

Modeling Dosing Design in Oracle Clinical

OCUG DRUG Focus Group
Breakout session

- October 10, 2007
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Overview

- Study Dosing Design
- CASE STUDY: Multi-drug, multi-dosing period (crossover) study design
- Setup of OC for successful un-blinding and reporting

STUDY DESIGNS

- **PARALLEL** – study subjects receive one TREATMENT per randomized group.
- **CROSSOVER** – study subjects receive one SEQUENCE of TREATMENTS per randomized group.

PARALLEL STUDY TYPE

- Each subject will receive only one treatment during duration of study

Dosing periods

Treatment Sequences

	1	2	3
A	A	A	A
B	B	B	B
C	C	C	C
D	D	D	D

CROSSOVER STUDY TYPE

- LATIN SQUARE - all possible combinations of treatments

Dosing periods

Treatment Sequences

	1	2	3
ABC	A	B	C
ACB	A	C	B
BAC	B	A	C
BCA	B	C	A
CAB	C	A	B
CBA	C	B	A

CASE STUDY:

A randomized, placebo controlled, three-period crossover design study on the effects of VITAMIN E on the efficacy of ACTIVE DRUG.

CASE STUDY DESIGN

- 3 treatments to be compared
 - Placebo
 - ACTIVE DRUG
 - ACTIVE DRUG + Vitamin E
- All 36 subjects will receive ALL 3 treatments
- 3 period crossover, multi-drug design
- Two Pills Per day (AM/PM) for Six Days
- The randomized groups differ only in the SEQUENCE in which the treatments are given

DEFINE IN ORACLE CLINICAL

- Treatment Definition
- Randomization Definition
- Interval/CPE Design
- Treatment Regimen Definition
- Regimen to Interval Assignment

First, Create Treatment Definition

OPA (Randy Hogg - OP5\$HOGGR at OCP02 on 06-JUL-05)

Action Move Clear Data Query Special Help Window

Maintain Treatment Patterns

Treatment Patterns for study TEST , Version 1

Pattern Code	Treatment Pattern Name	Label Code
ABC	Placebo > TESTDRUG > TESTDRUG + VITAMIN E	
ACB	Placebo > TESTDRUG + VITAMIN E > TESTDRUG	
BAC	TESTDRUG > Placebo > TESTDRUG + VITAMIN E	
BCA	TESTDRUG > TESTDRUG + VITAMIN E > Placebo	
CAB	TESTDRUG + VITAMIN E > Placebo > TESTDRUG	
CBA	TESTDRUG + VITAMIN E > TESTDRUG > Placebo	

Back Save Single Regimens in Treatment Pattern Drugs Copy Treatment Pattern

Here are the treatment sequences defined for CASE STUDY. Separator character is > in this case.

Next, Create Randomization Definition

- Navigator
 - Favorites
 - OC OCL 4.5.0
 - Admin
 - Plan
 - Design
 - Studies
 - Investigators and Sites
 - Treatments
 - Strata
 - Schedule
 - Randomization
 - Version Randomization
 - Strata Randomization
 - Version Blocked Randomization
 - Treatment Patterns
 - Easy Randomization
 - Block Definitions
 - Block Definition Block Sizes
 - Treatment Assignments
 - Strata Blocked Randomization
 - Randomization Batch Load
 - Randomization Maintenance
 - Patient Positions
 - Test a Study Design
 - DCI Form Local Study Settings
 - Design Reports

OPA (Randy Hogg - OPS\$HOGGR at OCP02 on 07-JUL-05)

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ORACLE

Create Quick Version Level Randomizations

Study	Version	Live ?	Number Of Kits Reqd	Starting Kit Code	Number of Rpl Kits Reqd	Starting Repl. Kit Code	Block Size	Sh
TEST	1	<input checked="" type="checkbox"/>	36	1			6	Li
		<input type="checkbox"/>						
		<input type="checkbox"/>						
		<input type="checkbox"/>						
		<input type="checkbox"/>						
		<input type="checkbox"/>						
		<input type="checkbox"/>						
		<input type="checkbox"/>						
		<input type="checkbox"/>						
		<input type="checkbox"/>						

Exit Save Treatment Patterns Show Randomizations

A code for the Clinical Study

<OSC>

Define Randomization Set Up

Click Treatment Patterns



After the ratios are entered,
just press the
RANDOMIZE button.

OPA (Randy Hogg - OPS\$HOGGR at OCP02 on 07-JUL-05)

Action Move Clear Data Query Special Help Window

ORACLE

Create Quick Version Level Randomizations

Treatment Patterns for Study TEST, Version 1

Pattern	Name	Ratio	Size Mult
ABC	Placebo > TESTDRUG > TESTDRUG + VITAMIN E	1	1
ACB	Placebo > TESTDRUG + VITAMIN E > TESTDRUG	1	1
BAC	TESTDRUG > Placebo > TESTDRUG + VITAMIN E	1	1
BCA	TESTDRUG > TESTDRUG + VITAMIN E > Placebo	1	1
CAB	TESTDRUG + VITAMIN E > Placebo > TESTDRUG	1	1
CBA	TESTDRUG + VITAMIN E > TESTDRUG > Placebo	1	1

Back Save **Randomize**

Treatment Assignments

- Strata Blocked Randomization
- Randomization Batch Load
- Randomization Maintenance

Record: 1/6 <OSC>



Here's what a finished randomization list with block size 6 might look like.

TEST07JUL2005140009AAA.INF - Notepad

File Edit Format Help

```
RANDO NUMBER =  
PROJECT      = Demonstration Study Randomization  
INDICATION   =  
INVESTIGATOR =  
COUNTRY      =  
STUDY        = TEST  
ABC=Placebo > TESTDRUG > TESTDRUG + VITAMIN E  
ACB=Placebo > TESTDRUG + VITAMIN E > TESTDRUG  
BAC=TESTDRUG > Placebo > TESTDRUG + VITAMIN E  
BCA=TESTDRUG > TESTDRUG + VITAMIN E > Placebo  
CAB=TESTDRUG + VITAMIN E > Placebo > TESTDRUG  
CBA=TESTDRUG + VITAMIN E > TESTDRUG > Placebo
```

- 1 CBA
- 2 BCA
- 3 BAC
- 4 ACB
- 5 CAB
- 6 ABC

- 7 CBA
- 8 BAC
- 9 ABC
- 10 CAB
- 11 ACB
- 12 BCA

- 13 CBA
- 14 ABC
- 15 ACB
- 16 CAB
- 17 BAC
- 18 BCA

- 19 BAC
- 20 CAB
- 21 CBA
- 22 BCA
- 23 ABC
- 24 ACB



Next, Define Intervals and Clinical Planned Events (CPEs). Consult CRF.

Two pills per day for 6 days - one TAB (AM) + 1 CAP (PM) on CRF dosing page

DATE OF VISIT (dd-MMM-yyyy)

Investigator :

Please print all details, and INITIAL and DATE all corrections. Indicate where applicable.

SITE ID

CENTER ID

SUBJECT INITIALS

DOSING RECORD

	DATE OF DOSING (dd-MMM-yyyy)	CARD NUMBER	AM	PM	REASON FOR DOSE CHANGE OR ANY MISSED MEDICATION
Tuesday	<input type="text"/>	<input type="text"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Wednesday	<input type="text"/>	<input type="text"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Thursday	<input type="text"/>	<input type="text"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Friday	<input type="text"/>	<input type="text"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Saturday	<input type="text"/>	<input type="text"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Sunday	<input type="text"/>	<input type="text"/>	<input type="checkbox"/>	<input type="checkbox"/>	

To track the dosing details for each dosing period separately, define three separate dosing Intervals, or Phases.

DPA (Randy Hogg - OPS\$HOGGR at OCP02 on 06-JUL-05)

Action Move Clear Data Query Special Help Window

Maintain Intervals

Phases for Study TEST, Version 1

Phase Name	Short Name	Previous Phase	Phase Type	Time Unit
SCREENING	SCRN		SCREEN	DAY
BASELINE	BASELINE	SCREENING	BASELN	DAY
DOSE_PERIOD_1	D1	BASELINE	DOSING	DAY
DOSE_PERIOD_2	D2	DOSE_PERIOD_1	DOSING	DAY
DOSE_PERIOD_3	D3	DOSE_PERIOD_2	DOSING	DAY
END OF STUDY	EOS	DOSE_PERIOD_3	FOLL_UP	DAY

The INTERVALS button from "easy design" gets you here.

Back Save Single **Periods** Resequen

- Active Substances
- Qry Active Substances
- Drugs
- Qry Drugs

The name of the Phase.

Record: 1/6

<OSC>



To track each of 2 pills given per day within a single CPE, use 2 DCM repeats and define PERIODS under each dosing interval.

OPA (Randy Hogg - OPS\$HOGGR at OCP02 on 07-JUL-05)

Action Move Clear Data Query Special Help Window

Maintain Intervals

Periods for Phase DOSE_PERIOD_1

Period Name	Short Name	Previous Period	Period Type	Time Unit	Minimum Duration	Maximum Duration
PILL 1	PILL 1		DOSING	DAY	0	0
PILL 2	PILL 2	PILL 1	DOSING	DAY	0	0

Back Save Single Sub-Periods Resequence



Define 2 days for each of the 3 dosing periods. That makes 6 CPEs with dosing records.

OPA (Randy Hogg - OPS\$HOGGR at OCP02 on 07-JUL-05)

Action Move Clear Data Query Special Help Window

Easy Design - Clinical Studies

Clinical Planned Events for Study TEST, Version 1

Event Name	Interval Name	Optional	Visit No.	T
DAY0	SCREENING	<input type="checkbox"/>	1	<input type="checkbox"/>
DAY1	BASELINE	<input type="checkbox"/>	2	<input type="checkbox"/>
DAY2	DOSE_PERIOD_1	<input type="checkbox"/>	3	<input type="checkbox"/>
DAY3	DOSE_PERIOD_1	<input type="checkbox"/>	4	<input type="checkbox"/>
DAY4	DOSE_PERIOD_2	<input type="checkbox"/>	5	<input type="checkbox"/>
DAY5	DOSE_PERIOD_2	<input type="checkbox"/>	6	<input type="checkbox"/>
DAY6	DOSE_PERIOD_3	<input type="checkbox"/>	7	<input type="checkbox"/>
DAY7	DOSE_PERIOD_3	<input type="checkbox"/>	8	<input type="checkbox"/>
DAY8	END OF STUDY	<input type="checkbox"/>	9	<input type="checkbox"/>
		<input type="checkbox"/>		<input type="checkbox"/>

Back Save Single

- Investigators and Sites
- Treatments
 - Active Substances
 - Orv. Active Substances

FRM-40400: Transaction complete: 6 records applied and saved.
Record: 9/9 <OSC>

The EVENTS button from "easy design" gets you here!



Next we need to define the Treatment Regimens that underlie each Treatment Pattern sequence.

OPA (Randy Hogg - OPS\$HOGGR at OCP02 on 06-JUL-05)

Action Move Clear Data Query Special Help Window



Maintain Treatment Patterns

Treatment Patterns for study TEST , Version 1

Pattern Code	Treatment Pattern Name	Label Code
ABC	Placebo > TESTDRUG > TESTDRUG + VITAMIN E	
ACB	Placebo > TESTDRUG + VITAMIN E > TESTDRUG	
BAC	TESTDRUG > Placebo > TESTDRUG + VITAMIN E	
BCA	TESTDRUG > TESTDRUG + VITAMIN E > Placebo	
CAB	TESTDRUG + VITAMIN E > Placebo > TESTDRUG	
CBA	TESTDRUG + VITAMIN E > TESTDRUG > Placebo	

Back Save Single Regimens in Treatment Pattern Drugs Copy Treatment Pattern

- Version Randomization
- Strata Randomization
- Version Blocked Randomization
- Treatment Patterns

A code for the type of Treatment Pattern
Record: 1/6 ... List of Valu... <OSC>



Lets start with the ABC sequence. With cursor on that one, click on DRUGS.

OPA (Randy Hogg - OPS\$HOGGR at OCP02 on 06-JUL-05)

Action Move Clear Data Query Special Help Window

Maintain Treatment Patterns

Treatment Patterns for study TEST , Version 1

Pattern Code	Treatment Pattern Name	Label Code
ABC	Placebo > TESTDRUG > TESTDRUG + VITAMIN E	
ACB	Placebo > TESTDRUG + VITAMIN E > TESTDRUG	
BAC	TESTDRUG > Placebo > TESTDRUG + VITAMIN E	
BCA	TESTDRUG > TESTDRUG + VITAMIN E > Placebo	
CAB	TESTDRUG + VITAMIN E > Placebo > TESTDRUG	
CBA	TESTDRUG + VITAMIN E > TESTDRUG > Placebo	

Back Save Single Regimens in Treatment Pattern **Drugs** Copy Treatment Pattern

- Version Randomization
- Strata Randomization
- Version Blocked Randomization
- Treatment Patterns

A code for the type of Treatment Pattern
Record: 1/6 ... List of Valu... <OSC>



Query for correct Drug.
We can use a pre-defined company drug record for a placebo.
Next press REGIMENS.

OPA (Randy Hogg - OPS\$HOGGR at OCP02 on 07-JUL-05)

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Maintain Treatment Patterns

Drugs (Query Only)

Drug Id	Drug Name	Substance Code	Form
5401	DOUBLE BLIND PLACEBO	90	

Back

Regimens for this Drug

- Treatment Patterns
- Qry Treatment Patterns
- Treatment Pattern Codes

The Id of the Drug

Record: 1/1

<OSC>



This is the regimen we want! Next press ADD THIS REGIMEN.

OPA (Randy Hogg - OPS\$HOGGR at OCP02 on 07-JUL-05)

Action Move Clear Data Query Special Help Window

ORACLE

Maintain Treatment Patterns

Treatment Regimens for Drug DOUBLE BLIND PLACEBO

Lab Abbr	Name	Drug Description	Route Admin
PLACEBO	Double Blind Placebo Tablet QD Oral	DOUBLE BLIND PLACEBO	PO

Back Single **Add this Regimen to Treatment Pattern**

- Treatment Patterns
- Qry Treatment Patterns
- Treatment Pattern Codes

The abbreviation used by labeling.
Record: 1/1 <OSC>



Follow the same steps to define all Treatment Regimens for first Treatment Pattern sequence

OPA (Randy Hogg - OPS\$HOGGR at OCP02 on 07-JUL-05)

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Maintain Treatment Patterns

Treatment Regimens for Placebo > TESTDRUG > TESTDRUG + VITAMIN E

Label

Code

Treatment Regimen Name

A	Double Blind Placebo Tablet QD Oral
C	Vitamin E (TPGS) 500 mg
A2	Double Blind Placebo Capsule QD Oral
B	TESTDRUG 5mg QD PO

Back

Save

Details of this Treatment Regimen

Assign Regimen to Intervals

Query Intervals

Processes

Events

Query Events

A code to be printed on the labels of this regimen

Record: 1/4

<OSC>

PREMIER
RESEARCH

Finally, assign regimens to each Period by selecting the ASSIGN REGIMENS button.

OPA (Randy Hogg - OPS\$HOGGR at OCP02 on 07-JUL-05)

Action Move Clear Data Query Special Help Window



Maintain Treatment Patterns

Treatment Regimens for Placebo > TESTDRUG > TESTDRUG + VITAMIN E

Label Code	Treatment Regimen Name
A	Double Blind Placebo Tablet QD Oral
C	Vitamin E (TPGS) 500 mg
A2	Double Blind Placebo Capsule QD Oral
B	TESTDRUG 5mg QD PO

Back Save Details of this Treatment Regimen **Assign Regimen to Intervals**

- Query Intervals
- Processes
- Events
- Query Events

A code to be printed on the labels of this regimen

Record: 3/4

<OSC>



Study Intervals assigned to Double Blind Placebo Capsule QD Oral

Assigned?	Label Code	Type	Name
<input type="checkbox"/>		BASELN	BASELINE
<input type="checkbox"/>		DOSING	DOSE_PERIOD_1
<input type="checkbox"/>		DOSING	PILL 1
<input checked="" type="checkbox"/>		DOSING	PILL 2
<input type="checkbox"/>		DOSING	DOSE_PERIOD_2
<input type="checkbox"/>		DOSING	PILL 3
<input checked="" type="checkbox"/>		DOSING	PILL 4
<input type="checkbox"/>		DOSING	DOSE_PERIOD_3
<input type="checkbox"/>		DOSING	PILL 5
<input type="checkbox"/>		DOSING	PILL 6
<input type="checkbox"/>		FOLL_UP	END OF STUDY

Back Save Assign Regimen to this Interval Deassign Regimen from this Interval

- Query Intervals
- Processes
- Events
- Query Events

A code to be printed on the labels of this regimen

Record: 3/13

<OSC>



QUESTIONS ???