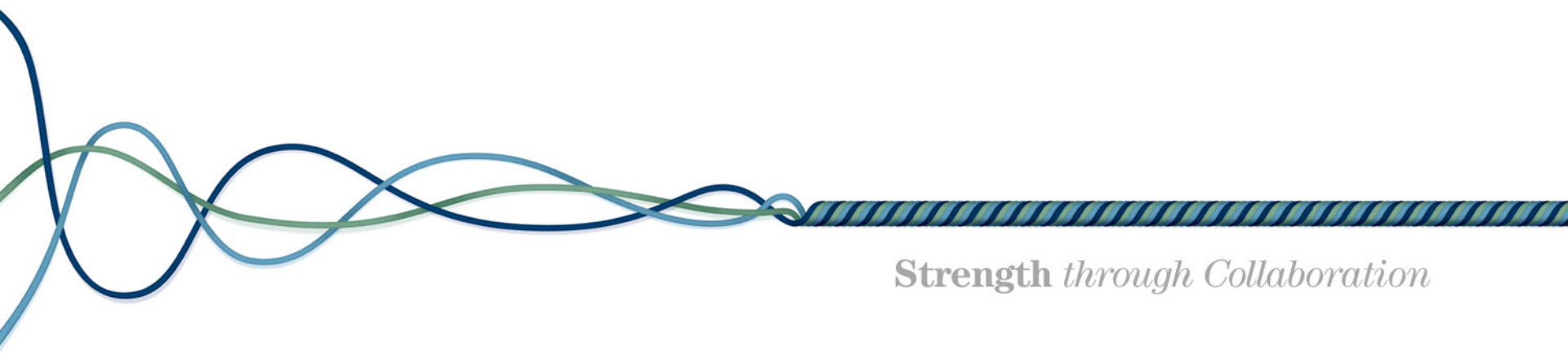
CDISC Public Webinar – Standards Updates and Additions

Nov 6 2015



Agenda

- CTR: Clinical Trial Registries, a CDISC-ODM Extension
  - Jozef Aerts, University of Applied Sciences, Graz, Austria
  - Paul Houston, CDISC
- CDISC Online Education & Event Updates
  - John Ezzell, CDISC

Question & Answer

- ‘Panelist’: Question

OR

- ‘Presentation’: Question

Examples:

Jozef: What is CTR?

OR

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

CDISC Public Webinar

CTR: Clinical Trial Registries

a CDISC-ODM extension

Jozef Aerts
Professorship for Medical Informatics
Insitute for eHealth
University of Applied Sciences FH Joanneum
Graz, Austria

Scope of the Project

- CTR&R - Clinical Trial Registries & Results
  - but excluding the "results" part
  - So limited to "design" part

1.2 Project Description

The purpose of this project is to evaluate requirements and models originally developed for the registry portion of a previously-initiated HL7 Clinical Trials Registry and Results project, update the requirements as necessary to meet current EudraCT requirements while trying to address any gaps with the current ***clinicaltrials.gov*** *registry requirements, and develop and document a BRIDG-compatible, CDISC ODM-based XML schema implementation of these requirements that can be used to electronically exchange registry information between a study sponsor and a registry organization.*

Source: Clinical Trial Registration and Results Workgroup - Requirements document

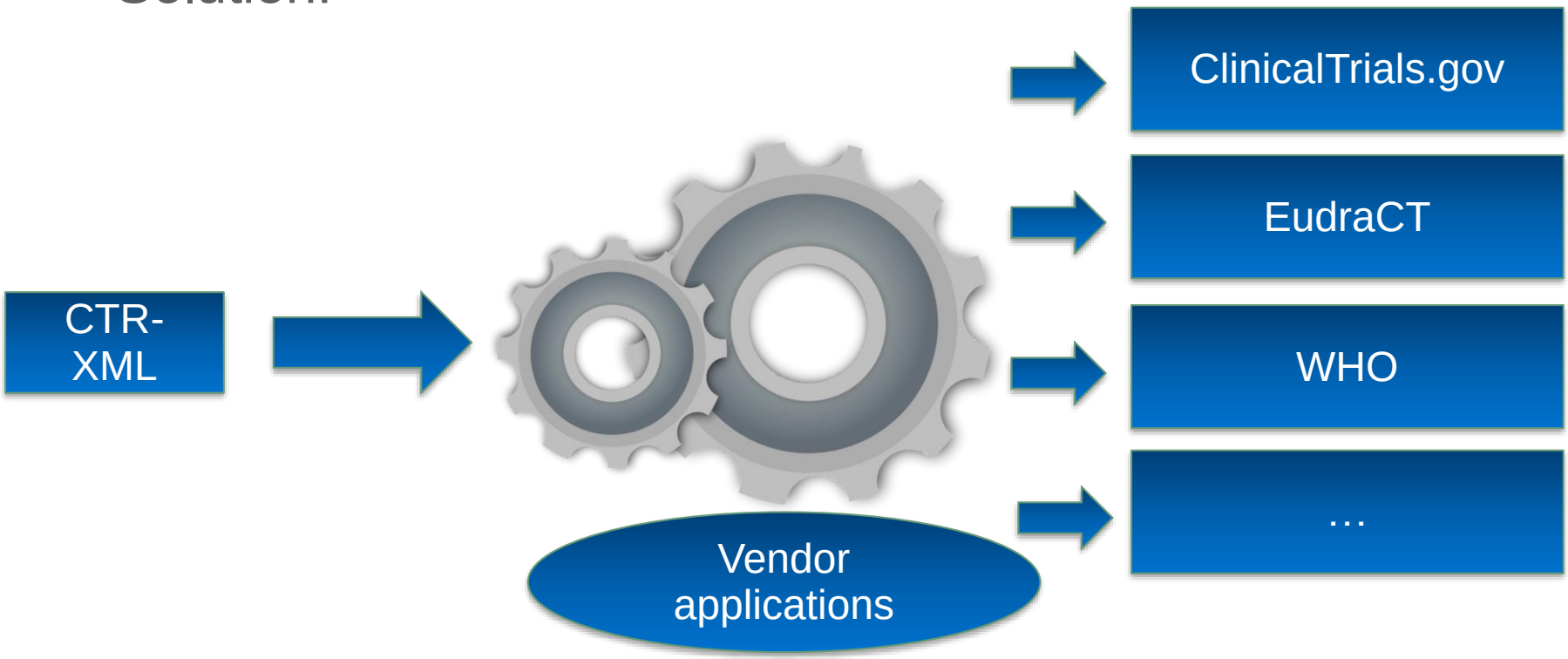
What problem are we trying to solve?

- For different clinical trial registries, sponsor companies and investigators must submit the same information over and over again
  - To different websites
  - Or using different formats
  - That is partially already in the study design (ODM/SDM-XML)

- Can a format be developed so that the information must be added only once?

The idea of „write once, submit several“

- Problem: it will take some time to convince all clinical trial registries to accept the CDISC format
- Solution:



Requirements

- CTR-XML must at least contain all common data elements of ClinicalTrials.gov and EudraCT
- Must implement the 20 WHO "data elements" (http://www.who.int/ictrp/network/trds/en/)
- Must reuse all information that is already in CDISC ODM anyway (electronic protocol)
  - E.g. eligibility criteria

Design principles

- If the information is already in ODM, use it (e.g. Study name)
- If the information is already in SDM-XML, use it (e.g. Eligibility criteria)
- If the information is already in SDTM (as a study design parameter), use it
  - Using SDM-XML "sdm:Parameter" name-value pairs
- If it is a name-value pair, use "sdm:Parameter" with existing or new CDISC Controlled Terminoloy
  - E.g. "planned number of participants"
- Use CDISC-CT as much as possible

Use of sdm:Parameter - example

```
<sdm:Summary>
   <sdm:Parameter OID="PAR.ADDON" ShortName="ADDON"
                  Term="Test product is added on to existing treatment">
      <sdm:Value ctr:CodeListOID="CL.TEST">Y</sdm:Value>
   </sdm:Parameter>
   <sdm:Parameter OID="PAR.AEDICT" ShortName="AEDICT" Term="Adverse event dictionary">
      <sdm:Value>MedDRA version 8.0 (partially masked by request of MSSO)</sdm:Value>
   </sdm:Parameter>
   <sdm:Parameter OID="PAR.AGEMAX" ShortName="AGEMAX" Term="Planned maximum age of subjects">
      <sdm:Value>No maximum</sdm:Value>
   </sdm:Parameter>
   <sdm:Parameter OID="PAR.AGEMIN" ShortName="AGEMIN" Term="Planned minimum age of subjects">
      <sdm:Value>50 years</sdm:Value>
   </sdm:Parameter>
   <sdm:Parameter OID="PAR.AGESPAN" ShortName="AGESPAN" Term="Age span">
      <sdm:Value>ADULT (18-65)</sdm:Value>
      <sdm:Value>ELDERLY (&gt; 65)</sdm:Value>
   </sdm:Parameter>
   <sdm:Parameter OID="PAR.BLIND" ShortName="BLIND" Term="Trial blinding scheme">
      <sdm:Value>DOUBLE BLIND</sdm:Value>
   </sdm:Parameter>
```

Advantage: automatic creation of SDTM "TS" (Trial Summary) dataset

Design principles

- Match EudraCT & ClinicalTrials.gov elements to
  - Either ODM elements
  - Or SDM-XML elements (including sdm:Parameter)
  - New XML elements
    - In a separate, new namespace
- Allow language localization

```
<sdm:Parameter OID="PAR.INDIC" ShortName="INDIC" Term="Trial indications">
  <!-- example of an Parameter-Value with translations -->
  <sdm:Value>
    <TranslatedText xml:lang="en">Mild to Moderate Alzheimer's Disease</TranslatedText>
    <TranslatedText xml:lang="de">Anfängende bis fortgeschrittene Alzheimer</TranslatedText>
  </sdm:Value>
</sdm:Parameter>
```

What when there is a semantic mismatch?

- "Trial phase" has different enumerations in ClinicalTrials.gov, EudraCT and CDISC-CT

- In such a case, use the attribute "Scope"

```
<sdm:Parameter OID="PAR.TPHASE" ShortName="TPHASE" Term="Trial Phase">
    <sdm:Value>Phase 2b Trial</sdm:Value><!-- CDISC value -->
    <sdm:Value ctr:Scope="EudraCT">Therapeutic Exploratory (Phase II)</sdm:Value>
    <sdm:Value ctr:Scope="ClinicalTrials.gov">Phase 2</sdm:Value>
</sdm:Parameter>
```

EudraCT extensions

- EudraCT requires information that is very specific and does not appear in any other clinical trial registry format

- In such cases, EudraCT v10 XML is used, as a "vendor" extension, in the EudraCT namespace "http://eudract.emea.europa.eu/schema/clinical_trial"

EudraCT example extension

```
<StudyName>
   <ctr:StudyNameLocalizations>
      <TranslatedText xml:lang="en">Xanomeline (LY246708) in english</TranslatedText>
      <TranslatedText xml:lang="de">Xanomeline (LY246708) auf Deutsch</TranslatedText>
      <TranslatedText xml:lang="fr">Xanomeline (LY246708) en Francais</TranslatedText>
   </ctr:StudyNameLocalizations>
</StudyName>
<StudyDescription>Safety and Efficacy of the Xanomeline Transdermal Therapeutic System (TTS) in Patients
<ProtocolName>H2Q-MC-LZZT(c)</ProtocolName>
<!-- CTR extensions -->
<ctr:Authorities>...</ctr:Authorities>

<MetaDataVersion Description="LZZT study design version 1" Name="LZZT study design version 1"
                 OID="LZZT_1">
   <!-- first come all the normal ODM elements -->
   <!-- then come the SDM-XML elements -->
   <!-- additional CTR elements that come under the Study element -->

   <!-- ************************************ -->
   <!-- medicinal_product is only for EudraCT -->
   <!-- ************************************ -->
   <ct:medicinal_product_information xmlns:ct="http://eudract.emea.europa.eu/schema/clinical_trial">
      <ct:medicinal_product>
         <ct:imp_category>
            <ct:eutct_id>112345678901</ct:eutct_id>
            <ct:eutct_version>10</ct:eutct_version>
         </ct:imp_category>
         <ct:imp_member_state>
            <ct:trade_name_in_ms>SuperDrug</ct:trade_name_in_ms>
            <ct:ev_identifiable_product_code></ct:ev_identifiable_product_code>
            <ct:ma_holder></ct:ma_holder>
```

What can we do with this new Standard?

- It gives technology vendors the opportunity to develop "add once – submit many" applications
- It gives us the opportunitity to strive for a worldwide standard accepted by all clinical trial registries
- As such, we believe it will get the same role as ODM has obtained in the last 15 years for EDC systems

What‘s in the distribution package?

- The specification
- The set of XML-Schemas
  - Entry schema: ctr1-0-0.xsd
- 2 example files

<Study OID="LZZT" ctr:StudyType="Interventional" ctr:ResponsiblePartyType="Sponsor">
<GlobalVariables>
<!-- StudyName: corresponding to WHO 'scientific title', CT.gov 'official title' and EudraCT 'scientific rationale'
<!-- ORIGINAL ODM:
<StudyName>Xanomeline (LY246708)</StudyName> -->
<StudyName>
<ctr:StudyNameLocalizations>
<TranslatedText xml:lang="en">Xanomeli lish</Translate
<TranslatedText xml:lang="de">Xan meli utsch</Translat
<TranslatedText xml:lang="fr) is</Translat
tudyNameLocalizations>
e>
ript Ef of line Tra herapeutic d
ame>H2Q-MC-LZZT(c)</Pro
<!-- CTR extensions -->
<ctr:Authorities>
<!-- FDA information -->
<ctr:FDAInformation IsFDARegulatedIntervention="Yes" IsINDNDEProtocol="Yes" H
<!-- Institutional Review Boards /
<ctr:InstitutionalReviewBoardEt roval="S
i
T.ANTHO CL.CONTACTROLES" ContactRole="CENTRAL CONTACT"/>
dEthicsCommittee>
cities -->
yCode="USA" CodeListOID="CL.COUNTRIES" Name="Federal Government">
izationOID="ORG.USFEDGOV"/>
yCod fe
izat
yCode="GER" CodeListOID="CL.COUNTRIES" Name="Paul-Ehrlich-Institut">
izationOID="ORG.PAULEHRLICH"/>
title" goes into the ODM element "StudyName" -->

CTR-XML

ClinicalTrials.gov

EudraCT

WHO

.....

Vendor applications

Question Time ...

CTR Stage 2 – Project ‘Optimus’

Paul Houston
Head of European Operations (CEF)

Protocol Representation Implementation Model - executable

Clinical Trial Registration & Results 2

Project Goals

- Project ‘Optimus’ as a second stage of CDISC CTR will focus on defining fully structured protocol and results summary elements. The CTR_2 standard will therefore utilize and necessitate the development of a new Protocol standard – PRIMe. The goal of the new standards being:
- driving further harmonisation of International Registry requirements between stakeholders
- to advance the beginning to end support of clinical trials
- Ensure that IDMP elements are mapped to CTR_2 and PRIMe

PRIMe Deliverables

- A definitive Protocol schema that can be implemented in software.
- A protocol model implemented in SHARE and integrated into a beginning-to-end CDISC metadata model.
- RDF and XML export formats.
- Extensions to SDM, SDTM, CDASH and ADaM where appropriate.
- harmonization with TransCelerate protocol work
- A short user guide to explain how to use the SHARE content and tools, including examples
- Controlled vocabulary sets with relationships expressed to the foundational standards

PRIMe Drivers

- To enable traceability of all protocol and Statistical Analysis Plan elements throughout the study
- Improve protocol quality and minimize amendments though re-use and consistency checks
- Improves the quality and efficiency of clinical research by explicitly aligning study objectives and endpoints with the data being captured and analyzed.
- Give greater flexibility, structure and reliability to biomarker design and analysis
- Provide new opportunities to create protocol-driven process automation and generation of study artifacts.

CTR_2 Deliverables

A set of standard elements represented in an extended version of ODM and where appropriate mapped to the standards metadata model in SHARE.

Summary result data elements as defined by the stakeholders and extensible as desired (ADaM and Define-XML data set configurations to present summary results)

A short user guide to explain how to use the SHARE content and tools, including examples.

Controlled vocabulary sets with relationships expressed to the foundational standards

CTR_2 Drivers

- A set of standard elements represented in an extended version of ODM and where appropriate mapped to the standards metadata model in SHARE.
- Summary result data elements as defined by the stakeholders and extensible as desired (ADaM and Define-XML data set configurations to present summary results)
- A short user guide to explain how to use the SHARE content and tools, including examples.
- Controlled vocabulary sets with relationships expressed to the foundational standards

Combined drivers

- Achieve true beginning to end support of clinical trial elements
- Create great efficiencies within drug development programs
- Easier reuse of trial designs
- Data quality gains through information management improvements
- Enabling re-use of content
- IDMP inclusion to increase the depth and quality of information relating to medicinal products , substances etc
- Support better Pharmacovigilance and research
  - Effective searching against clinical trial databases etc…

Timeline – 12 months

Project Stage	Project Stage Description	Timeline for Completion
Kick off	**Kick off**	Month 1
Stage 0	Scoping & Planning	Month 1-2
Stage 1	Concept Modeling (face to face at Europe Interchange 25-26 April)	Month 2-5
Stage 2	Standards Development	Month 5- 8
Stage 3a	Internal Review	Month 8-10
Stage 3b	Public Review	Month 10-11
Stage 3c	Publication	Month 12

Stakeholders

Stakeholders:

EMA, NIH, WHO,Trialscope, EFPIA , FDA, PMDA, Transcelerate, BRIDG Semantic Coordination Committee , CDISC Foundational Standards teams,

CDISC is looking for volunteers and/or sponsors. Estimated project budget is $218,000 for the 3 FTEs in the core team.

Others invitation for volunteers is open.

For more information please Contact phouston@cdisc.org Please forward on the CTR Webinar and these slides to your colleagues that maybe interested.

A big thank you for our sponsors for CTR stage 1 Biogen Idec and all our volunteers and thanks to our attendees today for your time and support today.

Q&A Session

CDISC Education Events Announcements

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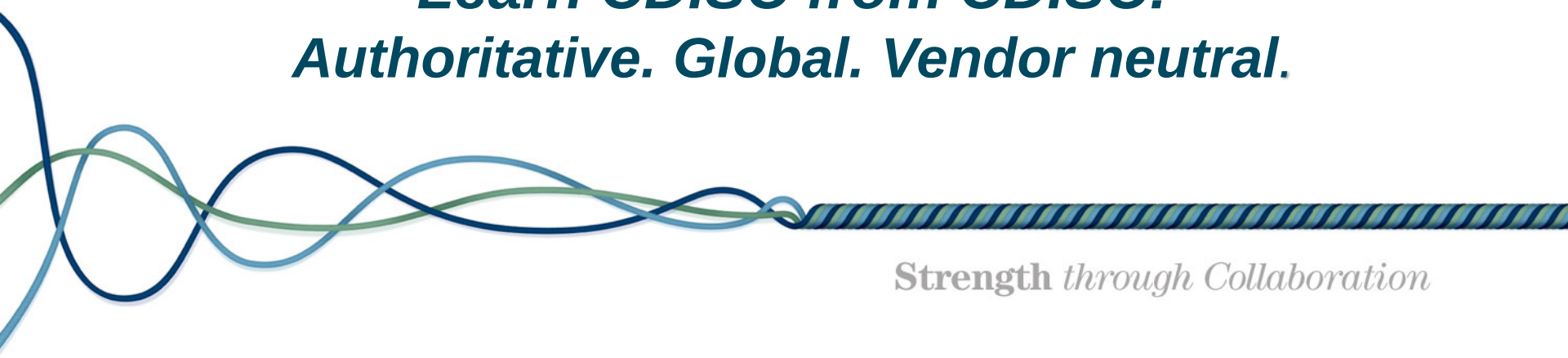

Standard currently out for review

- COPD v1 TA User Guide
  - Visit http://cdisc.org/therapeutic#copd for more information
  - Comments due 30 November 2015
- Tuberculosis v2 TA User Guide
  - Visit http://cdisc.org/therapeutic for more information
  - Comments due 30 November 2015

Click here to submit your comments.

Upcoming North America Public Courses and Events

Location	Dates	Courses Offered	Host
Chicago, IL (International Interchange)	9, 12-13 Nov	See website	CDISC
Morrisville, NC	9-12 Feb 2016	SDTM, CDASH, ADaM	SynteractHCR
Audubon, PA	2-11 Mar 2016	Courses corresponding to standards listed in Data Standards Catalog. See web.	BIOCLINICA
Emeryville, CA	11-15 April 2016	Courses corresponding to standards listed in Data Standards Catalog. See web.	Santen
Visit cdisc.org/public-courses for information on other CDISC Public Training events.			

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

Upcoming Europe Public Courses and Events

Location	Dates	Courses Offered	Host
Berkshire, UK	26-29 Jan 2016	SDTM, ADaM, Define-XML	QUINTILES
Paris, France	8-11 Mar 2016		SANOFI
Europe Interchange in Vienna, Austra	25-29 Apr 2016, Registration Opens Dec 2015 on CDISC Website: http://cdisc.org/interchange		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.

Full 2016 Public Training Schedule is online
Check CDISC website for up-to-date information on Public Courses

Upcoming Asia Public Courses and Events

Location	Dates	Courses Offered	Register by:	Early Registration Discounts	Host
Tokyo, Japan	14-18 Dec 2015	SDTM, CDASH, ADaM, ODM, Define-XML	13 Nov 2015	*13 Nov 2015*	CAC EXICARE Corporation

Visit http://cdisc.org/public-courses for information on other CDISC Public Training events in Asia.

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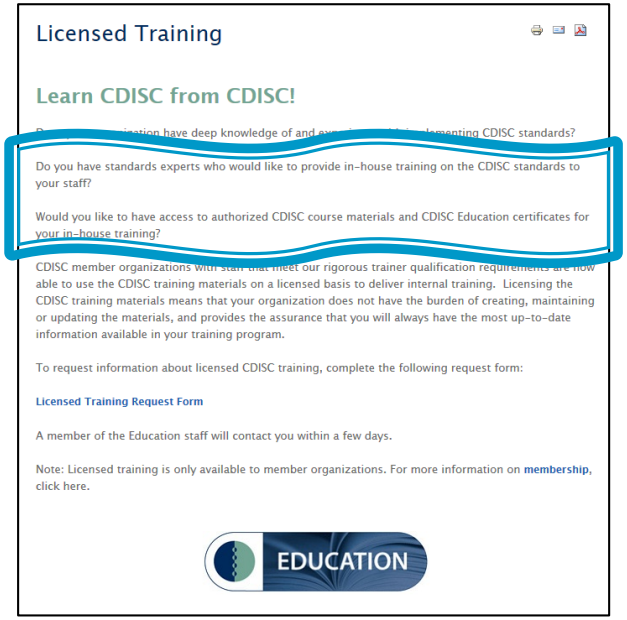

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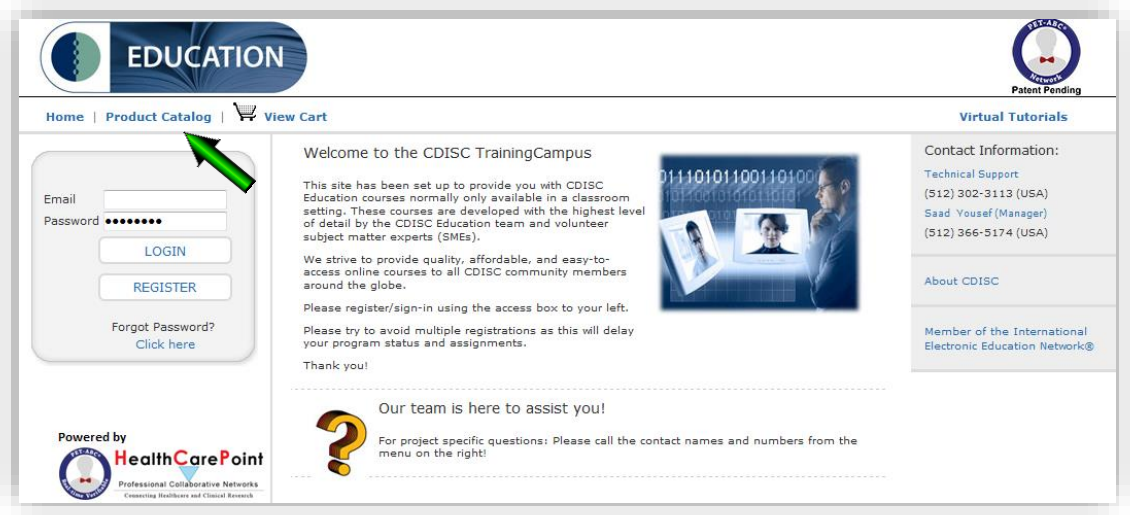
Cdisc.trainingcampus.net

- 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**
  - Tuberculosis v2 TA Public Review
- **Date**: 17 Nov 2015, 10:00-11:30 AM CST
- **Speakers:**
  - Laura Butte, C-Path
  - Bess LeRoy, C-Path
- Register here.

Webinar details also at www.cdisc.org/webinars

Next Members Only Webinar

- **Agenda:**
  - Ophthalmology (OE) Domain
- **Date**: 19 Nov 2015, 10:00-11:30 AM CST
- **Speakers:**
  - Kim Truett, KCT Data
- Register here.

Webinar details also at www.cdisc.org/webinars

Any more questions?

Thank you for attending this webinar.

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