

## What is RE domain?

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### ABSTRACT

Asthma, chronic obstructive pulmonary disease (COPD), and other lung related diseases make up one of the most important areas in clinical trials. Respiratory System Findings (RE domain) was introduced in the Therapeutic Area Data Standards User Guide for Asthma in 2013 and the Therapeutic Area Data Standards User Guide for Chronic Obstructive Pulmonary Disease in 2016. The SDTMIG 3.3 has included it as one of the new domains since 2015. The controlled terminology has included the Respiratory Test Code and Respiratory Test Name for years. Since the SDTMIG 3.3 will be finalized in a time to come, now is a good time to review what RE domain is for and understand its nuances. Some useful background of Respiratory will be introduced and a suggested way for Data Management to handle the controlled terminology will be shared as well.

### INTRODUCTION

Respiratory System Findings (RE) is a findings domain that contains physiological and morphological findings related to the respiratory system. RE was suggested from few TAUGs and includes the organs that are involved in breathing such as the nose, throat, larynx, trachea, bronchi and lungs. This draft version of the domain is intended for inclusion in SDTM Implementation Guide 3.3 which is found in CDISC Wiki.

Since the SDTMIG 3.3 will likely be finalized in the near future, it is a good time to review some details of RE domain and understand its nuances. The required and expected variables as well as other permissible variables will be reviewed.

Note that ERT is a leading cloud platform solutions provider that captures quality efficacy and safety endpoints, harmonizes data from any clinical source system, and delivers real-time insights for optimum trial performance.

### Required variables in RE

RE has six required variables below, similar to most findings Domains:

STUDYID	Study Identifier	Char		Identifier	Unique identifier for a study.	Req
DOMAIN	Domain Abbreviation	Char	RE	Identifier	Two-character abbreviation for the domain.	Req
USUBJID	Unique Subject Identifier	Char		Identifier	Identifier used to uniquely identify a subject across all studies for all applications or submissions involving the product.	Req
RESEQ	Sequence Number	Num		Identifier	Sequence number to ensure uniqueness of records within a dataset for a subject. May be any valid number (including decimals) and does not have to start at 1.	Req
RETESTCD	Short Name of Respiratory Test	Char	(RETESTCD)	Topic	Short name of the measurement, test, or examination. It can be used as a column name when converting a dataset from a vertical format to a horizontal format. The value in RETESTCD cannot be longer than 8 characters, nor can it start with a number (e.g., "1TEST" is not valid). RETESTCD cannot contain characters other than letters, numbers, or underscores. Examples: "FEV1", "FVC".	Req
RETEST	Name of Respiratory Test	Char	(RETEST)	Synonym Qualifier	Verbatim name of the test or examination used to obtain the measurement or finding. The value in RETEST cannot be longer than 40 characters. Examples: "Forced Expiratory Volume in 1 Second", "Forced Vital Capacity".	Req

**STUDYID**, **DOMAIN**, **USUBJID**, and **RESEQ** are required Identifier variables in all domains based on one of the three general observation classes, i.e. The Interventions Observations Class, The Events Observation Class, and The Findings Observation Class per the chapter 2.2.4 in SDTM v1.4 and above SDTM versions.

**RETESTCD** is the topic variable of RE and **RETEST** is the Synonym Qualifier of RETESTCD. Both of RETESTCD and RETEST are subject to follow the CDISC Controlled Terminologies. The detail of how to handle these two variables will be discussed in later section.

### Expected variables in RE

There are five expected variables in RE:

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REORRES	Result or Finding in Original Units	Char		Result Qualifier	Result of the procedure measurement or finding as originally received or collected.	Exp
RESTRESC	Character Result/Finding in Std Format	Char		Result Qualifier	Contains the result value for all findings, copied or derived from REORRES in a standard format or in standard units. RESTRESC should store all results or findings in character format; if results are numeric, they should also be stored in numeric format in RESTRESN.	Exp
RELOBXFL	Last Observation Before Exposure Flag	Char	(NY)	Record Qualifier	Operationally-derived indicator used to identify the last non-missing value prior to RFXSTDTC. The value should be "Y" or null.	Exp
VISITNUM	Visit Number	Num		Timing	Clinical encounter number. Numeric version of VISIT, used for sorting.	Exp
REDTC	Date/Time of Collection	Char	ISO 8601	Timing	Date/time of procedure or test.	Exp

**REORRES** and **RESTRESC** are Result Qualifiers which describe the specific results associated with the topic variable in Respiratory System Findings.

**VISITNUM** is a Timing Variable. It is the numeric version of VISIT variable and is used for sorting.

**REDTC** is a Timing Variable as well. It is a Character variable with Collection date and time of an observation and is represented in ISO 8601 character format.

**RELOBXFL** is a Record Qualifier and has been introduced in SDTM v1.5. RELOBXFL is an Operationally-derived indicator. It is used to identify the last non-missing value prior to RFXSTDTC. The valid values are "Y" or null. RFXSTDTC is the first date/time of exposure to any protocol-specified treatment or therapy. RELOBXFL and RFXSTDTC will be used to address the need for a consistent definition of a value that can serve as a reference with which to compare post-treatment values.

## Selected Permissible variables in RE

This section is for the explanation of some of permissible variables selected as an attempt to help the readers with less experience with Respiratory Domain.

**SPDEVID** is an Identifier variable which is for Sponsor-defined identifier for a device. This is used for EG and RE domains. This variable is explained further in the first example (RE1).

**RECAT** is a Grouping Qualifier to be used to categorize observations across subjects.

**REPOS** is a Record Qualifier to capture the Position of the subject during a measurement or examination. Examples include "SUPINE", "STANDING", "SITTING", which are from OID CL.C71148.POSITION of the CDISC Controlled Terminologies.

**REORREF** and **RESTREFN** are Variable Qualifier variables which are populated with the predicted reference value. These variables are needed because pulmonary function test results are compared to a single predicted normal value rather than to a normal range. There are multiple publications of predicted values available; these values may be calculated online. However, when maintaining continuity is important, the National Health and Nutrition Examination Survey (NHANES) III reference values are most appropriate to apply as they have been recommended for North America in 2005 ATS/ERS documents. Since lung function depends on body dimensions and physiological changes throughout growth, the values depend on such factors as age, sex, weight and ethnicity. It is worth noting that Age is a part of PHI and that there have been many discussions how to capture/calculate Age since the recent introduction of GDPR and other PHI rules.

**REMETHOD** is a Record Qualifier. It is the Method used to create the result. It is from CL.C85492.METHOD of the CDISC Controlled Terminologies.

**REREPNUM** is a Record Qualifier. It is the instance numbers of a test that is repeated within a given time frame for multiple measurements of pulmonary function. Normally 1st, 2nd, and 3rd attempts are represented in the variable REREPNUM. One of the three attempts will be flagged as the best result in BRESFL, which is Best Result Flag.

**IRESFL** Best test review set unacceptable: Indicates if test set such as FEV1 and FVC is unacceptable or not. Normally, the grading from OverRead provides the values of acceptable, borderline, and unacceptable.

## Examples

Spirometry testing is highly dependent on subject's effort. Normally the test is repeated three times and up to eight times to ensure reproducibility. Therefore, spirometry cannot be used on subjects who cannot comprehend and follow the instructions given, including young children.

When spirometry tests are performed, the subject usually makes 3 to 8 efforts, each of which produces results. Since only the best result for each test is used in analyses there are two ways to collect and create RE domain. In Example 1, the sponsor collected only the best results. On the other hand, in Example 2, all attempts were collected.

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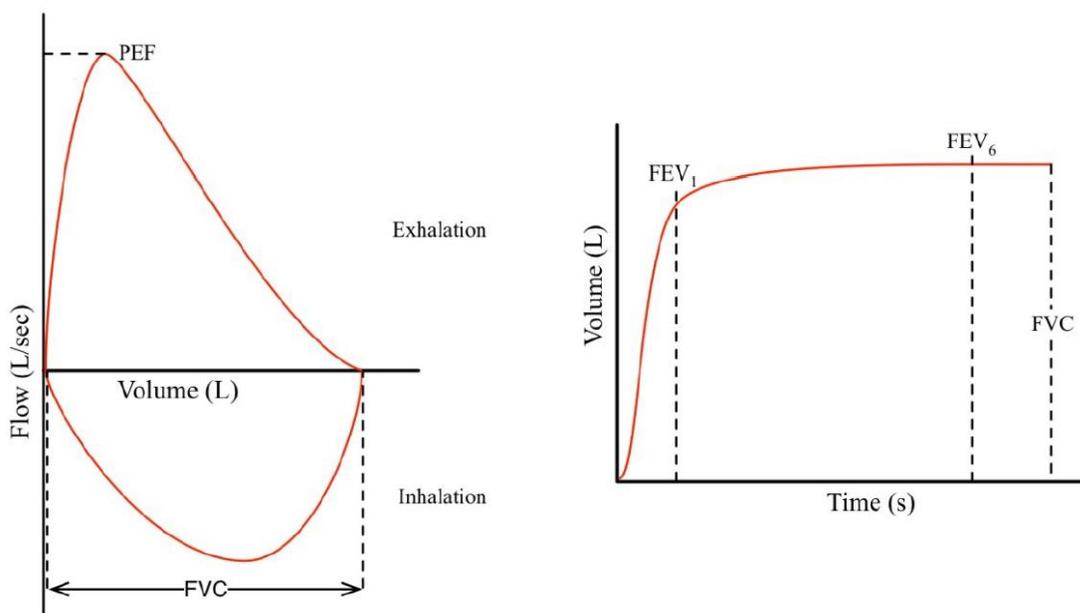
Note that the examples show results from several spirometry tests using either a spirometer or a peak flow meter.

**Example 1**

re.xpt

Row	STUDYID	DOMAIN	USUBJID	SPDEVID	RESEQ	RETESTCD	RETEST	REORRES	REORRESU	REORREF	...	VISITNUM	VISIT	REDTC
1	XYZ	RE	XYZ-001-001	ABC001	1	FEV1	Forced Expiratory Volume in 1 Second	2.73	L	3.37		2	VISIT 2	2013-06-30
2	XYZ	RE	XYZ-001-001	ABC001	2	FVC	Forced Vital Capacity	3.91	L	3.86		2	VISIT 2	2013-06-30
3	XYZ	RE	XYZ-001-001	ABC001	3	FEV1PP	Percent Predicted FEV1	81	%			2	VISIT 2	2013-06-30
4	XYZ	RE	XYZ-001-001	ABC001	4	FVCP	Percent Predicted Forced Vital Capacity	101.3	%			2	VISIT 2	2013-06-30
5	XYZ	RE	XYZ-001-001	DEF999	5	PEF	Peak Expiratory Flow	6.11	L/s	7.33		4	VISIT 4	2013-07-17

A flow-volume loop and a volume-time curve are shown the Figure 1 below. In the flow-volume loop, which is left side of the Figure 1, volume is shown on the x-axis; therefore, volume measurements such as FVC are measured horizontally. Flow (L/sec) is shown on the y-axis, with negative values during inspiration and positive values during expiration. Peak expiratory flow (rate) is measured vertically at the highest point of the loop. FEV1 is derived from the volume-time curve. FEV6 is Forced Expiratory Volume in 6 seconds.



**Figure 1. Flow-Volume Loop and Volume-Time Curve\***

\* Therapeutic Area Data Standards User Guide for Chronic Obstructive Pulmonary Disease

**Rows 1-2:**

The results for the spirometry tests are collected in FEV1 and FVC.

The predicted values in REORREF are calculated in the device based on the subject's age, sex, weight, and ethnicity.

The spirometer used in the tests is identified by the SPDEVID.

**Rows 3-4:**

The results for FEV1 and FVC as percentages of the predicted values are calculated. Note that the results are derived but output by the spirometer device. REORREF should be null as there are no reference results for percent predicted tests.

**Row 5:**

The result of the peak flow meter test is collected in PEF.

The predicted values is calculated and collected in REORREF.

Since the result is obtained with a different device, a peak flow meter, this is identified by the SPDEVID.

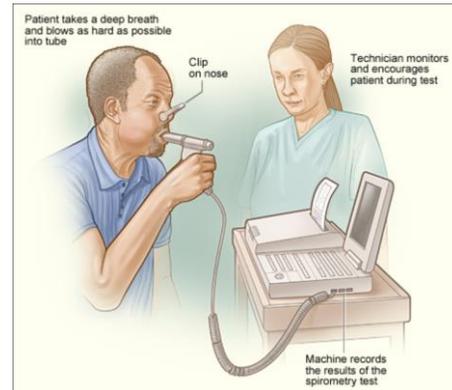
What is RE domain?, continued

di.xpt

Row	STUDYID	DOMAIN	SPDEVID	SPSEQ	DIPARMCD	DIPARM	DIVAL
1	XYZ	DI	ABC001	1	DEVTYPE	Device Type	SPIROMETER
2	XYZ	DI	DEF999	1	DEVTYPE	Device Type	PEAK FLOW METER



<https://www.ert.com/safety-efficacy/respiratory/>



[https://en.wikipedia.org/wiki/Spirometer#/media/File:Spirometry\\_NIH.jpg](https://en.wikipedia.org/wiki/Spirometer#/media/File:Spirometry_NIH.jpg)

**Figure 2.** Example spirometer device and an image for test



<https://www.ert.com/safety-efficacy/respiratory/>



<https://www.aboutkidshealth.ca/Article?contentid=1486&language=English>

**Figure 3.** Example peak flow meter device and an image for test

### Example 2

This example focuses on a subject with four attempts at the FEV1 pulmonary function test. Data about all attempts were collected. Since the best result to be used in analyses, the spirometry report included an indicator of which was the best result. The report also included an indicator that one of the attempts was considered to have produced an inadequate result with the related reasons which is shown in suppre.xpt.re.xpt

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Row	STUDYID	DOMAIN	USUBJID	SPDEVID	RESEQ	RETESTCD	RETEST	REORRES	REORRESU	RESTRESN	RESTRESU	REREPNUM	VISITNUM	VISIT	REDTC
1	XYZ	RE	XYZ-001-001	ABC001	1	FEV1	Forced Expiratory Volume in 1 Second	1.94	L	1.94	L	1	2	VISIT 2	2013-04-23
2	XYZ	RE	XYZ-001-001	ABC001	2	FEV1	Forced Expiratory Volume in 1 Second	1.88	L	1.88	L	2	2	VISIT 2	2013-04-23
3	XYZ	RE	XYZ-001-001	ABC001	3	FEV1	Forced Expiratory Volume in 1 Second	1.88	L	1.88	L	3	2	VISIT 2	2013-04-23
4	XYZ	RE	XYZ-001-001	ABC001	4	FEV1	Forced Expiratory Volume in 1 Second	1.57	L	1.57	L	4	2	VISIT 2	2013-04-23

**Rows 1-3:**

A subject can test 3 to 8 times usually. The first three individual test results for FEV1 are shown as measured by spirometry.

**Row 4:**

The same subject's fourth test result for FEV1 is shown. Note that this result is much less than the others.

suppre.xpt

Supplemental qualifiers were used to indicate which was the best result and to provide information on the attempt that was considered to produce inadequate results.

Row	STUDYID	RDOMAIN	USUBJID	IDVAR	IDVARVAL	QNAM	QLABEL	QVAL	QORIG	QVAL
1	XYZ	RE	XYZ-001-001	RESEQ	1	BRESFL	Best Result Flag	Y	CRF	
2	XYZ	RE	XYZ-001-001	RESEQ	4	IRESFL	Inadequate Results Flag	Y	CRF	
3	XYZ	RE	XYZ-001-001	RESEQ	4	IRREA1	Inadequate Result Reason 1	COUGHING WAS DETECTED IN THE FIRST PART OF THE EXPIRATION	CRF	
4	XYZ	RE	XYZ-001-001	RESEQ	4	IRREA2	Inadequate Result Reason 2	FEV1 REPEATABILITY IS UNACCEPTABLE	CRF	

**Row 1:**

The record with RESEQ = "1" was the best test result, indicated by Best Result Flag, BRESFL = "Y".

**Rows 2-4:**

The record with RESEQ = "4" was inadequate since Inadequate Results Flag, IRESFL = "Y".

In addition, the two reasons why this was the case are represented by QNAM = "IRREA1" and "IRREA2".

**Terminology for RETESTCD and RETEST**

The topic variable, RETESTCD and the synonym variable, RETEST in RE follow CDISC SDTM Controlled Terminology (CT).

Here is an easy way to use the CT by using JMP.

1. Find the current version from the CDISC SDTM directory on an NCI File Transfer Protocol (FTP) site:
2. <https://evs.nci.nih.gov/ftp1/CDISC/SDTM/>
  - SDTM Terminology.html is used for this example. However there are a few different types of files on can down load from the NIH site.
3. Open the SDTM Terminology.html in a Web Brower and copy the address: <https://evs.nci.nih.gov/ftp1/CDISC/SDTM/SDTM%20Terminology.html>
4. Open JMP and select "internet open" from the File menu, paste the NIH address, and click "OK":



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OID	Name (CDISC Submission Value)
21980	CLC111106.RETESTCD
21981	Respiratory Test Code (RETESTCD)
21982	DLCO
21983	DLCOHC
21984	DLCOHCPP
21985	DLCOHCVA
21986	DLCOHVAP
21987	DLCOM
21988	DLCOPP
21989	DLCOVA
21990	DLCOVAPP
21991	ELSTNCE
21992	ERV
21993	ERVPP
21994	EV_05FVC
	EV_1FVC

8. Select “Subset” from the Tables menu. Enter “RETESTCD” in the “Output table name” text box and click “OK” on the pop-up window:

Subset - JMP

Creates a new data table from the selected rows and columns of the source data table, or within each group generated with the 'by' columns.

Subset by

Rows

All rows

Selected Rows

Random - sampling rate : 0.5

Random - sample size : 1000

Stratify

Columns

All columns  Selected columns

Keep by columns

Output table name:

Link to original data table

Copy formula

Suppress formula evaluation

Keep dialog open

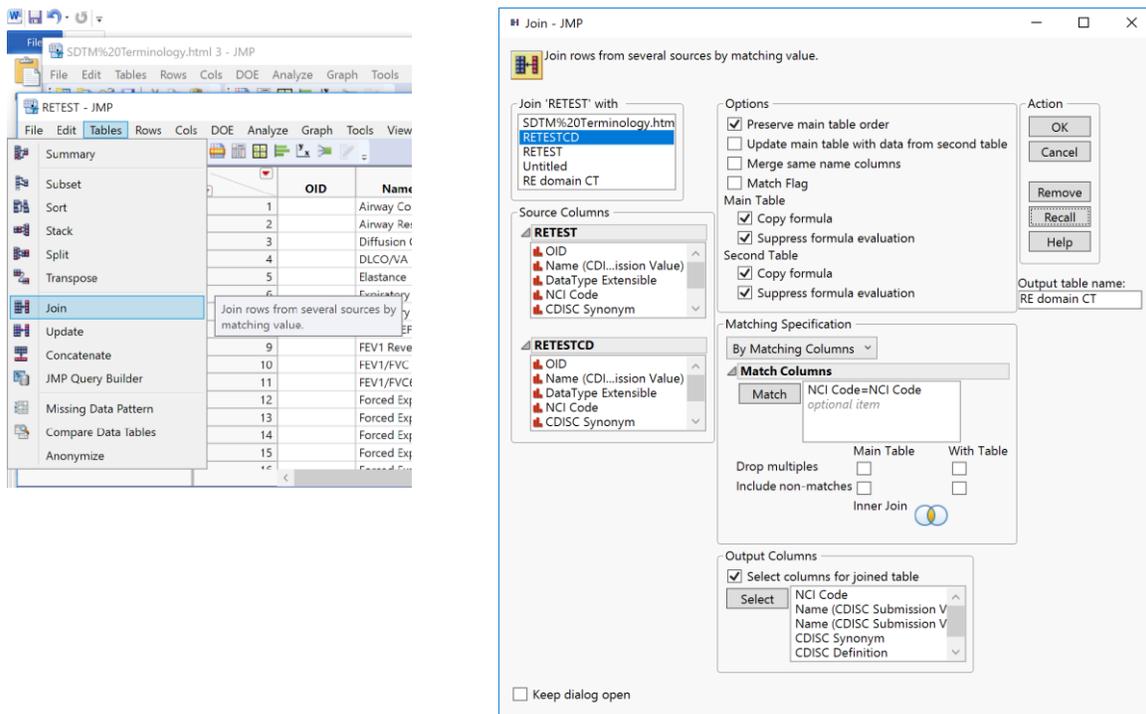
Buttons: OK, Cancel, Recall, Help, Save Default Options

9. Create “RETEST” table by following the step 5, 6, and 7

10. Select “Join” from the Tables menu. Select “NCI Code” from both fo RETEST and RETESTCD for “Match Columns”. Select “NCI Code”, “Name (CDISC Submission Value) of RETEST, “Name (CDISC Submission

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Value) of RETESTCD”, “CDISC Synonym”, “CDISC Definition”, “Preferred Term” for “Output Columns” and click “OK”. Type “RE domain CT” in the “Output table name.” text box.



11. Now the RE subset of CT has been created with TESTCD and TEST.

NCI Code	Name (CDISC Submission Value) of RETEST	Name (CDISC Submission Value) of RETESTCD	CDISC Synonym
1 C124422	Airway Conductance	GAW	Airway Conductance
2 C120927	Airway Resistance	RAW	Airway Resistance
3 C38083	Diffusion Capacity of Lung for CO	DLCO	Diffusion Capacity of Lung for CO; TLCO; Transfer Factor of Lun...
4 C120830	DLCO/VA	DLCOVA	DLCO/VA
5 C135493	Elastance	ELSTNCE	Elastance
6 C111200	Expiratory Reserve Volume	ERV	Expiratory Reserve Volume
7 C147484	Expiratory Vital Capacity	EVC	Expiratory Vital Capacity
8 C139249	FEV at PEF	FEV_PEF	FEV at PEF; Forced Expiratory Volume at Peak Expiratory Flow
9 C112285	FEV1 Reversibility	FEV1REV	FEV1 Reversibility
10 C111359	FEV1/FVC	FEV1FVC	FEV1/FVC
11 C123565	FEV1/FVC6	FEV1FVC6	FEV1/FVC6
12 C119545	Forced Expiratory Flow 25-75%	FEF2575	Forced Expiratory Flow 25-75%
13 C139253	Forced Expiratory Flow 50%	FEF50	Forced Expiratory Flow 50%
14 C139250	Forced Expiratory Flow in 0.05 Second	FEF_05	Forced Expiratory Flow in 0.05 Second

- Note that CDISC Synonym, CDISC Definition, and Preferred Term are identical between RETESTCD and RETEST.

## CONCLUSION

AMERICAN THORACIC SOCIETY posted Recommendations for a Standardized Pulmonary Function Report in December 2017. One of the conclusions in this document was “A uniform format for the presentation of PFT results in reports to users and in the medical record can reduce potential miscommunication or misunderstanding.” Therefore, now is a good timing to invest some time to understand RE domain. Understanding the contents of RE domain should help statisticians, data managers, and other non-medical staff to learn about Pulmonary Functional Test and handle the data with good quality. As always few people without enough experiences in medical areas will find it easy to understand the detail of any domain in CDISC. Since RE domain format itself are not far different from other finding domains, the author has focused on some of major TEST names and the background of introducing some variables so that any beginners in RE domain may understand the nuisances better.

The last section was delegated how to handle RE domain Controlled Terminology easily that would help Clinical Data Management staff to maintain the standard terminology. Note that both of RETESTCD and RETEST are extensible so that sponsor specific additional values can be added. However, it is always better way to use the controlled terminology unless there are no synonyms available in CT. If any a new terminology is used, the sponsor specific value must be marked as an extended value in define.xml.

## REFERENCES

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## ACKNOWLEDGMENTS

I would like to thank Bob Jacobs for his continuing support of the work on CDISC.

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