



# Overview of ADaM Radhika Chawda

## **Outline**

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# **CDISC-Introduction**

- 1997 : Started as a Volunteer group
- 2000 : Formed an Independent, non-profit organization

<u>CDISC</u> is a global, open, multidisciplinary, non-profit organization that has established standards to support the acquisition, exchange, submission and archive of clinical research data and metadata.

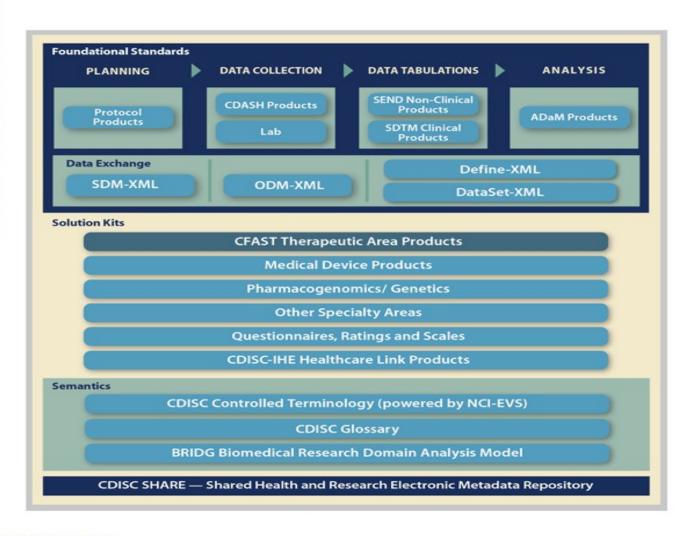
2014: +- 200 organization

# CDISC-Introduction



## **CDISC Foundation Standards**

#### Standards

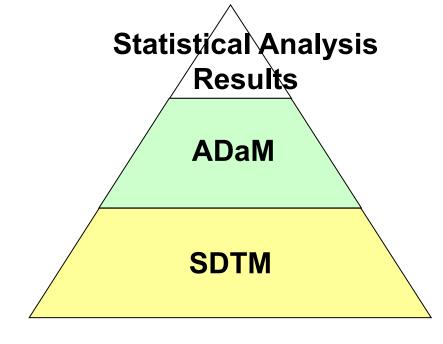


#### Introduction to ADaM

- Used for statistical analysis and reporting
- One proc away

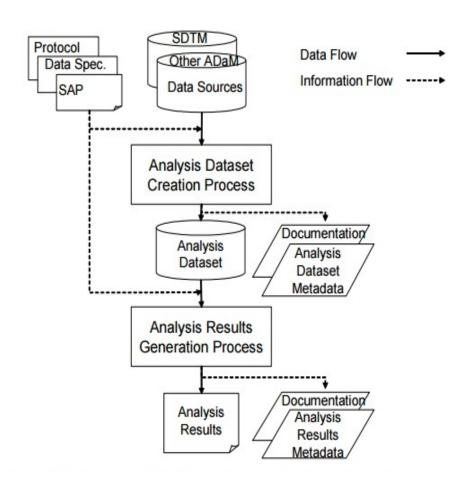
Authoritative source for all data derivations used in statistical

analyses



## Introduction to ADaM

#### **Process Flow**



# Need for ADaM

1. While SDTM purpose is to ensure that data is collected in a standard way, ADaM purpose is to provide data that is ready for analysis.

#### 2. Traceability Purpose

Traceability enables the user to understand the relationship between the analysis datasets, SDTM and source datasets.

#### 3. Health Authorities Purpose:

ADaM allows Health Authorities reviewers to replicate existing analyses or conduct new analyses with minimal or no data manipulation.

## Principles

- Analysis datasets and their associated metadata must:
  - · facilitate <u>clear and unambiguous communication</u>
  - provide <u>traceability</u> between the analysis data and its source data (ultimately SDTM)
  - be <u>readily useable</u> by commonly available software tools
- Analysis datasets must:
  - be accompanied by <u>metadata</u>
  - · be <u>analysis-ready</u>

- Traceability:
  - Enables the understanding of the data's lineage
  - Facilitates data flow transparency
  - Permits the understanding of the relationship among
    - · analysis results
    - · analysis datasets
    - · SDTM domains

- Metadata Traceability:
  - Required for <u>ADaM compliance</u>
  - Established by <u>describing the algorithm used</u> or steps taken to derive or populate an analysis value from its immediate predecessor
  - Also used to establish the <u>relationship between an</u> <u>analysis result & analysis dataset(s)</u>

#### Example of Metadata Traceability

	STUDY	PTNO	SEX	SEXDC
1	9999-0001	1	1	Male
2	9999-0001	2	2	Female
3	9999-0001	3	1	Male

		STUDYID	USUBJID	SUBJID	SEX	SEXN	SEXDC
	1	9999-0001	9999-0001-000001	000001	M	1	Male
	2	9999-0001	9999-0001-000002	000002	F	2	Female
Ī	3	9999-0001	9999-0001-000003	000003	М	1	Male

- Data Point Traceability:
  - Should be implemented if practically <u>feasible</u>.
  - To maintain traceability from SDTM to ADaM, SDTM variables that are copied into ADaM datasets should not be modified.
  - Helps to <u>trace the path</u> of a complex data manipulation.
  - Established by providing clear links in the data (e.g., via use of SEQ variable) to the specific data values used as input for an analysis value.

## Example of Datapoint Traceability: LOCF

USUBJID	AVISIT	PARAMCD	AVAL	PARCAT1	PARAMTYP	DTYPE
803 XYZ-20008		GAPS0101		GAPS01		
804 XYZ-20008	Screening	IPSS0101	3	IPSS01		
805 XYZ-20008	Screening	IPSS0102	2	IPSS01		
806 XYZ-20008	Screening	IPSS0103	5	IPSS01		
807 XYZ-20008	Screening	IPSS0104	1	IPSS01		
808 XYZ-20008	Screening	IPSS0105	2	IPSS01		
809 XYZ-20008	Screening	IPSS0106	5	IPSS01		
810 XYZ-20008	Screening	IPSS0107	3	IPSS01		
811 XYZ-20008	Screening	IPSS0108	4	IPSS01		
812 XYZ-20008	Screening	IPSS0199	21	IPSS01	DERIVED	
813 XYZ-20008	Screening	SFI0101	4	SFI01		
814 XYZ-20008	Screening	SFI0102	2	SFI01		
815 XYZ-20008	Screening	SFI0103	2	SFI01		
816 XYZ-20008	Screening	SFI0199	8	SFI01	DERIVED	
817 XYZ-20008	Visit 3	SFI0101	4	SFI01		
818 XYZ-20008	Vîsit 3	SFI0102	3	SFI01		
819 XYZ-20008	Visit 3	SFI0103	3	SFI01		
820 XYZ-20008	Visit 3	SFI0199	10	SFI01	DERIVED	
821 XYZ-20008	Visit 5	SFI0199	10	SFI01	DERIVED	LOCF
822 XYZ-30002		GAPS0101		GAPS01		

#### **ADaM Data Structure**

- Subject Level analysis Structure: One record per subject Eg: ADSL
- Occurrence Data Structure(ODS): Contains all the event domains of SDTM. Eg: ADAE
- Basic Data Structure(BDS): Mostly contain the <u>finding domains</u> of SDTM. Eg: ADLB
- Others

## Standard ADaM Variables

Required Variables: The variable must be included in the dataset

E.g.: STUDYID, USUBJID, SUBJID, SITEID, etc.

<u>Conditionally Required Variables</u>: The variable <u>must be included</u> in the dataset in <u>certain</u> circumstances.

E.g.: FASFL, SAFFL, ITTFL, COMPLFL, etc.

<u>Permissible Variables</u>: The variable <u>may be</u> <u>included</u> in the dataset, but is not required.

E.g.: SITEGRy, TRTxxPN, etc.

#### **ADaM Variable Conversions**

- Variables with xx, y, and zz Parameters:
  - · xx Parameter:

The xx parameter represents a two-digit period. Valid values are 01-99. E.g.: TRTxxP etc.

· y Parameter:

The y parameter represents a single-digit grouping or category, an analysis criterion, or an analysis range. Valid values are 1–9. E.g.:SITEGRy etc.

zz Parameter:

The zz parameter represents a two-digit index for the zzth record selection algorithm. E.g.: ANLzzFL etc.

## **ADaM Variable Conversions**

#### Naming Conventions:

- Names of date imputation flag variables end in DTF and time imputation flag variables end in TMF.
- 2 Character flag (or indicator) variables end in FL and the names of the corresponding numeric flag variables end in FN.
- Any ADaM variable whose name is the same as an SDTM variable must be a copy of the SDTM variable, and its label, meaning, and values must not be modified.
- All ADaM variable names must be no more than 8 characters in length, start with a letter (not underscore), and be comprised only of letters (A-Z), underscore (\_), and numerals (0-9). All ADaM variable labels must be no more than 40 characters in length. All ADaM character variables must be no more than 200 characters in length.

**Note for point 4**: In SDTM if a character variable has length more than 200 then the remaining portion is added in SUPP domain but in ADaM its in the same domain.

#### **ADaM Variable Conversions**

#### Timing Variable Conventions:

- Variables whose names :
  - · end in DT are numeric dates
  - end in DTM are numeric datetimes
  - end in TM are numeric times
  - end in DY are relative day variables
- Names of timing start variables end with:
  - an S followed by the two characters indicating the type of timing (e.g., SDT, STM)
  - an E followed by the two characters indicating the type of timing (e.g., EDT, ETM)

## **ADaM Treatment Variables**

- Treatment variables are required to be present in all analysis datasets
- Planned Treatment (TRTxxP char, TRTxxPN numeric)
- Actual Treatment (TRTxxA char, TRTxxAN numeric)
- Actual Treatment variables are required when it does not matches with the planned treatment

# **ADaM Treatment Variables**

Variable Name	Label	Туре	Source
TRTxxP	Planned Treatment for Period xx	Char	TRTxxP might be derived from the SDTM DM variable ARM. At least TRT01P is required
TRTxxPN	Planned Treatment for Period xx (N)	Num	The numeric code variable for TRTxxP.  One-to-one mapping to TRTxxP within a study
TRTxxA	Actual Treatment for Period xx	Char	Subject-level identifier that represents the actual treatment for the subject for period xx. Required when actual treatment does not match planned.
TRTxxAN	Actual Treatment for Period xx (N)	Num	TRTxxAN Actual Treatment for Period xx (N). One-to-one mapping to TRTxxA within a study

## **ADaM Common Variables**

- USUBJID, STUDYID
- Demographic Variables eg: AGE, RACE, SEX etc.
- Population Flags eg: ITTFL, SAFFL, FASFL etc.
- Baseline Flag variable i.e ABLFL
- Treatment Variables eg:TRTxxP,
   TRTxxA

#### **ADSL**

- One record per subject
- Contains key variables that describe study design and a subject's experience in a trial:
  - Treatment variables planned AND actual
  - Population flags
  - Completion status
  - Important dates
  - Disease history
  - Baseline Information
  - Demographic variables
  - Stratification variables
- Variables integral to design and/or randomization
- Structure and content make this analysis dataset a cornerstone for any trial

## **ADSL**

#### Notes:

- To create this basic ADSL dataset, it is necessary to review the following sections in SAP to understand how the analysis was planned: Population definitions, Schedule of assessments, Definition of baseline values, Analysis covariates and Definition of prior/concurrent medications.
- The Demographics Domain Model (DM) and Exposure (EX) domains from the SDTM model are typically required.
- **Screen Failures**: Whether analysis datasets include data for subjects not analyzed (e.g., screen failures) is a sponsor decision and should be communicated with the reviewers or users of the data. If these data are included, they should be incorporated in the appropriate analysis datasets such as ADSL (as opposed to separate datasets for non-analyzed subjects) using appropriate flag variables to clearly differentiate these records. The metadata must specify that these data are included and how to distinguish them.

## **ADSL**

#### Important Points:

- ADSL dataset is required
- There is only one ADSL per study
- ADSL is one record per USUBJ ID
- All applicable subject-level population flags must be present in ADSL
- ADSL must have at least one population flag
- ADSL must have the variables STUDYID, USUBJ ID, SUBJ ID, SITEID, AGE, AGEU, SEX, RACE, ARM, and these must match SDTM variables in metadata and values
- ADSL must have at least one TRTxxP variable
- Selected trial dates TRTSTDT, TRTENDT

- BDS dataset contains one or more records per subject, per analysis parameter, per analysis timepoint
- BDS Core Variables Classes:
  - Classes Pertaining to Analysis: Analysis Parameter
     What is being analyzed?
  - Analysis Timing
     ADaM time points may not be the same as SDTM time points
  - Analysis Descriptors
     Windowing, type of derivation of observation
  - Classes Pertaining to Traceability
     Data point traceability
    - --SEQ from SDTM
    - » SDTM VISIT/ VISITNUM
    - Source domain, source variable
    - Total scores, sub-scores, etc.

#### Important Points:

- BDS datasets may be derived from all classes of SDTM domains, other ADaM datasets and combination of those
- The four basic components of a BDS are the subject identification, study visit, the data value, and descriptors of that data parameter (PARAM and PARAMCD)
- An application of BDS is analysis data for the primary and secondary endpoints
- BDS contains variables for capturing both the baseline and change from baseline values

#### BDS Parameter Variables

- Parameter (PARAM) and Parameter Code (PARAMCD)

  PARAM) describes, and must uniquely and sufficiently identify, the contents of the relevant analysis value variable AVAL or AVALC. PARAMCD is the code for PARAM is map one to one
- 2. Differences between PARAM and SDTM xxTEST
  SDTM xxTEST is designed to work in conjunction with other variables called qualifiers in order to describe the collected result and PARAM is the only variable that describes AVAL or AVALC, qualifiers are not allowed.
- Parameter Category (PARCATy)

  PARCATy is used to group parameters into categories
- Parameter Type (PARAMTYP)
   Parameter Type (PARAMTYP) flags "derived" parameters

#### Derivation Type (DTYPE)

DTYPE serves two functions: when populated on a given record, (1) it indicates that the record is derived from other records within the same parameter and (2) it identifies the algorithm used to derive the analysis value (AVAL or AVALC) on the record

#### Baseline Type (BASETYPE)

BASETYPE refers to a definition of baseline that characterizes the value of BASE on that row in case of multiple baseline definition

#### Baseline Record Flag (ABLFL)

Baseline flag ABLFL must be set to "Y" on the row whose analysis value AVAL is used to populate BASE for that parameter and subject

#### Analysis Visit (AVISIT)

Analysis visit AVISIT is used to describe the analysis visit or conceptual timepoint characterizing the row

#### BDS Population Flags:

Subject-Level Population Flags: Subject-level population flags are contained in ADSL, and can be copied to BDS datasets.

E.g.: ITTFL

Record-Level Population Flags: Record-level population flag variable names end in RFL. A record-level flag is useful when there are reasons for excluding some records within subject and parameter from the analysis.

E.g.: PPROTRFL⊒'Y"

Parameter-Level Population Flags: Parameter-level population flag variable names end in PFL. A parameter-level flag is useful when observed data influence whether or not a subject is considered to be in a population for reporting purposes.

E.g.: for the analysis of a given parameter, a subject is included in the analysis if (1) the subject is a member of the ITT population, and (2) for the given parameter, the subject has a non-missing baseline value (BASE) and at least one non-missing post-baseline value of AVAL. For the subjects who meet both conditions, the parameter-level Full Analysis Set population flag FASPFL is set to "Y" on all rows for the parameter

## OCCDS and OTHERS

#### OCCDS:

Occurrence Data Structure(OCCDS) is the count of subjects with a given record or term, and often includes a structured hierarchy of dictionary coding categories. Eg: ADAE, ADCM, ADMH

#### OTHERS:

This class has no standard structure. The purpose is to support analyses that cannot be supported by the ADaM dataset structures that have been defined to date. These datasets follow the ADaM fundamental principles and all ADaM datasets and variable naming conventions. Other class is unlimited and grows each time someone needs something that is not yet addressed.

#### Rule 1 :

A parameter-invariant function of AVAL and BASE on the same row that does not involve a transform of BASE should be added as a new column.

**Example of Rule 1**: CHG or PCHG as both are derived from AVAL and BASE on the same row and are calculated for all the rows and there is no transformation of BASE.

	USUBJID	AVISIT	PARAM	PARAMCD	AVAL	PARCAT1	BASE	PARAMTYP	DTYPE	CHG	PCHG
1	XYZ-10001		GAPS01-Overall Efficacy,type 3	GAPS0101		GAPS01					
2	XYZ-10001	Screening	IPSS01-Incomplete emptying	IPSS0101	1	IPSS01	1				
3	XYZ-10001	Screening	IPSS01-Frequency	IPSS0102	1	IPSS01	1				
4	XYZ-10001	Screening	IPSS01-Intermittency	IPSS0103	1	IPSS01	1				
5	XYZ-10001	Screening	IPSS01-Urgency	IPSS0104	2	IPSS01	2				
6	XYZ-10001	Screening	IPSS01-Weak stream	IPSS0105	3	IPSS01	3				
7	XYZ-10001	Screening	IPSS01-Straining	IPSS0106	3	IPSS01	3				
8	XYZ-10001	Screening	IPSS01-Nocturia	IPSS0107	2	IPSS01	2				
9	XYZ-10001	Screening	IPSS01-Feel about Life	IPSS0108	3	IPSS01	3				
10	XYZ-10001	Screening	IPSS01- Total Score	IPSS0199	13	IPSS01	13	DERIVED			
11	XYZ-10001	Visit 5	IPSS01-Incomplete emptying	IPSS0101	0	IPSS01	1				
12	XYZ-10001	Visit 5	IPSS01-Frequency	IPSS0102	1	IPSS01	1				
13	XYZ-10001	Visit 5	IPSS01-Intermittency	IPSS0103	1	IPSS01	1				
14	XYZ-10001	Visit 5	IPSS01-Urgency	IPSS0104	2	IPSS01	2				
15	XYZ-10001	Visit 5	IPSS01-Weak stream	IPSS0105	1	IPSS01	3				
16	XYZ-10001	Visit 5	IPSS01-Straining	IPSS0106	1	IPSS01	3				
17	XYZ-10001	Visit 5	IPSS01-Nocturia	IPSS0107	2	IPSS01	2				
18	XYZ-10001	Visit 5	IPSS01-Feel about Life	IPSS0108		IPSS01	3				
19	XYZ-10001	Visit 5	IPSS01- Total Score	IPSS0199	8	IPSS01	13	DERIVED		-5	-38.46153
20	XYZ-10001	Screening	SFI01-Lack of Sex Drive	SFI0101	4	SFI01	4				
21	XYZ-10001	Screening	SFI01-Ability to get and keep Erections	SFI0102	2	SFI01	2				
22	XYZ-10001	Screening	SFI01-Ejaculation Problem	SFI0103	1	SFI01	1				
23	XYZ-10001	Screening	SFI01- Total Score	SFI0199	7	SFI01	7	DERIVED			
24	XYZ-10001	Visit 3	SFI01-Lack of Sex Drive	SFI0101	4	SFI01	4				
25	XYZ-10001	Visit 3	SFI01-Ability to get and keep Erections	SFI0102	2	SFI01	2				
26	XYZ-10001	Visit 3	SFI01-Ejaculation Problem	SFI0103	1	SFI01	1				
27	XYZ-10001	Visit 3	SFI01- Total Score	SFI0199		SFI01	7	DERIVED		0	
28	XYZ-10001	Visit 5	SFI01-Lack of Sex Drive	SFI0101		SFI01	4			-	
29	XYZ-10001	Visit 5	SFI01-Ability to get and keep Erections	SFI0102	4	SFI01	2			-	
30	XYZ-10001	Visit 5	SFI01-Ejaculation Problem	SFI0103	4	SFI01	1				
31	XYZ-10001	Visit 5	SFI01- Total Score	SFI0199	12	SFI01	7	DERIVED		5	71.428571
32	XYZ-10002		GAPS01-Overall Efficacy,type 3	GAPS0101		GAPS01					

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#### Rule 2 :

A transformation of AVAL that does not meet the conditions of Rule 1 should be added as a new parameter, and AVAL should contain the transformed value

#### Rule 3 :

A function of one or more rows within the same parameter for the purpose of creating an analysis timepoint should be added as a new row for the same parameter.

#### Rule 4 :

A function of multiple rows within a parameter should be added as a new parameter.

#### Rule 5 :

A function of more than one parameter should be added as a new parameter

Example of rule 2,3,4,5: The table in the next slide contain a variable PARAM which has the values "SFI01- Total Score" and "IPSS01- Total Score" are the function of more than one row or parameter.

l	USUBJID	AVISIT	PARAM	PARAMCD	AVAL	BASE	PARAMTYP	DTYPE	CHG	PCHG
1267 XYZ	Z-60014		GAPS01-Overall Efficacy,type 3	GAPS0101						
1268 XYZ	Z-60014	Screening	IPSS01-Incomplete emptying	IPSS0101	2	2				
1269 XYZ	Z-60014	Screening	IPSS01-Frequency	IPSS0102	2	2				
1270 XYZ	Z-60014	Screening	IPSS01-Intermittency	IPSS0103	3	3				
1271 XYZ	Z-60014	Screening	IPSS01-Urgency	IPSS0104	2	2				
1272 XYZ	Z-60014	Screening	IPSS01-Weak stream	IPSS0105	1	1				
1273 XYZ	Z-60014	Screening	IPSS01-Straining	IPSS0106	1	1				
1274 XYZ	Z-60014	Screening	IPSS01-Nocturia	IPSS0107	2	2				
1275 XYZ	Z-60014	Screening	IPSS01-Feel about Life	IPSS0108	4	4				
1276 XYZ	Z-60014	Screening	IPSS01- Total Score	IPSS0199	13	13	DERIVED			
1277 XYZ	Z-60014	Screening	SFI01-Lack of Sex Drive	SFI0101	2	2				
1278 XYZ	Z-60014	Screening	SFI01-Ability to get and keep Erections	SFI0102	2	2				
1279 XYZ	Z-60014	Screening	SFI01-Ejaculation Problem	SFI0103	2	2				
1280 XYZ	Z-60014	Screening	SFI01- Total Score	SFI0199	6	6	DERIVED			
1281 XYZ	Z-60014	Visit 3	SFI01-Lack of Sex Drive	SFI0101	3	2				
1282 XYZ	Z-60014	Visit 3	SFI01-Ability to get and keep Erections	SFI0102	3	2				
1283 XYZ	Z-60014	Visit 3	SFI01-Ejaculation Problem	SFI0103	3	2				
1284 XYZ	Z-60014	Visit 3	SFI01- Total Score	SFI0199	9	6	DERIVED		3	
1285 XYZ	Z-60014	Visit 5	SFI01- Total Score	SFI0199	9	6	DERIVED	LOCF	3	
1286 XYZ	Z-60015		GAPS01-Overall Efficacy,type 3	GAPS0101						
1287 XYZ	Z-60015	Screening	IPSS01-Incomplete emptying	IPSS0101	2	2				
1288 XYZ	Z-60015	Screening	IPSS01-Frequency	IPSS0102	3	3				
1289 XYZ	Z-60015	Screening	IPSS01-Intermittency	IPSS0103	1	1				
1290 XYZ	Z-60015	Screening	IPSS01-Urgency	IPSS0104	2	2				
1291 XYZ	Z-60015	Screening	IPSS01-Weak stream	IPSS0105	2	2				
1292 XYZ	Z-60015	Screening	IPSS01-Straining	IPSS0106	2	2				
1293 XYZ	Z-60015	Screening	IPSS01-Nocturia	IPSS0107	3	3				
	Z-60015	Screening	IPSS01-Feel about Life	IPSS0108	4	4				
	Z-60015	Screening	IPSS01- Total Score	IPSS0199	15	15	DERIVED			
1296 XYZ	Z-60015	Visit 5	IPSS01-Incomplete emptying	IPSS0101	3	2				
	Z-60015	Visit 5	IPSS01-Frequency	IPSS0102	2	3				
	Z-60015	Visit 5	IPSS01-Intermittency	IPSS0103	3	1				

#### **Rule 6**:

When there is more than one definition of baseline, each additional definition of baseline requires the creation of its own set of rows.

	<b>USUBJID</b>	1	AVISITN	<b>A</b>	PARAMCD	1	AVAL	△ B	ASETYPE	1	ATPTN	1	APERIOD	(1)	ABLFL
1	XYZ-123-001-001		0	HR			60	STUDY	LEVEL						
2	XYZ-123-001-001		1	HR			55	STUDY	LEVEL		-60	0	1		
3	XYZ-123-001-001		1	HR			55	STUDY	LEVEL		-	5	1	Y	
4	XYZ-123-001-001		1	HR			58	STUDY	LEVEL			5	1		
5	XYZ-123-001-001		1	HR			62	STUDY	LEVEL		6	0	1		
6	XYZ-123-001-001		2	HR			59	STUDY	LEVEL		-60	0	2		
7	XYZ-123-001-001		2	HR			60	STUDY	LEVEL		-	5	2		
8	XYZ-123-001-001		2	HR			58	STUDY	LEVEL			5	2		
9	XYZ-123-001-001		2	HR			57	STUDY	LEVEL		6	0	7	)	
10	XYZ-123-001-001		2	HR			59	PERIO	D 2		-	-	2	2	
11	XYZ-123-001-001		2	HR			60	PERIO	D 2		-	5	2	Y	
12	XYZ-123-001-001		2	HR			58	PERIO	D 2			5	2	)	
13	XYZ-123-001-001		2	HR			57	PERIO	D 2		6	0	2	2	

# \*Thank You for your attention

