

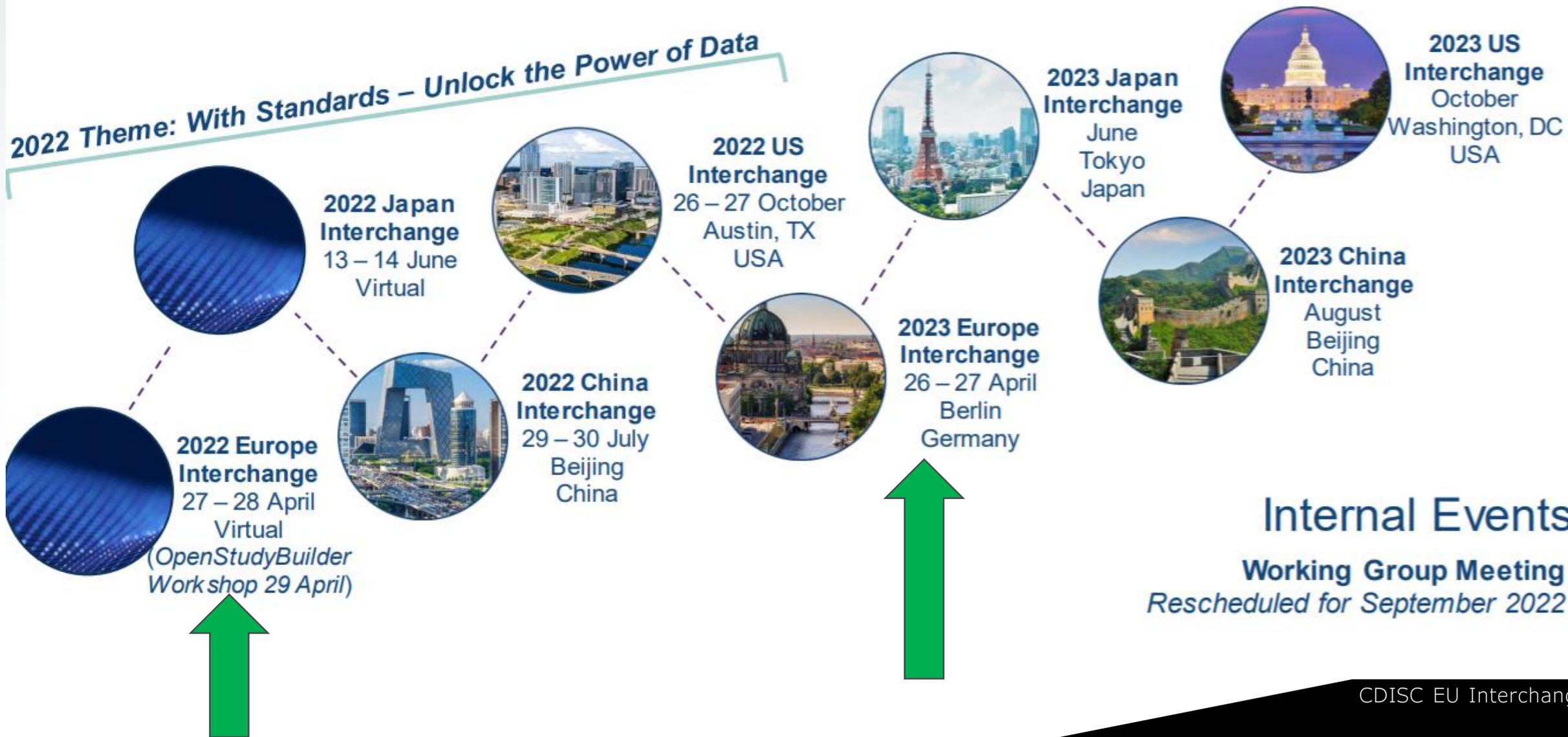
2022 EUROPE INTERCHANGE CDISC VIRTUAL CONFERENCE 27-28 APRIL

The CDISC logo, consisting of the lowercase letters 'cdisc' in a bold, blue, sans-serif font. Above the 'i' are three colored dots: red, yellow, and light blue.

MAURO CORTELLINI, DM

CDISC Events, 2022 - 2023

2022 Theme: *With Standards – Unlock the Power of Data*



Internal Events
Working Group Meeting
Rescheduled for September 2022

Meeting Agenda

 COSA: CDISC Open Source Alliance

 CORE: CDISC Open Rules Engine

 Real World Data from EMA



Meeting Agenda

-  COSA
-  CORE
-  Real World Data from EMA



CDISC Project: COSA

Mission:

The CDISC Open Source Alliance supports, promotes, and sometimes sponsors open source and free software development projects that create tools for implementing or developing CDISC standards to drive innovation in the CDISC community.



CDISC Project: COSA

COSA

The CDISC Open Source Alliance

Mission: The CDISC Open Source Alliance supports, promotes, and sometimes sponsors open source and free software development projects that create tools for implementing or developing CDISC standards to drive innovation in the CDISC community.

- Provide a directory for open source projects
- Conference sessions & webinars
- Hackathons & workshops
- Sandbox environment & test data
- Community building
- Information exchange
- Open-source best practices
- Licensing guidance



COSA is directed by a Governance Board that evaluates projects for inclusion in the **COSA Repository Directory**, sets the project inclusion criteria, and determines what committees are needed to lead COSA activities.

On 23Sep e-mail: *'First COSA-approved tools are now freely available via the [COSA Repository Directory](#)'*

18Nov2021 dedicated COSA webinar

Mar 2022 → 9 projects deployed in total

COSA Repository Directory

The following repositories are officially recognized by COSA as being open-source projects focused on implementing or developing CDISC standards innovation in the CDISC community. All COSA projects must meet the [inclusion criteria](#) to be considered for inclusion the Repository Directory.

View All 9

Define-XML 7

ADaM 4

Dataset-XML 3

ARM 3

SDTM 2

ODM 1

CDISC CT 1

CDASH 1



Admiral
ADaM in R Asset Library.



odmLib
odmLib is a Python library that simplifies creating and processing ODM and its extensions, such as Define-XML.



Tplyr
Tplyr is a grammar of data format and summary, designed to simplify the creation of clinical safety summaries.



Open Study Builder
The OpenStudyBuilder is a new approach to working with studies that once fully implemented will drive end-to-end consistency and more efficient processes.



Define-XML XSL Stylesheets
This projects provides a Define-XML v2.0 and v2.1 XSL stylesheet



R4DSXML
R4DSXML is R package for import both CDISC Dataset-XML and Define-XML as R data frame.

Q: Which is the added value to have CDISC on board instead of single WGs?

Jun 2022 → 11 projects
deployed in total

COSA Repository Directory

The following repositories are officially recognized by COSA as being open-source projects focused on implementing or developing CDISC standards to drive innovation in the CDISC community. All COSA projects must meet the [inclusion criteria](#) to be considered for inclusion the Repository Directory.



View All 11

Define-XML 7

ADaM 5



Digital Data Flow

The DDF initiative aims to modernize clinical trials by enabling a digital workflow that allows for automated creation of study content and configuration of study systems to support clinical trial execution.



tidyCDISC

tidyCDISC is a shiny app to easily create custom tables and figures from ADaM-ish data sets.



Number is slowing increasing, but... do you remember the 'Gli scacchi e il Faraone' novel?

When many people are working with the same aim, at the beginning improvement is low... until ecosystem reaches a turning point

CDISC Project: COSA eLearnings

<https://www.cdisc.org/cosa>

Overview

Webinars

Past eLearnings

COSA Spotlight
CDISC Open Source Alliance

- Tplyr**
- Define-XML XLS Stylesheets**
- OpenStudyBuilder**

- Sam Hume, VP, Data Science, CDISC
- Charles Shadle, Head of Data Science Operations, CDISC
- Mike Stackhouse, Chief Innovation Officer, Atorus Research
- Eli Miller, Informatics Application Developer, Atorus Research
- Lex Jansen, Sr. Director, Data Science Development, CDISC
- Henrik Lyngge, Vice President, Novo Nordisk A/S
- Mikkel Traun, Principal Programmer, Novo Nordisk A/S

1:33:45

cdisc.org

CDISC Open Source Alliance (COSA) Spotlight Q1 2022

CDISC Open Source Alliance (COSA) Spotlight

Bhavin Busa, VP of Clinical Data Services & Operations, Vita Data Sciences
Sam Hume, VP Data Science, CDISC
Dmitry Kolosov, Expert Statistical Programmer, Parexel,

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THU 18 NOV
11:00AM-12:30PM ET

1:54:48

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CDISC Open Source Alliance (COSA) Spotlight Q4 2021

COSA Spotlight Q2 2022

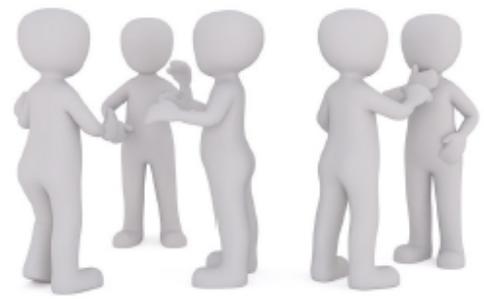
Next eLearning: *Tomorrow, 30Jun2022. 17-18.30 Italian time*

30 June 2022, 11 am - 12:30pm EDT

CDISC Project: COSA

How does COSA work?

- Board
 - Bi-weekly meeting
 - Next steps
 - Applications
 - Various topics



Name	Company
Bhavin Busa	Vita Data Sciences
Dmitry Kolosov	Parexel and Open-source developer
Jeff Fattic	Microsoft
Katja Glaß	Katja Glass Consulting
Mike Stackhouse	Atorus
Mikkel Traun	Novo Nordisk
Sam Hume	CDISC
Charles Shadle	CDISC, ex officio

CDISC Project: COSA

COSA Participation

- Application process documented, form available <https://cosa.cdisc.org/application>

➤ Get in contact

- [LinkedIn](#), Mail (cosa@cdisc.org)
- Contact with board members
- Become a board member

The screenshot shows the 'Application Editor' interface for the CDISC Open Source Alliance. The page has a dark blue header with the CDISC logo and navigation links: DIRECTORY, ABOUT, EVENTS, APPLICATION, and OTHER. Below the header, the page title is 'Application > Editor'. The main content area is titled 'Application Editor' and contains three buttons: 'SAVE', 'LOAD', and 'PREVIEW'. The form is divided into two columns: 'Project Information' and 'Detailed Description'. The 'Project Information' column has three input fields: 'Project Name', 'Project Owner', and 'Project Contact', each with a question mark icon. The 'Detailed Description' column has three input fields: 'Problem', 'Solution', and 'Open Source Considerations', each with a question mark icon.

CDISC Project: COSA

<https://cosa.cdisc.org>

Meeting Agenda

 COSA

 CORE

 Real World Data from EMA



RWD: DARWIN EU Example



Update on DARWIN EU®

Data Analysis and Real World
Interrogation Network

28 April 2022



RWD: DARWIN EU Example

By 2025 the use of Real-World Evidence will have been enabled and the value will have been established across the spectrum of regulatory use cases

- European Medicines Regulatory Network (EMRN) strategy to 2025 -

Foster the value of RWD and incorporate in decision making

HMA / EMA Big Data Steering Group

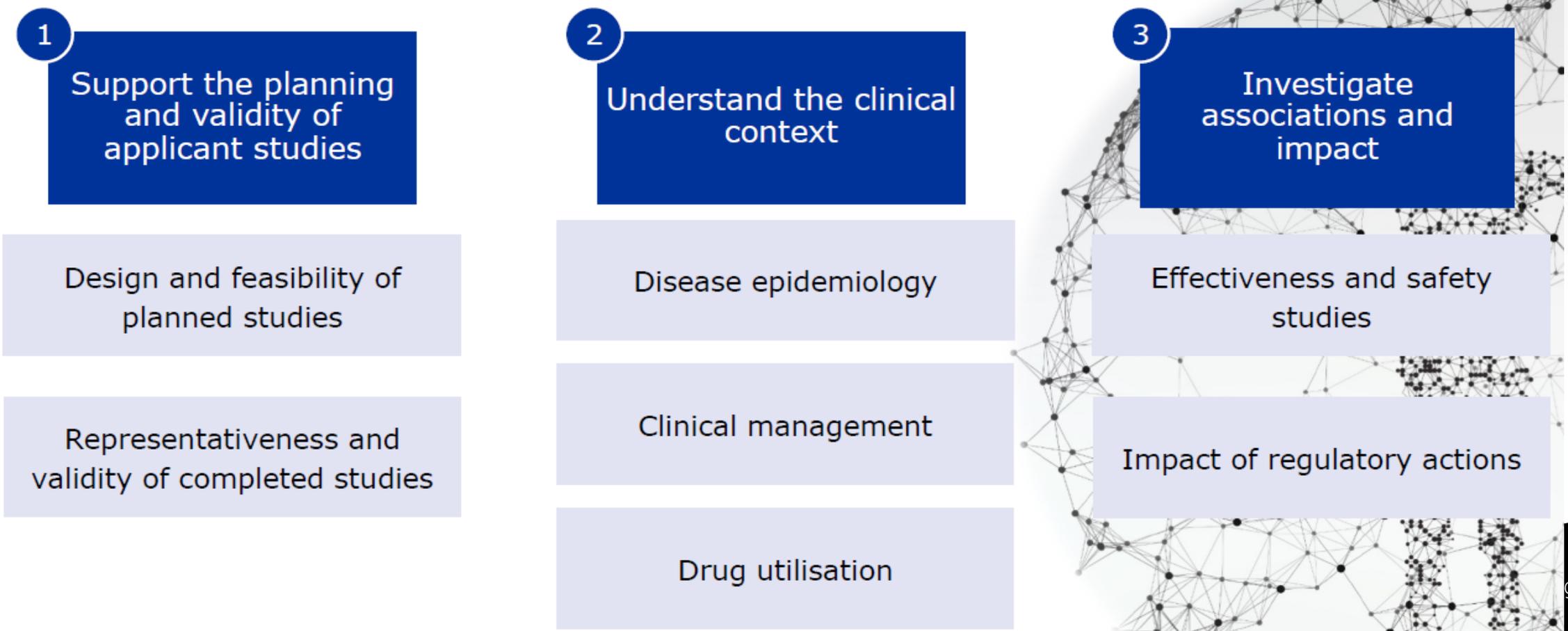
The European Medicines Agency (EMA) and Heads of Medicines Agencies (HMA) set up a **joint task force** to describe the big data landscape from a regulatory perspective and identify practical steps for the European Medicines Regulatory Network to make best use of big data in support of innovation and public health in the European Union (EU). This led to the creation of the **Joint HMA/EMA Big Data Steering Group** and **Big Data Steering Group Work Plan**.



DARWIN is the top priority in the workplan

RWD: DARWIN EU Example

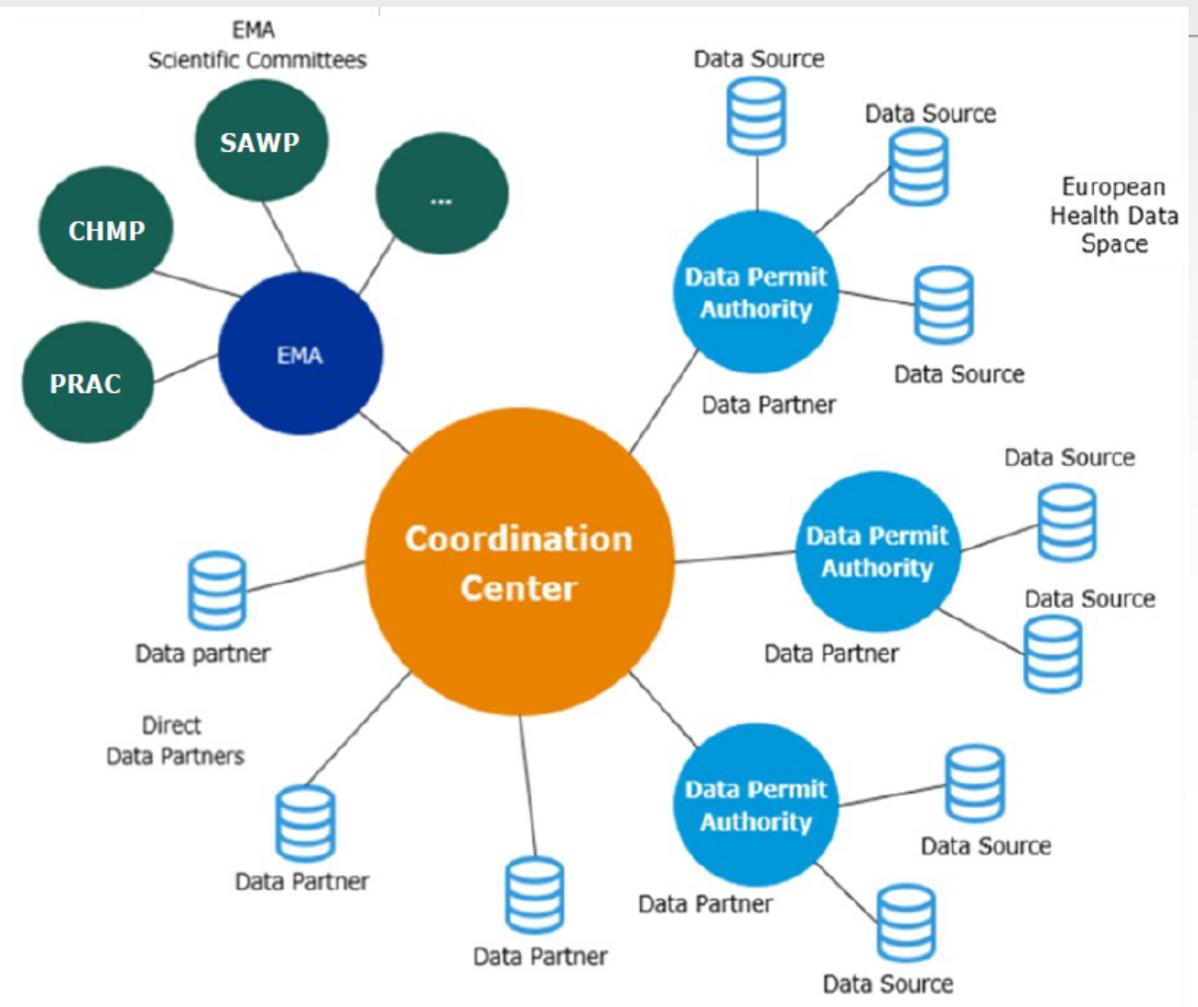
Three main areas for which RWD analyses can support committees' decision-making



RWD: DARWIN EU Example

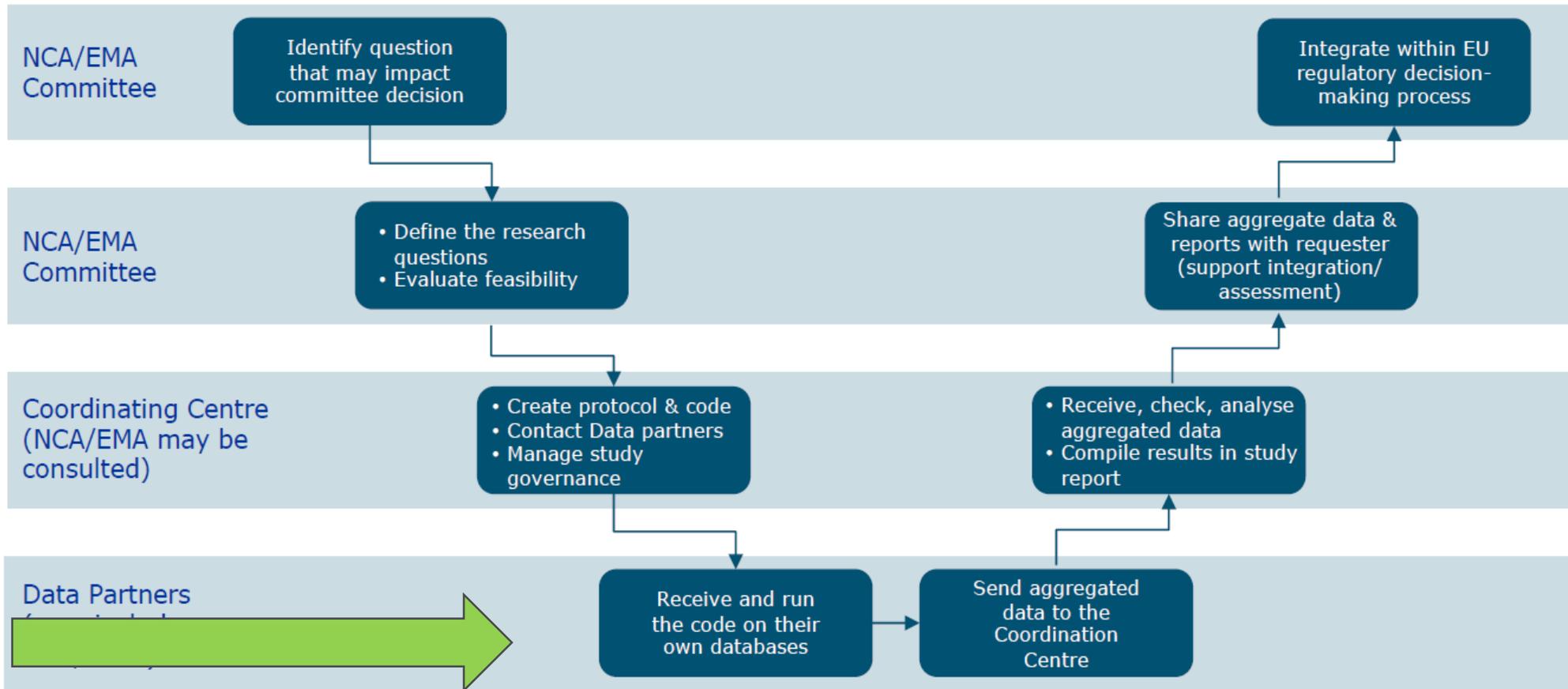
DARWIN EU® is a federated **network of data, expertise and services** that supports better decision-making throughout the product lifecycle by generating reliable **evidence from real world healthcare data**

- FEDERATED NETWORK PRINCIPLES**
- Data stays **local**
 - **Use of Common Data Model** (where applicable) to perform studies in a timely manner and increase consistency of results



The principles for data access via DARWIN EU® include the data staying locally at the data partners' sites and the use of a Common Data Model (CDM).

What is the DARWIN EU[®] process for conducting studies?



For regular updates on DARWIN EU[®] Subscribe to the [Big Data Highlights](#) newsletter by sending an email to: bigdata@ema.europa.eu

Meeting Agenda

 COSA

 CORE

 Real World Data from EMA



CORE Rules Delivery Planning



Phase 1

CORE Engine

- SDTMIG v3.4 Conformance Rules
- Sample SEND, ADaM, and Regulatory Rules
- Machine Executable

Phase 2

- SDTMIG v3.2 and v3.3 Conformance Rules
- SENDIG Rules
- ADaMIG Rules
- Regulatory Authority Rules

Phase 3

- Evaluate and Develop New Content
- Refinement of Existing Rules

Complete Q2 2022

Complete Q1 2023
SDTMIG v3.2 and v3.3 Rules

Complete Q2 2023
SENDIG Rules

Complete Q3 2023
ADaMIG Rules

Begin Q1 2023

Publish the Rules in the CDISC Library and the engine under the CDISC Open Source Alliance (COSA)

CDISC CORE

<https://core.cdisc.org/>

CDISC CORE and P21

Q: *P21 had implemented CORE in validation tool?*

A: We've seen the announcement from P21 that had implemented support to CORE in their validated release. [...] However, CORE engine should be available for all.

Q: *Is CORE complementing or replacing P21?*

A: That's really not the point. Folks out-there are going to be able to use the open source engine [...] or company-like P21. The idea is they are going to refer to CORE to verify the output and the results, if the result are equal it is very good.

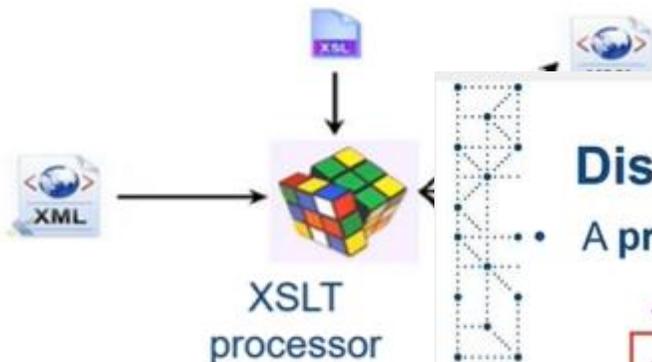


Thank You

Back Up slides

Displaying Define-XML

- eXtensible Stylesheet Language Transformations (XSLT) is a language that lets you transform XML documents into other XML documents, into HTML documents, or into any other text-based document (CSV, JSON, code, ...), or even a PDF file.
- XSLT is a language "for transforming the structure and content of an XML document"



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Displaying Define-XML

- A processor instruction associates a stylesheet with an XML file

```
<?xml version="1.0" encoding="UTF-8"?>
<?xml-stylesheet type="text/xsl" href="define2-0-0.xsl"?>
```

```
<ODM
  xmlns="http://www.cdisc.org/ns/odm/v1.3"
  xmlns:xlink="http://www.w3.org/1999/xlink"
  xmlns:def="http://www.cdisc.org/ns/def/v2.0"
  ODMVersion="1.3.2"
  ...
```

- A stylesheet processor can use the processor instruction to automatically apply the stylesheet ... *(but not in modern browsers on your local PC)*

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Available Stylesheets

- CDISC provided sample stylesheets:
 - 2005 - Define-XML v1.0 (“CRT-DDS”)
 - 2011 - Metadata Submission Guideline (MSG) for SDTMIG (Define-XML v1.0)
 - 2014 - Define-XML v2.0
 - 2015 - Analysis Results Metadata (ARM) v1.0 for Define-XML v2.0
 - 2019 - Define-XML v2.1
- PHUSE working group published an updated and much style
 - 2018 – Define-XML 2.0

Available Stylesheets

The latest Define-XML v2.0 and v2.1 stylesheets:

- Conform to web standards and follow accessibility guidelines
- Renders to HTML that is supported in modern browsers (Chrome, Firefox, MS Edge, Safari)
 - Internet Explorer is retiring soon
- Use JavaScript, but degrade gracefully when JavaScript is disabled
- Implement a special style for printing purposes (recommended: landscape)

- But where do you go with issues and bugs?
- Where do you find the latest stylesheets?

The COSA Project



Define-XML XSL Stylesheets

This projects provides a Define-XML v2.0 and v2.1 XSL stylesheet

- Provides a central location on GitHub for the latest Define-XML stylesheets
- Central location for submitting issues / feature requests
- Documentation of stylesheet usage
(example: how to transform Define-XML to HTML outside of the browser)
- Scope is narrow: use case of electronic submissions to regulatory agencies
- Will not depend on the availability of an XSLT processor in the browser
 - Modern browsers do not allow transforming a local Define-XML document to HTML using an XSLT stylesheet reference for reasons of security
 - XSLT processors in the browser only support XSTL 1.0 (1999!)
 - Use an external XSLT processor to transform to HTML that can be opened in any browser



The Define-XML XSL Project: What's next

- Style sheet localization: **one** stylesheet for **many** languages
- The stylesheet uses a parameter (**interfaceLang**) to look up translations in a dictionary

```
<?xml version="1.0" encoding="utf-8"?>
<dictionary>
  <entry term="Class">
    <TranslatedText xml:lang="zh">类</TranslatedText>
    <TranslatedText xml:lang="ja">クラス</TranslatedText>
  </entry>
  <entry term="Code List">
    <TranslatedText xml:lang="zh">代码列表</TranslatedText>
    <TranslatedText xml:lang="ja">コードリスト</TranslatedText>
  </entry>
  <entry term="Codelist">
    <TranslatedText xml:lang="zh">代码列表</TranslatedText>
    <TranslatedText xml:lang="ja">コードリスト</TranslatedText>
  </entry>
  <entry term="Collapse all VLM">
    <TranslatedText xml:lang="zh">折叠所有VLM</TranslatedText>
    <TranslatedText xml:lang="ja">すべてのVLMを折りたたむ</TranslatedText>
  </entry>
  <entry term="Comment">
    <TranslatedText xml:lang="zh">注释</TranslatedText>
    <TranslatedText xml:lang="ja">コメント</TranslatedText>
  </entry>
</dictionary>
```



For not English-oriented Ras:
instead of creating multiple
Stylesheets, just one with the
option to switch language

CDISC-Sample

- Supplemental Documents
- Datasets
- Controlled Terminology
- Methods

Expand all VLM

Collapse all VLM

Datasets								
Dataset	Description	Class	Structure	Purpose	Keys	Documentation	Location	
ADSL	Subject-Level Analysis	SUBJECT LEVEL ANALYSIS DATASET	one record per subject	Analysis	USUBJID	Screen Failures are excluded since they are not needed for this study analysis	adsl.xpt	
ADQSADAS	ADAS-Cog Analysis	BASIC DATA STRUCTURE	One record per subject per parameter per analysis visit per	Analysis	USUBJID, PARAMCD, AVISIT, ADT	See referenced dataset creation program and Analysis Data Reviewer's	adqsadas.xpt	

CDISC-Sample

- 補足文書
- データセット
- 統制用語
- メソッド

すべてのVLMを展開する

全てのVLMを折りたたむ

データセット								
データセット	要約	クラス	構造	目的	キー	ドキュメンテーション	ロケーション	
ADSL	Subject-Level Analysis	SUBJECT LEVEL ANALYSIS DATASET	one record per subject	Analysis	USUBJID	Screen Failures are excluded since they are not needed for this study analysis	adsl.xpt	
ADQSADAS	ADAS-Cog Analysis	BASIC DATA STRUCTURE	One record per subject per parameter per	Analysis	USUBJID, PARAMCD, AVISIT, ADT	See referenced dataset creation program and Analysis Data Reviewer's	adqsadas.xpt	

CDISC-Sample

- 补充文件
- 数据集
- 受控术语
- 方法

展开所有VLM

收起所有VLM

数据集								
数据集	描述	类	结构	目的	按键	文献资料	位置	
ADSL	Subject-Level Analysis	SUBJECT LEVEL ANALYSIS DATASET	one record per subject	Analysis	USUBJID	Screen Failures are excluded since they are not needed for this study analysis	adsl.xpt	
ADQSADAS	ADAS-Cog Analysis	BASIC DATA STRUCTURE	One record per subject per parameter per analysis visit per	Analysis	USUBJID, PARAMCD, AVISIT, ADT	See referenced dataset creation program and Analysis Data Reviewer's	adqsadas.xpt	



39:21



Directory › tidyCDISC



Project Owner

Aaron Clark

Repository

<https://github.com/Biogen-Inc/tidyCDISC>

Landing Page

<https://biogen-inc.github.io/tidyCDISC/>

Open Source License

AGPL-3.0

Problem

Creating static tables, listings, and figures, (TLGs) can be an iterative process with multiple revisions, which can take a large amount of person-hours. Furthermore, products that allow interactive exploration of ADaM data primarily are proprietary and do not allow the code that generated the interactive visualization, limiting its use for reproducibility.

Solution

{tidyCDISC} is an application designed with the shiny package in R that allows a user to import ADaM data, create tables using a drag-and-drop interface, figures, and patient profiles. The code that generated the drag-and-drop table can then be exported as an R script, capable of running independently from the shiny program.

List of {tidyCDISC} presentations:

- [Phuse single day event](#)
- [R/Medicine](#)
- [R in Pharma](#)
- [tidyCDISC Youtube Channel](#)
- [Appsilon Shiny Conference 2022](#)

Data Upload/Preview

Data upload

ADSL file is mandatory & BDS/ OCCDS files are optional
Inspect Uploaded Data

- ADSL
- ADVS
- ADAE
- ADLBC

Data Preview for ADAE

Show 10 entries

Search:

STUDYID	CTRTID	LETRNID	TRTA	TETAN	AGE	AGEGR1	ADTGR2N	RACE	SEX	TA
1	USM4P000001	101	01_201-1101	Placebo	0	60-65		WHITE	1	1
2	CDISCHE0701	101	01_201-1101	Placebo	0	60-65		WHITE	1	1
3	CDISCHE0701	101	01_201-1101	Placebo	0	60-65		WHITE	1	1
4	CDISCHE0701	101	01_201-1101	Placebo	0	60-65		WHITE	1	1
5	CDISCHE0701	101	01_201-1101	Placebo	0	60-65		WHITE	1	1
6	CDISCHE0701	101	01_201-1101	Placebo	0	60-65		WHITE	1	1

Riproduci (k)

Filter Data

Commonly Used Tables: NONE

ADVS

- DIABP
- HEIGHT
- PULSE
- SYSBP
- TEMP
- WEIGHT

ADLBC

Variables

DiABP X

RACE X

SYSBP X

Stats

MEAN X

FREQ X

ANOVA X

Stats

CHG

ANOVA

MEAN

FREQ

Table Title:

Download Table

Download Type: CSV HTML

	Placebo N=86	Xanomeline High Dose N=84	Xanomeline Low Dose N=84
Descriptive Statistics of Diastolic Blood Pressure (mmHg) at Week 6			
Missing	0	0	0
Mean	74.48	75.26	74.9
SD	10.2	9.9	9.18
Median	74	76	76
Q1 Q3	70 80	70 82	70 80
Min Max	48 110	52 98	50 100
Summary Counts of Race			
AMERICAN INDIAN OR ALASKA NATIVE	NA	1 (1.19)	NA
BLACK OR AFRICAN AMERICAN	8 (9.3)	9 (10.71)	6 (7.14)
WHITE	78 (90.7)	74 (88.1)	78 (92.86)
ANOVA of Systolic Blood Pressure (mmHg) at Week 8			
p-value			0.683
Test Statistic			0.38
Mean Sum of Squares			111.87