

Protocol deviation programming

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DS03 – PHUSE EU Connect 2022



AGENDA

- Introduction: PD overview
- PD programming cycle
- PD tracking file
- DV creation
- Summary



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#DataStrategy #DataIntegration
#DataViz #DataStandards
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#MedicalReview #SDTM
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#Protocol #Coding

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INTRODUCTION: PD OVERVIEW

Protocol Deviation Definition

Any change, divergence, or departure from the study design or procedures defined in the approved protocol.

- **Compliance** of investigational sites with protocol
- Reveal systematic errors

INTRODUCTION: PD OVERVIEW

- Examples:
 - Unplanned instances of protocol non-compliance
 - Treatment administration not in accordance with protocol
 - Eligibility criteria not met but patient included in the study
- Protocol deviations can be either **major** or **minor**
- Importance level is defined by the sponsor
- Reporting Important PDs in CTR

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PD PROGRAMMING CYCLE

- Inputs: SDTM datasets, PD_PRERM file, PD classification sheet
- Outputs: PD_PRERM file , PD_POSTRM file
- **Steps:**
 1. Derive PDs programmatically
 2. PD Categorisation
 3. Import manual PDs from SDTM.DV and SDTM.SUPPDV
 4. Combining manual and programmable PDs
 5. Compare with last PD_POSTRM
 6. Generate PD_PRERM/PD_POSTRM

PD PROGRAMMING: #1

- Generate PD dataset from SDTM datasets
- **Steps:**
 1. Initial program parameters: Libraries/Macros
 2. PD macro functions for PD codes
 3. Combining PD datasets generated by each PD macro
- PD macros examples:
 - Prohibited Medication
 - Randomization failure
 - Eligibility criteria
 - Out of Window treatment administration
 - Study procedure or assessment

PD PROGRAMMING: #2

- Based on protocol/SAP, a PD classification sheet is prepared before FPFV to describe PD categories and subcategories
- Merge programmable PDs combination with PD classification sheet to get PD categories and subcategories

CODE	CATEG	SCATEG
100	INCLUSION/EXCLUSION	INC1
101	INCLUSION/EXCLUSION	EXCL2
200	INVESTIGATIONAL PRODUCT	DOSE INTAKE
300	CONCOMITANT MEDICATION	PROHIBITED CONCOMITANT MEDICATION
400	RANDOMIZATION FAILURE	TREATMENT ALLOCATION

PD PROGRAMMING: #3

- Check SDTM.DV existence
- Import SDTM.DV and SDTM.SUPPDV
- Merge DV and SUPPDV

```
/*Check DV existence*/  
%macro mrg;  
  %global DV;  
  %let DV= ;  
  %if %sysfunc(exist(SDTM.DV)) %then %do ;  
    data DV;  
      set SDTM.DV;  
      %let DV=DV;  
    run;  
  %end;  
%mend mrg;
```

PD PROGRAMMING: #4

- Rename variables based on expected PD dataset output
- Combining Programmable and Manual deviations
- Merging with other SDTM domains to get required variables

PD PROGRAMMING: #5

1. Retrieve duplicates
2. Exclude subjects from both PD_POSTRM and PD_PRERM datasets
3. Combine PD_POSTRM and PD_PRERM
4. Handle duplicates by considering the Deviation Description in the merge
5. Set a new merge with Duplicates
6. Get rid of old PDs
7. Remove duplicates across PD types
8. Remove records of subjects with overall code who receive any other code

PD PROGRAMMING: #5

- Status since last review:
 - LOCKED: Reviewed and saved for output
 - NEW: Detected for the first time
 - UPDATED: Having changes in some attributes comparing to previous version
 - OLD: Having been removed from current SDTM DV
 - DUPLICATE: Attributed during Review meeting

PD PROGRAMMING: #6

- Programmatic detection is useful for: classifying PDs as major or minor
- Classifying PDs:
 - Important
 - Non-important
- Generate PD_PRERM and PD_POSTRM

PD PROGRAMMING: #6

Example:

Studyid	Usubjid	Country	Site_Identifier	Investigator_Identifier	Code	Protocol_Deviation_Term	Protocol_Deviation_Description	Deviation_CAT
XX	A	USA	A1	B1	100	Age criteria	Age is less then 18 years at the day of study start	Inclusion/exclusion
XX	B	FRA	A2	B2	200	Investigational product	Visit 3 : unknown route of administration	Investigational product
XX	C	USA	A3	B3	300	CM medication	Visit 2 : Patient took OLANZAPINE	CONCOMITANT MEDICATION
XX	D	FRA	A4	B4	300	CM medication	Visit 2 : Patient took PIPRAZOLE	CONCOMITANT MEDICATION
XX	E	FRA	A5	B5	300	CM medication	Visit 2 : Patient took OLANZAPINE	CONCOMITANT MEDICATION
XX	F	USA	A6	B6	400	Treatment allocation	Subject number allocation without treatment	RANDOMIZATION FAILURE
XX	G	USA	A7	B7	100	Age criteria	Age is less then 40 years at the day of study start	Inclusion/exclusion
XX	H	FRA	A8	B8	100	Age criteria	Age is less then 40 years at the day of study start	Inclusion/exclusion
XX	I	USA	A9	B9	101	Chronic disease	Patient has a chronic disease	Inclusion/exclusion
XX	J	USA	A10	B10	200	Missing tretament	Visit 2 : Treatment not provided	Investigational product
XX	K	USA	A11	B11	300	CM medication	Visit 4 : Patient took OLANZAPINE	CONCOMITANT MEDICATION
XX	L	FRA	A12	B12	200	Missing dose	Visit 5 : Missing second dose	Investigational product
XX	M	USA	A13	B13	101	Chronic disease	Patient has a chronic disease	Inclusion/exclusion
XX	N	USA	A14	B14	101	Chronic disease	Patient has a chronic disease	Inclusion/exclusion
XX	O	FRA	A15	B15	200	Missing treatment	Visit 3 : Treatment not provided	Investigational product
XX	P	USA	A16	B16	101	Chronic disease	Patient has a chronic disease	Inclusion/exclusion
XX	Q	USA	A17	B17	200	Missing tretament	Visit 2 : Treatment not provided	Investigational product

PD PROGRAMMING: #6

DEVIATION_SCAT	Deviation_date	PD_GRADE	Subject_Elimination	Type	VISIT_NUMBER	PD_status
INC1	21-Jan-20	Major	Yes	Prog	1	Old
DOSE INTAKE	3-Jan-20	Minor	No	Man	3	Duplicate
PROHIBITED CONCOMITANT MEDICATION	25-Mar-20	Major	Yes	Prog	2	New
PROHIBITED CONCOMITANT MEDICATION	29-Jan-20	Minor	No	Man	2	New
PROHIBITED CONCOMITANT MEDICATION	25-Jun-20	Major	Yes	Prog	2	Duplicate
TREATMENT ALLOCATION	26-Feb-20	Major	No	Prog	1	Old
INC1	27-Jan-20	Major	Yes	Man		Old
INC1	28-Aug-20	Major	Yes	Prog		Old
EXCL2	29-Jan-20	Major	Yes	Prog	1	Duplicate
DOSE INTAKE	30-Jan-20	Minor	No	Man	2	Duplicate
PROHIBITED CONCOMITANT MEDICATION	31-May-20	Major	Yes	Prog	4	New
DOSE INTAKE	1-Feb-20	Minor	No	Man	5	Locked
EXCL2	2-Feb-20	Major	Yes	Prog	1	New
EXCL2	25-Mar-20	Major	Yes	Prog	1	Locked
DOSE INTAKE	4-Feb-20	Minor	No	Prog	3	Locked
EXCL2	2-Oct-20	Major	Yes	Man	4	Duplicate
DOSE INTAKE	18-Aug-20	Minor	No	Prog	2	New

AGENDA

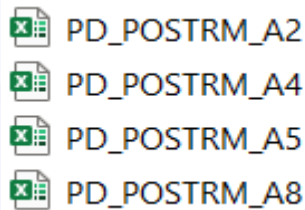
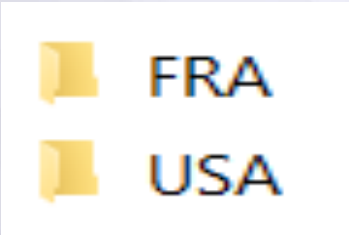
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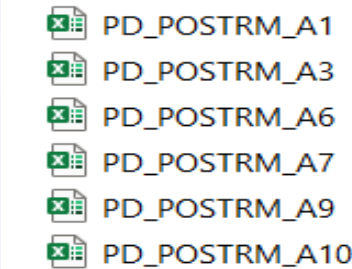
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PD TRACKING FILE

- AFTER PD REVIEW MEETING:
 - Splitting the PD_POSTRM by site and put them in respective folders
 - Input: PD_POSTRM
 - Outputs: Site tracking sheet for every site



FRA			
10/17/2022 5:30 PM	Microsoft Excel W...	11 KB	
10/17/2022 5:30 PM	Microsoft Excel W...	11 KB	
10/17/2022 5:30 PM	Microsoft Excel W...	11 KB	
10/17/2022 5:30 PM	Microsoft Excel W...	11 KB	



USA			
10/17/2022 5:30 PM	Microsoft Excel W...	11 KB	
10/17/2022 5:30 PM	Microsoft Excel W...	11 KB	
10/17/2022 5:30 PM	Microsoft Excel W...	11 KB	
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DV CREATION

- PD_POSTRM file will be used in updating the SDTM.DV dataset
- Creating SDTM.DV in accordance to CDISC standards (refer to SDTMIG section 6.2.4)
- Structure: One record per protocol deviation per subject
- Assumptions:
 - Key variables: STUDYID, USUBJID, DVTERM, DVSTDTC
 - Not for entry criteria information unless specified in the protocol

DV CREATION

- Main DV variables:
 - DVTERM: Verbatim name of the PD
 - DVCAT: Category of the protocol deviation
 - DVSCAT: Subcategory of the protocol deviation
- SUPPDV may contain PD additional information:
 - PDTYPE: Important/Non-important
 - PDDESCzz: PD description
- DV data example:

Row	STUDYID	DOMAIN	USUBJID	DVSEQ	DVTERM	DVDECOD	EPOCH	DVSTDTC
1	ABC123	DV	123101	1	IVRS PROCESS DEVIATION - NO DOSE CALL PERFORMED.	TREATMENT DEVIATION	TREATMENT	2003-09-21
2	ABC123	DV	123103	1	DRUG XXX ADMINISTERED DURING STUDY TREATMENT PERIOD	EXCLUDED CONCOMITANT MEDICATION	TREATMENT	2003-10-30
3	ABC123	DV	123103	2	VISIT 3 DOSE <15 MG	TREATMENT DEVIATION	TREATMENT	2003-10-30
4	ABC123	DV	123104	1	TOOK ASPIRIN	PROHIBITED MEDS	TREATMENT	2003-11-30

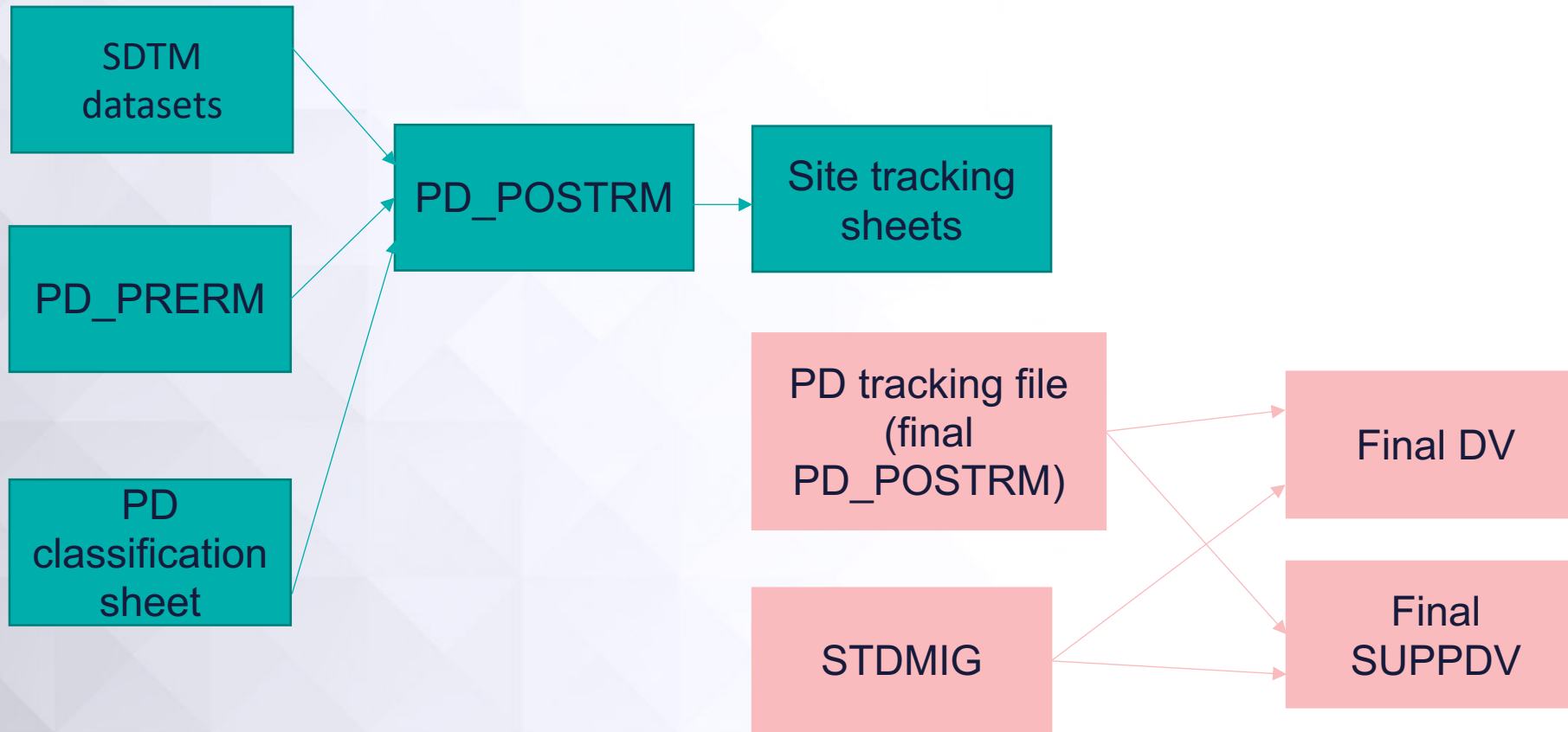
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SUMMARY





THANK YOU FOR YOUR ATTENTION
Q&A

CONTACT



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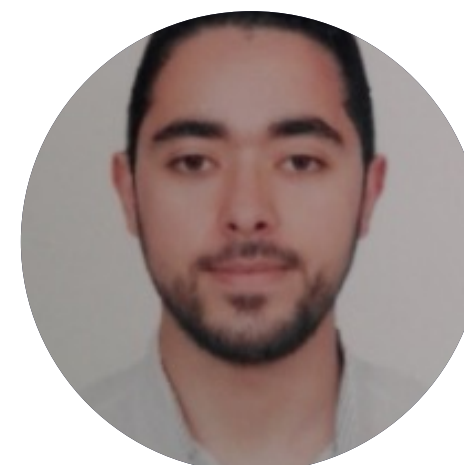
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