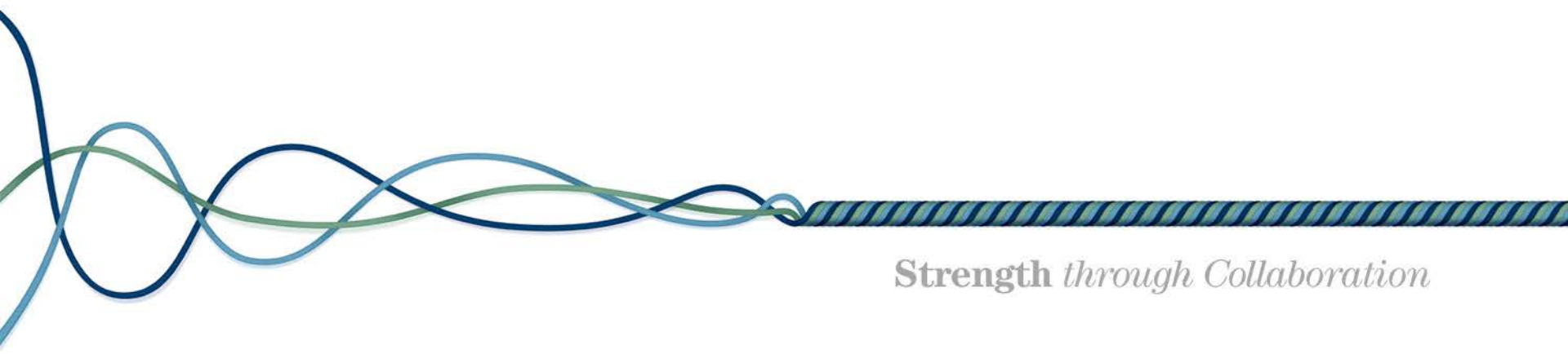
CDISC Public Webinar – Standards Updates and Additions

23 July 2015



Agenda

- Virology Therapeutic-Area User Guide (TAUG) v2.0, Public Review
  - Jon Neville, C-Path
  - Laura Butte, C-Path

- CDISC Online Education & Event Updates
  - John Ezzell, CDISC

Question & Answer

- ‘Panelist’: Question

OR

- ‘Presentation’: Question

Examples:

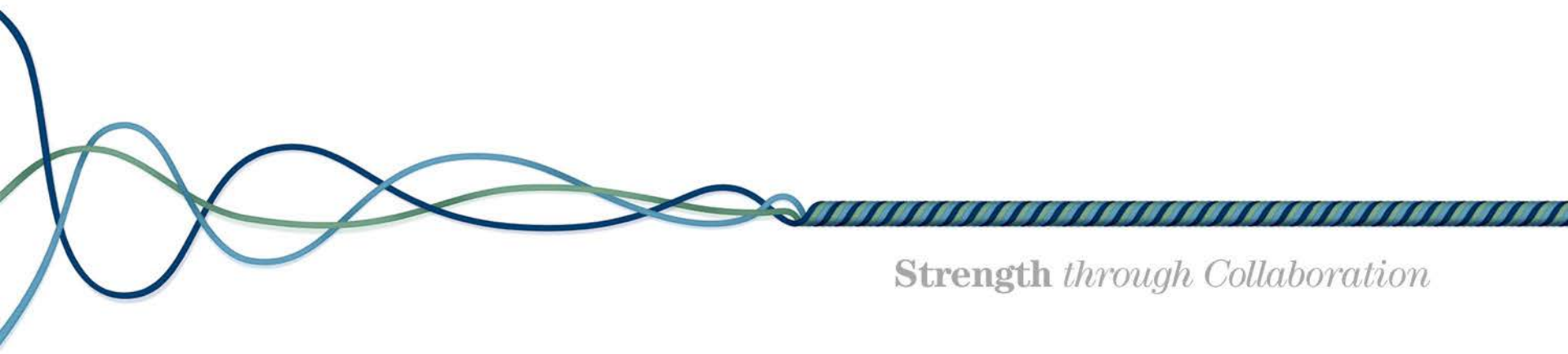
Amy: What are new updates in the Virology TAUG?

OR

CDISC: When can we start registering for the US Interchange?

Virology Therapeutic-Area User Guide (TAUG) v2.0, Public Review

Presented by Jon Neville,
Critical Path Institute



Project Background

- Goal
  - Update Virology v1.0 to align with more recent development work, particularly in CFAST therapeutic areas
  - Create a high-level go-to source for virus studies (intervention/prophylaxis)
- Focus
  - Drug sensitivity testing (phenotypic and genotypic data)
  - A more robust approach to handling virus nomenclature
  - Multiple new concepts/examples based on recent development in Influenza and Chronic Hepatitis C
  - Update user guide layout (concept-based as opposed to SDTM domain-based)
- Inputs
  - Virology v1.0
  - Existing User Guides: Pharmacogenomics (PGx), Influenza and Chronic Hepatitis C
  - FDA Guidance

Review Status Summary

- Internal Review
  - Concluded June 11th
  - Team received and responded to ~40 comments
- CDISC SRC Review
  - Received and addressed ~100 comments
  - Approval to post for public review on July 21
- Public Review
  - **Happening now!**
  - Anyone welcome to review and comment
  - Comment period closes **08/24/2015**

Concepts Covered in v2.0

- Diagnosis and laboratory confirmation of infection
- Viral resistance (drug sensitivity testing)
- Viral Load
- Immune response
- **Virus Nomenclature**
- Analysis Data

Changes from v1.0

- Guide is organized by concept, not SDTM domain
- Immune response examples added (IS domain).
- Analysis data section added
- **Proposed deprecation of Viral Resistance (VR) domain: Resistance data will be modeled in the Microbiology Susceptibility (MS) domain**
- **New approach to nomenclature: draft Organism Identifiers (OI) domain and ORGNAMID variable**
  - **Proposed deprecation of --NSTRN variable**

Guide Layout- CFAST TAUG Style

CONTENTS

Host Immune Response: Immunogenicity Specimen (IS) Domain

4.3.1 Examples for Host Immunogenic Response

Example 1

IS – Assumptions for the Immunogenicity Specimen Assessment Domain Model

1. The Immunogenicity Specimen Assessments (IS) domain model holds assessments which describe whether a therapy provoked/caused/induced an immune response. The response can be either positive or negative. For example, a vaccine is expected to induce a beneficial immune response, while a cellular therapy such as erythropoiesis stimulating agents may cause an adverse immune response.

hemagglutination. The standard result titer is expressed as the inverse of this dilution.

Row 2: Shows the results of an MN titer. ISORRES shows that a 1:64 dilution of subject serum was the most dilute sample capable of neutralizing Influenza virus in the assay. The standard result titer is expressed as the inverse of this dilution.

is.xpt

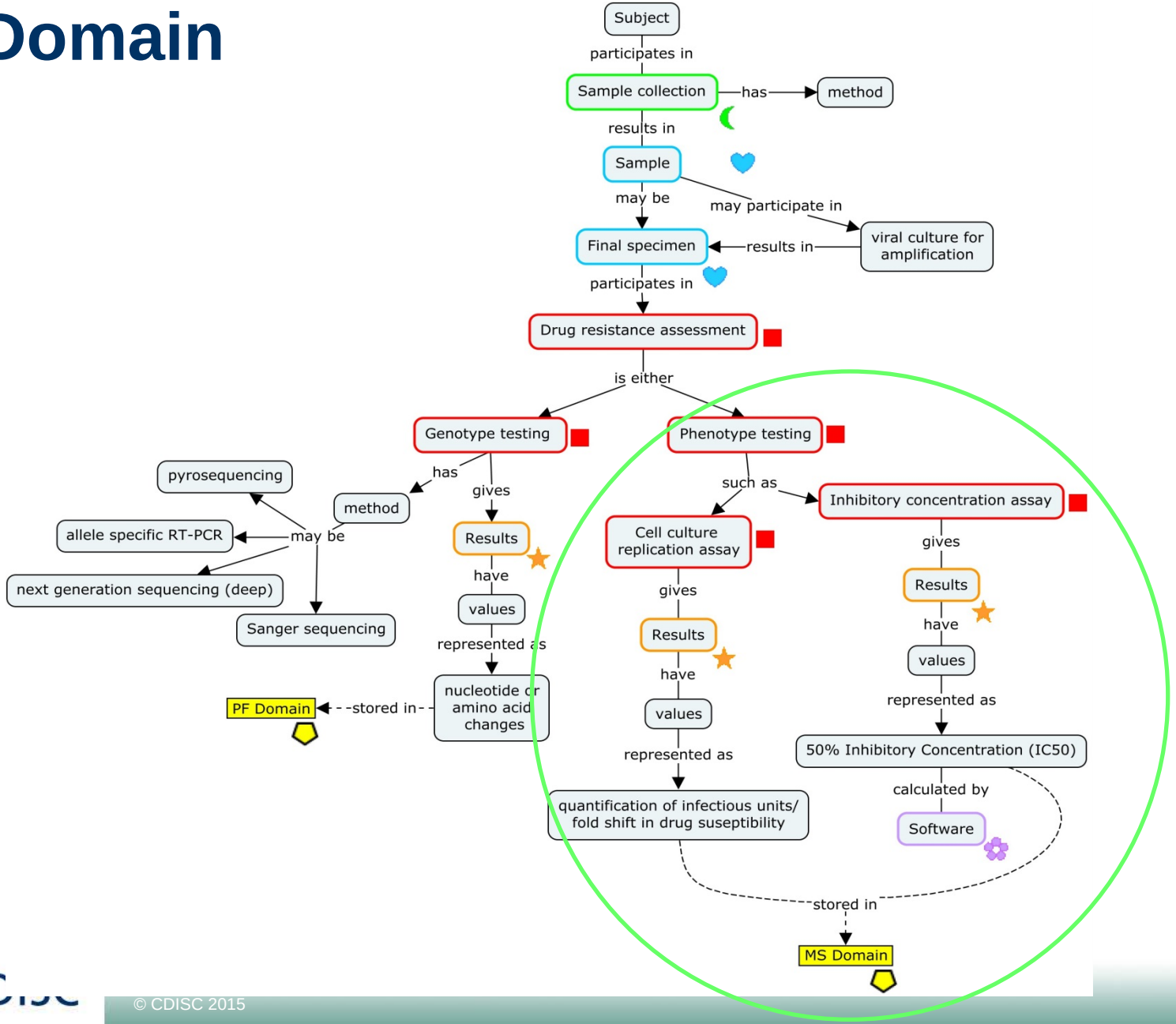
Row	STUDYID	DOMAIN	USUBJID	ISSEQ	ISREFID	ISNSPCES	ISTESTCD	ISTEST	ISCAT	ISORRES	ISORRESU	ISSTRESC
1	INFL456	IS	INF02-01	1	SAMPBL0201	Influenza A	INFAHIT	Hemagglutination Inhibition Antibody Titer	SEROLOGY	1:32	dilution	32
2	INFL456	IS	INF02-02	2	SAMPBL0202	Influenza A	INFAMNT	Microneutralization Antibody Titer	SEROLOGY	1:64	dilution	64

Row	ISSTRESN	ISSTRESU	ISSPEC	ISMETHOD	ISDTC
1 (cont)	32	titer	SERUM	HEMAGGLUTINATION INHIBITION ASSAY	2011-08-08
2 (cont)	64	titer	SERUM	MICRONEUTRALIZATION ASSAY	2011-08-08

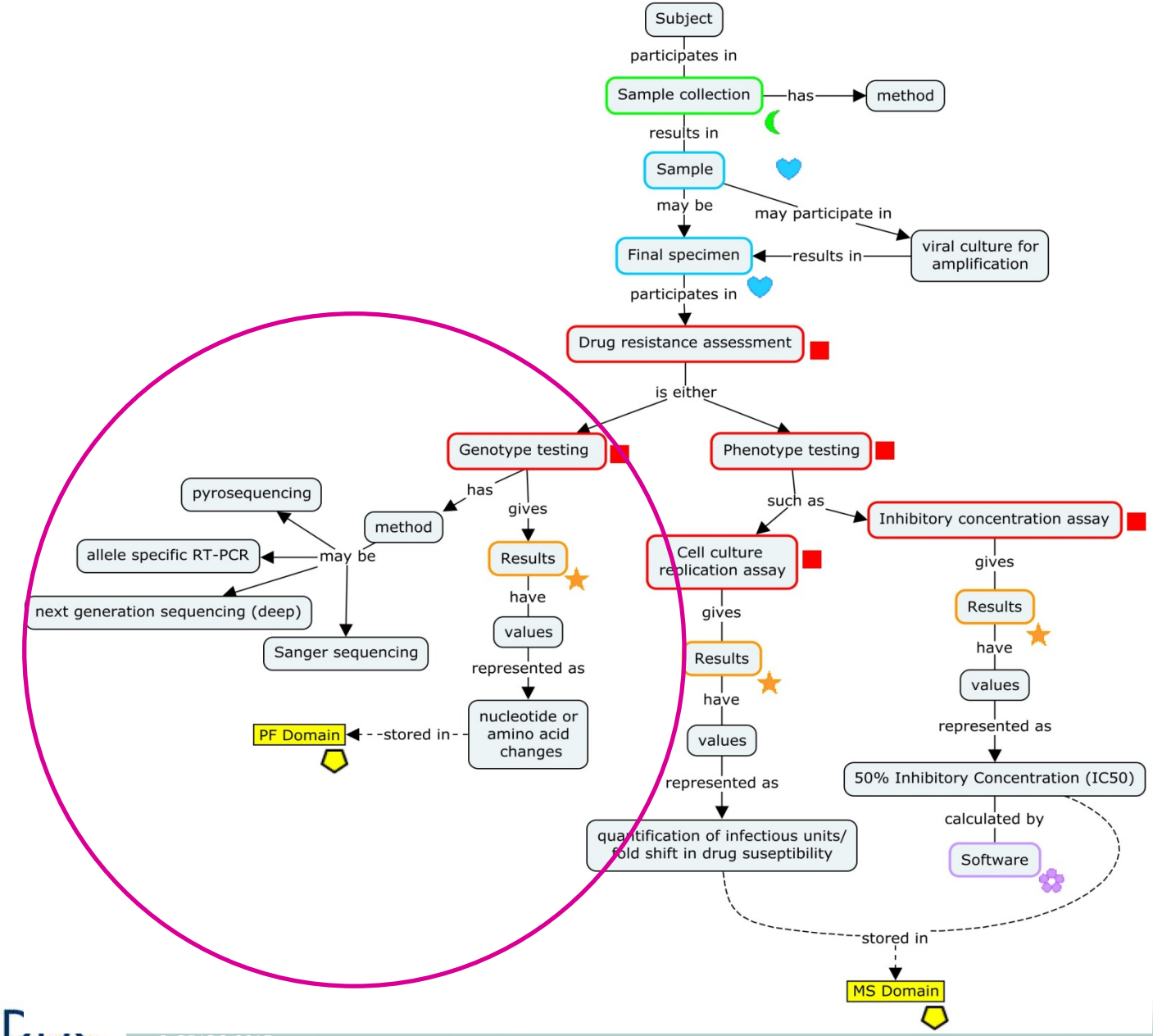
Analysis Data Section

- Identification of co-morbidities of interest
- Subgrouping subjects
- Virus taxonomy: distinguishing between baseline and follow-up
- Subject-level variables associated with efficacy response
- Analysis data for genotypic and phenotypic findings

Phenotypic Viral Resistance, now in MS Domain



Genotypic Viral Resistance: PF Domain



Nomenclature: The problem

- The terminology for classification/naming of different viruses at levels below species varies greatly.
- VR domain variables allowed for a two-level hierarchy only: --NSPCES (non-host species) and –NSTRN (Non-host strain)

There are typically more than two levels required to describe viruses

"Strain" is not necessarily the only name, nor even a valid name, for sub-species taxonomy

Virus Nomenclature Issue

--NSPCES

	HIV	Influenza A	Hep C	Hep B	HPV
SPECIES level	**Species**	**Species**	**Species**	**Species**	**Species**
Subspecies Level 1	Type	Subtype	Genotype	Genotype	Type
Subspecies Level 2	Group	Strain	Subtype	Sub-genotype	
Subspecies Level 3	Subtype (or Clade)			Recombination Type	
Subspecies Level 4	Subclade				

--NSTRN?

Nomenclature, cont'd

Example 2

This example shows how to represent data from an NA inhibition assay that is assessing influenza susceptibility to a neuraminidase inhibitor during an antiviral treatment trial. This assessment was done at three time points over a five-day period. Each time point compares a known reference strain to a subject-derived sample strain that has previously been identified as being of the same lineage based on genetic markers (thus the strain name ending in "-like"). Information about sample collection method, analysis software, and software version used to calculate the IC50 values are represented in SUPPVR and linked to the parent domain via VRSEQ. Information about the commercial kit used are represented in the Device Identifiers domain (DI), and linked to the VR domain via SPDEVID. Note that the values in VRGENTYP and VRGENRI are chosen based on the target molecule of the study drug, a neuraminidase inhibitor.

Some Required and Expected variables have been omitted in consideration of space and clarity. Controlled terminology is still under development, thus some values in the examples are not CDISC controlled terms. Verify demonstrated terminology against current standards before adopting it.

Rows 1, 4, and 7: Show the response of the virus extracted from the subject based on drug concentrations required to produce 50% inhibition of the standard virus growth.

Rows 2, 5, and 8: Show a reference viral sample response based on drug concentrations required to produce 50% inhibition of the standard virus growth.

Rows 3, 6, and 9: Show the fold change of the response of the virus extracted from the subject compared to the reference viral sample response based on drug concentrations required to produce 50% inhibition of the standard virus growth. This is the subject sample result divided by the reference result.

Row 10: Shows the net assessment of the trend in fold change (rows 3, 6 and 9) based on how the sample virus susceptibility to drug changed with respect to the control strain over the three time points. VRORRES/VRSTRESC show "Reduced Susceptibility".

vr.xpt

Row	STUDYID	DOMAIN	USUBJID	SPDEVID	VRSEQ	VRGRPID	VRREFID	VRGENTYP	VRGENRI	VRTESTCD	VRTEST
1	INFL123	VR	INF01-01	10	1	1	SAMPMU0101	PROTEIN	NEURAMINIDASE	IC50T	IC50 Subject Sample Result
2	INFL123	VR	INF01-01	10	2	1	SAMPMU0101	PROTEIN	NEURAMINIDASE	IC50R	IC50 Reference Control Result
3	INFL123	VR	INF01-01		3	1	SAMPMU0101	PROTEIN	NEURAMINIDASE	IC50FCR	IC50 Fold Change from Reference
4	INFL123	VR	INF01-01	12	4	1	SAMPMU0101	PROTEIN	NEURAMINIDASE	IC50T	IC50 Subject Sample Result
5	INFL123	VR	INF01-01	12	5	1	SAMPMU0101	PROTEIN	NEURAMINIDASE	IC50R	IC50 Reference Control Result
6	INFL123	VR	INF01-01		6	1	SAMPMU0101	PROTEIN	NEURAMINIDASE	IC50FCR	IC50 Fold Change from Reference
7	INFL123	VR	INF01-01	12	7	1	SAMPMU0101	PROTEIN	NEURAMINIDASE	IC50T	IC50 Subject Sample Result
8	INFL123	VR	INF01-01	12	8	1	SAMPMU0101	PROTEIN	NEURAMINIDASE	IC50R	IC50 Reference Control Result
9	INFL123	VR	INF01-01		9	1	SAMPMU0101	PROTEIN	NEURAMINIDASE	IC50FCR	IC50 Fold Change from Reference
10	INFL123	VR	INF01-01		10	1	SAMPMU0101	PROTEIN	NEURAMINIDASE	ICNETAS	Inhibitory Concentration Net Assessment

Row	VRSPCIES	VRNSTRN	VRDRUG	VRORRES	VRORRESU	VRSTRESC
1 (cont)	INFLUENZA A	A/California/7/2009 (H1N1)-like	Investigamavir	0.20	nM	0.20
2 (cont)	INFLUENZA A	A/California/7/2009 (H1N1)	Investigamavir	0.21	nM	0.21
3 (cont)	INFLUENZA A		Inv			
4 (cont)	INFLUENZA A	A/California/7/2009 (H1N1)-like	Inv			
5 (cont)	INFLUENZA A	A/California/7/2009 (H1N1)	Inv			
6 (cont)	INFLUENZA A		Inv			
7 (cont)	INFLUENZA A	A/California/7/2009 (H1N1)-like	Inv			
8 (cont)	INFLUENZA A	A/California/7/2009 (H1N1)	Inv			
9 (cont)	INFLUENZA A		Investigamavir	21		21
10 (cont)	INFLUENZA A		Investigamavir	Reduced Susceptibility		Reduced Susceptibility

This works! The values listed in VRNSTRN are in fact STRAINS of Influenza A

Nomenclature Issue

2.3.1 Examples for Influenza Drug Sensitivity Testing

Example 1

This example shows a longitudinal assessment of genetic variation in the influenza neuraminidase gene from two subjects. These assessments look for changes in the Arginine (R) residue at position 292 in the neuraminidase protein over a period of five days, because this change is known to confer drug resistance[17]. PFORRES shows the one letter amino acid abbreviation more commonly seen in literature. PFSTRESC shows the result using standard Human Genome Variation Society (HGVS) nomenclature.

Some Required and Expected variables have been omitted in consideration of space and clarity. Controlled terminology is still under development, thus some values in the examples are not CDISC controlled terms. Verify demonstrated terminology against current standards before adopting it.

Row 1: Shows that the baseline assessment found no variation in R292 for subject INF01-01. Note that the experimental result (PFORRES) and the reference result (PFORREF) are the same. The standard result (PFSTRESC) value of "p.(=)" indicates there is no change detected.

Rows 2-3: Show that R292 residue mutated to Lysine (K) on day 2 and remained that way through day 5 for subject INF01-01. Note that the experimental result (PFORRES) has changed to "K"

Rows 4-6: Show that the baseline, day 2, and day 5 assessments found no variation in R292 for subject INF01-02.

pf.xpt

Row	STUDYID	DOMAIN	USUBJID	PFSEQ	PFGENTYP	PFGENRI	PFTESTCD	PFTEST	PFCAT
1	INFLU123	PF	INF01-01	1	PROTEIN	NEURAMINIDASE	AA	AMINO ACID	PROTEIN VARIATION
2	INFLU123	PF	INF01-01	2	PROTEIN	NEURAMINIDASE	AA	AMINO ACID	PROTEIN VARIATION
3	INFLU123	PF	INF01-01	3	PROTEIN	NEURAMINIDASE	AA	AMINO ACID	PROTEIN VARIATION
4	INFLU123	PF	INF01-02	1	PROTEIN	NEURAMINIDASE	AA	AMINO ACID	PROTEIN VARIATION
5	INFLU123	PF	INF01-02	2	PROTEIN	NEURAMINIDASE	AA	AMINO ACID	PROTEIN VARIATION
6	INFLU123	PF	INF01-02	3	PROTEIN	NEURAMINIDASE	AA	AMINO ACID	PROTEIN VARIATION

Row	PFSPCIES	PFNSTRN	PFORRES	PFORREF	PFGENLOC	PFSTRESC	VISITNUM	VISIT	PFDTC
1 (cont)	INFLUENZA A	H3N2	R	R	292	p.(=)	1	BASELINE	2012-03-01
2 (cont)	INFLUENZA A	H3N2	K	R	292	p.Arg292Lys	2	DAY 2	2012-03-02
3 (cont)	INFLUENZA A	H3N2	K	R	292	p.Arg292Lys	3	DAY 5	2012-03-05
4 (cont)	INFLUENZA A	H3N2	R	R	292	p.(=)	1	BASELINE	2012-03-01
5 (cont)	INFLUENZA A	H3N2	R						
6 (cont)	INFLUENZA A	H3N2	R						

This doesn't work well. The values listed in PFNSTRN are Influenza Subtypes, not Strains.

Nomenclature solution: Organism Identifiers (OI) domain

- OI is a special purpose domain that is modeled after the Device Identifiers (DI) domain
- It allows for parsed nomenclature values to be condensed on a single identifier variable, ***ORGNAMID***
- ORGNAMID can be used in relevant findings domains such as MS, PF, LB
- ORGNAMID is a link to the OI domain where fully parsed taxonomy values reside
- Relieves burden from parent domain (MS, PF, etc)

ORGNAMID and OI Dataset

ms.xpt

Row	STUDYID	DOMAIN	USUBJID	MSSEQ	MSGRPID	ORGNAMID	MSTESTCD	MSTEST	MSDRUG	MSORRES	MSORRESU	MSSTRESC
1	COINF1	MS	COINF1-01	1	1	HIV1MC	IC50S	IC50 Subject Result	Experimenavir	0.2	nM	0.2
2	COINF1	MS	COINF1-01	2	1	HIV1MB	IC50R	IC50 Reference Control Result	Experimenavir	0.21	nM	0.21
3	COINF1	MS	COINF1-01	3	1		IC50FCR	IC50 Fold Change from Reference	Experimenavir	0.95		0.95
4	COINF1	MS	COINF1-01	4	2	HCV2C	IC50S	IC50 Subject Result	Heprevir	1.35	nM	1.35
5	COINF1	MS	COINF1-01	5	2	H77	IC50R	IC50 Reference Control Result	Heprevir	1.21	nM	1.21

oi.xpt

Row	STUDYID	DOMAIN	ORGNAMID	OISEQ	OIPARMCD	OIPARM	OIVAL
1	STUDY123	OI	HIV1MC	1	SPCIES	Species	HIV
2	STUDY123	OI	HIV1MC	2	TYPE	Type	1
3	STUDY123	OI	HIV1MC	3	GROUP	Group	M
4	STUDY123	OI	HIV1MC	4	SUBTYP	Subtype	C
5	STUDY123	OI	HIV1MB	1	SPCIES	Species	HIV
6	STUDY123	OI	HIV1MB	2	TYPE	Type	1
7	STUDY123	OI	HIV1MB	3	GROUP	Group	M
8	STUDY123	OI	HIV1MB	4	SUBTYP	Subtype	B
9	STUDY123	OI	HCV2C	1	SPCIES	Species	HCV
10	STUDY123	OI	HCV2C	2	GENTYP	Genotype	2
11	STUDY123	OI	HCV2C	3	SUBTYP	Subtype	c
12	STUDY123	OI	H77	1	SPCIES	Species	HCV
13	STUDY123	OI	H77	2	GENTYP	Genotype	1
14	STUDY123	OI	H77	3	SUBTYP	Subtype	a

ORGNAMID

- ORGNAMID is sponsor defined, with the following constraints:
  - A unique ORGNAMID must represent a unique identity as represented in its combination of OIPARMCD/OIVAL pairs.
  - Study sponsors should populate ORGNAMID with intuitive name values based on either:
    - the name of the organism as reported by a lab, or
    - published references/databases where applicable and appropriate (e.g., when reference strain H77 is used in a HCV study, ORGNAMID for this strain should be populated with “H77” or “HCV1a-H77”).

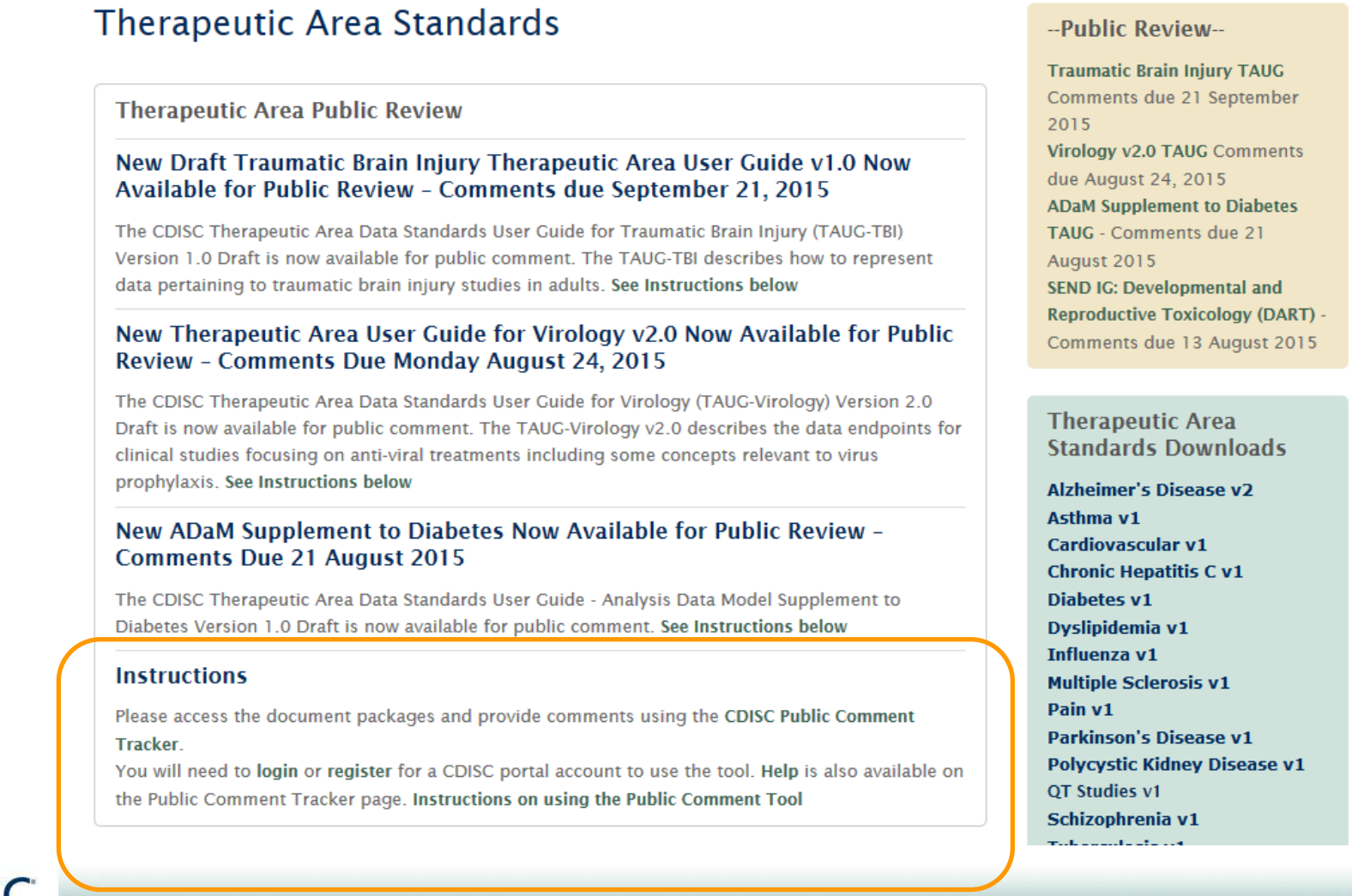
Quick Summary

- TAUG-Virology v2.0 available for public review until **08/24/15**
- MS domain will be replacing VR domain for phenotypic drug sensitivity testing data
- New OI domain/ ORGNAMID variable addresses nomenclature issues
- Not all concepts represented in the guide were discussed in this presentation
- If you plan to review, please take note of **section 1.6**, **known issues** (some were discussed here today)
- We are on track to publish by end of September 2015

Comments may also be sent to Laura Butte, Project Manager, at LButte@c-path.org

Reviewing and commenting

Go to www.cdisc.org/therapeutic, scroll down



Therapeutic Area Standards

Therapeutic Area Public Review

New Draft Traumatic Brain Injury Therapeutic Area User Guide v1.0 Now Available for Public Review – Comments due September 21, 2015

The CDISC Therapeutic Area Data Standards User Guide for Traumatic Brain Injury (TAUG-TBI) Version 1.0 Draft is now available for public comment. The TAUG-TBI describes how to represent data pertaining to traumatic brain injury studies in adults. **See Instructions below**

New Therapeutic Area User Guide for Virology v2.0 Now Available for Public Review – Comments Due Monday August 24, 2015

The CDISC Therapeutic Area Data Standards User Guide for Virology (TAUG-Virology) Version 2.0 Draft is now available for public comment. The TAUG-Virology v2.0 describes the data endpoints for clinical studies focusing on anti-viral treatments including some concepts relevant to virus prophylaxis. **See Instructions below**

New ADaM Supplement to Diabetes Now Available for Public Review – Comments Due 21 August 2015

The CDISC Therapeutic Area Data Standards User Guide - Analysis Data Model Supplement to Diabetes Version 1.0 Draft is now available for public comment. **See Instructions below**

Instructions

Please access the document packages and provide comments using the **CDISC Public Comment Tracker**.
You will need to **login** or **register** for a CDISC portal account to use the tool. **Help** is also available on the Public Comment Tracker page. **Instructions on using the Public Comment Tool**

--Public Review--

Traumatic Brain Injury TAUG Comments due 21 September 2015
Virology v2.0 TAUG Comments due August 24, 2015
ADaM Supplement to Diabetes TAUG - Comments due 21 August 2015
SEND IG: Developmental and Reproductive Toxicology (DART) - Comments due 13 August 2015

Therapeutic Area Standards Downloads

Alzheimer's Disease v2
Asthma v1
Cardiovascular v1
Chronic Hepatitis C v1
Diabetes v1
Dyslipidemia v1
Influenza v1
Multiple Sclerosis v1
Pain v1
Parkinson's Disease v1
Polycystic Kidney Disease v1
QT Studies v1
Schizophrenia v1

Funding for this project was provided by the U.S. Food and Drug Administration

Q&A Session

CDISC Education Events Announcements

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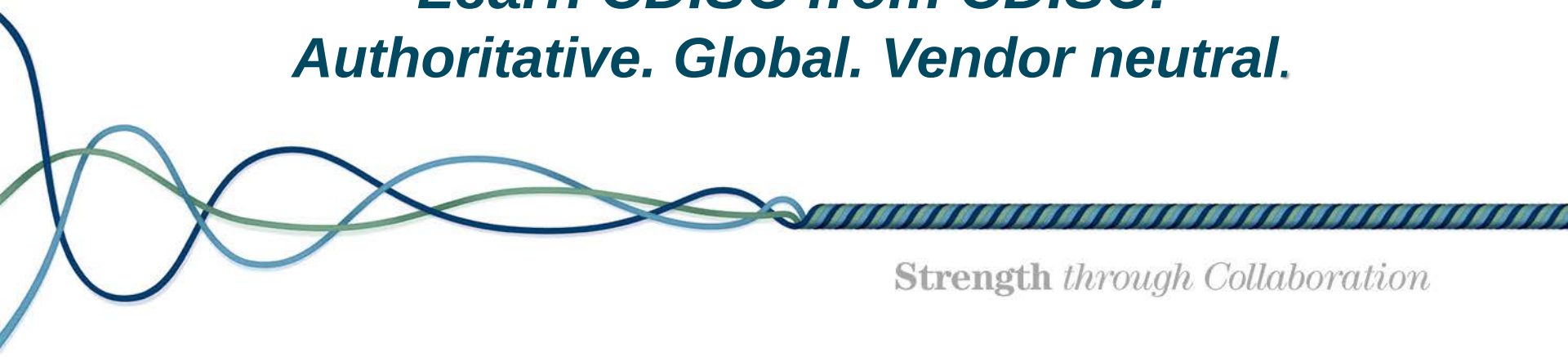

Standards currently out for review

- Traumatic Brain Injury TAUG
  - Visit http://cdisc.org/therapeutic for more information.
  - Comments due 21 Sept 2015
- Virology v2.0 TAUG
  - Visit http://cdisc.org/therapeutic for more information.
  - Comments due 24 August 2015
- ADam Supplement for Diabetes
  - Visit http://cdisc.org/therapeutic for more information.
  - Comments due 21 August 2015
- SEND IG: Developmental and Reproductive Toxicology (DART)
  - Visit http://www.cdisc.org/send for more information.
  - Comments due 13 August 2015
- Click here to submit your comments.

Upcoming North America Public Courses and Events

Location	Dates	Courses Offered	Register By	Early Registration Discounts	Host
Durham, NC	27-31 July 2015	SEND, SDTM, ADaM	27 June 2015	*Expired*	Duke Clinical Research Institute, Duke University Medical Center
Gaithersburg, MD	1-4 Sep 2015	SDTM, CDASH, ADaM	1 Aug 2015	*Expired*	MedImmune
Whippany, NJ	29 Sep – 2 Oct	SDTM, CDASH, ADaM	29 Aug 2015	*Expired*	Bayer HealthCare
Seattle, WA	6-9 Oct 2015	SDTM, ADaM, ODM/Define-XML Combo	6 Sep 2015	*Expired*	Axio Partners in Research
Chicago, IL (Interchange)	9-13 Nov	Visit http://www.cdisc.org/public-courses for more details!	26 Oct 2015	*31 July 2015*	CDISC

Registration deadline indicates online deadline. Onsite registration is available before each event begins. Additional 2015 public training events can be found @ http://cdisc.org/public-courses.

Check CDISC website for up-to-date information on Public Courses

Upcoming Europe Public Courses and Events

Location	Dates	Courses Offered	Online Registration Deadline	Early Registration Discounts	Host
Eschborn (Frankfurt), Germany	28-31 Jul 2015	SDTM, CDASH, ADaM	28 June 2015	*Expired*	ACCOVION
Brussels, Belgium	7-10 Sep 2015	SDTM, CDASH, ADaM	7 August 2015	*Expired*	Business & Decision Life Sciences

Registration deadline indicates online deadline. Onsite registration is available before each event begins. Additional 2015 public training events can be found @ http://cdisc.org/public-courses.

Check CDISC website for up-to-date information on Public Courses

Upcoming Asia Public Courses and Events

Location	Dates	Courses Offered	Online Registration Deadline	Early Registration Discounts	Host
Guangzhou, China	8-11 Sep 2015	SDTM, CDASH, ADaM	8 August 2015	*Expired*	Guangdong Provincial Hospital of Chinese Medicine
Osaka, Japan	14-18 Sep 2015	SDTM, CDASH, ADaM, ODM, Define-XML	14 Aug 2015	*Expired*	EXiCARE
Beijing, China	20-23 Oct 2015	SDTM, CDASH, ADaM, ODM, Define-XML	20 Sep 2015	*Expired*	PPD®
Shanghai, China	26-29 Oct 2015	SDTM, CDASH, ADaM, ODM, Define-XML	20 Sep 2015	*Expired*	gsk GlaxoSmithKline 葛兰素史克

Registration deadline indicates online deadline. Offline registration deadlines for each event available up until start date. Additional public training events can be found @ http://cdisc.org/public-courses.

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- Your instructor delivers training
- Training when your staff needs it
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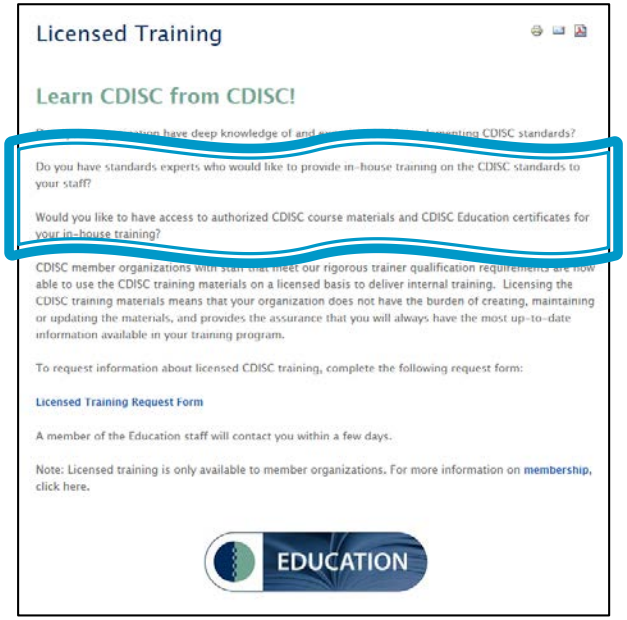
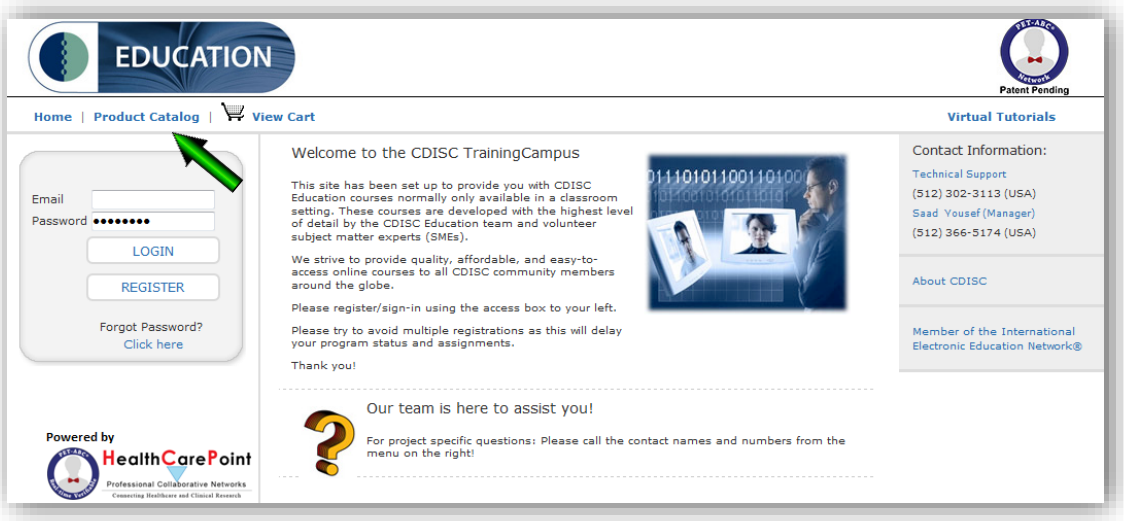


CDISC Online Training

Cdisc.trainingcampus.net

- Online training created with support from CDISC standards development teams
- New CDISC trainings developed in tandem with standards development
- Online courses benefits:
  - flexibility
  - more content
  - greater depth
  - updated frequently



Next Public Webinar

- **Agenda:**
  - Breast Cancer TA Public Review
  - ADaM Supplement for Diabetes TA Public Review
- **Date**: 12 August 2015, 11:00-12:30 PM EST
- **Speakers:**
  - John Owen, CDISC
  - Susan Kenney, Maximum Likelihood
  - Mario Widel, Eli Lilly
  - Rachael Zirkle, Eli Lilly
- Register here.

Webinar details also at www.cdisc.org/webinars

Next Members Only Mini-Training

- **Agenda:**
  - Implementation of Oncology-Specific SDTM Domains
- **Date**:
  - 20 Aug 2015, 08:00 - 09:30 AM *Central European Time (01:00 - 02:-30 AM Central USA Time)*
- **Speakers:**
  - Jan De Cleir, SGS Life Science Services
- Register here.

Webinar details also at www.cdisc.org/webinars

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Any more questions?

Thank you for attending this webinar.

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