China CFDA Data Submission Regulatory Requirements and Updates

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Biography

Victor Wu

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Chair, China CDISC Coordinating Committee

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TOC

- CDISC in China
- Data Submission in China
- Current Status & the Future
- Thoughts on Implementation

CDISC in China (2007-2017)

Nov: Sandy Lei (JNJ) introduce CDISC

Nov: 1st interchange

Sep: 2nd CDISC interchange

Jun: Data Standardization Committee
Aug: Data Standardization WG

Sep: CDISC Interchange 2017

Jun: Half day Training (Becky Kush and Sandy Lei)

Jun: C3C established

Dec: CDISC UG

May: C-STAR

May: CDISC Standards CN released for public review

CFDA Guidance

Since 2009, Every year: CDISC public training-BJ/SH

Since 2008: CDISC UG Activities

Since 2013: CDISC Seminar: Quarterly

China CDISC Coordinating Committee C3C

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Clinical Trial Data Submission Requirements Chronology

Before 1999: No GCP

1999：China GCP

2005-2007：Published a number of guidelines

2007：Provisions for Drug Registration

- database submission was required in NDA

2012

Jan: Held the Data Management and Data Standards Seminar

May: Technical Guidance For Clinical trial Data Management

Clinical Trial Data Submission Requirements Chronology (cont')

2013

- Jun: Set up the China Clinical Trial Data Standard Steering Committee
- Jul: Published the implementation plan of standardizing the clinical trial data management
- Aug: Set up 5 China clinical trial data standard working groups(SDTM etc.)

2014-2015：Quarterly Seminar

China Clinical Trial Data Standard (CTDS) – CDE Initiative

- **Established China CTDS Steering Committee (in June 2013)**

  http://www.cde.org.cn/news.do?method=viewInfoCommon&id=313177

- **Kicked off Working Groups in August 2013**
  - 1) CDASH
  - 2) SDTM
  - 3) ADaM
  - 4) CT - Controlled Terminology
  - 5) TCM - Traditional Chinese Medicine

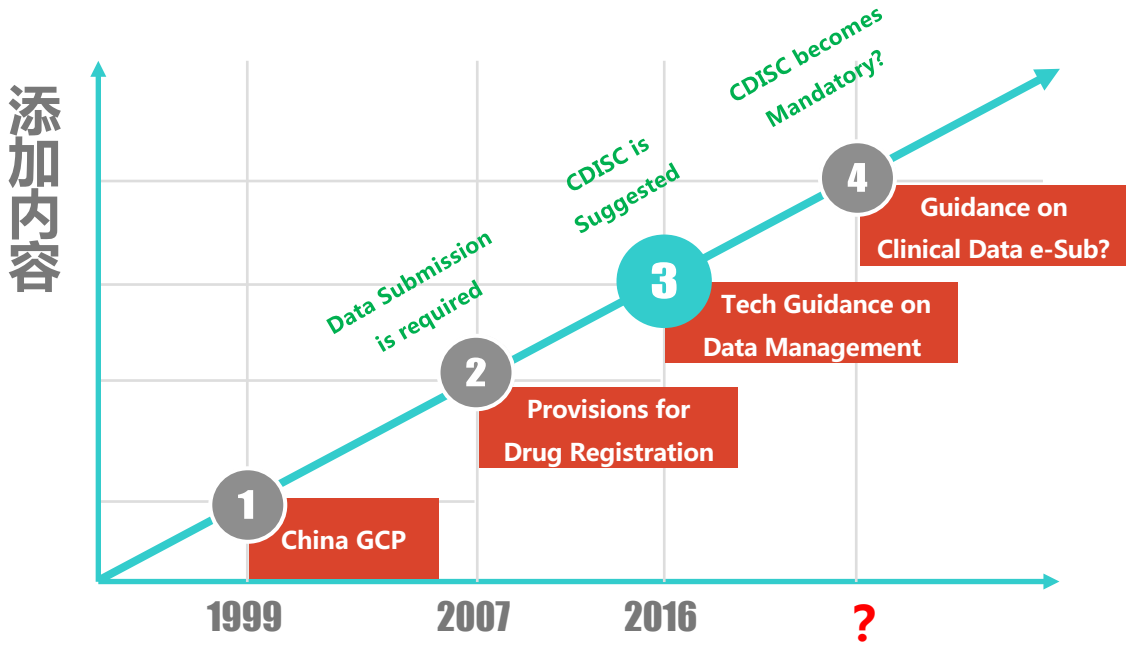
Clinical Trial Data Submission Requirements Chronology (cont')

- **2016： Guidance on Clinical Data Management Plan & report and Statistical Analysis Plan & Report.**
  - Raw database and analysis database and meta data should be submitted(with xpt format)

- **2016： Technical Guidance on Data Management**
  - …Suggested to adopt CDISC standards to submit raw database and analysis database.

- **2017： Notice on supplemental materials of clinical trial database**

Clinical Data Submission in China



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标准在审评中的作用

- **Where is data needed? 哪呢？**
- **What dose it mean?! 什么意思？**
- **The data was coded in different way, pool them?! 汇总分析？**

Regulatory Consideration on Data Standardization

Data Standardization

- ✓ Learn from the internationally recognized mature standard system - CDISC
- ✓ Don't start from scratch
- ✓ Complement and develop CDISC standard based on the data characteristics in China
- ✓ Taken a leading role in developing traditional Chinese medicine standard
- ✓ Reach a consensus through extensive discussion

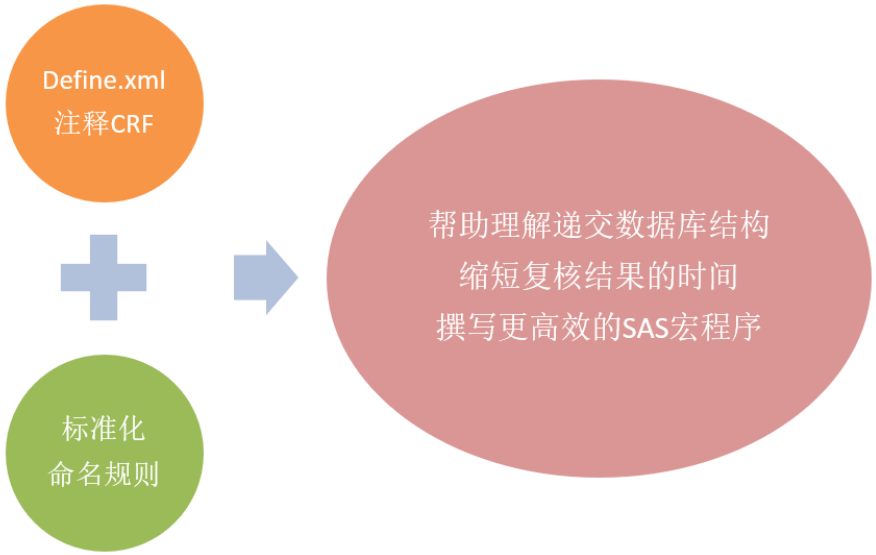
Janhong Pan, CDE
Presented on DIA QSF 2017 Beijing

Statistical Review and Data Standardization

- ✓ Statistical review includes review of data quality and statistical analysis, and high quality clinical data is the basis for drug review
- ✓ For fast access and easy handling of submitted clinical data
- ✓ Meta-analysis
- ✓ To determine non-inferiority margins etc.
- ✓ ……

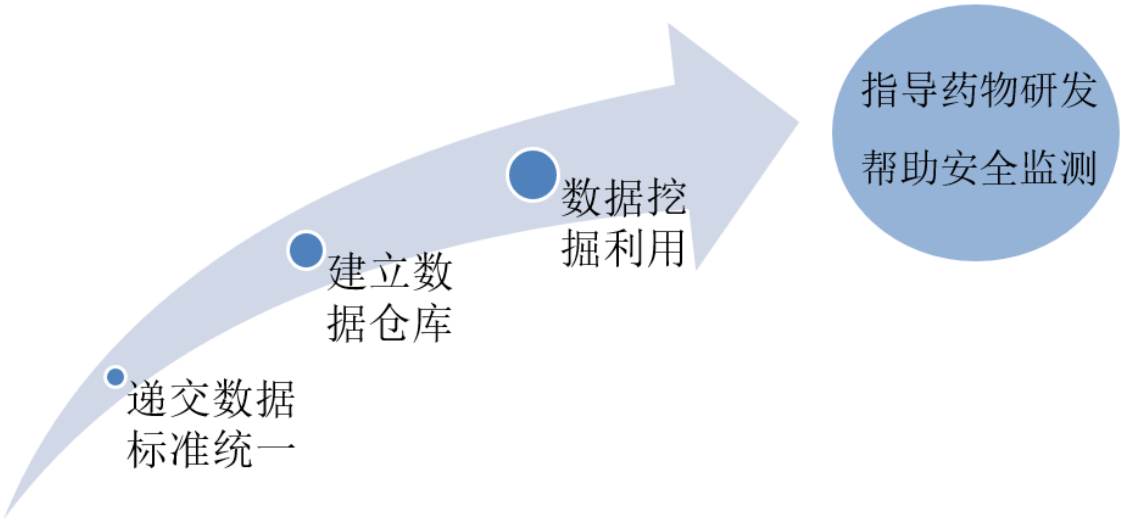
Regulatory Consideration on Data Standardization(cont')

提高统计审评效率



Xin Zeng, CDE,
Presented on CDISC China Interchange 2017 Beijing

建立数据仓库



Requirements of Clinical Data Submission in China
中国数据递交要求

2007：Provisions for Drug Registration

- **database submission was required in NDA**

2016：Guidance on Clinical Data Management Plan & report and Statistical Analysis Plan & Report.

- **Raw database and analysis database and meta data should be submitted(with xpt format)**

2016：Technical Guidance on Data Management

- **…Suggested to adopt CDISC standards to submit raw database and analysis database.**

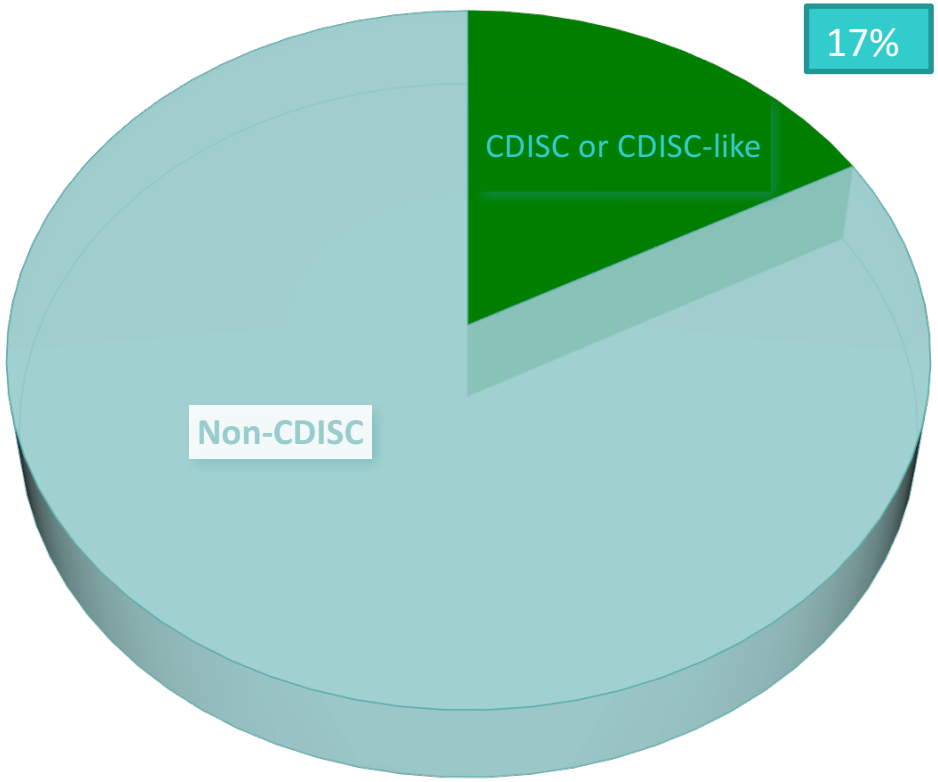
- **2007：《药品注册管理办法》**
  - 第三十九条　申请人完成临床试验后，应当向国家食品药品监督管理局**提交**临床试验总结报告、统计分析报告以及**数据库**。
- **2016：《药物临床试验数据管理与统计分析的计划和报告指导原则》**
  - **原始数据库、分析数据库**及相应的变量说明文件（数据库应为SAS XPORT 传输格式，**xpt**格式）
- **2016：《临床试验数据管理工作技术指南》**
  - 为了提高临床试验数据质量以及统计分析的质量和效率，方便数据的交流与汇总分析，在新药上市注册申请时，**建议**采用**CDISC**标准递交原始数据库和分析数据库。

File Format 文件格式

- **Raw database, analysis database and corresponding variable specifications (database should be XPORT format)**

- **XPT**
  - Limitation of Length:
    - Name: <=8
    - Label: <=40;
    - Value: <=200

Standard Status of Data Submitted by Local Sponsors



The Future

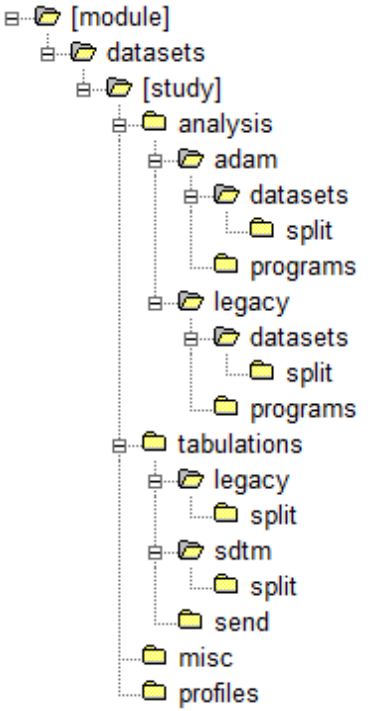
- **Data Standard**
  - CDISC
  - From Recommend to Mandatory?

- **File Format**
  - Dataset-xml: future
  - US FDA has already done pilot

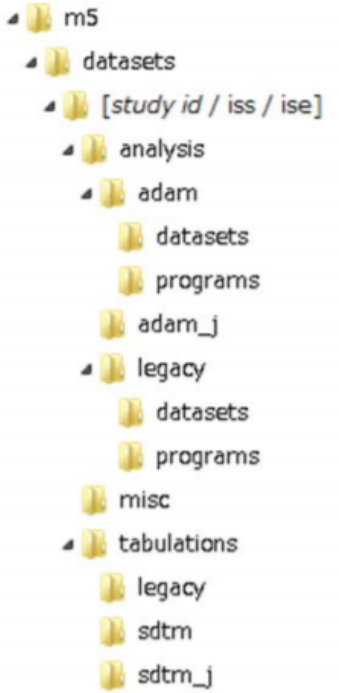
The Future

Folder Structure

FDA



PMDA



CFDA

?

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The Future

Language – In Chinese

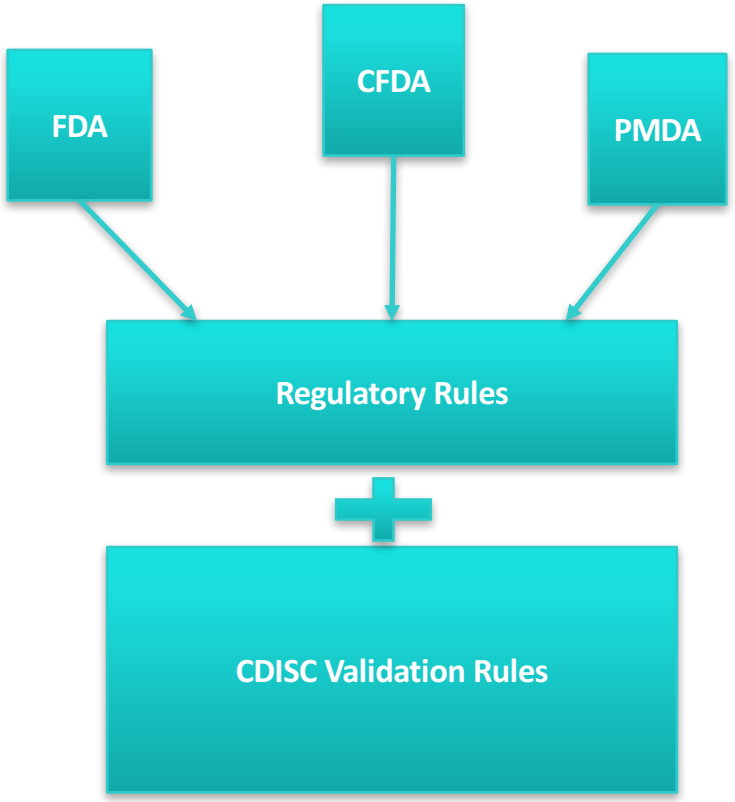
- Standardized Parts - Automatically
  - Metadata: Dataset attributes, Variable attributes
  - CT: Values

- Non-Standardized Parts
  - Free text of Chinese Chars in xxTRT/xxTERM: fine
  - Free text of Chinese Chars in [Other specifiy]: SUPPxx?
  - Chinese Chars in xxORRES: fine?
  - Chinese Chars in xxTEST: leave it as it is or translate?

The Future

- **Ideally?**

Validation Rules



Validation Rules (CFDA):

- less strict than CDISC Validation rules?

Validation Tools:

- local vendors? (Open and Free)

The Future

TCM

- **CDISC is leading to develop CDISC TA standards:**
  - Angina Pectoris – TCM
  - Symptoms, Signs; Tongue and Pulse:
    - WB (whole body)?
    - FA?
    - A new domain?
      - QS: not validated tools

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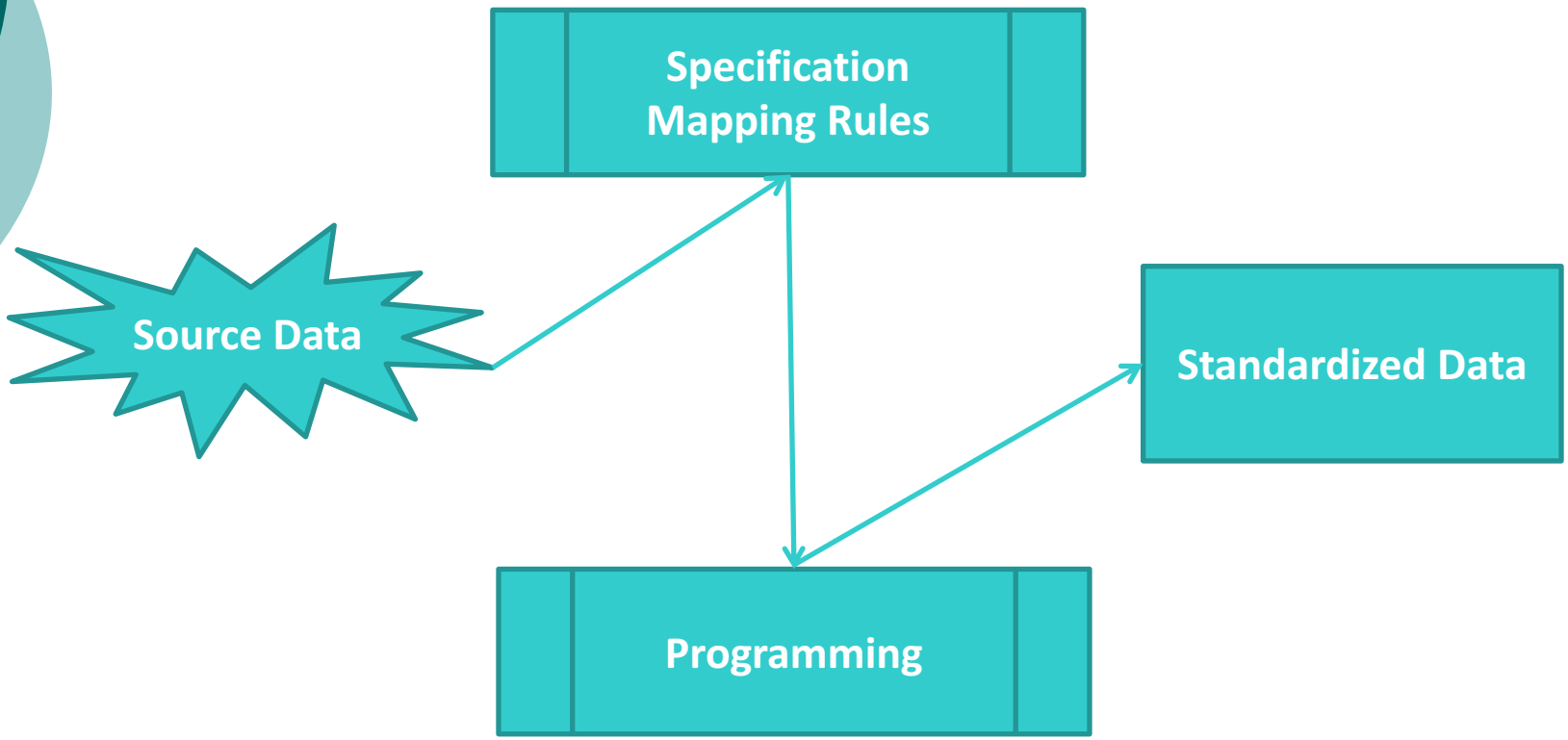
Why it has to be difficult to learn or implement?

Struggling on What?
Mapping rules or Programming, or Both?



Standardized vs Non-standardized

- **Dataset level**
  - Name
  - Description
  - Structure
  - Allowed Variables
- **Variable level**
  - Name
  - Label
  - Type
  - Format
- **Value level**
  - Controlled Terminology

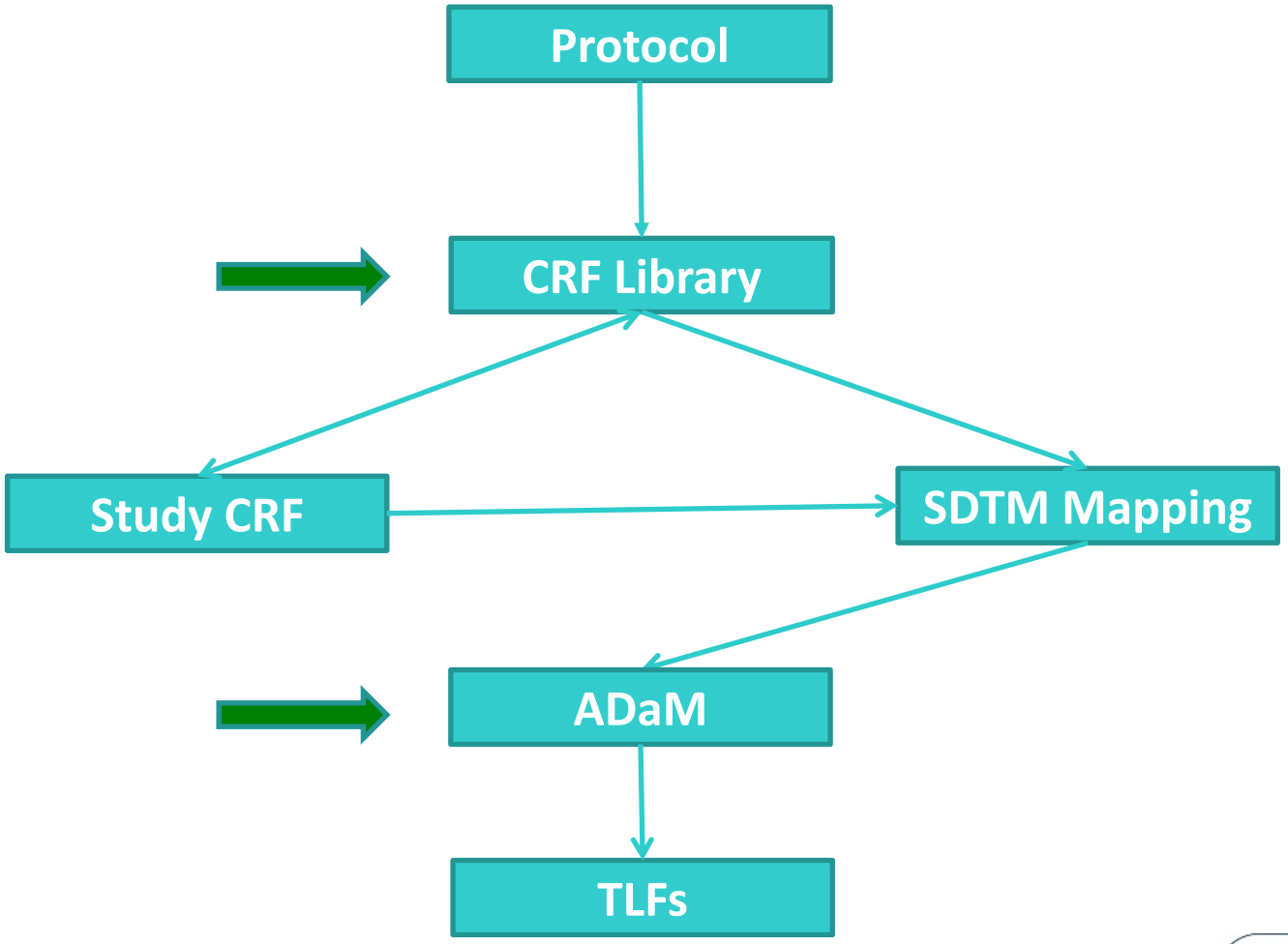
It is nonsense or practicable?

Any specific programming skills needed?

- **Dataset Level:**
  - Re-Structure: transpose, Array
  - Vertical or Horizontal Combination: merge, set
- **Variable Level:**
  - Variable(s) -> New variable(s): statements, function
  - Type conversion: input, put..
- **Value level:**
  - Value(s)-> New Values: conditional statements, formats

1. **Most of the tasks could be done by macros**
2. **When reading the tasks in this way, we already have the logics on how to design the macros**

Where we can start from before it becomes company level practice?



Q & A

Thanks

Strength *through collaboration.*

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