

Analysis Results Metadata for Define-XML v2

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Agenda

- Why Analysis Metadata Results?
- History of ADaM Metadata & Define-XML
- Analysis Results Metadata v1 for Define-XML v2
- What's Next

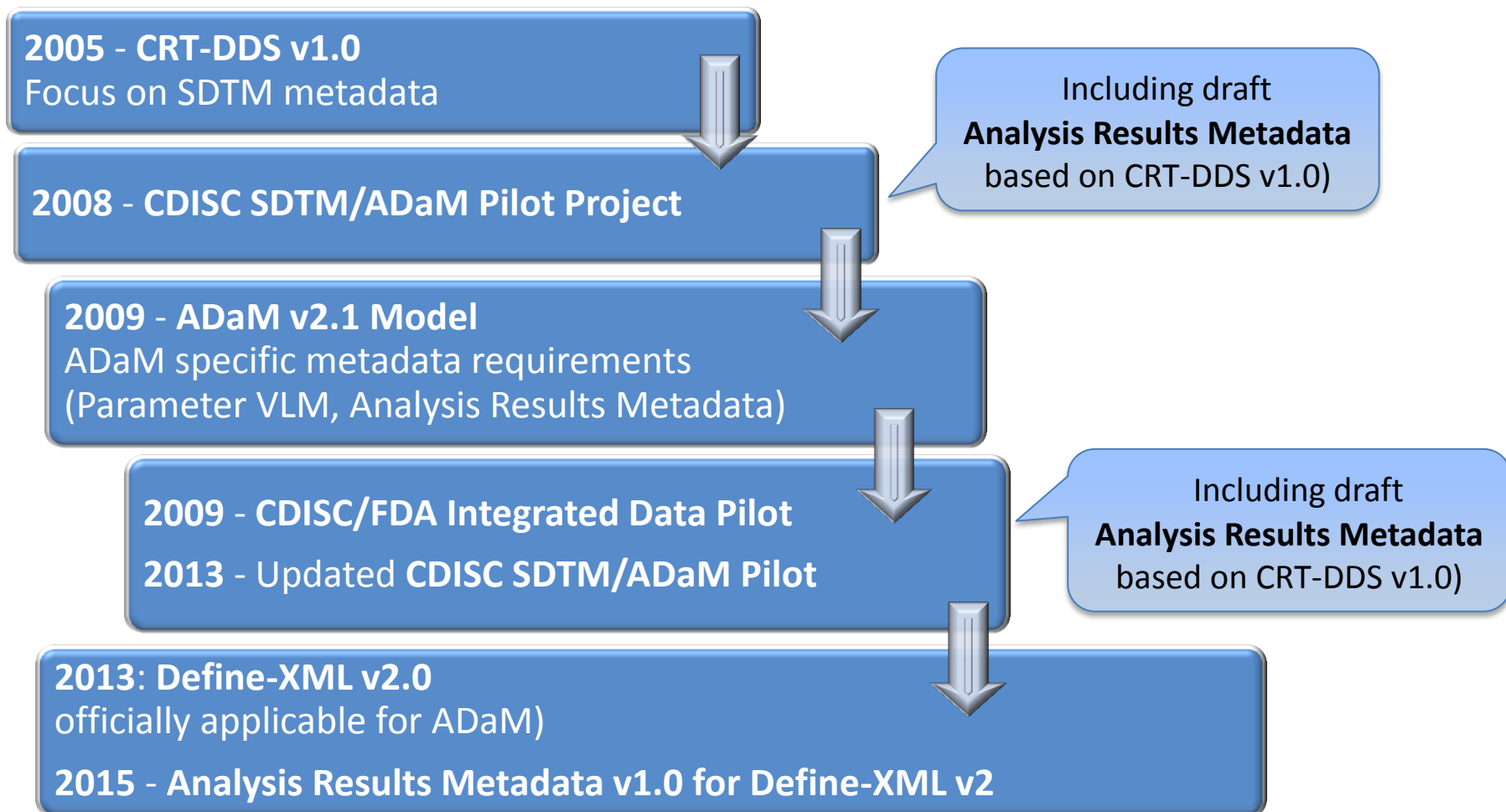


Why Analysis Results Metadata?

- **Traceability** is a fundamental principle in ADaM:
 - It enables the reader to understand the data flow from **collection** to **SDTM** and **ADaM** to **Analysis Results**
- Analysis Results Metadata provides **traceability** from **results** in a statistical display to the **data** in the analysis datasets
- Analysis Results Metadata includes:
 - Identification of critical analysis displays and particular results
 - Details on analysis performed (reason, underlying analysis dataset(s), selection criteria, documentation, programming statements)
- Facilitates documentation and reproduction of the analysis results
- Not needed - or even advisable - for every analysis in a submission



ADaM Metadata and Define-XML history



ADaM Results Metadata – Pilot 1 (2008)

Analysis Results Metadata (Summary) for Study CDISC_Pilot

[Table 14-1.01 - Summary of Populations](#)

[Table 14-1.02 - Summary of End of Study Data](#)

[Table 14-1.03 - Summary of Number of Subjects by Site](#)

[Table 14-2.01 - Summary of Demographic and Baseline Characteristics](#)

[Table 14-3.01 - Primary Endpoint Analysis: ADAS Cog \(11\) - Change from Baseline to Week 24 -- LOCF](#)

...

[Table 14-3.11 - ADAS Cog \(11\) -- Repeated Measures Analysis of Change from Baseline to Week 24](#)

Analysis	Table 14-3.11 - ADAS Cog (11) -- Repeated Measures Analysis of Change from Baseline to Week 24
Description	Likelihood based repeated measures analysis of ADAS-Cog(11) change from baseline at Week 24, includes LS Means at Week 24, pairwise comparisons between treatment groups - windowed values with no imputation for missing values, Efficacy population
Reason	pre-specified in SAP
Data References	ADAS-Cog Analysis (ADQSADAS) [where EFFICACY='Y' and AWEEK>0 and ITTV='Y' and ITYPE ne 'LOCF' and PARAMCD='ACTOT']
Documentation	SAP Section 10.1.1 , SAP Template 10 , Adjusted means for the change from baseline at week 24 and pairwise comparisons between treatment groups at Week 24 using a repeated measures model with treatment group (as class variable); site (as class variable); time;treatment*time interaction; baseline score and baseline*time interaction terms; and an unstructured covariance matrix. SAS code used to perform repeated measures analysis: PROC MIXED DATA=EFF(WHERE=(AWEEK>0 AND ITTV='Y' AND ITYPE NE 'LOCF' AND PARAMCD='ACTOT')); CLASS USUBJID SITEGRP AWEEK TRTPN; MODEL CHG = TRTPN SITEGRP AWEEK TRTPN*AWEEK BASE BASE*AWEEK / OUTP=PRED DDFM=KR; REPEATED AWEEK / SUBJECT=USUBJID TYPE=UN; LSMEANS TRTPN / DIFF CL; RUN;



ADaM Results Metadata – Pilot 2 (2009)

Analysis Results

Display Identifier	Display Name	Result Identifier	Analysis Variable	Reason	Dataset	Selection Criteria
Table 14-1.1	Patient Disposition (Safety Population)	Total Number of Safety Patients	SAFFL	Pre-specified in SAP	ADSL	SAFFL eq 'Y'
Table 14-1.1	Patient Disposition (Safety Population)	Frequency of Patients Completing/Discontinuing	COMPFL	Pre-specified in SAP	ADSL	SAFFL eq 'Y'

Table 14-4.4.5.3	Total Events in Study Epoch by Peak Dose Based on Number of Patients Experiencing the Event (Cumulative Dose: gt q2 - le q3) (Safety Population)	Frequency of Abnormal Laboratory Events	PARAM	Pre-specified in SAP	ADLB	dosmaxgn=3; saffl='Y'; anl2fl='Y'; group by aepoch
Table 14-4.4.5.4	Total Events in Study Epoch by Peak Dose Based on Number of Patients Experiencing the Event (Cumulative Dose: gt q4) (Safety Population)	Frequency of Adverse Events by Preferred Term	DECODCUR	Pre-specified in SAP	ADAE	dosmaxgn=4; saffl='Y'; group by aepoch
Table 14-4.4.5.4	Total Events in Study Epoch by Peak Dose Based on Number of Patients Experiencing the Event (Cumulative Dose: gt q4) (Safety Population)	Frequency of Abnormal Vital Signs Events	PARAM	Pre-specified in SAP	ADVS	dosmaxgn=4; saffl='Y'; anl2fl='Y'; group by aepoch
Table 14-4.4.5.4	Total Events in Study Epoch by Peak Dose Based on Number of Patients Experiencing the Event (Cumulative Dose: gt q4) (Safety Population)	Frequency of Abnormal Laboratory Events	PARAM	Pre-specified in SAP	ADLB	dosmaxgn=4; saffl='Y'; anl2fl='Y'; group by aepoch



ADaM Results Metadata – Pilot 1 Update (2013)

Analysis Results Metadata (Summary) for Study CDISCPIL01

[Table 14-1.01](#) Summary of Populations

[Table 14-1.02](#) Summary of End of Study Data (ITT population)

[Table 14-2.01](#) Summary of Demographic and Baseline Characteristics (ITT population)

[treatment group comparison for continuous variables](#)

[treatment group comparison for categorical variables](#)

[Table 14-3.01](#) Primary Endpoint Analysis: ADAS-Cog - Summary at Week 24 - LOCF (Efficacy Population)

[dose response analysis for ADAS-Cog changes from baseline](#)

[pairwise comparisons to placebo for ADAS-Cog changes from baseline](#)

Table_14-3.01

Display	Table 14-3.01 Primary Endpoint Analysis: ADAS-Cog - Summary at Week 24 - LOCF (Efficacy Population)
AnalysisResult	dose response analysis for ADAS-Cog changes from baseline
Analysis Parameter(s)	ACTOT=Adas-Cog(11) Subscore
Analysis Variable(s)	CHG
Reason	Primary Endpoint Analysis; pre-specified in SAP
Data References (incl. Selection Criteria)	ADQSADAS [EFFFIL="Y" and ANL01FL="Y" and AVISIT="Week 24" and PARAMCD="ATOT"]
Documentation	SAP Section 10.1.1 Linear model analysis of CHG for dose response; using randomized dose (0 for placebo; 54 for low dose; 81 for high dose) and site group in model. Used PROC GLM in SAS to produce p-value (from Type III SS for treatment dose).
Programming Statements	<pre>proc glm data = ADQSADAS; where EFFFIL='Y' and ANL01FL='Y' and AVISIT='Week 24' and PARAMCD="ATOT"; class sitegr1; model CHG = trtpn sitegr1; run;</pre>
AnalysisResult	pairwise comparisons to placebo for ADAS-Cog changes from baseline
Analysis Parameter(s)	ACTOT=Adas-Cog(11) Subscore



ADaM Results Metadata – Pilots

- No formal specification
- Draft XML schemas (or no schema at all)
- Based on CRT-DDS 1.0 (Define-XML 1.0)
 - Limited document referencing capabilities
 - No WhereClause support
 - Limited comment support



ADaM Results Metadata – Pilots

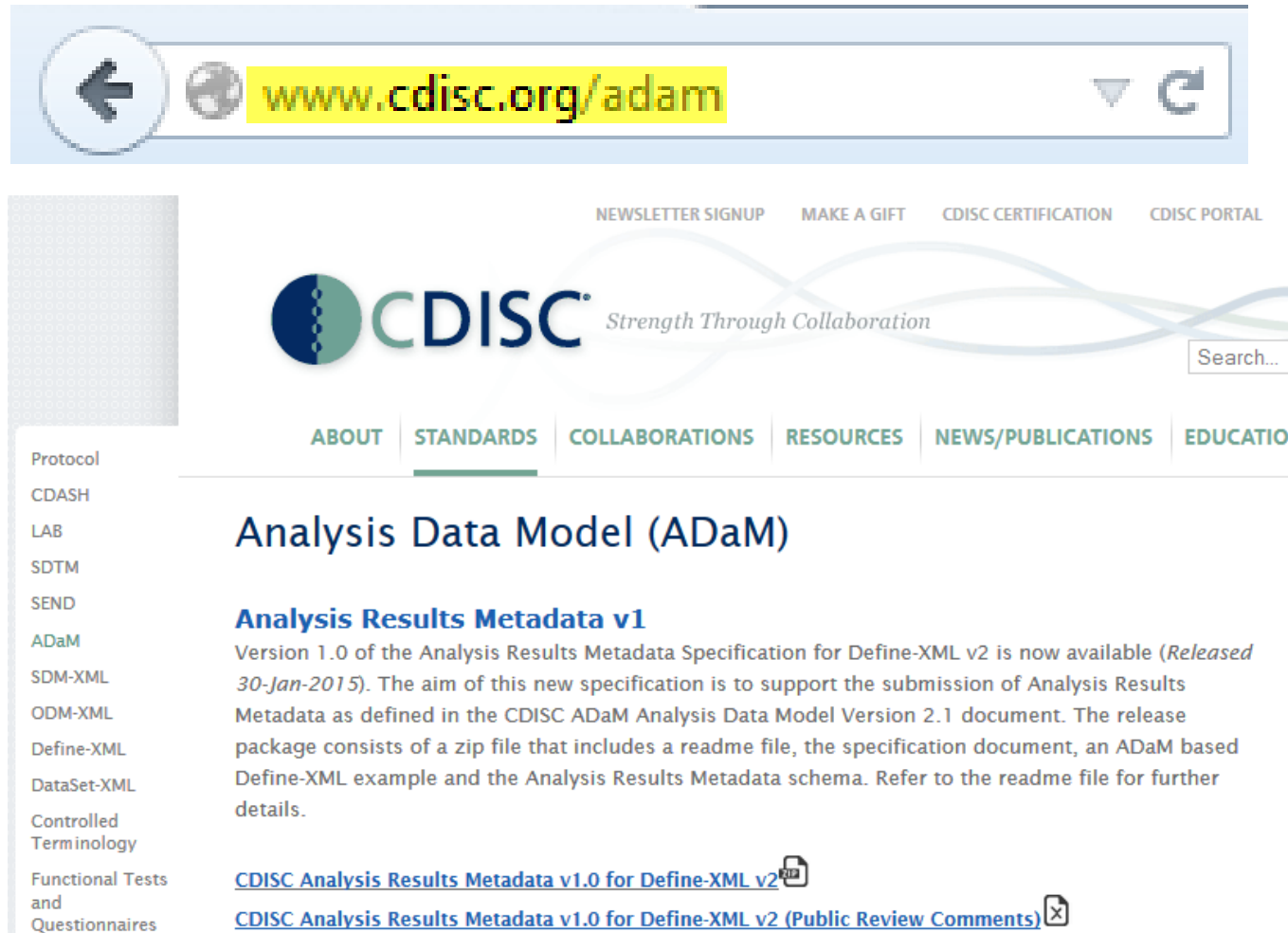
```
<cp01:AnalysisResultsMetadata>
  <cp01:ARMEEntry OID="ARM-Entry001" Reason="pre-specified in SAP">
    <cp01:AnalysisName>
      <cp01:SingleTextOrLink>
        <crt:DocumentRef leafID="ARM-Leaf0001"> - Summary of Populations
      </crt:DocumentRef>
    </cp01:SingleTextOrLink>
  </cp01:AnalysisName>
  <Description>
    <TranslatedText xml:lang="en"><![CDATA[Summary of number of subject
  ]></TranslatedText>
```

```
<adamref:AnalysisResults DisplayIdentifier="Table 14-1.1"
  DisplayName="Patient Disposition (Safety Population)"
  ResultIdentifier="Total Number of Safety Patients" Reason="Pre-specified in SAP">
  <adamref:AnalysisVariable Name="SAFFL"/>
  <adamref:AnalysisDataset Name="ADSL"/>
  <adamref:SelectionCriteria>SAFFL eq 'Y'</adamref:SelectionCriteria>
  <adamref:Documentation leafID="ARM-Leaf0001">
    <TranslatedText xml:lang="en">Patient Disposition (Safety Population)</TranslatedText>
  </adamref:Documentation>
</adamref:AnalysisResults>
```

```
<adamref:AnalysisResultDisplays>
  <adamref:ResultDisplay DisplayIdentifier="Table_14-1.01" OID="Table_14-1.01"
    DisplayLabel="Summary of Populations" leafID="Table_14-1.01">
    <adamref:AnalysisResults
      OID="Table_14-1.01.R.1"
      Reason="pre-specified in SAP">
      <adamref:AnalysisVariable ItemOID="ADSL.ITTFL"/>
      <adamref:AnalysisVariable ItemOID="ADSL.SAFFL"/>
      <adamref:AnalysisVariable ItemOID="ADSL.EFFFL"/>
      <adamref:AnalysisVariable ItemOID="ADSL.COMP24EI"/>
```



ADaM Results Metadata v1 for Define-XML v2



The screenshot shows the CDISC website with the URL www.cdisc.org/adam in the browser address bar. The CDISC logo and tagline "Strength Through Collaboration" are visible. The navigation menu includes links for ABOUT, STANDARDS, COLLABORATIONS, RESOURCES, NEWS/PUBLICATIONS, and EDUCATION. The left sidebar lists various CDISC standards and resources, including Protocol, CDASH, LAB, SDTM, SEND, ADaM, SDM-XML, ODM-XML, Define-XML, DataSet-XML, Controlled Terminology, Functional Tests and Questionnaires, and NEWS/PUBLICATIONS. The main content area features the heading "Analysis Data Model (ADaM)" and a subheading "Analysis Results Metadata v1". The text below the subheading states: "Version 1.0 of the Analysis Results Metadata Specification for Define-XML v2 is now available (*Released 30-Jan-2015*). The aim of this new specification is to support the submission of Analysis Results Metadata as defined in the CDISC ADaM Analysis Data Model Version 2.1 document. The release package consists of a zip file that includes a readme file, the specification document, an ADaM based Define-XML example and the Analysis Results Metadata schema. Refer to the readme file for further details." Below this text are two links: "CDISC Analysis Results Metadata v1.0 for Define-XML v2" and "CDISC Analysis Results Metadata v1.0 for Define-XML v2 (Public Review Comments)".

Protocol
CDASH
LAB
SDTM
SEND
ADaM
SDM-XML
ODM-XML
Define-XML
DataSet-XML
Controlled Terminology
Functional Tests and Questionnaires

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CDISC Strength Through Collaboration

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Analysis Data Model (ADaM)

Analysis Results Metadata v1

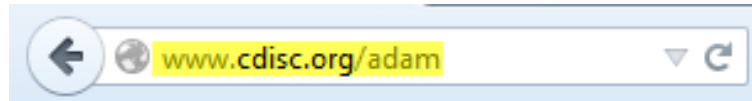
Version 1.0 of the Analysis Results Metadata Specification for Define-XML v2 is now available (*Released 30-Jan-2015*). The aim of this new specification is to support the submission of Analysis Results Metadata as defined in the CDISC ADaM Analysis Data Model Version 2.1 document. The release package consists of a zip file that includes a readme file, the specification document, an ADaM based Define-XML example and the Analysis Results Metadata schema. Refer to the readme file for further details.

[CDISC Analysis Results Metadata v1.0 for Define-XML v2](#)

[CDISC Analysis Results Metadata v1.0 for Define-XML v2 \(Public Review Comments\)](#)



ADaM Results Metadata v1 for Define-XML v2



Analysis Results Metadata Specification Version 1.0 for Define-XML Version 2

Prepared by
CDISC ADaM Metadata Sub-Team

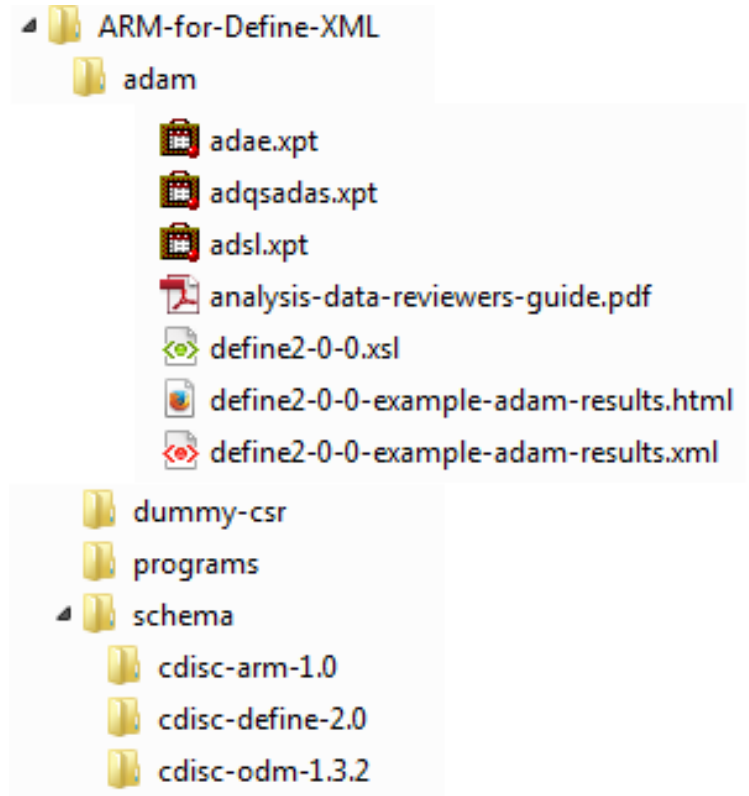
Notes to Readers

- This is the specification for the Analysis Results Metadata extension of Version 2.0 of the CDISC Define-XML standard.
- This document is intended for companies and individuals involved in the analysis of clinical data that will be submitted to regulatory authorities.

Revision History

Date	Version	Summary of Changes
2015-01-27	1.0	Final version 1.0 incorporating all changes identified during the public comment period
2014-09-10	1.0 DRAFT	Draft for public review

Warranties Notice: see Appendix C



ADaM Results Metadata v1 for Define-XML v2

- Formal Technical Specifications

5.3.9. arm:ProgrammingCode Element

arm:ProgrammingCode is the parent element for programming statements and/or a reference to the program used to perform the specific analysis.

Element Name:	arm:ProgrammingCode
Element XPath:	/ODM/Study/MetaDataVersion/arm:AnalysisResultDisplays/arm:ResultDisplay/ arm:AnalysisResult/arm:ProgrammingCode
Element Textual Value:	<i>None</i>
Usage	<u>Requirement:</u> Optional <u>Cardinality:</u> Zero or One
Attributes:	Context
Child Elements:	arm:Code, def:DocumentRef

Attribute	Usage	Allowable Values	Description
Context	Optional	Text Sample: “SAS Version 9.2”	The name and version of the computer language used for the actual programming statements provided.

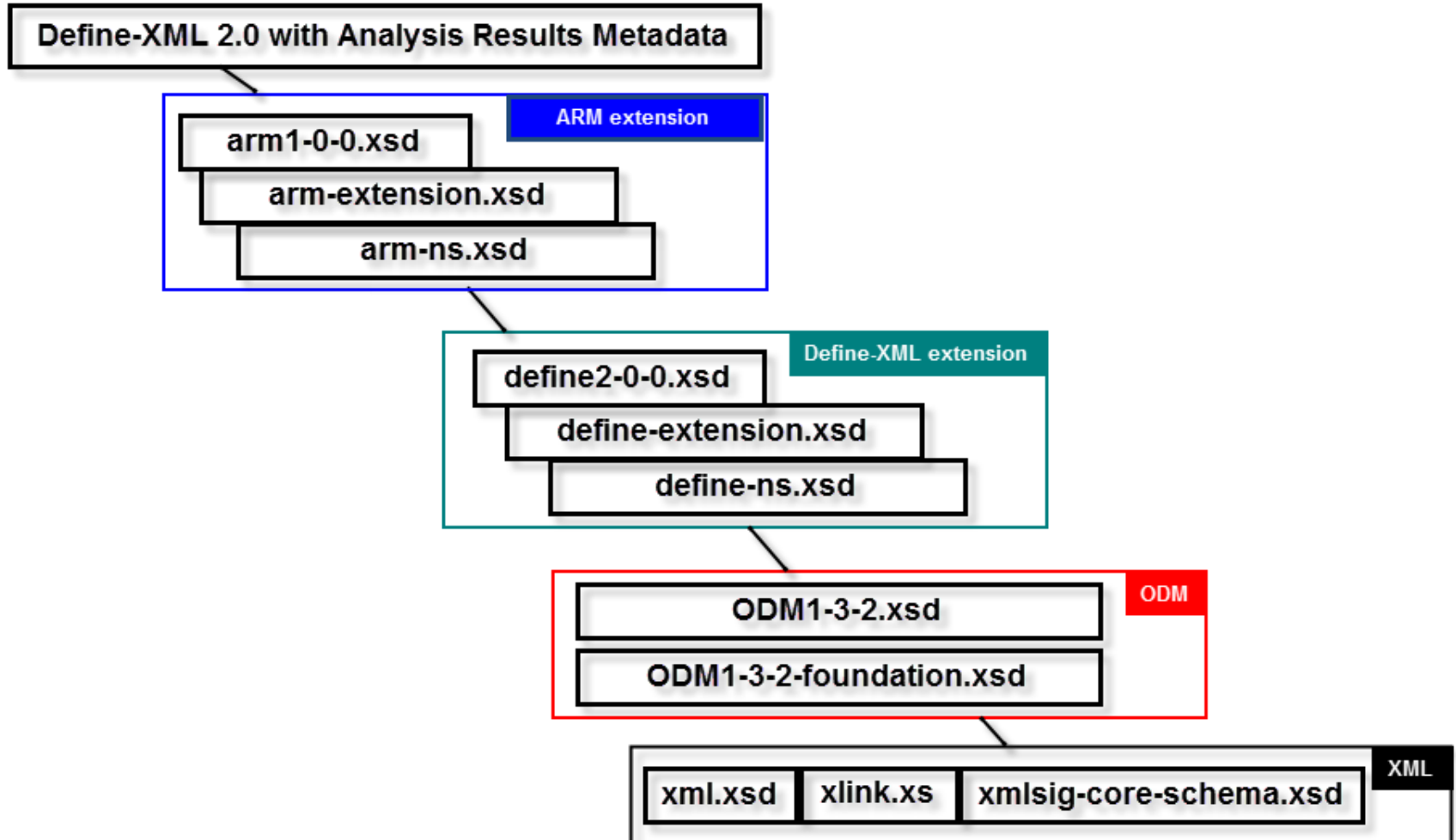


ADaM Results Metadata v1 for Define-XML v2

- For Define-XML v2 **only**
- Utilizes various Define-XML v2 constructs
 - WhereClause
 - Document reference support
 - Comment support
- It is recommended to move to Define-XML v2



ADaM Results Metadata v1 for Define-XML v2



ADaM Results Metadata v1 for Define-XML v2

- Updated Define-XML v2 XSL Stylesheet
- Works for ADaM, SDTM, SEND (with or without Results Metadata)
 - Bug fixes
 - Many improvements for linking to external PDF documents with physical page references or named destinations
 - Added Study metadata display

Standard	ADaM-IG 1.0
Study Name	CDISC-Sample
Study Description	CDISC-Sample Data Definition
Protocol Name	CDISC-Sample
Metadata Name	Study CDISC-Sample, Data Definitions
Metadata Description	Study CDISC-Sample, Data Definitions



Analysis Results Metadata – Metadata Fields*

Table 5.3.1 Analysis Results Metadata Fields

Analysis Results Metadata Field	Description
DISPLAY IDENTIFIER	A unique identifier for the specific analysis display (such as a table or figure number)
DISPLAY NAME	Title of display, including additional information if needed to describe and identify the display (e.g., analysis population)
RESULT IDENTIFIER	Identifies the specific analysis result within a display. For example, if there are multiple p-values on a display and the analysis results metadata specifically refers to one of them, this field identifies the p-value of interest. When combined with the display identifier provides a unique identification of a specific analysis result.
PARAM	The analysis parameter in the BDS analysis dataset that is the focus of the analysis result. Does not apply if the result is not based on a BDS analysis dataset.
PARAMCD	Corresponds to PARAM in the BDS analysis dataset. Does not apply if the result is not based on a BDS analysis dataset.
ANALYSIS VARIABLE	The analysis variable being analyzed
REASON	The rationale for performing this analysis. It indicates when the analysis was planned (e.g., "Pre-specified in Protocol," "Pre-specified in SAP," "Data Driven," "Requested by Regulatory Agency") and the purpose of the analysis within the body of evidence (e.g., "Primary Efficacy," "Key Secondary Efficacy," "Safety"). The terminology used is sponsor defined. An example of a reason is "Primary Efficacy Analysis as Pre-specified in Protocol."
DATASET	The name of the dataset used to generate the analysis result. In most cases, this is a single dataset. However, if multiple datasets are used, they are all listed here.
SELECTION CRITERIA	Specific and sufficient selection criteria for analysis subset and / or numerator – a complete list of the variables and their values used to identify the records selected for the analysis. Though the syntax is not ADaM-specified, the expectation is that the information could easily be included in a WHERE clause or something equivalent to ensure selecting the exact set of records appropriate for an analysis. This information is required if the analysis does not include every record in the analysis dataset.
DOCUMENTATION	Textual description of the analysis performed. This information could be a text description, pseudo code, or a link to another document such as the protocol or statistical analysis plan, or a link to an analysis generation program (i.e., a statistical software program used to generate the analysis result). The contents of the documentation metadata element contains depends on the level of detail required to describe the analysis itself, whether or not the sponsor is providing a corresponding analysis generation program, and sponsor-specific requirements and standards. This documentation metadata element will remain free form, meaning it will not become subject to a rigid structure or controlled terminology.
PROGRAMMING STATEMENTS	The software programming code used to perform the specific analysis. This includes, for example, the model statement (using the specific variable names) and all technical specifications needed for reproducing the analysis (e.g., covariance structure). The name and version of the applicable software package should be specified either as part of this metadata element or in another document, such as a Reviewer's Guide (see Appendix B for more information about a Reviewer's Guide).

- Display Identifier
- Display name
- Result Identifier
- Parameter (Code/Decode)
- Analysis Variable
- Reason
- Dataset
- Selection Criteria
- Documentation
- Programming Statements

* Version 2.1 of the Analysis Data Model (ADaM) Document, December 17, 2009

ADaM Results Metadata v1 for Define-XML v2

Analysis Results Metadata Field	Description
DISPLAY IDENTIFIER	A unique identifier for the specific analysis display (such as a table or figure number)
DISPLAY NAME	Title of display, including additional information if needed to describe and identify the display (e.g., analysis population)
RESULT IDENTIFIER	Identifies the specific analysis result within a display. For example, if there are multiple p-values on a display and the analysis results metadata specifically refers to one of them, this field identifies the p-value of interest. When combined with the display identifier provides a unique identification of a specific analysis result.

```
<arm:AnalysisResultDisplays>
  <arm:ResultDisplay OID="RD.Table_14-3.01" Name="Table 14-3.01">
    <Description>
      <TranslatedText xml:lang="en">Primary Endpoint Analysis: ADAS-Cog - Summary at Week 24 - LOCF (Efficacy Pop
    </TranslatedText>
    </Description>
    <def:DocumentRef leafID="LF.Table-14-3.01">
      <def:PDFPageRef PageRefs="2" Type="PhysicalRef"/>
    </def:DocumentRef>
    <arm:AnalysisResult
      OID="AR.Table_14-3.01.R.1" ParameterOID="IT.ADQSADAS.PARAMCD"
      AnalysisReason="SPECIFIED IN SAP" AnalysisPurpose="PRIMARY OUTCOME MEASURE">
        <Description>
          <TranslatedText xml:lang="en">Dose response analysis for ADAS-Cog changes from baseline</TranslatedText>
        </Description>
      </arm:AnalysisResult>
    </arm:ResultDisplay>
  </arm:AnalysisResultDisplays>
```



ADaM Results Metadata v1 for Define-XML v2

Analysis Results Metadata Field	Description
DISPLAY IDENTIFIER	A unique identifier for the specific analysis display (such as a table or figure number)
DISPLAY NAME	Title of display, including additional information if needed to describe and identify the display (e.g., analysis population)
RESULT IDENTIFIER	Identifies the specific analysis result within a display. For example, if there are multiple p-values on a display and the analysis results metadata specifically refers to one of them, this field identifies the p-value of interest. When combined with the display identifier provides a unique identification of a specific analysis result.

Analysis Results Metadata (Summary) for Study CDISC-Sample

[Table 14-3.01](#) Primary Endpoint Analysis: ADAS-Cog - Summary at Week 24 - LOCF (Efficacy Population)

[Dose response analysis for ADAS-Cog changes from baseline](#)

[Pairwise comparisons to placebo for ADAS-Cog changes from baseline](#)

[Table 14-5.02](#) Incidence of Treatment Emergent Serious Adverse Events by Treatment Group

[Incidence of Treatment Emergent Serious Adverse Events by Treatment Group](#)

Analysis Results Metadata (Detail) for Study CDISC-Sample

Table 14-3.01

Display	Table 14-3.01 Primary Endpoint Analysis: ADAS-Cog - Summary at Week 24 - LOCF (Efficacy Population)
Analysis Result	Dose response analysis for ADAS-Cog changes from baseline



ADaM Results Metadata v1 for Define-XML v2

PARAM	The analysis parameter in the BDS analysis dataset that is the focus of the analysis result. Does not apply if the result is not based on a BDS analysis dataset.
PARAMCD	Corresponds to PARAM in the BDS analysis dataset. Does not apply if the result is not based on a BDS analysis dataset.
ANALYSIS VARIABLE	The analysis variable being analyzed
REASON	The rationale for performing this analysis. It indicates when the analysis was planned (e.g., "Pre-specified in Protocol," "Pre-specified in SAP," "Data Driven," "Requested by Regulatory Agency") and the purpose of the analysis within the body of evidence (e.g., "Primary Efficacy," "Key Secondary Efficacy," "Safety"). The terminology used is sponsor defined. An example of a reason is "Primary Efficacy Analysis as Pre-specified in Protocol."

```
<arm:AnalysisResult
  OID="AR.Table_14-3.01.R.1"
  ParameterOID="IT.ADQSADAS.PARAMCD"
  AnalysisReason="SPECIFIED IN SAP"
  AnalysisPurpose="PRIMARY OUTCOME MEASURE">
  <Description>
    <TranslatedText xml:lang="en">Dose response analysis for ADAS-Cog changes from baseline</TranslatedText>
  </Description>
  <arm:AnalysisDatasets>
    <arm:AnalysisDataset ItemGroupOID="IG.ADQSADAS" >
      <def:WhereClauseRef WhereClauseOID="WC.Table_14-3.01.R.1.ADQSADAS" />
      <arm:AnalysisVariable ItemOID="IT.ADQSADAS.CHG"/>
    </arm:AnalysisDataset>
  </arm:AnalysisDatasets>
```



ADaM Results Metadata v1 for Define-XML v2

PARAM	The analysis parameter in the BDS analysis dataset that is the focus of the analysis result. Does not apply if the result is not based on a BDS analysis dataset.
PARAMCD	Corresponds to PARAM in the BDS analysis dataset. Does not apply if the result is not based on a BDS analysis dataset.
ANALYSIS VARIABLE	The analysis variable being analyzed
REASON	The rationale for performing this analysis. It indicates when the analysis was planned (e.g., "Pre-specified in Protocol," "Pre-specified in SAP," "Data Driven," "Requested by Regulatory Agency") and the purpose of the analysis within the body of evidence (e.g., "Primary Efficacy," "Key Secondary Efficacy," "Safety"). The terminology used is sponsor defined. An example of a reason is "Primary Efficacy Analysis as Pre-specified in Protocol."

Analysis Result	Dose response analysis for ADAS-Cog changes from baseline
Analysis Parameter(s)	PARAMCD = "ACTOT" (Adas-Cog(11) Subscore)
Analysis Variable(s)	CHG (Change from Baseline)
Analysis Reason	SPECIFIED IN SAP
Analysis Purpose	PRIMARY OUTCOME MEASURE
Data References (incl. Selection Criteria)	ADQSADAS [PARAMCD = "ACTOT" and AVISIT = "Week 24" and EFFFL = "Y" and ANL01FL = "Y"]



ADaM Results Metadata v1 for Define-XML v2

PARAM	The analysis parameter in the BDS analysis dataset that is the focus of the analysis result. Does not apply if the result is not based on a BDS analysis dataset.
PARAMCD	Corresponds to PARAM in the BDS analysis dataset. Does not apply if the result is not based on a BDS analysis dataset.
ANALYSIS VARIABLE	The analysis variable being analyzed
REASON	The rationale for performing this analysis. It indicates when the analysis was planned (e.g., "Pre-specified in Protocol," "Pre-specified in SAP," "Data Driven," "Requested by Regulatory Agency") and the purpose of the analysis within the body of evidence (e.g., "Primary Efficacy," "Key Secondary Efficacy," "Safety"). The terminology used is sponsor defined. An example of a reason is "Primary Efficacy Analysis as Pre-specified in Protocol."

	Code	Codelist Code	Codelist Extensible (Yes/No)	Codelist Name	CDISC Submission Value	CDISC Synonym(s)
1	C117745		Yes	Analysis Purpose	ANLPURP	Analysis Purpose
2	C98724	C117745		Analysis Purpose	EXPLORATORY OUTCOME MEASURE	Exploratory Outcome Measure
3	C98772	C117745		Analysis Purpose	PRIMARY OUTCOME MEASURE	Primary Outcome Measure
4	C98781	C117745		Analysis Purpose	SECONDARY OUTCOME MEASURE	Secondary Outcome Measure
5	C117744		Yes	Analysis Reason	ANLREAS	Analysis Reason
6	C117750	C117744		Analysis Reason	DATA DRIVEN	
7	C117751	C117744		Analysis Reason	REQUESTED BY REGULATORY AGENCY	
8	C117752	C117744		Analysis Reason	SPECIFIED IN PROTOCOL	
9						



ADaM Results Metadata v1 for Define-XML v2

DATASET	The name of the dataset used to generate the analysis result. In most cases, this is a single dataset. However, if multiple datasets are used, they are all listed here.
SELECTION CRITERIA	Specific and sufficient selection criteria for analysis subset and / or numerator – a complete list of the variables and their values used to identify the records selected for the analysis. Though the syntax is not ADaM-specified, the expectation is that the information could easily be included in a WHERE clause or something equivalent to ensure selecting the exact set of records appropriate for an analysis. This information is required if the analysis does not include every record in the analysis dataset.

```
<arm:AnalysisDatasets def:CommentOID="COM.JOIN-ADSL-ADAE">
  <arm:AnalysisDataset ItemGroupOID="IG.ADAE">
    <def:WhereClauseRef WhereClauseOID="WC.Table_14-5.02.R.1.ADAE" />
    <arm:AnalysisVariable ItemOID="IT.ADAE.AEBODSYS"/>
    <arm:AnalysisVariable ItemOID="IT.ADAE.AEDECOD"/>
  </arm:AnalysisDataset>
  <arm:AnalysisDataset ItemGroupOID="IG.ADSL">
    <def:WhereClauseRef WhereClauseOID="WC.Table_14-5.02.R.1.ADSL"/>
  </arm:AnalysisDataset>
</arm:AnalysisDatasets>

<def:CommentDef OID="COM.JOIN-ADSL-ADAE">
  <Description>
    <TranslatedText xml:lang="en">Get denominators for percentages from ADSL and counts and numerator
  </Description>
</def:CommentDef>
```



ADaM Results Metadata v1 for Define-XML v2

DATASET	The name of the dataset used to generate the analysis result. In most cases, this is a single dataset. However, if multiple datasets are used, they are all listed here.
SELECTION CRITERIA	Specific and sufficient selection criteria for analysis subset and / or numerator – a complete list of the variables and their values used to identify the records selected for the analysis. Though the syntax is not ADaM-specified, the expectation is that the information could easily be included in a WHERE clause or something equivalent to ensure selecting the exact set of records appropriate for an analysis. This information is required if the analysis does not include every record in the analysis dataset.

Data References (incl. Selection Criteria)	ADAE [TRTEMFL = "Y" and AESER = "Y"] ADSL [SAFFL = "Y"] Get denominators for percentages from ADSL and counts and numerators from ADAE. Join ADAE with ADSL based on the unique subject identifier (USUBJID) keeping only records in ADAE for the numerator.
---	--



ADaM Results Metadata v1 for Define-XML v2

DOCUMENTATION	Textual description of the analysis performed. This information could be a text description, pseudo code, or a link to another document such as the protocol or statistical analysis plan, or a link to an analysis generation program (i.e., a statistical software program used to generate the analysis result). The contents of the documentation metadata element contains depends on the level of detail required to describe the analysis itself, whether or not the sponsor is providing a corresponding analysis generation program, and sponsor-specific requirements and standards. This documentation metadata element will remain free form, meaning it will not become subject to a rigid structure or controlled terminology.
PROGRAMMING STATEMENTS	The software programming code used to perform the specific analysis. This includes, for example, the model statement (using the specific variable names) and all technical specifications needed for reproducing the analysis (e.g., covariance structure). The name and version of the applicable software package should be specified either as part of this metadata element or in another document, such as a Reviewer's Guide (see Appendix B for more information about a Reviewer's Guide).

```
<arm:Documentation>
  <Description>
    <TranslatedText xml:lang="en">Linear model analysis of CHG for dose response; using randomized do
  </TranslatedText>
  </Description>
  <def:DocumentRef leafID="LF.SAP-SEC-10.1.1">
    <def:PDFPageRef PageRefs="4" Type="PhysicalRef"/>
  </def:DocumentRef>
</arm:Documentation>
<arm:ProgrammingCode Context="SAS version 9.2">
<arm:Code>
ta = ADQSADAS;
FL='Y' and ANL01FL='Y' and AVISIT='Week 24' and PARAMCD="ACTOT";
EGR1;
= TRTPN SITEGR1;

</arm:Code>
</arm:ProgrammingCode>
```

ADaM Results Metadata v1 for Define-XML v2

DOCUMENTATION	Textual description of the analysis performed. This information could be a text description, pseudo code, or a link to another document such as the protocol or statistical analysis plan, or a link to an analysis generation program (i.e., a statistical software program used to generate the analysis result). The contents of the documentation metadata element contains depends on the level of detail required to describe the analysis itself, whether or not the sponsor is providing a corresponding analysis generation program, and sponsor-specific requirements and standards. This documentation metadata element will remain free form, meaning it will not become subject to a rigid structure or controlled terminology.
PROGRAMMING STATEMENTS	The software programming code used to perform the specific analysis. This includes, for example, the model statement (using the specific variable names) and all technical specifications needed for reproducing the analysis (e.g., covariance structure). The name and version of the applicable software package should be specified either as part of this metadata element or in another document, such as a Reviewer's Guide (see Appendix B for more information about a Reviewer's Guide).

```
<arm:Documentation>
  <Description>
    <TranslatedText xml:lang="en">Unique count of subjects that experienced an Adverse Event by Pr
    </TranslatedText>
  </Description>
  <def:DocumentRef leafID="LF.SAP-SEC-11.2">
    <def:PDFPageRef PageRefs="5" Type="PhysicalRef"/>
  </def:DocumentRef>
</arm:Documentation>
<arm:ProgrammingCode Context="SAS version 9.2">
  <def:DocumentRef leafID="LF.at14-5-02.sas" />
</arm:ProgrammingCode>
```



ADaM Results Metadata v1 for Define-XML v2

DOCUMENTATION	Textual description of the analysis performed. This information could be a text description, pseudo code, or a link to another document such as the protocol or statistical analysis plan, or a link to an analysis generation program (i.e., a statistical software program used to generate the analysis result). The contents of the documentation metadata element contains depends on the level of detail required to describe the analysis itself, whether or not the sponsor is providing a corresponding analysis generation program, and sponsor-specific requirements and standards. This documentation metadata element will remain free form, meaning it will not become subject to a rigid structure or controlled terminology.
PROGRAMMING STATEMENTS	The software programming code used to perform the specific analysis. This includes, for example, the model statement (using the specific variable names) and all technical specifications needed for reproducing the analysis (e.g., covariance structure). The name and version of the applicable software package should be specified either as part of this metadata element or in another document, such as a Reviewer's Guide (see Appendix B for more information about a Reviewer's Guide).

Documentation	Linear model analysis of CHG for dose response; using randomized dose (0 for placebo; 54 for low dose; 81 for high dose) and site group in model. Used PROC GLM in SAS to produce p-value (from Type III SS for treatment dose). SAP Section 10.1.1
Programming Statements	[SAS version 9.2] <pre>proc glm data = ADQSADAS; where EFFFL='Y' and ANL01FL='Y' and AVISIT='Week 24' and PARAMCD="ACTOT"; class SITEGR1; model CHG = TRTPN SITEGR1; run;</pre>



ADaM Results Metadata v1 for Define-XML v2

DOCUMENTATION	Textual description of the analysis performed. This information could be a text description, pseudo code, or a link to another document such as the protocol or statistical analysis plan, or a link to an analysis generation program (i.e., a statistical software program used to generate the analysis result). The contents of the documentation metadata element contains depends on the level of detail required to describe the analysis itself, whether or not the sponsor is providing a corresponding analysis generation program, and sponsor-specific requirements and standards. This documentation metadata element will remain free form, meaning it will not become subject to a rigid structure or controlled terminology.
PROGRAMMING STATEMENTS	The software programming code used to perform the specific analysis. This includes, for example, the model statement (using the specific variable names) and all technical specifications needed for reproducing the analysis (e.g., covariance structure). The name and version of the applicable software package should be specified either as part of this metadata element or in another document, such as a Reviewer's Guide (see Appendix B for more information about a Reviewer's Guide).

Documentation	Unique count of subjects that experienced an Adverse Event by Preferred Term, System Organ Class, and Treatment Group and percentages based on the number of subjects in the safety population within each treatment group. The total number of times an event occurred was recorded by Preferred Term, System Organ Class, and Treatment Group. Fisher's exact test was used for treatment comparison of event rates. SAP Section 11.2
Programming Statements	[SAS version 9.2] at14-5-02.sas



ADaM Results Metadata v1 for Define-XML v2

Analysis Results Metadata (Summary) for Study CDISC-Sample

Table 14-3.01 Primary Endpoint Analysis: ADAS-Cog - Summary at Week 24 - LOCF (Efficacy Population)

[Dose response analysis for ADAS-Cog changes from baseline](#)

[Pairwise comparisons to placebo for ADAS-Cog changes from baseline](#)

Table 14-5.02 Incidence of Treatment Emergent Serious Adverse Events by Treatment Group

[Incidence of Treatment Emergent Serious Adverse Events by Treatment Group](#)

Analysis Results Metadata (Detail) for Study CDISC-Sample

Table 14-3.01

Display	Table 14-3.01 Primary Endpoint Analysis: ADAS-Cog - Summary at Week 24 - LOCF (Efficacy Population)
Analysis Result	Dose response analysis for ADAS-Cog changes from baseline
Analysis Parameter(s)	PARAMCD = "ACTOT" (Adas-Cog(11) Subscore)
Analysis Variable(s)	CHG (Change from Baseline)
Analysis Reason	SPECIFIED IN SAP
Analysis Purpose	PRIMARY OUTCOME MEASURE
Data References (incl. Selection Criteria)	ADQSADAS [PARAMCD = "ACTOT" and AVISIT = "Week 24" and EFFFL = "Y" and ANL01FL = "Y"]
Documentation	Linear model analysis of CHG for dose response; using randomized dose (0 for placebo; 54 for low dose; 81 for high dose) and site group in model. Used PROC GLM in SAS to produce p-value (from Type III SS for treatment dose). SAP Section 10.1.1
Programming Statements	[SAS version 9.2] <pre>proc glm data = ADQSADAS; where EFFFL='Y' and ANL01FL='Y' and AVISIT='Week 24' and PARAMCD="ACTOT"; class SITEGR1; model CHG = TRTPN SITEGR1; run;</pre>

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PMDA – New Study Data Technical Conformance Guide (April 27, 2015) *

4.1.2.1 データセットの定義書

SDTM、ADaM データセットに関する定義書はそれぞれ CDISC における Define-XML 形式により、内容の表示が可能なスタイルシートへの参照を含む XML 形式のファイルにまとめた上で、提出フォルダに当該スタイルシートと共に格納して提出すること。定義書のファイル名は「define.xml」とする。定義書の内容としては、データセット、変数、変数の取り得る値、及び統制用語やコードに関する定義が含まれる。統制用語、辞書等の情報にはバージョンを含めること。

承認審査のために用いられる申請資料において表示される解析結果と解析データセットとの関係の把握が容易であることは、臨床試験データを用いた承認審査を円滑に進めるために重要である。よって、ADaM データセットに関する定義書には、4.1.1.3 に示す有効性、安全性の主要な結果及び用法・用量の設定の根拠に関わる臨床試験結果を得るための解析について、解析結果と対応する解析データセットや利用される変数等との関係を示す解析結果メタデータ (Analysis Results Metadata) が含まれることが望ましい。解析結果メタデータにおいては、各解析について以下の項目が含まれることが望ましい。

- 治験総括報告書に表示される解析結果を示す図表番号等及び表示名
- 解析の内容と実施理由
- 使用するパラメータ名とコード
- 解析対象となる変数
- 使用するデータセット
- 解析対象となるレコードの選択基準
- 解析計画書における対応する記載、解析プログラム名、解析方法の概略
- 解析方法に対応する解析用プログラムの抜粋

解析結果メタデータの形式については可能な限り CDISC による Analysis Results Metadata Specification for Define-XML を参考とすることとするが、定義書に含めて提出することが困難な場合には、eCTD 通知及び eCTD 取扱い通知によって定められている PDF により別途提出することが可能である。なお、定義書において、説明等が日本語により作成されていても差し支えない。

* PMDA Technical conformance guide (in Japanese) <http://www.pmda.go.jp/files/000204728.pdf>



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PMDA – New Study Data Technical Conformance Guide (April 27, 2015) *

- It is desired that define.xml for ADaM includes Analysis Results Metadata.
- Regarding formats for Analysis Results Metadata, CDISC's Analysis Results Metadata Specification for Define-XML should be used as a reference, wherever possible.
- However, if it is difficult for sponsor to submit Analysis Results Metadata by including it in define.xml, it can also be submitted in PDF format specified in eCTD-relevant notices.
- By the way, it is also allowed to create explanation and so on in define.xml in Japanese.

* PMDA Technical conformance guide (in Japanese) <http://www.pmda.go.jp/files/000204728.pdf>



ADaM Results Metadata v1 for Define-XML v2

What's next?

- The ADaM Metadata Team is developing validation checks for The Analysis Results Metadata extension
- These can then be implemented by validating applications (OpenCDISC, ...)
- But you can already validate your Define-XML v2 (+ ARM) against the XML Schema (**you should!**)
- FDA reference in the Data Standards Catalog?

Clinical study data definition	Define	XML	CDISC	1.0	N/A	CDER, CBER, CDRH	Ongoing		12/17/2016 [1] 12/17/2017 [2]		CDISC.org - Define-XML
Clinical study data definition	Define	XML	CDISC	2.0	N/A	CDER, CBER, CDRH	08-07-2013		12/17/2016 [1] 12/17/2017 [2]		CDISC.org - Define-XML



Thank you!

Questions?

