes back with 74 pills and lost 1 pill. Form 11 is completed to indicate F11Q6A = 0 (No drugs dispensed) and on Form 5 col. c will be 80. Fill out col. d = 1 and put 74 (73 pills still in the bottle and 1 pill the patient lost) in col. f and 1 in col. g. Col. h will be calculated as 5 and the compliance will be calculated as 71%. Put a 0 in col. k (Even though 7 more pills are placed in the patients dispenser).
- 3) Repeat step 2 until a new bottle has to be dispensed. When a fresh bottle is opened start with step 1.

18.4.3 Option #2 for dispensing

Rather than filling out a Form 5 every time meds are placed in the patients pill dispenser, the Form 5 can be completed a) when the “fresh” bottle is dispensed AND b) at the next “protocol” visit when a “pill count” is done. During the weekly interim visits, the Form 5 does not have to be completed since for the medications being placed in the dispensers there have not been new/fresh bottles of medications dispensed.

- 1) At visits where new medications are being dispensed:
 - a. Complete Form 11 and indicate new medications were dispensed.
 - b. Complete Form 5 indicating medications dispensed (i.e. 80).
- 2) Complete Form 5 at next protocol visit after conducting the pill count.

Form 5's for interim visits are not required.

18.5 Procedure for Emergency Unblinding of the Randomized Medication

Part 1 How to request emergency unblinding.

For an emergency unblinding between the hours of 7:00 a.m. and 5:00 p.m. (Eastern Time), the AASK PI or designated back-up may telephone: Jennifer Gassman (216) 444-9938, Tom Greene (216)444-9933, Dr. Dallas Hall (404)712-4722 or Dr. O.T. Randall (202) 865-4881 and provide a very detailed clinical explanation for unblinding. Explain what will be done differently on the basis of which blinded med the person was on. Also, provide the following information:

My name is Dr. X
I am from Center # ____
I want to be unblinded for patient (ID#, Name Code)

For an emergency unblinding between the hours of 5:00 p.m and 7:00 a.m. (Eastern Time), the AASK PI or designated back-up may telephone the Cleveland Clinic Hospital Pharmacy at (216) 444-6590 and say:

My name is Dr. X
I am from Center # ____
I want to be unblinded for patient (ID#, Name Code)
The AASK Study Book is located in the I.V. Room

Part 2 Who is authorized to request emergency unblinding?

Only the following PI's and designated back-ups are authorized to request emergency unblinding.

<u>Center Name</u>	<u>Principal Investigator/Co-Principal Investigator</u>
0. UCSD	Daniel O'Connor, M.D., P.I. Robert Parmer, M.D., Co-P.I. (back-up)
1. CWRU	Jackson Wright, M.D., Ph.D., P.I. Michael Smith, M.D., Co-P.I. (back-up)
2. Emory	Dallas Hall, M.D., P.I. Babatunde Olutade, M.D., Co-P.I. (back-up)
3. Harbor-UCLA	Joel Kopple, M.D., P.I. Khaja Ahmed, M.D., Co-P.I. (back-up)
4. Howard	Otelio Randall, M.D., P.I.

5. Johns Hopkins
Tamrat Retta, M.D., Ph.D., Co-P.I. (back-up)
Lawrence Appel, M.D., M.P.H., P.I.
Joseph Coresh, M.D., Ph.D., Co-P.I. (back-up)
6. MLK/Drew
Keith Norris, M.D., P.I.
Edwina Barnett, M.D., Co-P.I. (back-up)
7. MUSC
DeAnna Cheek, M.D., P.I.
Florence Hutchinson, M.D., Co-P.I. (back-up)
8. Meharry
Marquetta Faulkner, M.D., P.I.
Femi Odunusi, M.D., Co-P.I. (back-up)
9. Harlem
Velvie Pogue, M.D., P.I.
Donna Dowie, M.D. (back-up)
10. Morehouse
William Cleveland, M.D., P.I.
Angus Howard, M.D., Co-P.I. (back-up)
11. Mt. Sinai
Robert Phillips, M.D., Ph.D., P.I.
Michael Lipkowitz, M.D., Co-P.I. (back-up)
12. OSU
Lee Hebert, M.D., P.I.
Kwame Osei, M.D., Co-P.I. (back-up)
13. Rush
George Bakris, M.D., P.I.
Jim Lash, M.D., Co-P.I. (back-up)
14. Alabama
Stephen Rostand, M.D., P.I.
Denise Thornley-Brown, M.D., Co-P.I. (back-up)
15. Florida
Craig Tisher, M.D., P.I.
John Peterson, M.D., Co-P.I. (back-up)
16. Miami
Jacques Bourgoignie, M.D., P.I.
Gabriel Contreras, M.D., Co-P.I. (back-up)
17. Michigan
Kenneth Jamerson, M.D., P.I.
Freidrich Port, M.D., Co-P.I. (back-up)
18. So. Calif.
Shaul Massry, M.D., P.I.
Vito Campese, M.D., Co-P.I. (back-up)
19. Texas
John Middleton, M.D., P.I.
Helen Mitchell, M.D., Co-P.I. (back-up)
20. Vanderbilt
Julia Breyer, M.D., P.I.
Gerald Schulman, M.D., Co-P.I. (back-up)