



Science For A Better Life

# FDA Review Principles Applied on CRO Oversight

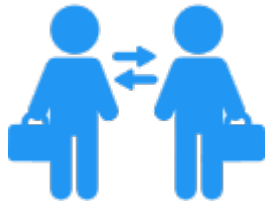
October 13th 2015, Sascha Ahrweiler, Version 0.2



## Agenda

- Introduction
- FDA Data Review
- Application To Sponsor and CRO Collaboration
- Impact on People Development
- Conclusions

# Introduction



## Common Setup in Sponsor – CRO Collaboration

Sponsor outsources a clinical study to CRO

Work package: CRF database, SDTM, ADaM, TLFs

CRO delivers work package to Sponsor



## Sponsor follows Hands-Off Approach (no Oversight)

When sponsor uses the CRO delivery for submissions

Detects issues in CRO delivery

Blame the CRO for not meeting expectations



## Sponsor performs Full Quality Control

Sponsor validates that CRO deliveries are 100% correct

Sponsor detects issues in CRO delivery

Complain that the CRO requires handholding



# Introduction

 How to establish a successful Sponsor-CRO Collaboration?

 Let's take a look at a Collaboration that HAS to work and HOW that works



FDA



Sponsor

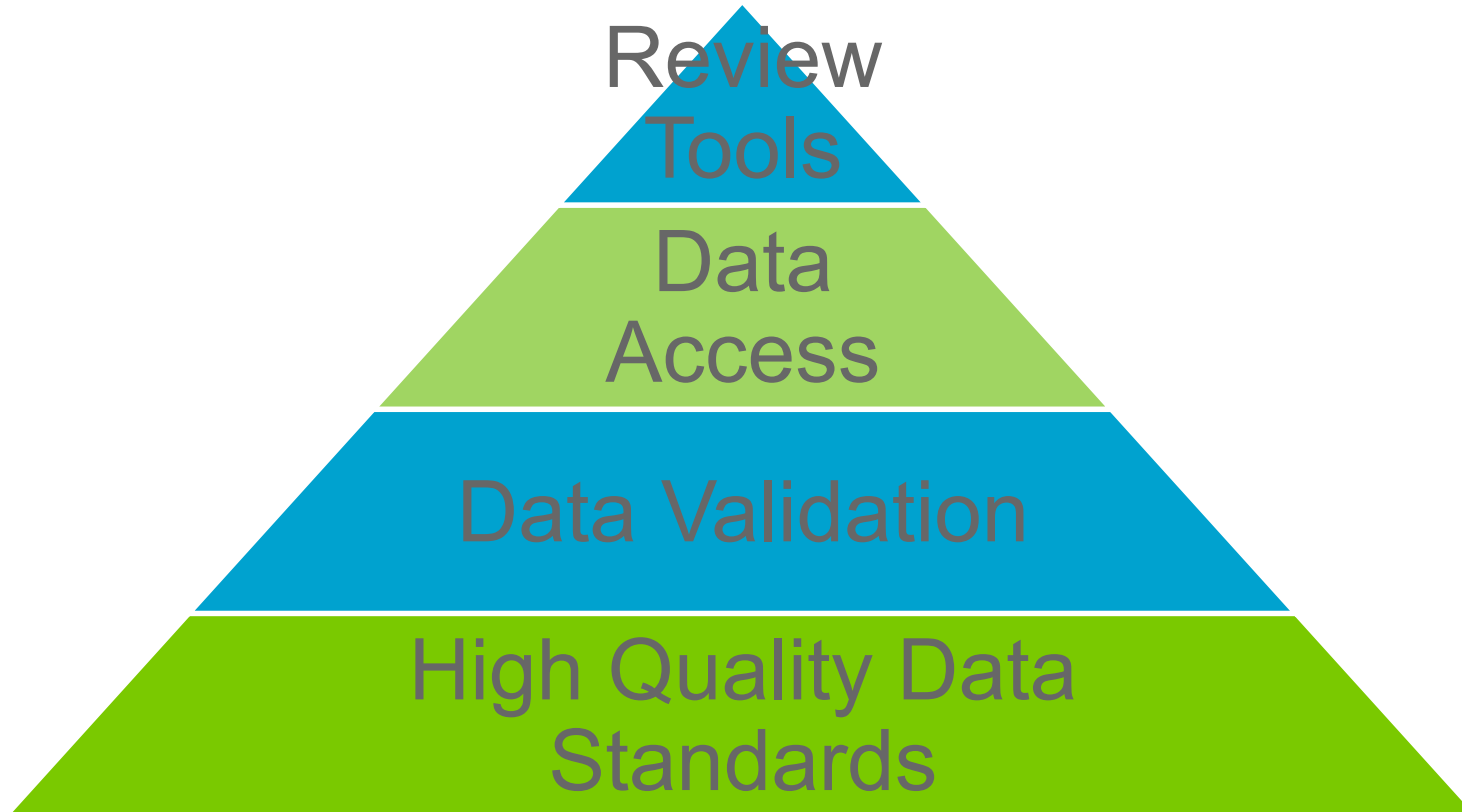
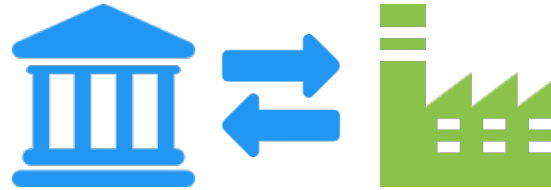


CRO



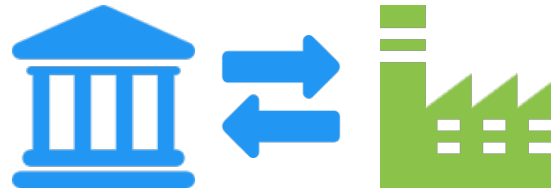
Impact on People Development

# FDA Data Review



**Source:** Building a Modern Review Environment and Opportunities to Collaborate Around Common Goals, Chuck Cooper, PhUSE AC 2012

# FDA Data Review



## High Quality Data Standard is Foundation for efficient FDA Review

- FDA develops internal expertise to learn and use data standards
  - CDISC: SDTM, ADaM, metadata, ...
  - PhUSE CS: ADRG, SDRG, ...

## Standards Well defined and Communicated

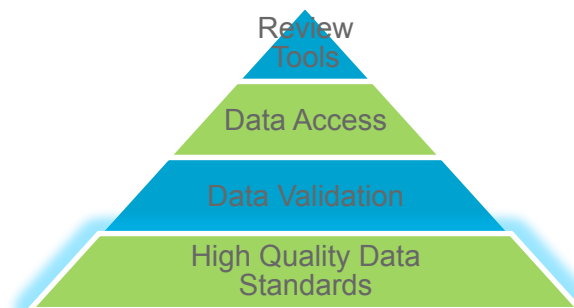
- Submission packages defined in guidances
  - eSubmission Guidance for Industry, December 2014
- Standards defined in Data Standards Catalog

## Consultancy/Discussion at pre-IND stage

- Standardization plan (formats, terminologies,...)



## Clear Exchange of Expectations



# Sponsor and CRO



## Well Defined Sponsor Standards

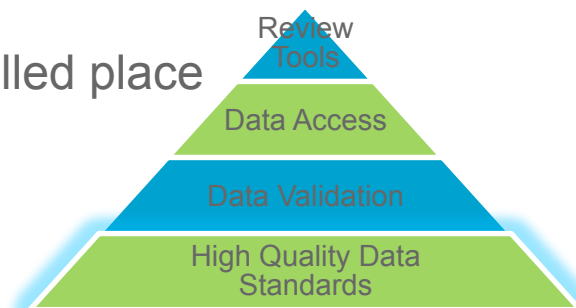
- Develop internal expertise to learn and use standards
- Same standards as communicated by FDA
- Interpretation gaps **must** be closed
  - Sponsor SDTM and ADaM Interpretation Guides
  - Project Standards!
- Handling of Controlled Terminology
  - Extensible Codelists!



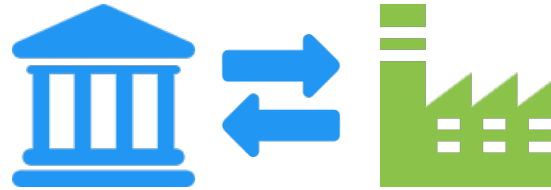
## Standards Clearly Communicated

- Submission packages defined in one version controlled place
- Well defined delivery package

 **What do you Expect? What do you NOT Expect?**



# FDA Data Review



## Validate Adherence to Data Standards

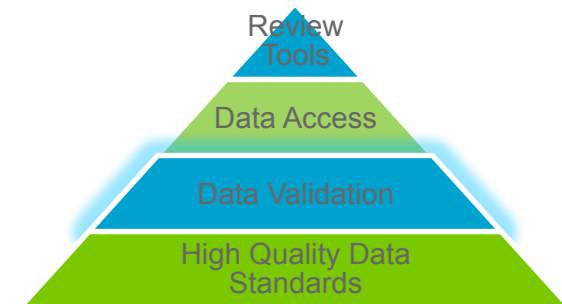
- Before Data is uploaded to JANUS warehouse
- Before Medical Data Review starts

## Conformance vs. Quality Checks

- Conformance: eg. SDTM: value in domain columns match name of domain
- Quality Check: Age falls within a pre-specified range
- Consistency within Data (eg. Death Cases, EPOCH,...)

## Usage of Tools

- OpenCDISC to check formal topics
- Standard programs to check other topics



# Sponsor and CRO



## Validate Adherence to Data Standards

- Before Data is uploaded to Sponsor data repository
- Before Data is used for Post Study Processes (eg. submissions)

## Conformance vs. Quality Checks

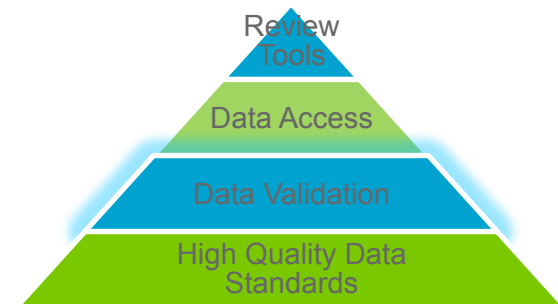
- Conformance: Rules of Sponsor SDTM and ADaM Interpretation Guides
- Quality Checks: Project Standards

## Usage of other Tools than SAS

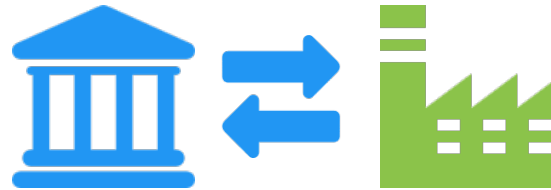
- OpenCDISC to check formal topics
  - Review of CRO OpenCDISC reports
- Standard programs to check other topics
  - eg. macros to calculate project specific ranges



**Clear Rules and Process for Acceptance**



# FDA Data Review

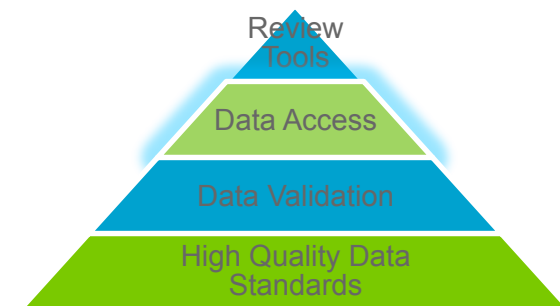


## Ensure Data Access for Medical and Statistical Data Review

- Upload to JANUS warehouse
- All Data from same compound or Drug Class available
- Tools can connect to Data
- Custom Data Views

## Submission/Study Change Management

- Version control of submitted Data



**Ensure Data is Ready for Review**

# Sponsor and CRO



## Ensure Data Access for Statistical Analysts and Other Functions

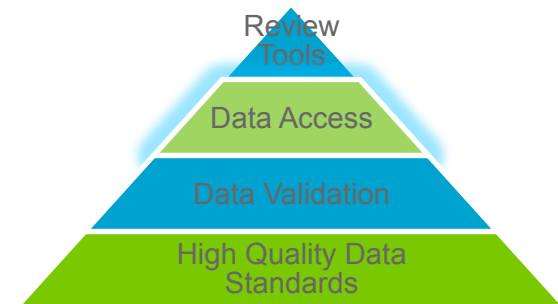


- Upload to Data Pool
  - No surprises when data is processed later (eg. other attributes)
- All Data from same compound/project available
  - Helpful for Data Content Review
- Tools can connect to Data
- Custom Data Views (eg. for medical data reviewer)

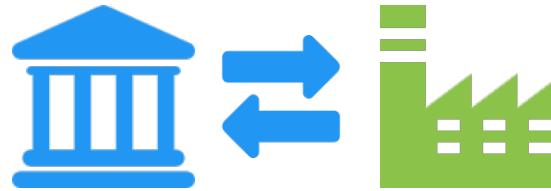
## Study Data Change Management

- Version control of submitted Data
  - Communication!

**Ensure that Data can be used for Post Processing**



# FDA Data Review



## Review Data with Review Tools

- Commercially available Tools: JReview, SAS JMP/Clinical
- Home Grown Systems: FIRRS, MAED
  - Eg. for Standard Safety Analysis
- Combination of Statistical and Medical Knowledge
- Reconciliation between Sponsors Analysis and different Methods

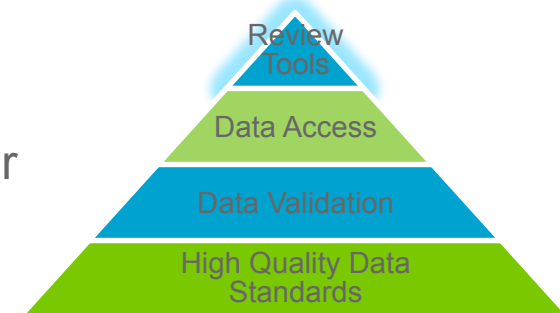
## Review Catalog

- Eg. JReview Standard Review Catalog
- What kind of Analysis should be performed?

## Documentation of Findings

- Communicate Analytical Review Findings to Sponsor

**Analytical Data Review to check Data Content**



# Sponsor and CRO



## Use Data Mining Tools and Techniques for Data Review



- Tools: JReview, SAS JMP/Clinical
- Home Grown Macro library: Project specific Macros for complex Variables
  - Eg. Bleeding Cycles for WHC
- Don't recreate all results, but play with Data to understand it!

## Checklist of Standard Analysis Checks



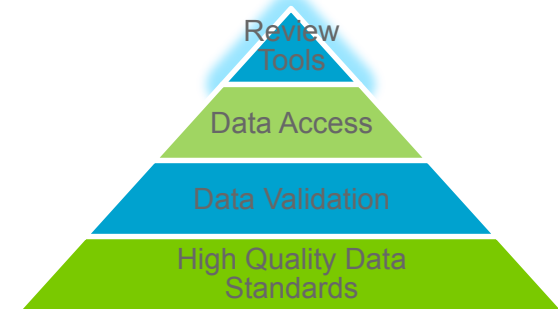
- Review Plan should include Project specific Checks
- Comparison with previous or Data Pool Analysis Results

## Documentation of Analysis and Findings

- For Communication of Findings to CRO
- For Knowledge for Post Processing



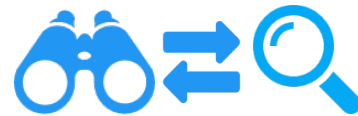
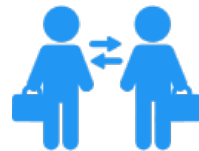
**Analytical Data Review to check and learn**



# Conclusion

FDA Review Techniques can be translated and applied to Sponsor-CRO model

Clear exchange of Expectations with well defined ownership and responsibilities



Define an appropriate oversight model

People Development to gain Data Knowledge despite outsourced Studies





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# Thank you!

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