



INTEGO
GROUP

DH12: Brace Yourself for Smooth Unblinding

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Table of Contents

01 Randomization and Blinding as the Most Effective Design Techniques to Avoid Bias

02 Unblinding Process in a Clinical Trial Data Flow

03 Impact an Unblinding Process Could Have on Data

04 Challenges of Unblinding and How to Overcome Them

05 Overview of an Unblinding Plan Document

06 Conclusions



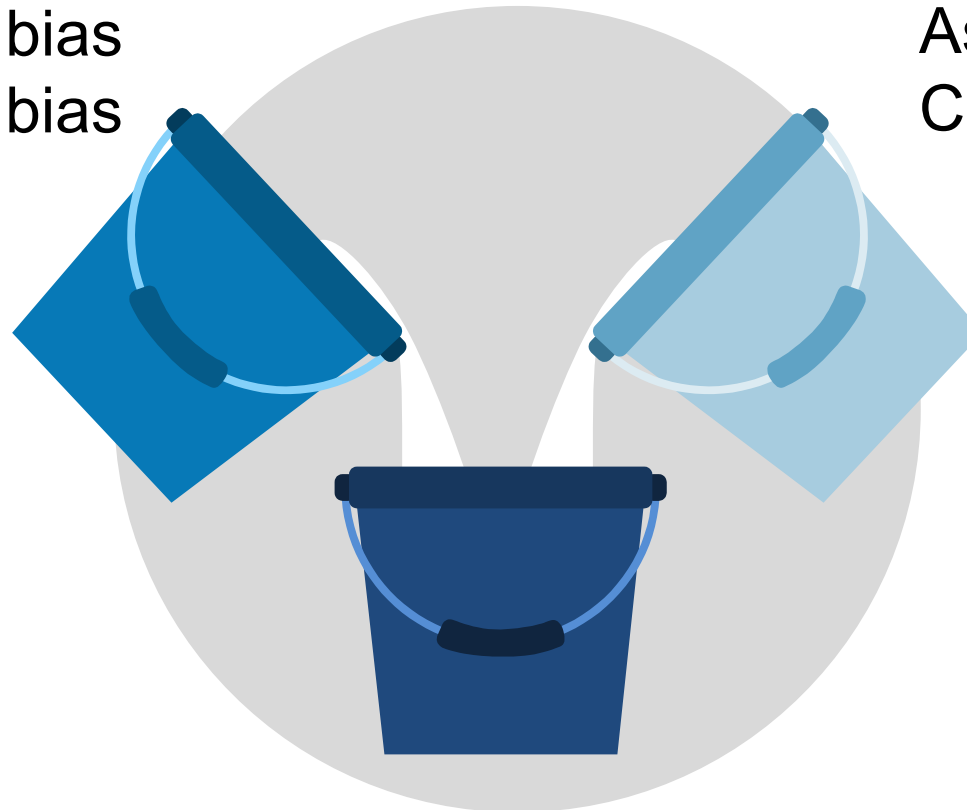
Randomization and Blinding as the Most Effective Design Techniques to Avoid Bias



Bias. Common types of bias

Selection and allocation bias
Attitude bias

Assessment bias
Confirmation bias



Bias

Blinding and Randomization

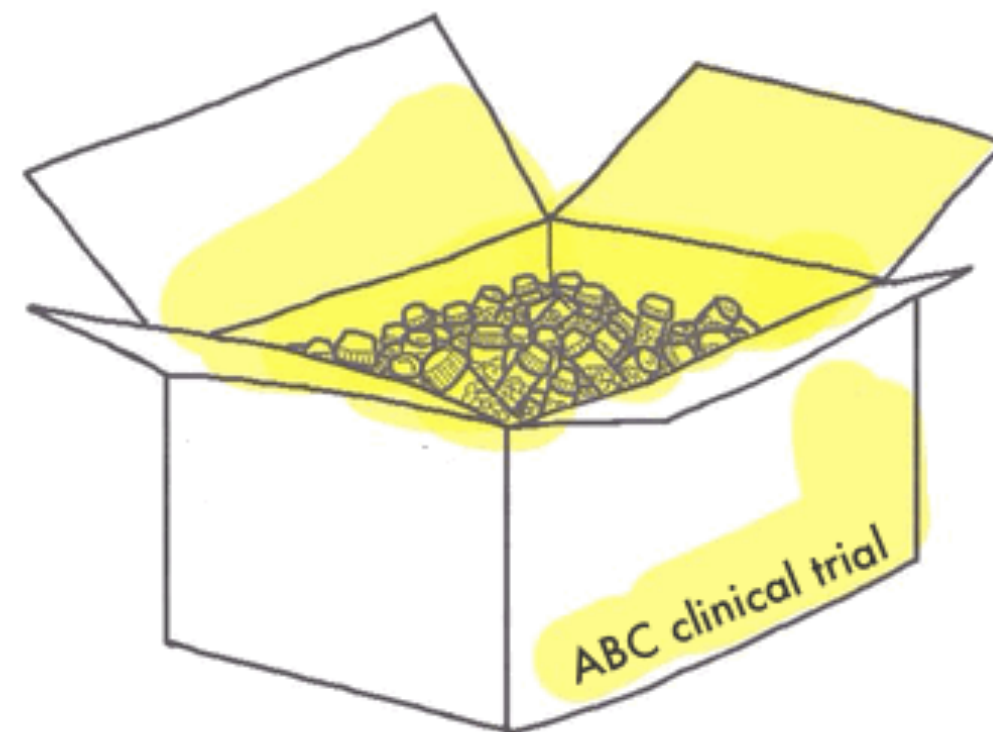
Blinding

Blinding or masking is intended to limit the occurrence of conscious and unconscious bias in the conduct and interpretation of a clinical trial arising from the influence which the knowledge of treatment may have on all participants of the trial.

Randomization

Randomization introduces a deliberate element of chance into the assignment of treatments to subjects in a clinical trial. It also tends to produce treatment groups in which the distributions of prognostic factors, known and unknown, are similar.

Drug Kits



Interactive Response Technology

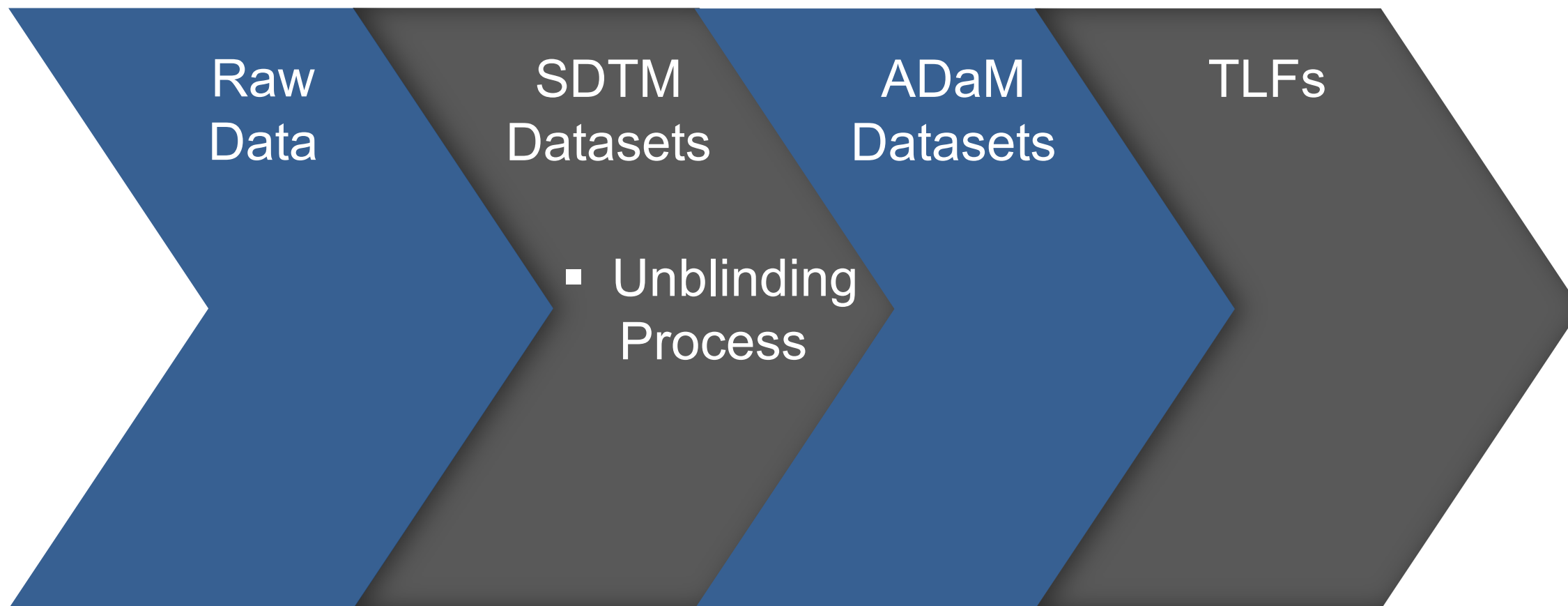




Unblinding Process in a Clinical Trial Data Flow



Clinical Trial Data Flow



Impact – SDTM Level

DM Domain

Variable Name	Variable Label	Type
ARMCD	Planned Arm Code	Char
ARM	Description of Planned Arm	Char
ACTARMCD	Actual Arm Code	Char
ACTARM	Description of Actual Arm	Char

EX Domain

Variable Name	Variable Label	Type
EXTRT	Name of Treatment	Char
EXDOSE	Dose	Num
EXDOSTXT	Dose Description	Char

Impact – ADaM Level

ADSL		
Variable Name	Variable Label	Type
TRT01P	Planned Treatment for Period 01	Char
TRT01A	Actual Treatment for Period 01	Char
TRTSDTM	Datetime of First Exposure to Treatment	Num
TRTEDTM	Datetime of Last Exposure to Treatment	Num

ADEX	
PARAMCD	PARAM
DURD	Study drug duration
TDOSE	Total administered dose
DUREXPD	Overall duration of exposure



Impact an Unblinding Process Could Have on Data



Example 1 – Exposure (EX) Domain

ex.xpt

Row	STUDYID	DOMAIN	USUBJID	EXTRT	EXDOSE	EXDOSU	EXSTDTC	EXENDTC	EXKIT
1	ABC	EX	ABC5001	PLACEBO	0	mg	2020-01-08	2020-01-11	TTH0101
2	ABC	EX	ABC5001	PLACEBO	0	mg	2020-01-13	2020-01-18	TTH0102
3	ABC	EX	ABC5002	DRUG A	40	mg	2020-03-10	2020-03-18	TTH0201
4	ABC	EX	ABC5002	DRUG A	80	mg	2020-03-19	2020-03-22	TTH0202
5	ABC	EX	ABC5002	DRUG A	80	mg	2020-03-23	2020-04-01	TTH0203
6	ABC	EX	ABC5003	PLACEBO	0	mg	2019-11-16	2019-11-18	TTH0301
7	ABC	EX	ABC5003	PLACEBO	0	mg	2019-11-19	2019-12-14	TTH0301
8	ABC	EX	ABC5005	DRUG A	40	mg	2020-05-04	2020-05-08	TTH0501

Sample CRF:

Phase	Treatment
Study Drug	Blinded Drug A
Start Date	____ - ____ - ____
End Date	____ - ____ - ____

Sample CRF (cont):

Dose	____
Unit	mg
Dose Frequency	QD

Example 2 – Demographics (DM) Domain

dm.xpt

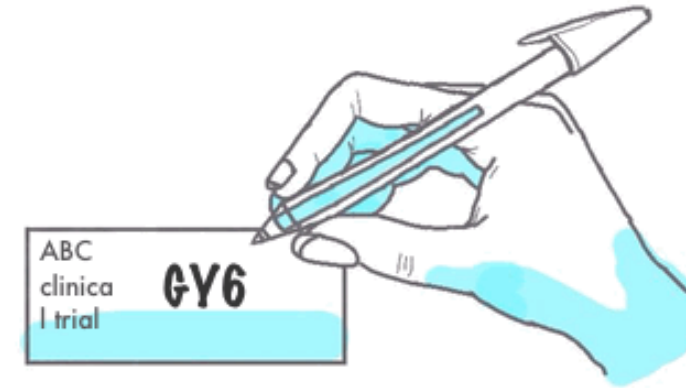
Row	STUDYID	DOMAIN	USUBJID	ARMCD	ARM	ACTARMCD	ACTARM
1	ABC	DM	ABC5001	ABO	DRUG A	ABO	DRUG A
2	ABC	DM	ABC5002	ABO	DRUG A	ABO	DRUG A
3	ABC	DM	ABC5003	ABO	DRUG A	ABO	DRUG A
4	ABC	DM	ABC5004	ABO	DRUG A	ABORT	Not Acted
5	ABC	DM	ABC5005	A	DRUG A	A	DRUG A



Challenges of Unblinding and How to Overcome Them



Kit List Dataset



Kit code	Treatment
AF5	Placebo
GY6	Drug A
YU1	Drug A
FT2	Placebo

Unblinding – Process

ex.xpt

Row	STUDYID	DOMAIN	USUBJID	EXTRT	EXDOSE	EXDOSU	EXKIT
1	ABC	EX	ABC5001	BLANDED DRUG A	00	mg	TTH0101
2	ABC	EX	ABC5001	BLANDED DRUG A	00	mg	TTH0102
3	ABC	EX	ABC5002	BLANDED DRUG A	40	mg	TTH0201
4	ABC	EX	ABC5002	BLANDED DRUG A	80	mg	TTH0202
5	ABC	EX	ABC5002	BLANDED DRUG A	80	mg	TTH0203
6	ABC	EX	ABC5003	BLANDED DRUG A	00	mg	TTH0301
7	ABC	EX	ABC5003	BLANDED DRUG A	80	mg	TTH0301
8	ABC	EX	ABC5005	BLANDED DRUG A	40	mg	TTH0501

Kit List

Row	KLTESTCD	KLKIT
1	PBO	TTH0101
2	PBO	TTH0102
3	A	TTH0201
4	A	TTH0202
5	A	TTH0203
6	PBO	TTH0301
7	PBO	TTH0301
8	A	TTH0501

Scenario 1

ex.xpt

Row	STUDYID	DOMAIN	USUBJID	EXTRT	EXDOSE	EXDOSU	EXKIT
1	ABC	EX	ABC5001	PLACEBO	0	mg	TTH0101
2	ABC	EX	ABC5001	PLACEBO	0	mg	TTH0102
3	ABC	EX	ABC5002	DRUG A	40	mg	TTH0201
4	ABC	EX	ABC5002	DRUG A	80	mg	TTH0202
5	ABC	EX	ABC5002	DRUG A	80	mg	TTH0203
6	ABC	EX	ABC5003	PLACEBO	0	mg	TTH0301
7	ABC	EX	ABC5003	PLACEBO	0	mg	TTH0301
8	ABC	EX	ABC5005	DRUG A	40	mg	TTH0501
9	ABC	EX	ABC5006	UNKNOWN	40	mg	TTH0601

Kit List

Row	KLTESTCD	KLKIT
1	PBO	TTH0101
2	PBO	TTH0102
3	A	TTH0201
4	A	TTH0202
5	A	TTH0203
6	PBO	TTH0301
7	PBO	TTH0301
8	A	TTH0501

Warning: EXKIT=TTH0601 does not exist in Kit List dataset



Scenario 2

ex.xpt

Row	DOMAIN	USUBJID	EXTRT	EXDOSE	EXDOSU	EXKIT
1	EX	ABC5001	PLACEBO	0	mg	TTH0101
2	EX	ABC5001	PLACEBO	0	mg	TTH0102
3	EX	ABC5002	DRUG A	40	mg	TTH0201
4	EX	ABC5002	DRUG A	80	mg	TTH0202
5	EX	ABC5002	DRUG A	80	mg	TTH0203
6	EX	ABC5003	PLACEBO	0	mg	TTH0301
7	EX	ABC5003	PLACEBO	0	mg	TTH0301
8	EX	ABC5005	DRUG A	40	mg	TTH0501
9	EX	ABC5007	DRUG A	40	mg	TTH0701
10	EX	ABC5007	PLACEBO	0	mg	TTH0702

**Warning: USUBJID=ABC5007
received different types of drug
during the same period**

dm.xpt

Row	DOMAIN	USUBJID	ACTARMCD	ACTARM
1	DM	ABC5001	PBO	PLACEBO
2	DM	ABC5002	A	DRUG A
3	DM	ABC5003	PBO	PLACEBO
4	DM	ABC5004	NOTRT	Not Treated
5	DM	ABC5005	A	DRUG A
6	DM	ABC5007	???	???



Scenario 3

ex.xpt

Row	STUDYID	DOMAIN	USUBJID	EXTRT	EXDOSE	EXDOSU	EXKIT1	EXKIT2	EXKIT1 (Desc.)	EXKIT2 (Desc.)
1	DEF	EX	DEF8001	BLANDED DRUG B	0000	mg	GY0111	GY0112	PLACEBO	PLACEBO
2	DEF	EX	DEF8001	BLANDED DRUG B	0000	mg	GY0121	GY0122	PLACEBO	PLACEBO
3	DEF	EX	DEF8002	BRUNED DRUG B	1000	mg	GY0231	GY0232	DRUG B	DRUG B
4	DEF	EX	DEF8002	BRUNED DRUG B	1000	mg	GY0233	GY0234	DRUG B	DRUG B
5	DEF	EX	DEF8002	BRUNED DRUG B	1000	mg	GY0235	GY0236	DRUG B	DRUG B
6	DEF	EX	DEF8003	BLANDED DRUG B	0000	mg	GY0341	GY0342	PLACEBO	PLACEBO
7	DEF	EX	DEF8003	BLANDED DRUG B	0000	mg	GY0343	GY0344	PLACEBO	PLACEBO
8	DEF	EX	DEF8005	BLANDED DRUG B	1000	mg	GY0551	GY0552	DRUG B	PLACEBO

**Warning: EXKIT1=GY0551 and
EXKIT2=GY0552 contain
different types of drug**



Scenario 4

dm.xpt

Row	DOMAIN	USUBJID	ARMCD	ARM
1	DM	ABC5001	PBO	PLACEBO
2	DM	ABC5002	A	DRUG A
3	DM	ABC5003	PBO	PLACEBO
4	DM	ABC5004	A	DRUG A
5	DM	ABC5005	A	DRUG A

Randomization List

Row	PTNUM	RNDARMCD	RNDARM
1	5001	PBO	PLACEBO
2	5002	A	DRUG A
3	5003	PBO	PLACEBO
4	5004	A	DRUG A
5	5005	A	DRUG A
6	5050	A	DRUG A

**Warning: subject PTNUM=5050
was randomized but is not
present in the Demographics
domain**





Overview of an Unblinding Plan Document



Unblinding Plan



Description of data to be used for unblinding



Instructions for the programming team on how to perform unblinding programming



Summary of the data changes after unblinding



Guidelines on how to deal with challenging cases

Assessment of the impact on analysis



Points of contact in case of different scenarios





Conclusions



What Has Been Covered

- Blinding and randomization as a way to minimize bias
- Impact that unblinding has on data
- Challenges from the author's experience
- Importance of the unblinding plan





THANK YOU

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