cdisc

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It's easy peasy submitting data to the NMPA, really?

Meet the Speaker

Chenkai Lv

Title: Data Scientist

Organization: Roche

Chenkai Lv is a data scientist in Roche PD Data Sciences function and has been working in Pharmaceutical Industry for over four years. He mainly works in oncology and contributes to several studies in solid tumor and hematology areas. He has experience in both global filing and China filing and is also a member of the eSub global team acting as the China Filing point of contact at Roche. Besides, he also contributes to some next-generation tools projects like R End-to-End packages development and eSub package translation pipeline set-up.

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Agenda

1. China Filing evolution and preparation
2. China Filing new topic: Translation
3. Early planning and smooth delivery
4. Discussion: eSub For Future in China
5. Key Takeaways

China Filing evolution and preparation

Old China (e)Sub Requirement

Rawdata Spec ✗
No Translation Requirement -
Rawdata SAS xpt's ✗
No Translation Requirement -
Analysis data Spec ✗
No Translation Requirement -
Analysis data SAS xpt's ✗
No Translation Requirement -
SAS programs ✗
(occasionally requested by CDE reviewers)
No Translation Requirement -

New guidance, Effective 1-Oct,2020

- ✓ Protocol
- ✓ eSub annotated CRF
  - Translate all except for Var name
- ✓ SDTM Define
  - Translate all except for Var name
- ✓ SDTM SAS xpt's
  - Translate Var & dataset label & MedDRA + WHODrug/GNE coding
- ✓ SDTM Reviewers Guide pdf (SDRG)
  - Translate all except for Var name
- ✓ ADaM Define
  - Translate all except for Var name
- ✓ ADaM SAS xpt's
  - Translate Var & dataset label & MedDRA + WHODrug/Legacy GNE or Roche coding List
- ✓ SAS programs
  - No explicit requirement for translating SAS or R programming comments
- ✓ ADaM Reviewers Guide pdf (ADRG)
  - Translate all except for Var name

NOTE: CDISC is not mandatory but recommended

NMPA (China)

Source Data

SDTM annotated CRF
[**Translation required**]

SDTM Define.XML **or PDF**
[**Translation required**]

SDTM SAS xpt's
- **Conformance** to NMPA validation rules.
- [**Translation required**]

SDTM Reviewers Guide (SDRG)
- **Explanation** of the validation rules.
- [**Translation required**]

Analysis Data

ADaM Define.XML **or PDF**
[**Translation required**]

ADaM SAS xpt's
- **Conformance** to NMPA validation rules.
- [**Translation required**]

Software programs (E.g. SAS)
(.txt format)

ADaM Reviewers Guide (ADRG)
- **Explanation** of the validation rules.
- [**Translation required**]

FDA

Source Data

SDTM annotated CRF

SDTM Define.XML

SDTM SAS xpt's
- Conformance to **FDA validation rules**

SDTM Reviewers Guide (SDRG)
- Explanation of the validation results against **FDA validation rules**

Analysis Data

ADaM Define.XML

ADaM SAS xpt's
- Conformance to **FDA validation rules**

Software programs (E.g. SAS, R)
(.txt format)

ADaM Reviewers Guide (ADRG)
- Conformance to **FDA validation rules**

PMDA (Japan)

Source Data

Similarly as FDA with **PMDA validation rules**

Analysis Data

Similarly as FDA with **PMDA validation rules**

EMA

Source Data

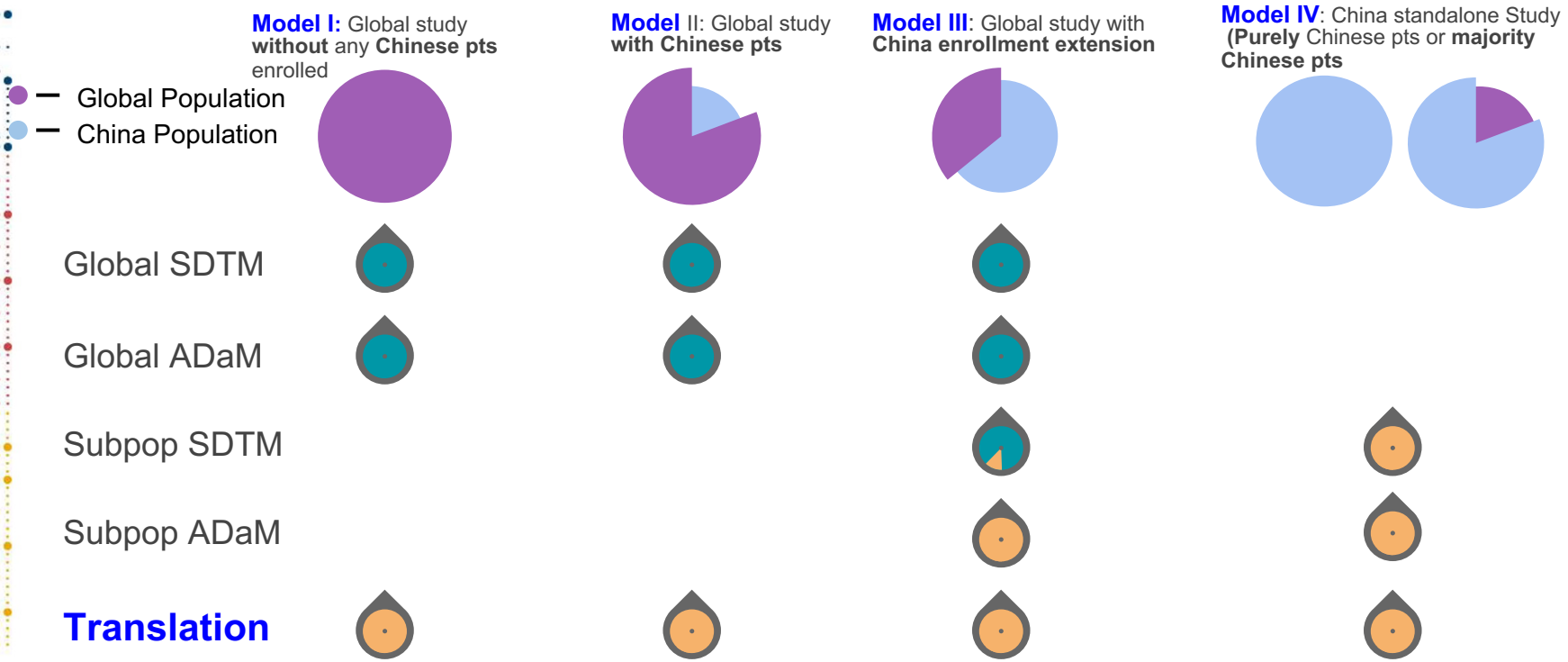
Piloting

Analysis Data

Piloting

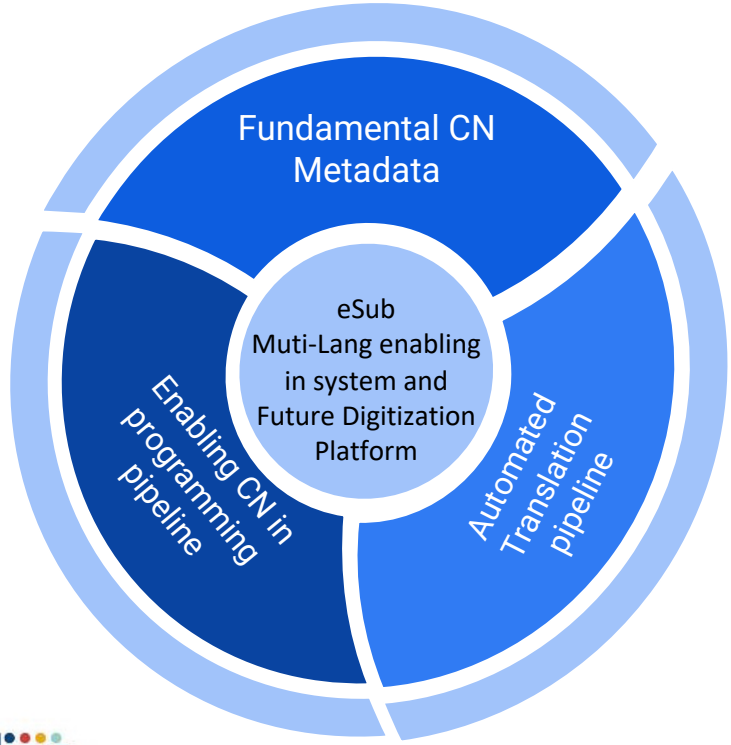
Global & Local Teams Support for China Filings

eSub Package preparation and Translation process



China Filing new topic: Translation

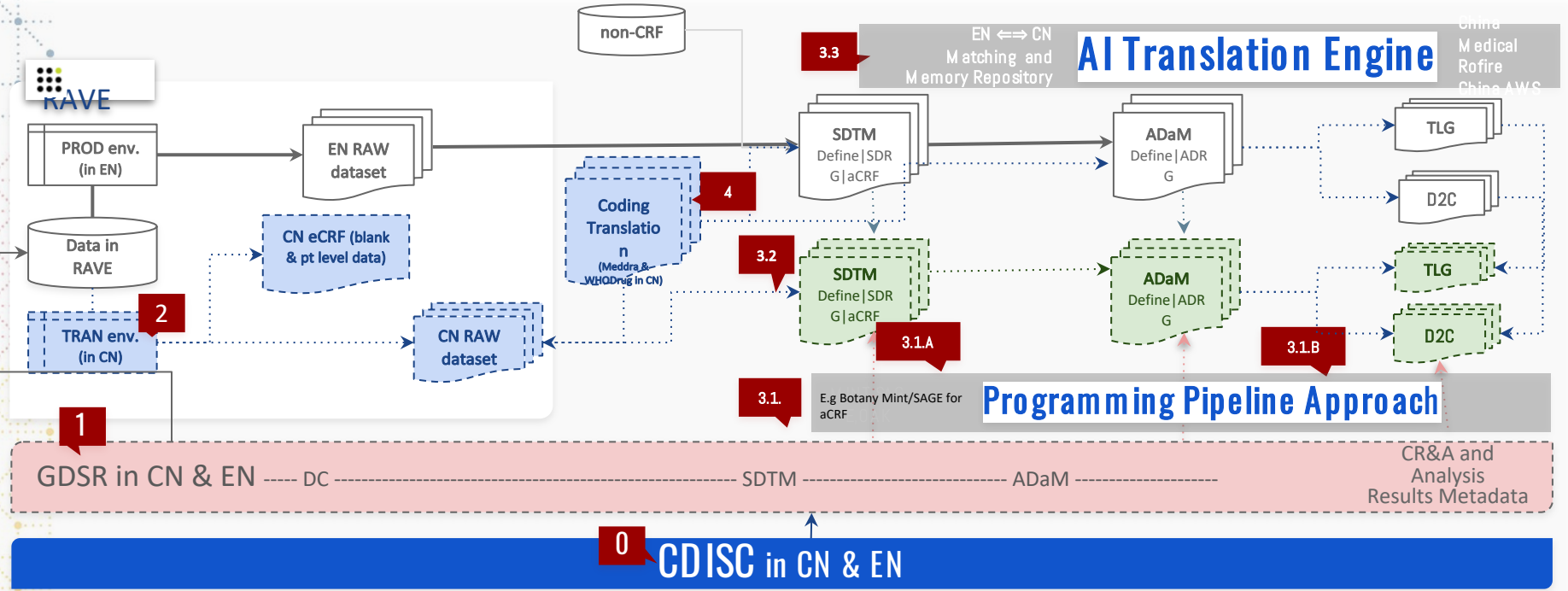
eSub Data package Translation Solution



- Fundamental metadata available
- Tools support
- Platform availability

E2E Implementation

- From data collection to analysis results
- From data to metadata & technical documents



Detailed Preparation & Responsibilities for translation of CDISC studies (not Legacy studies)

Pre-Requisite

9-10 weeks prior to NMPA filing date

Allow sufficient time for translation

Pre-Translation

Global eSub package available.
(Model I, II, III)

Model III Sub-pop packages & model IV

Chinese Blank CRF

China Vendor

China Study Team

Global Study Team

On-Translation

Parallel work

Translate SDTM Spec

Translate ADaM Spec

Translated Spec Review

Translate Annotation

Create bookmark

Manually check aCRF pages

Reviewer's Guide Translation (cSDRG/ADRG)

Post-Translation

Review and deliver

Convert to XML define

Check all the links

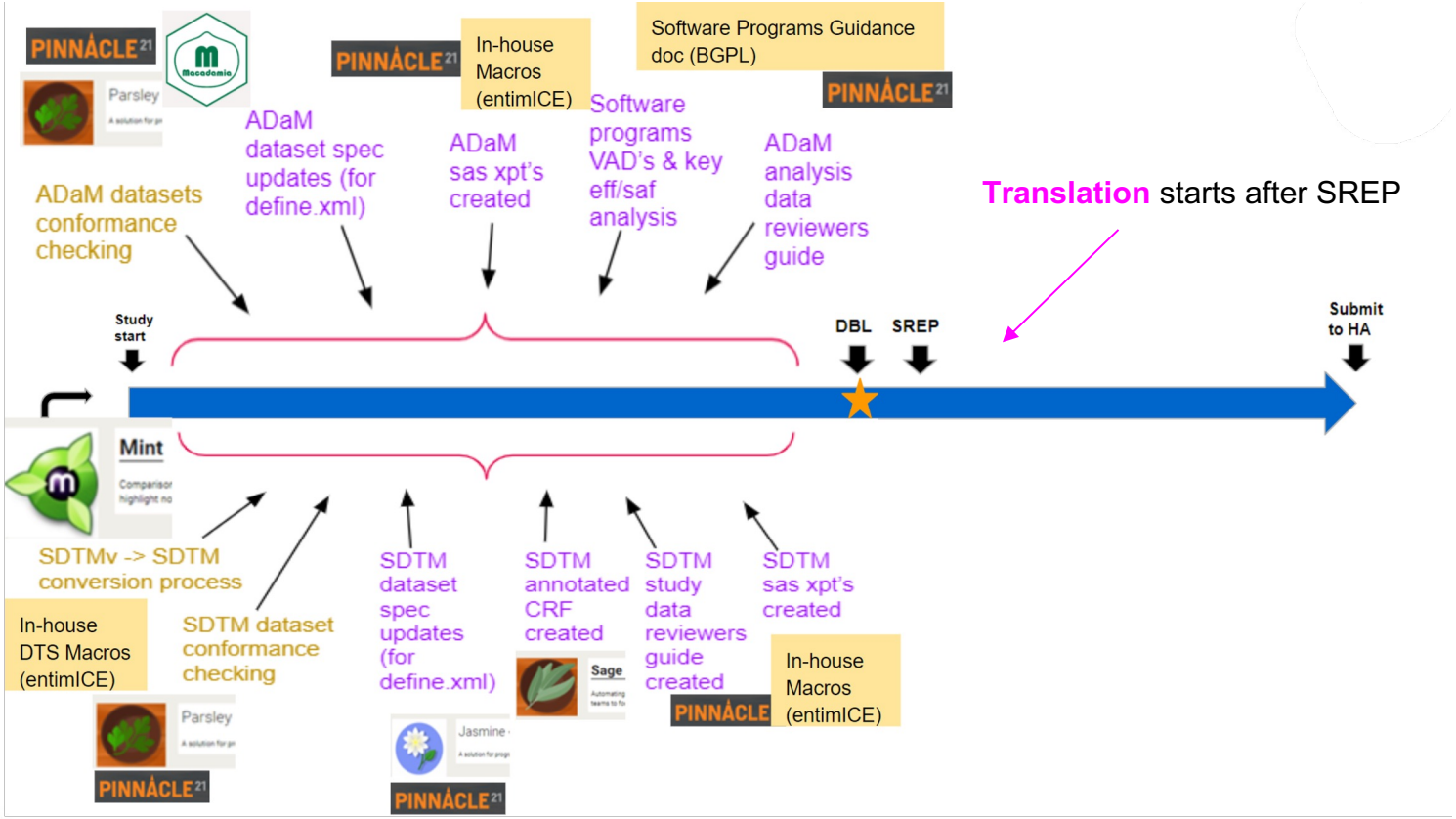
Datasets Translation

Whole package review

Translation tool update

Early planning and smooth delivery

Tools & Workflow



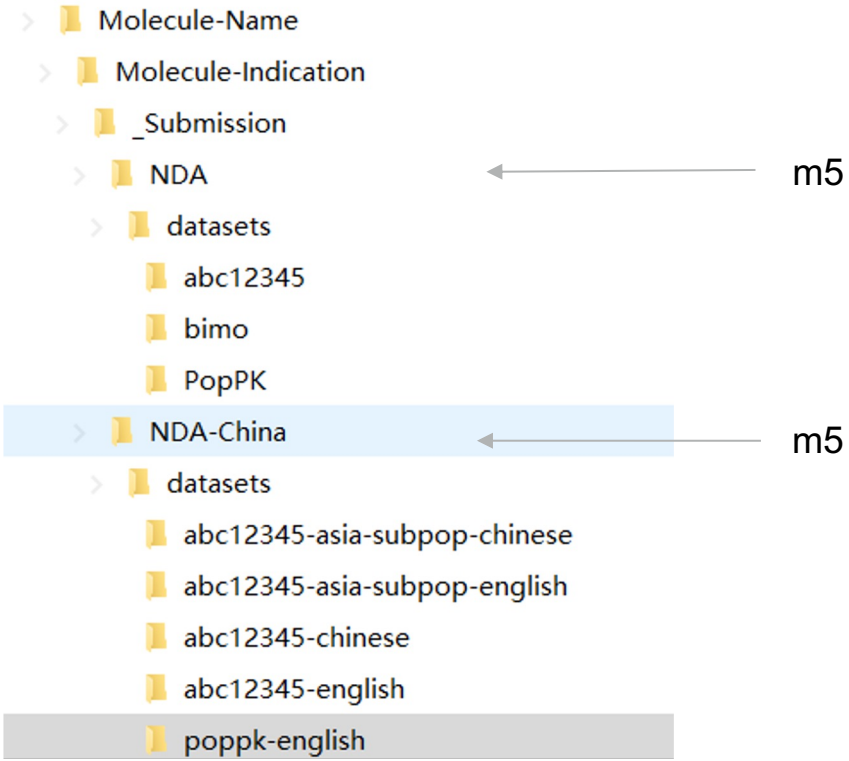
China Filing Data Collection Sheet (DCS) template

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T
1	eSubmission Packages	PDR-O Server folder name for eSub package drop by eSub Team	Database lock Date	Data Package Format (Legacy, CDISC, CDISC A)	Existing eSub package available? *(Yes / No)*	Content of eSub Package						SPA Lead Clin Pharm (C-P) Lead	eSub Entimice folder (Tabulation dataset location)	eSub Entimice folder (Analysis dataset location)	Data Science molecule team Deliver All pre-dbl dry run files to eSub Team *(6-8 wks pre-DBL) QA checks must be completed prior to delivery*	Data Science molecule team Deliver All Final files to eSub Team *(to allow 3 weeks for eSub review, correction and finalisation) QA checks must be completed prior to delivery*	Final English version of package ready *(9-10 weeks prior to filing date)*	Final Chinese version of package ready (translated from English) *(2-5 days prior to delivery to PDR)*	eSub Team Deliver Data Package to PDR-O *(last delivery 3weeks prior to FDA date)*	PDR-O Deliver to NMPA
2						acrf	Tabulation Data & Define file	Tabulation Reviewers Guide	Analysis Data & Define file	Analysis Reviewers Guide	Programs & programtoc									
3	Project XY12345 – Study-name *(Pivotal study)*	*project-study-name*	12-Jan-18	CDISC	No	Yes	Yes	Yes	Yes	Yes	Yes	SPA : Joe Bloggs				4-Mar-22	25-Mar-22	10-May-22	13-May-22	
4	Project XY12346 – Study-name *(Supporting*	*project-study-name*	12-Jan-18	CDISC	Yes	Yes	Yes	Yes	Yes	Yes	Yes	SPA : Joe Bloggs				4-Mar-22	25-Mar-22	10-May-22	13-May-22	3-Jun-22
5	Clinical Pharmacology *(Check for the need for translation)*	*project-clinpharm*	N/A	Legacy	No	n/a	n/a	n/a	Yes	n/a	Yes	C-P : Jo Bloggs	n/a			4-Mar-22	25-Mar-22	10-May-22	13-May-22	

eSub package delivery
Closely collaborate with Regulatory team

- Paper submission
  - Data scientist prepare data package and upload to shared server
  - Regulatory burn disc and submit to HA

- eCTD submission
  - Data scientist prepare data package
  - Work with Regulatory to pass checks
  - Upload to server and share the path with Regulatory
  - Regulatory package all the things and submit to HA



Discussion: eSub For Future in China

eCTD & One size fits all

eCTD: Different requirements from FDA

- File types: only accept pdf/txt/xpt/xml/xsl, Not .csv (PopPK has csv files)
- Folder structure:
  - No folders for bilingual submissions
  - No “misc” folder in current eCTD folder structure (not official solutions)
- Datasets no larger than 4GB (Different from FDA)
- PDF settings (ADRG, cSDRG, Programtoc, aCRF) in translated packages different to FDA requirements

One Size fits all

- Align requirements across HAs

R submission

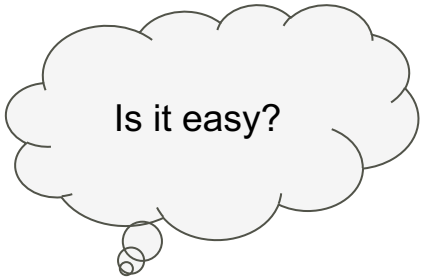
Current status - what can / cannot be submitted

Submission of:	FDA	PMDA	NMPA	Comment
Readable R code accepted ?	Y	Y	Y?	Upon prior agreement with the HA. Follow R consortium's (link) "Pilot R submission to the FDA" approach and influence other HA's to align if needed
Interactive displays accepted ?	Unknown	Unknown	Unknown	NOTE: Pilots are ongoing with the FDA and the R consortium (see pilot 2 from above link)

Submission of:	Can Roche currently submit these ?	Comment
Readable R code for TLG's	Y	Developed in validated programming environment
Readable R code for Datasets	Y	Developed in validated programming environment
Interactive displays	N	Awaiting outcome from R consortium pilot and a validated solution

Key takeaways

- CDISC data standards is mandated by the FDA and PMDA. For CDE the draft guidances also follow the CDISC standards.
- Four different China filing study models with different preparation work
- Important to start early interactions between China and global team
- Chinese metadata and E2E translation engine accelerates delivery
- Closely collaborate with Regulatory when delivering eSub package
- Be careful about the differences of eCTD filing requirements
- Collaborate in industry and CDE on R (program) submission for future



Thank You!

Open Source Clinical Reporting summeR

The main focus of this workshop is: open-source & collaboration in Pharma, sharing experience in using open-sourced R packages (such as Admiral and NEST packages) for

- SDTM mapping
- ADAM data creation
- TLG creation

https://insightsengineering.github.io/nest-2023-summeR/reg.html