CDISC Asthma Therapeutic Area Data Standards User Guide – Yes, it is interesting!

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cros nt

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- Rather dry – no statistics here
- Standards matter
- Must have been a lot of hard work!

What I am not going to talk about

RE – Specification for Respiratory System Findings Domain Model

re.xpt, Respiratory Physiology — Findings, Version 3.x.x. One record per finding or result per time point per visit per subject, Tabulation.

Variable Name	Variable Label	Type	Controlled Terms, Codelist or Format	Role	CDISC Notes	Core
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
SPDEVID	Sponsor Device Identifier	Char		Identifier	Sponsor-defined identifier for the device	Perm
RESEQ	Sequence Number	Num		Identifier	Sequence number to ensure uniqueness of subject records within a domain.	Req
REGRPID	Group ID	Char		Identifier	Used to tie together a block of related records in a single domain for a subject.	Perm
REREFID	Reference ID	Char		Identifier	Internal or external procedure identifier.	Perm
RESPID	Sponsor-Defined Identifier	Char		Identifier	Additional reference number. Perhaps pre-printed on the CRF as an external identifier or defined in the sponsor's operational database.	Perm
RETESTCD	Test or Examination Short Name	Char	(RETESTCD)		Line number from the procedure or test page. Short name of the measurement, test, or examination described in RETEST. It can be used as a column name when converting a dataset from a vertical to a horizontal format. The value in RETESTCD cannot be longer than 8 characters, nor can it start with a number (e.g., "1TEST"). RETESTCD cannot contain characters other than letters, numbers, or underscores. Examples: FEV1, FVC	Req
RETEST	Test or Examination Name		(TEST)	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
RECAT	Category for Test	Char	*	Grouping Qualifier	Used to categorize observations across subjects.	Perm
RESCAT	Subcategory for Test	Char	*	Grouping Qualifier	A further categorization.	Perm
REPOS	Position of Subject	Char	(POSITION)	Record Qualifier	Position of the subject during a measurement or examination. Examples: SUPINE, STANDING, SITTING.	Perm

Or at least not too much...

What I am going to talk about

- Background
- Purpose, focus and contents
- Examples
- What next?

‘In the bad old days…’

- Datasets from different studies were different
- Had to understand structure/set-up before we could think about running the analyses
- Took time
- Solution?

‘In the good old days…’

- Used to program as well as analyse
- Heavily involved in the data, got to know and understand it
- Now, in some cases, statisticians barely touch it!
- Solution?

We should know our…

Asthma Therapeutic Area User Guide (TAUG-Asthma)

- Released in December 2013 in order to improve standardisation of asthma studies
- Designed to help those developing and/or using CDISC standards
- Explain typical data collected in asthma studies
- Developed under the Coalition for Accelerating Standards and Therapies (CFAST) initiative

CFAST Partnership

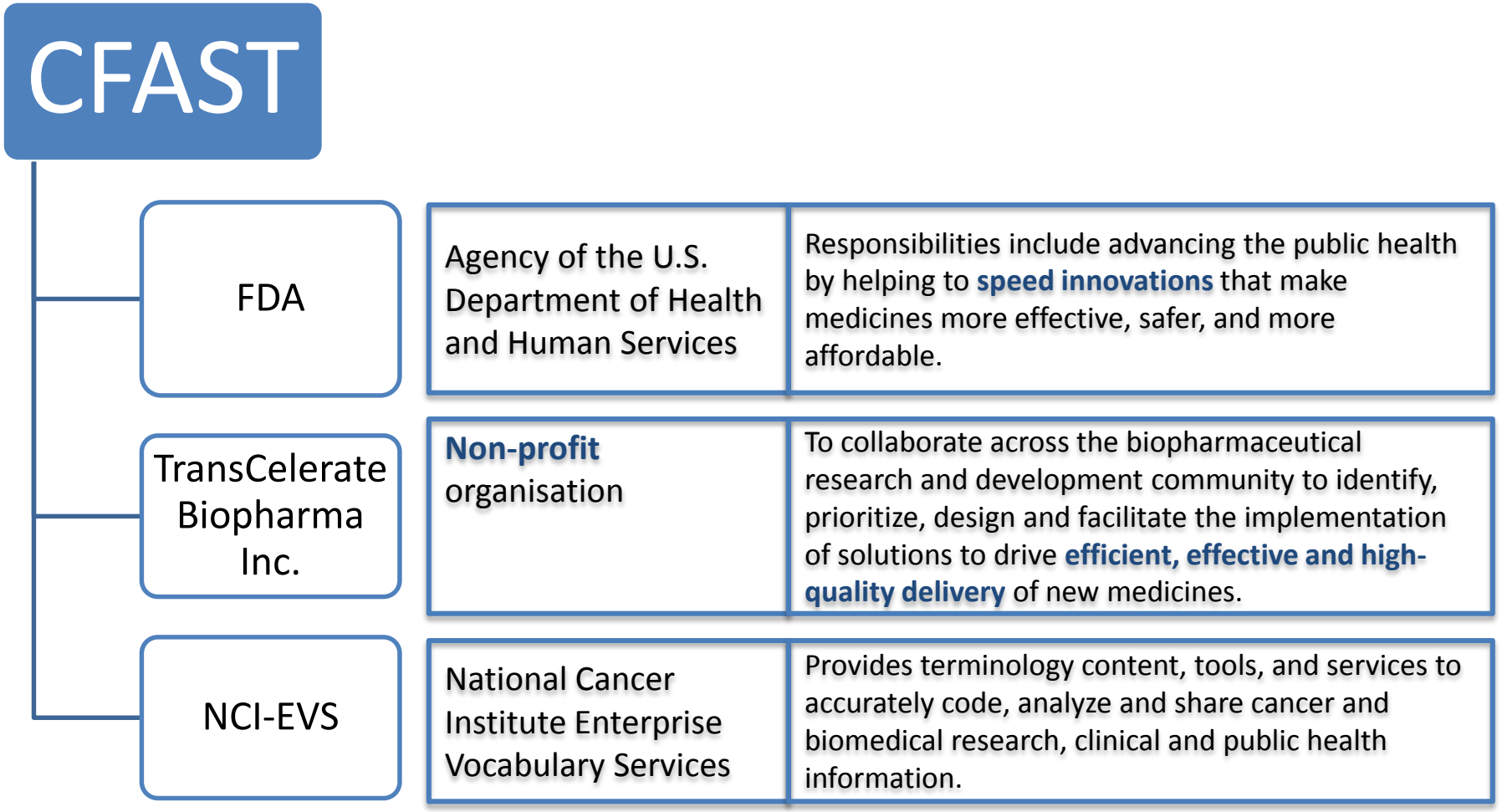
CFAST

Coalition for Accelerating Standards and Therapies

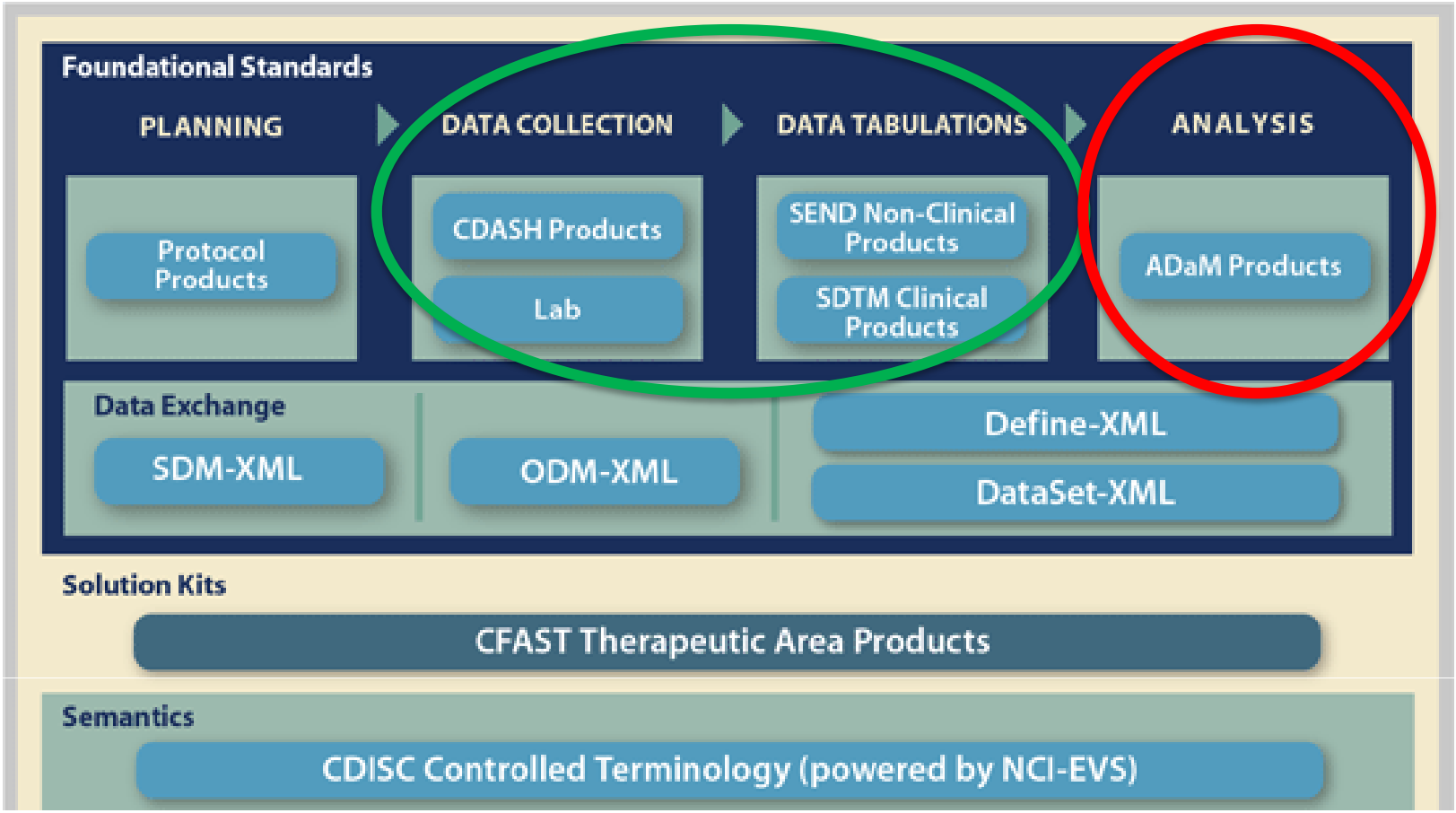
An initiative formed to accelerate clinical research and medical product development by creating and maintaining data standards, tools and methods for conducting research in therapeutic areas that are important to public health

CDISC	Global, open, multidisciplinary, **non-profit** organisation	To develop and support global, platform-independent data standards that enable information system interoperability to **improve medical research** and related areas of healthcare
C-Path	Independent, **non-profit**, public-private partnership with the FDA	To improve human health and well-being by developing new technologies and methods to **accelerate the development and review of medical products**

CFAST Major Collaborators



CDISC Standards & TAUG-Asthma



TAUG-Asthma: Purpose

… describes the **most common data** needed for asthma studies, so that those handling the data (e.g., data managers, **statisticians**, programmers) **understand the data** and can apply standards appropriately.

Descriptions … include **clinical situations** from which the data arise, and the **reasons** these data are **relevant** for asthma.

… to **define research concepts unambiguously**, so that consistent terminology can be used in asthma studies to **enable aggregation and comparison of data** across studies and drug programs.

TAUG-Asthma: Focus

- Focuses primarily on pulmonary physiology, exacerbations and biomarkers
- Less discussion of symptoms, QoL, asthma control and healthcare utilization
- Also covers allergen skin tests, as well as a subject's history of asthma and some elements of routinely collected data

TAUG-Asthma: Table of Contents

Section 1 Introduction

Section 2: Subject and Disease Characteristics

- Data usually collected once at beginning of the study (e.g. asthma history)

Section 3: Disease Assessments

- Data used to evaluate disease severity, control or progression (e.g. pulmonary function tests)

Section 4: Routine Data

- Background data (e.g. AEs/conmeds of special interest)

Example: Exhaled nitric oxide (FeNO)

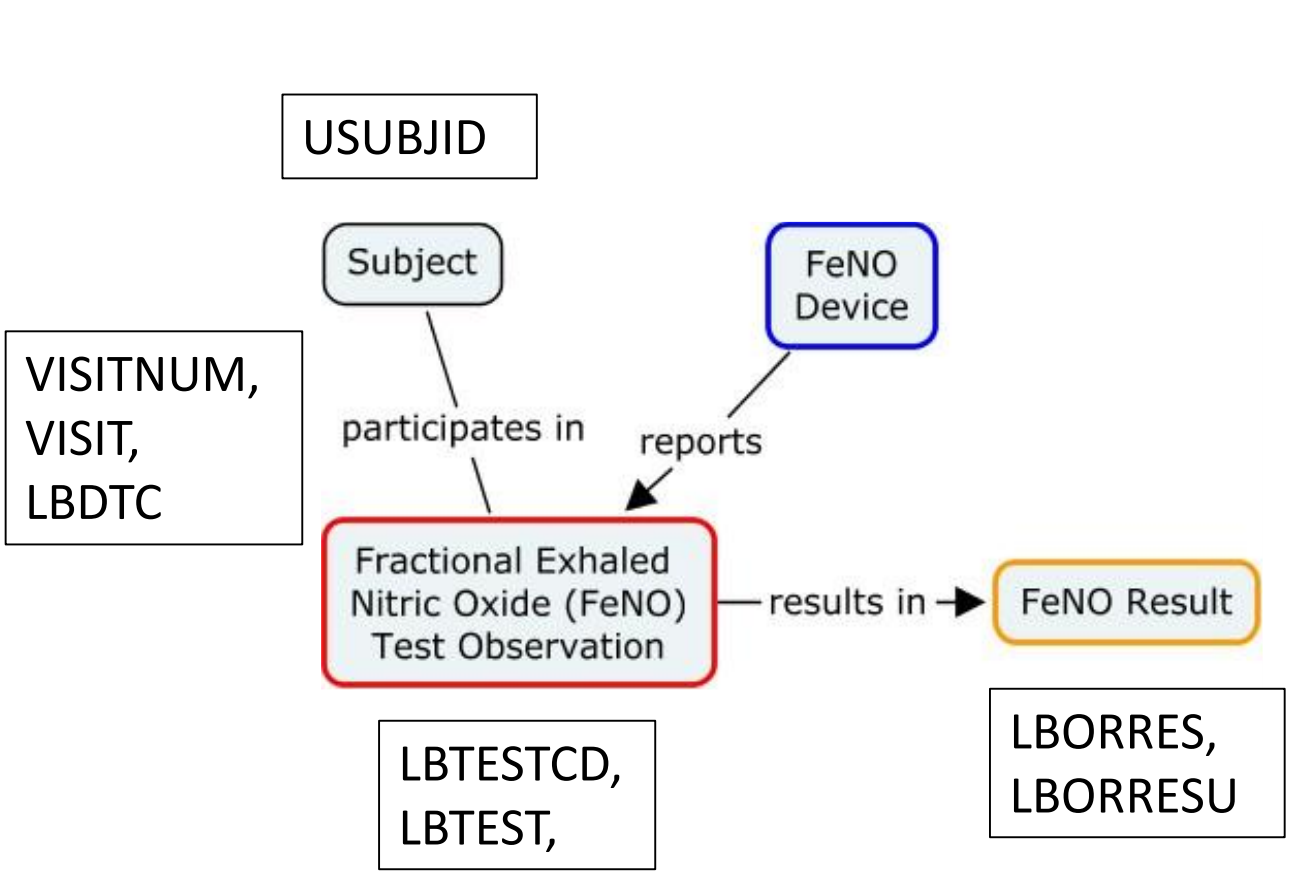
From TAUG-asthma:

It is increasingly recognized that the measurement of exhaled mediators in general, and nitric oxide in particular, constitutes a novel way to monitor separate aspects of diseases, such as asthma. In asthma, it has been proposed to use fractional exhaled nitric oxide (FeNO) to diagnose asthma, to monitor the response to anti-inflammatory medications, to verify adherence to therapy, and to predict upcoming asthma exacerbations. It is also proposed that adjusting anti-inflammatory medications guided by the monitoring of noninvasive markers such as FeNO could improve overall asthma control

It goes on:

Recommendations have been published detailing standardized procedures for both online and offline measurements of FeNO. Online measurement is more commonly used in clinical trials, using standardized equipment. A number of factors can impact the measurement of FeNO (e.g. time since last bronchodilator use, spirometry measurement, food or beverage consumption, strenuous exercise, and smoking) and should be standardized as much as possible. FeNO should be performed prior to spirometry.

Concept Map: Exhaled FeNO



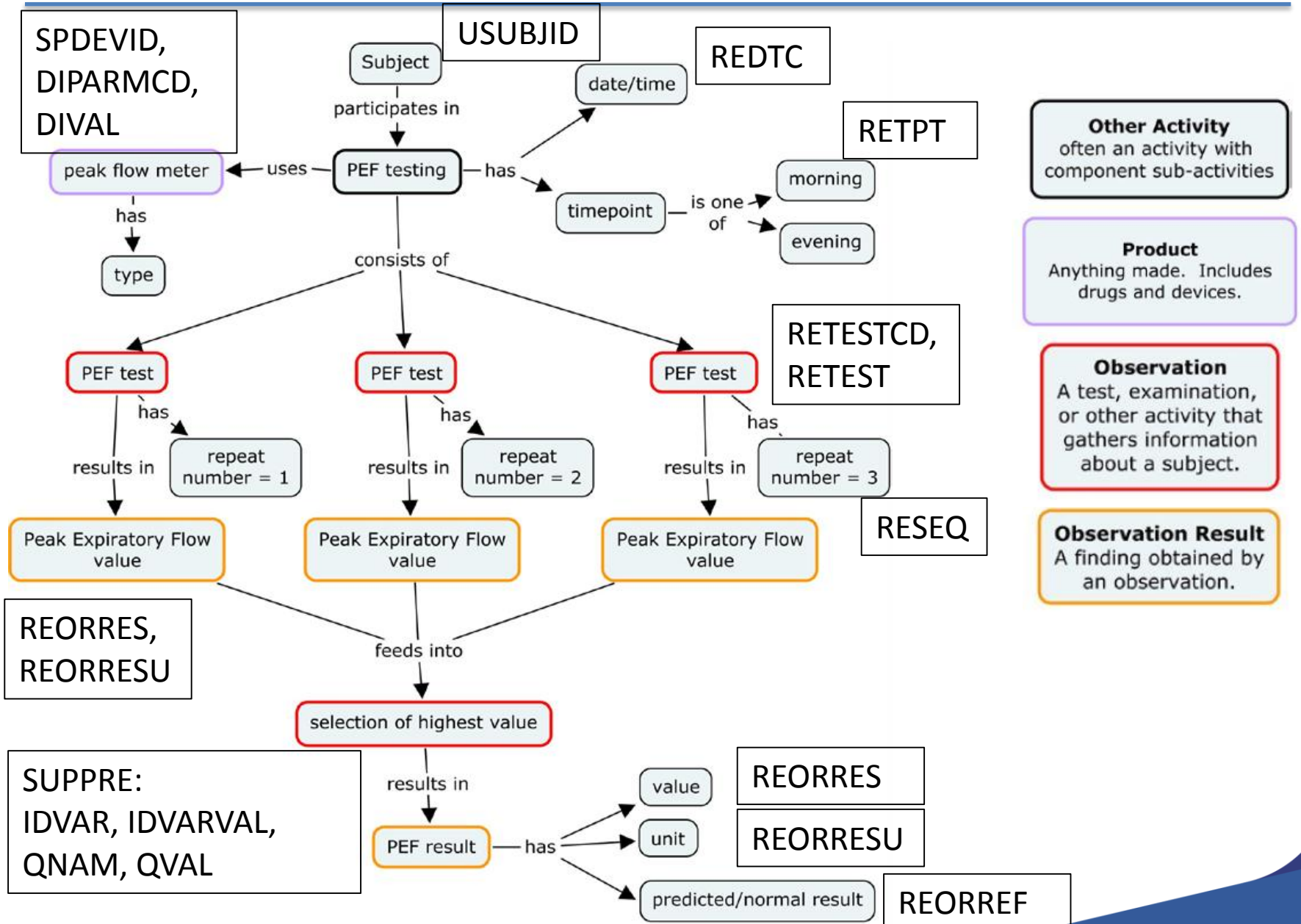
Dataset: Exhaled FeNO

lb.xpt

Row	USUBJID	LBSEQ	LBTESTCD	LBTEST	LBORRES	LBORRESU
1	A001-123	1	FENO	Fractional Exhaled Nitric Oxide	43	ppb
2	A001-123	2	FENO	Fractional Exhaled Nitric Oxide	35	ppb

Row	VISITNUM	VISIT	LBDTC	LBTPT
1 (cont)	1	SCREENING	2010-10-01T10:30:00	PRE
2 (cont)	1	SCREENING	2010-10-01T22:41:00	11 HOURS

Concept Map: Peak Flow



Dataset: Peak Flow

re.xpt

Row	USUBJID	SPDEVID	RESEQ	RETESTCD	LBTEST	REORRES	LBORRESU	VISIT
1	A001-123	XYZ1	1	PEF	Peak Expiratory Flow	410	L/min	VISIT 2
2	A001-123	XYZ1	2	PEF	Peak Expiratory Flow	460	L/min	VISIT 2
3	A001-123	XYZ1	3	PEF	Peak Expiratory Flow	425	L/min	VISIT 2

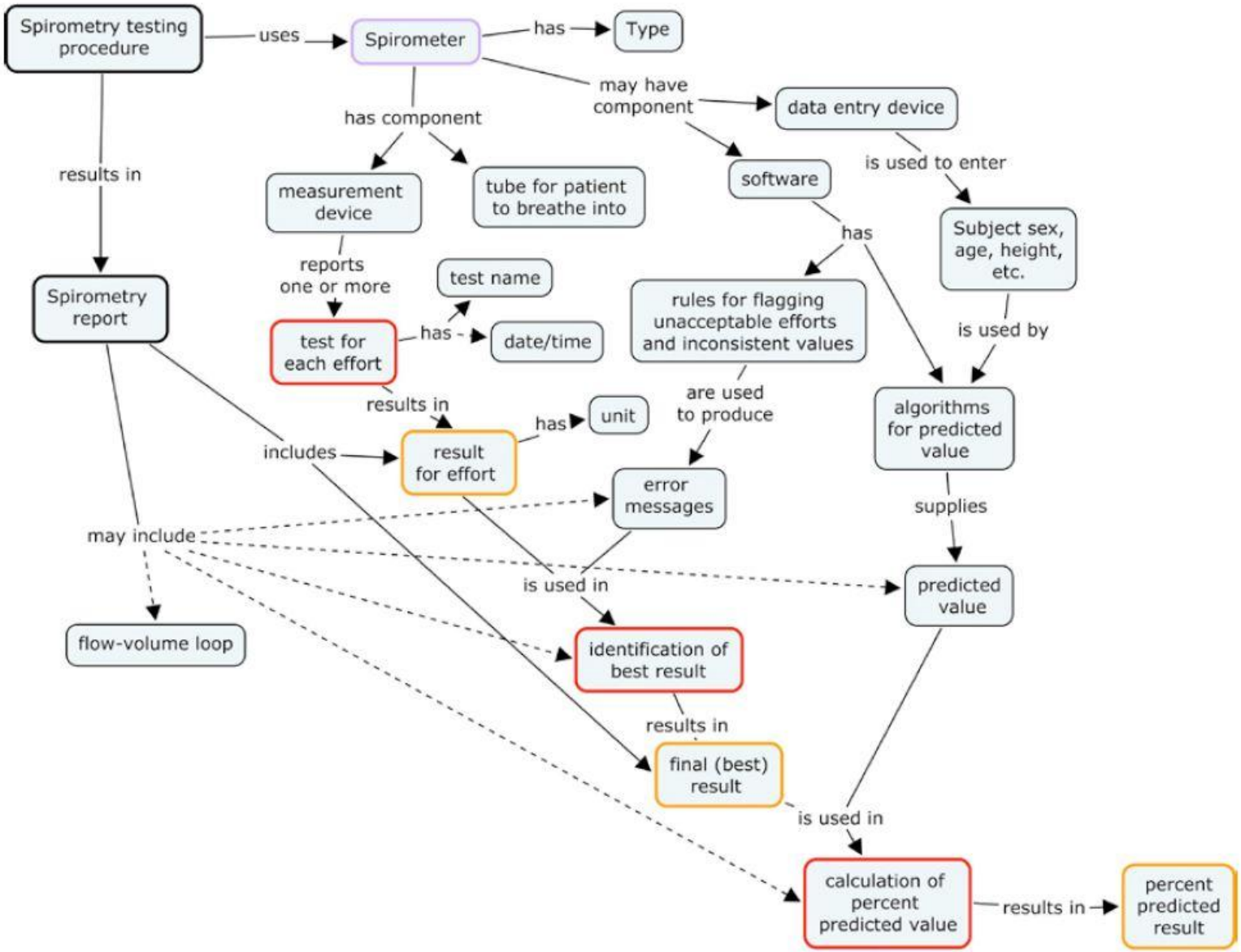
suppre.xpt

Row	USUBJID	IDVAR	IDVARVAL	QNAM	QLABEL	QVAL
1	A001-123	RESEQ	2	REBRESFL	Best Result Flag	Y

di.xpt

Row	SPDEVID	DISEQ	DIPARMCD	DIPARM	DIVAL
1	XYZ1	1	TYPE	Device Type	PEAK FLOW METER

Concept Map: Spirometry



Spirometry Test Results

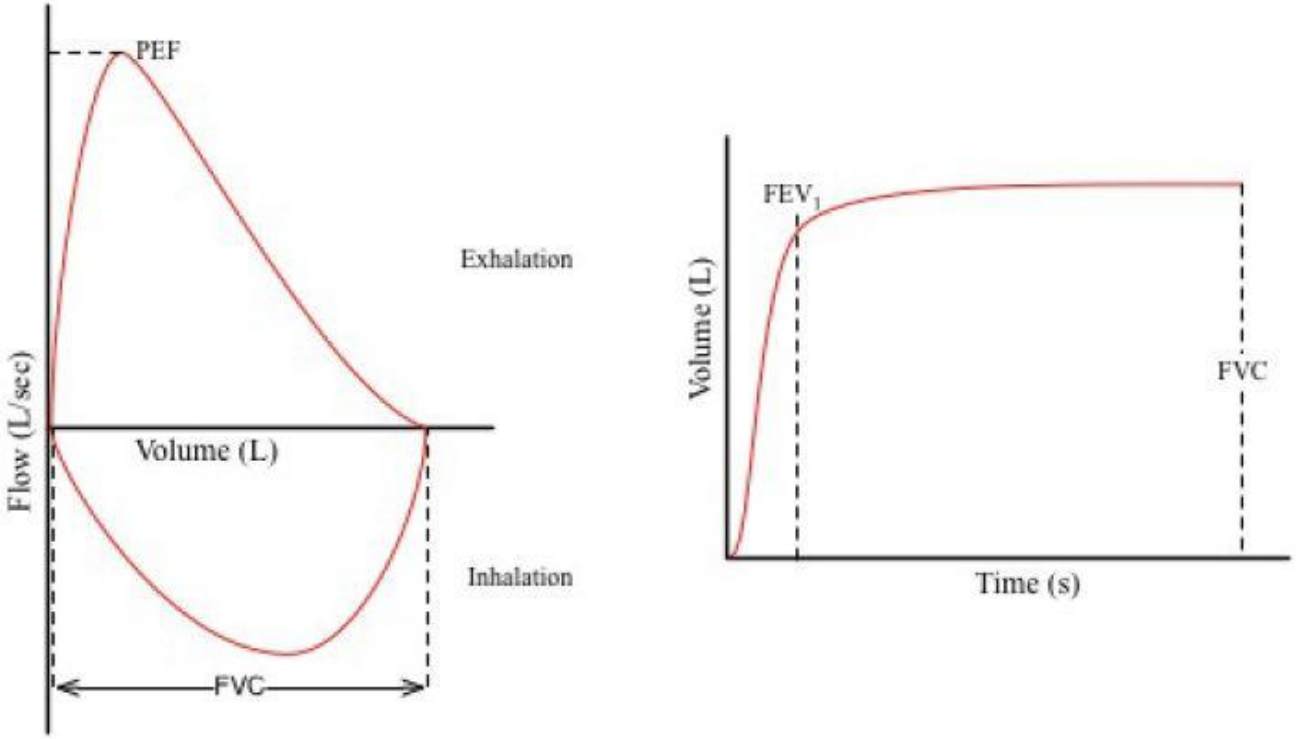
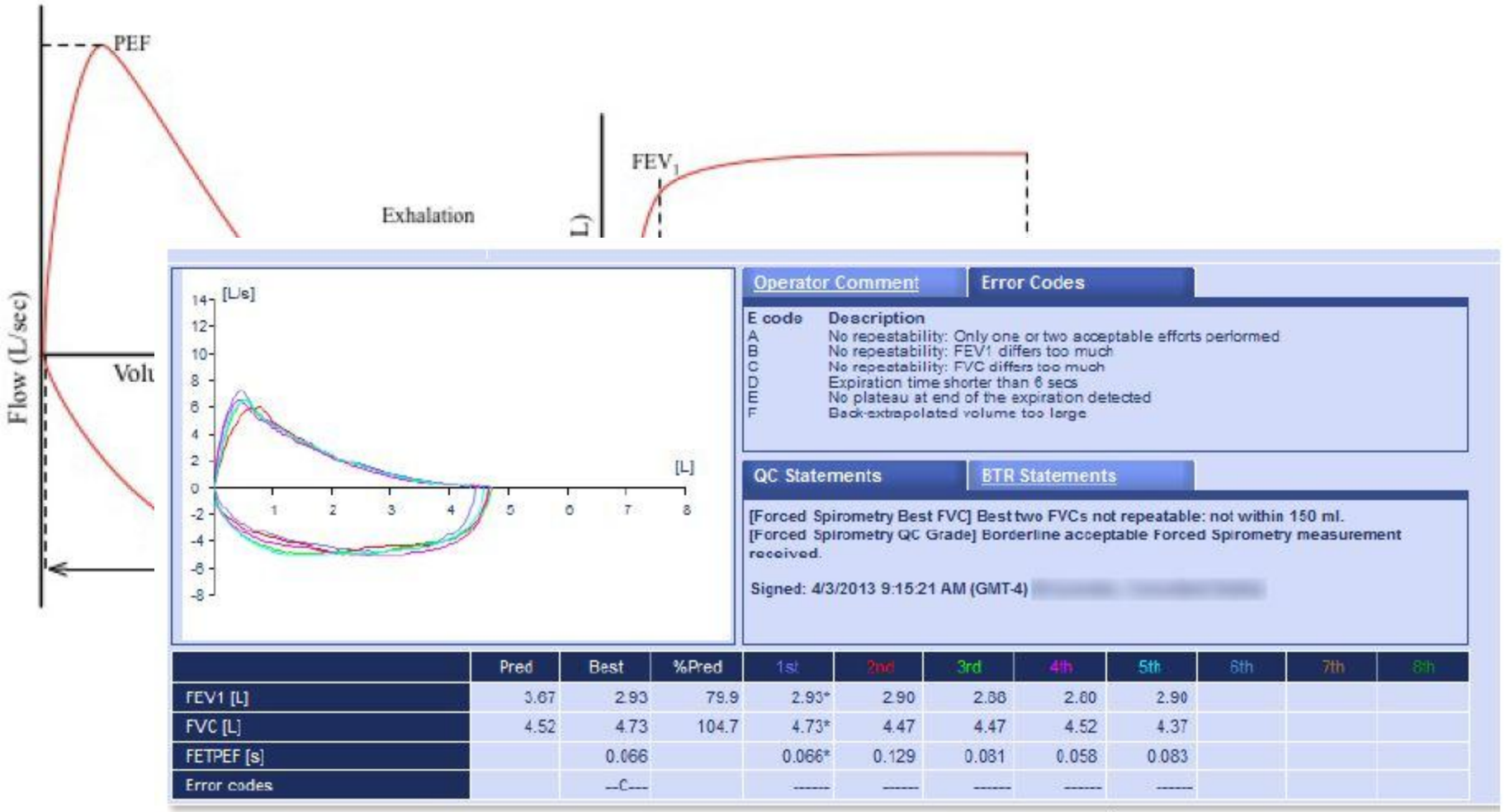


Figure 3.1.2.1-1: Flow-Volume Loop and Volume-Time Curve

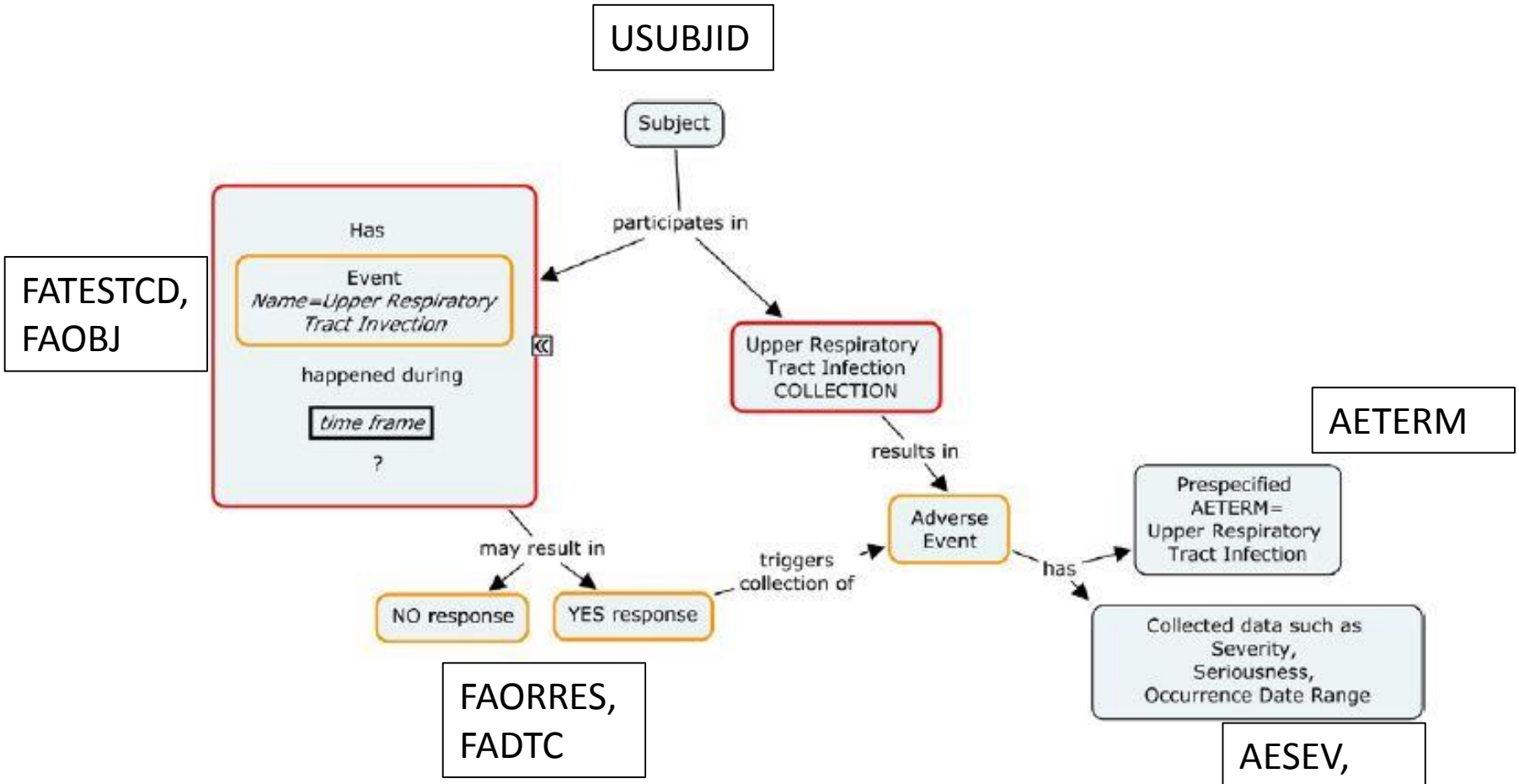
Spirometry Test Results



	Pred	Best	%Pred	1st	2nd	3rd	4th	5th	6th	7th	8th
FEV1 [L]	3.67	2.93	79.9	2.93*	2.90	2.86	2.60	2.90			
FVC [L]	4.52	4.73	104.7	4.73*	4.47	4.47	4.52	4.37			
FETPEF [s]		0.066		0.066*	0.129	0.081	0.058	0.083			
Error codes		--C---		------	------	------	------	------			

Figure 3.1.2.2-1: Sample Spirometry Report 1†

Concept Map: AESI



Dataset: AESI

faae.xpt

Row	USUBJID	FASEQ	FATESTCD	FAOBJ	FAORRES	FADTC
1	A001-123	1	OCCUR	Upper respiratory tract infection	Y	2013-05-24
2	A001-123	2	OCCUR	Sinusitis	N	2013-05-24
3	A001-123	3	OCCUR	Bronchitis	N	2013-05-24

ae.xpt

Row	USUBJID	AESEQ	AETERM	AEPRESP	AESEV	AESTDTC	AEENDTC
1	A001-123	1	Upper respiratory tract infection	Y	MILD	2013-05-20	2013-05-31

TAUG-Asthma: ADaM

For the Analysis Data Model (ADaM), the form of guidance has not yet been established, but will be in future iterations of this document.

TAUG-COPD

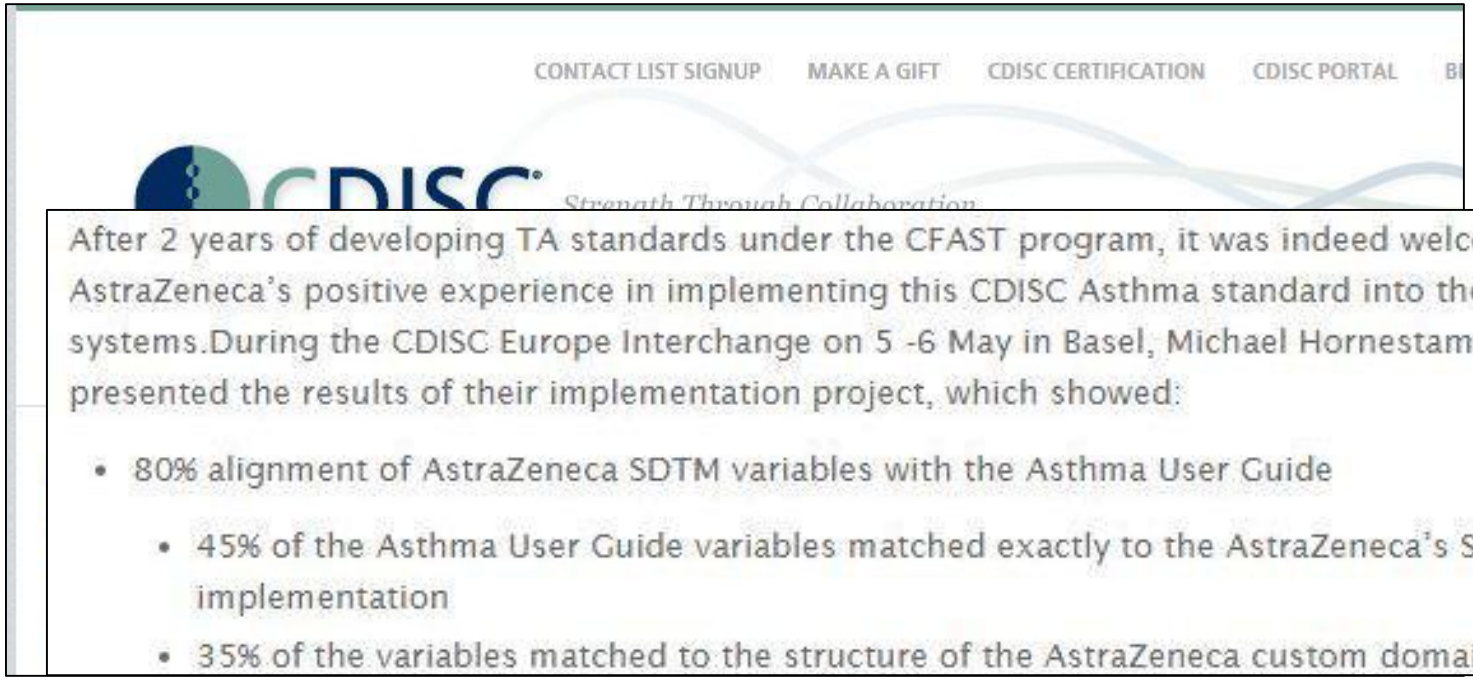
- Hot of the press a draft TAUG-COPD has been released for public review – comments due 7th December
- Includes examples of SDTM annotated CRFs
- Also has an additional section 5…

Section 5 Analysis Data

- Demonstrates the use of ADaM to create datasets to support the analysis of two endpoints common to COPD, namely exacerbations and the BODE Index (BMI, FEV1, 6 minute walk and dyspnea scale).

TAUG-Asthma and AstraZeneca

TAUG-Asthma and AstraZeneca



After 2 years of developing TA standards under the CFAST program, it was indeed welcome to hear of AstraZeneca's positive experience in implementing this CDISC Asthma standard into their systems.During the CDISC Europe Interchange on 5 -6 May in Basel, Michael Hornestam of AstraZeneca presented the results of their implementation project, which showed:

- 80% alignment of AstraZeneca SDTM variables with the Asthma User Guide
  - 45% of the Asthma User Guide variables matched exactly to the AstraZeneca's SDTM implementation
  - 35% of the variables matched to the structure of the AstraZeneca custom domains

TAUG-Asthma and AstraZeneca

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Further, the AZ team reported that it took only *1 FTE 2 weeks* to implement the Asthma standard and that the team viewed this as an opportunity to enhance the AstraZeneca standards.Their work confirmed that the AstraZeneca SDTM implementation was CDISC aligned before the differential analysis and acknowledged that their custom domains are structured according to industry standards.

The results of AstraZeneca's CDISC Asthma standard implementation clearly demonstrate the value and appropriateness of the CDISC standard. This standard complements and extends existing global industry standards for this important therapeutic area and could be implemented with minimal resource required.

Summary

- Standards matter
- Therapeutic area knowledge matters
- Understanding the data matters

The TAUG-Asthma has been created so that those working in asthma studies, including statisticians, understand the data and can work to a common underlying framework.

It should be of interest!

Asthma TAUG Workgroup

Name	Institution/Organization
Rhonda Facile, Team Leader	CDISC
Sharon Broderick	Boehringer Ingelheim
Melissa Cook	Accenture
Scott Getzin	Eli Lilly
Miho Hashio	Glaxo Smith Kline
Brooke Hinkson	Sanofi
Gloria Jones	Johnson & Johnson
Erin Muhlbradt	NCI EVS
Jaya Mukkamala	Genentech
Chris Price	Roche
Dianne Reeves	NCI EVS
Pam Rinaldi	Boehringer Ingelheim
Santosh Sutradhar	Pfizer
Madhavi Vemuri	Johnson & Johnson
Rosemary Watt	Johnson & Johnson
Brittny Weather	Johnson & Johnson
Diane Wold	Glaxo Smith Kline
Ron Fitzmartin	FDA Liaison
Xu Wang	FDA
Feng Zhou, M.D.	FDA