

ADRG Builder Python Application SM16 – PHUSE EU Connect 2024

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Inspired by **patients.**
Driven by **science.**





Agenda

1. Why an ADRG?
2. Why an Application?
3. ADRG Builder Python™ Application
4. Conclusion
5. Questions



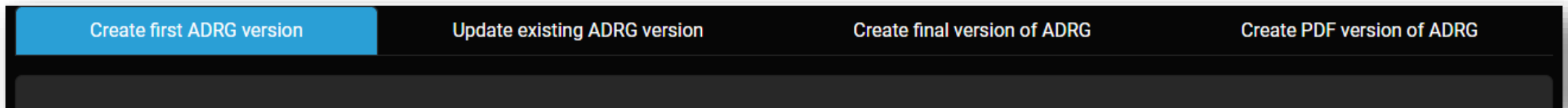
Why an ADRG?

- ❑ Recommended document according to the Study Data Technical Conformance Guide from the FDA.
- ❑ Provide authorities' reviewers with additional information presented in **ADaM define.xml file** with information that can't either be described properly or that cannot be represented in that format (i.e. tables, graphical images).
- ❑ Provide a summary of **ADaM conformance findings** (i.e. Pinnacle 21™ report).

Why an Application?

- ❑ Maintain a high level of **quality** and **consistency**.
- ❑ Reduce time by **automating** the creation of sections/sub-sections.
- ❑ Include standard analysis datasets text.
- ❑ Fully **automate** the insertion of P21 Enterprise report.
- ❑ Generate check report that highlights remaining issues and provide solutions.

4 tasks from the lifecycle of an ADRG creation



ADRG Builder Python Application

ADRG Template and Configuration JSON file

☐ Customized PHUSE ADRG Package version 1.2 template:

- ☐ Removed unnecessary text / information.
- ☐ Added “<<” and “>>” tags to identify areas of interest.
- ☐ Reconfigured some tables headers and format.

☐ Configuration JSON file:

- ☐ Regulate the structure and contents of the ADRG.
- ☐ Regulate styles for each section header.
- ☐ Ensure consistency for Table of Contents automatic creation.

ADRG Builder Python Application

First ADRG Version

- ☐ Select the ADaM define.xml to build the first ADRG version.
- ☐ Optionally exclude analysis dataset(s) from this first version.

The screenshot shows the 'Create first ADRG version' tab of the ADRG Builder application. At the top, there are four tabs: 'Create first ADRG version' (active), 'Update existing ADRG version', 'Create final version of ADRG', and 'Create PDF version of ADRG'. Below the tabs, the 'ADaM Define.xml File:' section contains a text input field with 'define-first.xml' and a 'Browse' button. The 'Analysis Datasets:' section features a list box with the following items: ☒ ADAE, ☒ ADCM, ☒ ADEASI, ☒ ADPGI, ☒ ADSL, and ☒ ADVS. To the right of the list box are 'Select All' and 'Clear All' buttons. At the bottom of the form are 'Submit' and 'Reset Fields' buttons.

- Cover Page
- Section 1.3
- Section 2.1
- Section 3.1
- Section 5.2
- Sections 5.2.x

First ADRG Version

Cover Page

Define.xml

```
<ODM ...>
  <Study OID="Study-ABC123">
    <GlobalVariables>
      <StudyName>ABC123</StudyName>
      <StudyDescription>
        PHASE 2, MULTIPLE DOSE, BLINDED STUDY OF DRUG XXX
      </StudyDescription>
      <ProtocolName>ABC123</ProtocolName>
    </GlobalVariables>
    <MetaDataVersion ...>
      ...
    </MetaDataVersion>
  </Study>
</ODM>
```

ADRG First Version

Analysis Data Reviewer's Guide

UCB

Study ABC123

ADRG Template Version 2019-07-18



First ADRG Version

Section 1.3

Define.xml

```
<MetaDataVersion OID="MDV.Study-ABC123"
  Name="Study ABC123 Data Definitions"
  Description="Study ABC123 Data Definitions"
  def:DefineVersion="2.1.0"
  <def:Standards>
    <def:Standard OID="STD.ADaMIG"
      Name="ADaMIG"
      Type="IG"
      Version="1.3"
      Status="FINAL"/>
    <def:Standard OID="STD.SDTMIG"
      Name="SDTMIG"
      Type="IG"
      Version="3.4"
      Status="FINAL"/>
    <def:Standard OID="STD.CT.ADaM"
      Name="CDISC/NCI"
      Type="CT"
      PublishingSet="ADaM"
      Version="2024-03-29"
      Status="FINAL"/>
    <def:Standard OID="STD.CT.SDTM"
      Name="CDISC/NCI"
      Type="CT"
      PublishingSet="SDTM"
      Version="2024-03-29"
      Status="FINAL"/>
  </def:Standards>
  ...
  <CodeList OID="CL.MEDICAL_EVENTS_DICT"
    <ExternalCodeList Dictionary="MedDRA" Version="22.1"/>
  </CodeList>
  <CodeList OID="CL.MEDICATIONS_DICT"
    <ExternalCodeList Dictionary="WHODD" Version="2023Q3"/>
  </CodeList>
</MetaDataVersion>
```

ADRG First Version

1.3 Study Data Standards and Dictionary Inventory

Standard or Dictionary	Versions Used
SDTM	Study Data Tabulation Model Version 2.0 Study Data Tabulation Model Implementation Guide: Human Clinical Trials Version 3.4
SDTM Controlled Terminology	2024-03-29
ADaM	ADaM Model Document Version 2.1 ADaM Implementation Guide Version 1.3 ADaM Structure for Occurrence Data (OCCDS) Implementation Guide Version 1.1
ADaM Controlled Terminology	2024-03-29
Data Definitions	define.xml v2.1.0
TAUG (if applicable)	
Medications Dictionary	WHODD 2023Q3
Medical Events Dictionary	Initial: Final: MedDRA 22.1
Other standards (optional)	

First ADRG Version

Section 1.3

Define.xml

```
<MetaDataVersion ...>
  <def:Standards>
    <def:Standard OID="STD.ADaMIG"
      Name="ADaMIG"
      Type="IG"
      Version="1.3"
      Status="FINAL"/>
    <def:Standard OID="STD.SDTMIG"
      Name="SDTMIG"
      Type="IG"
      Version="3.4"
      Status="FINAL"/>
    <def:Standard .../>
  </def:Standards>
  ...
</MetaDataVersion>
```

JSON look-up file

```
{
  "ADaMIG": {
    "1.3": [
      {
        "document": "ADaM Model Document Version 2.1"
      },
      {
        "document": "ADaM Implementation Guide Version 1.3"
      },
      {
        "document": "ADaM Structure for Occurrence Data (OCCDS) Implementation Guide Version 1.1",
        "class": ["OCCURRENCE DATA STRUCTURE"]
      },
      {
        "document": "Analysis Data Model Implementation Guide for Non-compartmental Analysis Input Data Version 1.0",
        "class": ["BASIC DATA STRUCTURE"],
        "subclass": ["NON-COMPARTMENTAL ANALYSIS"]
      },
      {
        "document": "Analysis Data Model Implementation Guide for Medical Devices Version 1.0",
        "class": ["DEVICE LEVEL ANALYSIS DATASET", "MEDICAL DEVICE OCCURRENCE DATA STRUCTURE", "MEDICAL DEVICE BASIC DATA STRUCTURE"]
      }
    ],
    "1.2": [...],
    "1.1": [...],
  },
  "SDTMIG": {
    "3.4": [
      {
        "document": "Study Data Tabulation Model Version 2.0"
      },
      {
        "document": "Study Data Tabulation Model Implementation Guide: Human Clinical Trials Version 3.4"
      }
    ],
    "3.3": [...],
    "3.2": [...],
  },
  "SDTMIG-AP": [...],
  "SDTMIG-MD": [...],
}
```

ADRG First Version

1.3 Study Data Standards and Dictionary Inventory

Standard or Dictionary	Versions Used
SDTM	Study Data Tabulation Model Version 2.0 Study Data Tabulation Model Implementation Guide: Human Clinical Trials Version 3.4
SDTM Controlled Terminology	2024-03-29
ADaM	ADaM Model Document Version 2.1 ADaM Implementation Guide Version 1.3 ADaM Structure for Occurrence Data (OCCDS) Implementation Guide Version 1.1
ADaM Controlled Terminology	2024-03-29

First ADRG Version

Sections 2.1 & 3.1

Define.xml

```
<ODM ...>
  <Study OID="Study-ABC123">
    <GlobalVariables>
      <StudyName ABC123 /StudyName>
      <StudyDescription>
        PHASE 2, MULTIPLE DOSE, BLINDED STUDY OF DRUG XXX
      </StudyDescription>
      <ProtocolName>ABC123</ProtocolName>
    </GlobalVariables>
    <MetaDataVersion ...>
      ...
    </MetaDataVersion>
  </Study>
</ODM>

<ItemDef OID="ADSL.BMIBLGR1" Name="BMIBLGR1" DataType="text" Length="20">
  <Description> ... </Description>
  <def:Origin Type="Derived" Source="Sponsor"/>
</ItemDef>
...
<ItemDef OID="ADPGI.BMIBLGR1" Name="BMIBLGR1" DataType="text" Length="20">
  <Description> ... </Description>
  <def:Origin Type="Predecessor">
    <Description><TranslatedText>ADSL.BMIBLGR1</TranslatedText></Description>
  </def:Origin>
</ItemDef>
```

ADRG First Version

2.1 Protocol Number and Title

Protocol Number: ABC123
Protocol Title: PHASE 2, MULTIPLE DOSE, BLINDED STUDY OF DRUG XXX
Protocol Versions: <<Protocol Versions>>

3.1 Core Variables

Core variables are those that are represented across all/most analysis datasets.

Variable Name	Variable Description
STUDYID	
USUBJID	
BMIBLGR1	
TRT01P	
TRTSEQP	
TRTSEQA	

First ADRG Version

Section 5.2

Define.xml

```
<ItemGroupDef OID="ADSL"
  Name="ADSL"
  Purpose="Analysis"
  SASDatasetName="ADSL"
  Repeating="No"
  IsReferenceData="No"
  def:Structure="One record per subject"
  def:ArchiveLocationID="LF.ADSL"
  def:CommentOID="COM.ADSL"
  def:StandardOID="STD.ADaMIG">
  <Description>
    <TranslatedText>Subject-Level Analysis Dataset</TranslatedText>
  </Description>
  <ItemRef .../>
  <def:Class Name="SUBJECT LEVEL ANALYSIS DATASET">
  <def:leaf ID="LF.ADSL" xlink:href="adsl.xpt">
    <def:title>adsl.xpt</def:title>
  </def:leaf>
</ItemGroupDef>
```

ADRG First Version

5.2 Analysis Datasets

Dataset Dataset Label	Class	Efficacy	Safety	Baseline or other subject characteristics	PK/PD	Primary Objective	Structure
ADSL Subject-Level Analysis Dataset	ADSL						One record per subject
ADAE Adverse Events Analysis Dataset	OCCDS						One record per adverse event per subject
ADCM Concomitant Medications Analysis Dataset	OCCDS						One record per recorded medication occurrence or constant-dosing interval per subject
ADEASI EASI Questionnaire Analysis Dataset	BDS						One record per Eczema Area and Severity Index (EASI) question per visit per subject
ADPGI PGI Analysis Dataset	BDS						One record per question per visit per subject
ADVS Vital Signs Analysis Dataset	BDS						One record per vital sign measurement per visit per date and time per timepoint per subject

First ADRG Version

Sections 5.2.x

Define.xml

```
<ItemGroupDef OID="ADAE" Name="ADAE" Purpose="Analysis" ...>
  <Description>
    <TranslatedText>Adverse Events Analysis Dataset</TranslatedText>
  </Description>
  <ItemRef .../>
</ItemGroupDef>
<ItemGroupDef OID="ADCM" Name="ADCM" Purpose="Analysis" ...>
  <Description>
    <TranslatedText>Concomitant Medications Analysis Dataset</TranslatedText>
  </Description>
  <ItemRef .../>
</ItemGroupDef>
<ItemGroupDef OID="ADEASI" Name="ADEASI" Purpose="Analysis" ...>
  <Description>
    <TranslatedText>EASI Questionnaire Analysis Dataset</TranslatedText>
  </Description>
  <ItemRef .../>
</ItemGroupDef>
<ItemGroupDef OID="ADSL" Name="ADSL" Purpose="Analysis" ...>
  <Description>
    <TranslatedText>Subject-Level Analysis Dataset</TranslatedText>
  </Description>
  <ItemRef .../>
</ItemGroupDef>
```

ADRG First Version

5.2.1 ADSL - Subject-Level Analysis Dataset

ADSL contains variables to support baseline characteristics and disposition analyses. The population indicator variables and covariates are defined in ADSL and copied into other analysis datasets as needed.

<< All subjects in domain DM, except for screen failures were included in ADSL. >>

5.2.2 ADAE - Adverse Events Analysis Dataset

ADAE contains variables to adverse events analyses.

<< All rows in domain AE were included in ADAE. >>

5.2.3 ADCM - Concomitant Medications Analysis Dataset

<<insert your text here>>

5.2.4 ADEASI - EASI Questionnaire Analysis Dataset

ADEASI is an Eczema Area and Severity Index (EASI) questionnaire dataset that supports the <<Primary/Secondary/Exploratory>> efficacy endpoint of the study.

The analysis EASI total score is derived as follow:

- For each Body Region, create a temporary score:
- Create a temporary sum of AVAL from the following 4 assessments (see parameters referenced in table below): Erythema, Edema/Papulation, Excoriation and Lichenification
- Multiply the temporary calculated above with the associated Region score value (AVAL from associated parameter referenced in table below).
- Multiply the value from the previous step with the value from column "Multiplier" of the associated Body Region (see reference table below).
- Sum all 4 Body Region temporary score calculated above to get the EASI total score. The minimum score is 0 and the maximum score is 72.
- Missing values are imputed based on <<XXX>> method.

Patients 8 years old or above:

Body Region	Erythema (0-3)	Edema/Papulation (0-3)	Excoriation (0-3)	Lichenification (0-3)	Region score (0-6)	Multiplier	Score per body region
Head / neck	PARAMCD="EASI0102"	PARAMCD="EASI0103"	PARAMCD="EASI0104"	PARAMCD="EASI0105"	PARAMCD="EASI0101"	0.1	(0-7.2)
Trunk	PARAMCD="EASI0107"	PARAMCD="EASI0108"	PARAMCD="EASI0109"	PARAMCD="EASI0110"	PARAMCD="EASI0106"	0.3	(0-21.6)
Upper extremities	PARAMCD="EASI0112"	PARAMCD="EASI0113"	PARAMCD="EASI0114"	PARAMCD="EASI0115"	PARAMCD="EASI0111"	0.2	(0-14.4)
Lower extremities	PARAMCD="EASI0117"	PARAMCD="EASI0118"	PARAMCD="EASI0119"	PARAMCD="EASI0120"	PARAMCD="EASI0116"	0.4	(0-28.8)

The final EASI score is the sum of the 4 region scores: (0-72)

ADRG Builder Python Application

Update existing ADRG version

- ☐ Select the ADRG to update
- ☐ Select the ADaM define.xml
- ☐ Optionally select a Pinnacle 21 Enterprise report
- ☐ Optionally exclude analysis dataset(s) from this updated version

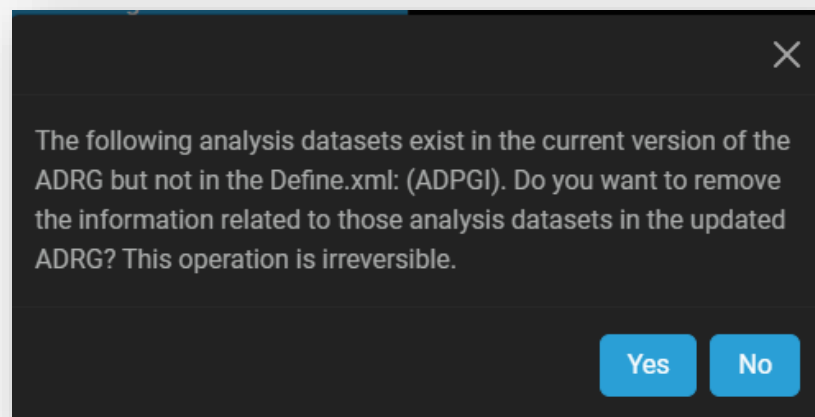
The screenshot shows the 'Update existing ADRG version' tab of the ADRG Builder Python Application. The interface includes four tabs at the top: 'Create first ADRG version', 'Update existing ADRG version' (active), 'Create final version of ADRG', and 'Create PDF version of ADRG'. Below the tabs, there are three input fields with 'Browse' buttons: 'ADRG File to Update:' with 'adrg-2024-mm-dd-hh-mm.docx', 'ADaM Define.xml File:' with 'define-second.xml', and 'P21E Report (Optional):' with 'ABC123-FDA-validation-report.xlsx' and a 'Remove' button. A list of analysis datasets is shown with checkboxes, all of which are checked: ADAE, ADCM, ADDE, ADDL, ADEASI, ADHO, ADLB, ADSF36, ADSL, and ADVS. To the right of the list are 'Select All' and 'Clear All' buttons. At the bottom are 'Submit' and 'Reset Fields' buttons.

- Cover Page
- Section 1.3
- Section 2.1
- Section 3.1
- Section 5.2
- Sections 5.2.x
- Section 6.1
- Section 6.2

ADRG Builder Python Application

Update existing ADRG version

- ☐ Analysis datasets in the ADRG but not found in the define.xml are flagged.
- ☐ Users can choose to either retain or remove these flagged analysis datasets from the ADRG.
- ☐ If users opt to remove the datasets, the corresponding information from sections 5.2 and 5.2.x are also removed.



Update existing ADRG version

Section 1.3

Define.xml

```
<MetaDataVersion ...>
  <def:Standards>
    <def:Standard />
    <def:Standard
      OID="STD.SDTMIG-MD"
      Name="SDTMIG-MD"
      Type="IG"
      Version="1.1"
      Status="FINAL" //
    </def:Standard>
    ...
  </def:Standards>

  ItemGroupDef OID="ADDL" Name="ADDL" Purpose="Analysis" ...>
    ...
    <def:Class Name="DEVICE LEVEL ANALYSIS DATASET"/>
    ...
  </ItemGroupDef>
  ...
</MetaDataVersion>
```

JSON look-up file

```
{
  "ADaMIG": {
    "1.3" : [
      {
        "document": "ADaM Structure for Occurrence Data (OCCDS) Implementation Guide Version 1.1",
        "class": ["OCCURRENCE DATA STRUCTURE"]
      },
      {
        "document": "Analysis Data Model Implementation Guide for Non-compartmental Analysis Input Data Version 1.0",
        "class": ["BASIC DATA STRUCTURE"],
        "subclass": ["NON-COMPARTMENTAL ANALYSIS"]
      }
    ],
    "1.2" : [
      {
        "document": "Analysis Data Model Implementation Guide for Medical Devices Version 1.0",
        "class": ["DEVICE LEVEL ANALYSIS DATASET", "MEDICAL DEVICE OCCURRENCE DATA STRUCTURE", "MEDICAL DEVICE BASIC DATA STRUCTURE"]
      }
    ],
    "1.1" : [
      {
        "document": "Study Data Tabulation Model Implementation Guide: Associated Persons Version 1.0"
      }
    ],
    "SDTMIG-AP": {
      "1.0" : [
        {
          "document": "Study Data Tabulation Model Implementation Guide: Associated Persons Version 1.0"
        }
      ]
    },
    "SDTMIG-MD": {
      "1.1" : [
        {
          "document": "Study Data Tabulation Model Implementation Guide for Medical Devices Version 1.1"
        }
      ]
    },
    "1.0" : [
      {
        "document": "Study Data Tabulation Model Implementation Guide: Associated Persons Version 1.0"
      }
    ]
  }
}
```

ADRG Updated Version

1.3 Study Data Standards and Dictionary Inventory	
Standard or Dictionary	Versions Used
SDTM	Study Data Tabulation Model Version 2.0
	Study Data Tabulation Model Implementation Guide: Human Clinical Trials Version 3.4
	Study Data Tabulation Model Implementation Guide for Medical Devices Version 1.1
SDTM Controlled Terminology	2024-03-29
ADaM	ADaM Model Document Version 2.1
	ADaM Implementation Guide Version 1.3
	ADaM Structure for Occurrence Data (OCCDS) Implementation Guide Version 1.1
	Analysis Data Model Implementation Guide for Medical Devices Version 1.0
ADaM Controlled Terminology	2024-03-29

Update existing ADRG version

Section 3.1

Original ADRG

3.1 Core Variables
Core variables are those that are represented across all/

Variable Name	Variable Description
STUDYID	Study Identifier
USUBJID	Unique Subject Identifier
BMIBLGR1	BMI at Baseline Analysis Group
TRT01P	Planned Treatment for Period 01
TRTSEQP	Planned Sequence of Treatment
TRTSEQA	Actual Sequence of Treatment

Variable no longer in Define.xml

ADRG Updated Version

3.1 Core Variables
Core variables are those that are represented across all/most analysis datasets.

Variable Name	Variable Description
STUDYID	Study Identifier
USUBJID	Unique Subject Identifier
TRT01P	Planned Treatment
TRTSEQP	Planned Sequence of Treatment
TRTSEQA	Actual Sequence of Treatment
SAFFL	

New variable in Define.xml

Update existing ADRG version

Section 5.2

Original ADRG

5.2 Analysis Datasets

Dataset Dataset Label	Class	Efficacy	Safety	Baseline or other subject characteristics	PK/PD	Primary Objective	Structure
ADSL Subject-Level Analysis Dataset	ADSL			X			One record per subject
ADAE Adverse Events Analysis Dataset	OCCDS		X				One record per adverse event per subject
ADCM Concomitant Medications Analysis Dataset	OCCDS		X				One record per recorded medication occurrence or constant-dosing interval per subject
ADEASI EASI Questionnaire Analysis Dataset	BDS	X				X	One record per Eczema Area and Severity Index (EASI) question per visit per subject
ADPGI PGI Analysis Dataset	BDS	X					One record per question per visit per subject
ADVS Vital Signs Analysis Dataset	BDS		X				One record per vital sign measurement per visit per date and time per timepoint per subject

ADRG Updated Version

5.2 Analysis Datasets

Dataset Dataset Label	Class	Efficacy	Safety	Baseline or other subject characteristics	PK/PD	Primary Objective	Structure
ADSL Subject-Level Analysis Dataset	ADSL			X			One record per subject
ADAE Adverse Events Analysis Dataset	OCCDS		X				One record per adverse event per subject
ADCM Concomitant Medications Analysis Dataset	OCCDS		X				One record per recorded medication occurrence or constant-dosing interval per subject
ADDE Device Event Analysis Dataset	MDOCCDS						One record per device event per subject
ADDL Device-Level Analysis Dataset	ADDL						One record per device per subject
ADEASI EASI Questionnaire Analysis Dataset	BDS	X				X	One record per Eczema Area and Severity Index (EASI) question per visit per subject

**New analysis
datasets in
Define.xml**

Update existing ADRG version

Sections 5.2.x

Original ADRG

5.2.1 ADSL - Subject-Level Analysis Dataset

ADSL contains variables to support baseline characteristics and disposition analyses. The population indicator variables and covariates are defined in ADSL and copied into other analysis datasets as needed.

<< All subjects in domain DM, except for screen failures were included in ADSL. >>

5.2.2 ADAE - Adverse Events Analysis Dataset

ADAE contains variables to adverse events analyses.

<< All rows in domain AE were included in ADAE. >>

5.2.3 ADCM - Concomitant Medications Analysis Dataset

<<insert your text here>>

5.2.4 ADEASI - EASI Questionnaire Analysis Dataset

ADEASI is an Eczema Area and Severity Index (EASI) questionnaire dataset following the ADaM Basic Data Structure (BDS) that supports the <<Primary/Secondary/Exploratory>> efficacy endpoint of the study.

The analysis EASI total score is derived as follow:

ADRG Updated Version

5.2.1 ADSL - Subject-Level Analysis Dataset

ADSL contains variables to support baseline characteristics and disposition analyses. The population indicator variables and covariates are defined in ADSL and copied into other analysis datasets as needed.

<< All subjects in domain DM, except for screen failures were included in ADSL. >>

5.2.2 ADAE - Adverse Events Analysis Dataset

ADAE contains variables to adverse events analyses.

<< All rows in domain AE were included in ADAE. >>

5.2.3 ADCM - Concomitant Medications Analysis Dataset

<<insert your text here>>

5.2.4 ADDE - Device Event Analysis Dataset

<<insert your text here>>

5.2.5 ADDL - Device-Level Analysis Dataset

ADDL contains variables to support medical devices disposition analyses.

<< All devices in DI were included in ADDL. >>

5.2.6 ADEASI - EASI Questionnaire Analysis Dataset

ADEASI is an Eczema Area and Severity Index (EASI) questionnaire dataset following the ADaM Basic Data Structure (BDS) that supports the <<Primary/Secondary/Exploratory>> efficacy endpoint of the study.

The analysis EASI total score is derived as follow:

Sections
renumbered

Update existing ADRG version

Section 6.1

Pinnacle 21 Enterprise Report

Pinnacle 21 Enterprise Data Package Validation Report			
Project: XXX Study: ABC123 Data Package: FDA		Report Generated: 2024-mm-ddThh:mm:ssZ Data Validated: 2024-mm-ddThh:mm:ssZ Enterprise Version: 5.1.1	
Issues	Progress	Data Fitness Score	Projected Score
47 Unresolved Issues	94% Excellent	68 Progressing	68 Progressing
Issues Breakdown	Changes from Last Validation	Package Details	Key Metrics
Issues by Status Open 47 Fix Now 0 Fix Later 0 To Close 0 To Close w/o Expl. 0 Closed 0	Issue Changes New Issues 0 Fixed Issues 0 Updated Issues 0 Unchanged Issues 47 View New/Updated View All Changes	Validation Engine FDA 2204.0 Standards Used ADaM-IG 1.3 Define-XML 2.1	How to Make Progress? Make Progress by fixing Issues, changing Issue Status, and adding Explanations. What is Data Fitness Score?

ADRG Updated Version

6.1 Conformance Inputs

Specify the software name and version for the analysis datasets

Pinnacle 21 Enterprise version 5.1.1

Specify the version of the validation rules (i.e. CDISC, FDA) for the analysis datasets

FDA Validation Engine version 2204.0

Specify the software name and version for the define.xml

Pinnacle 21 Enterprise version 5.1.1

Specify the version of the validation rules (i.e. CDISC, FDA) for the define.xml

FDA Validation Engine version 2204.0

Provide any additional compliance evaluation information:

<<Text here>>

Update existing ADRG version

Section 6.2

Pinnacle 21
Enterprise
Report

ADRG Updated
Version

Validation Issues										
Manage Issues in Enterprise										
Dataset	Rule ID	Message	Affected	Changed	Impact	Type	Status	Assignee	Sources	Explanation
ADEASI	AD0149B	Inconsistent value for AVALC	2	0	Medium	Error	Open		Mapping	For analysis purposes, values below the lower limit of quantification are treated as being equal to the lower limit of quantification. Hence, AVALC = "< 100" and AVALC="100" are both considered to have AVAL = 100.
ADAE	CT2002	ADURU value not found in 'Unit' extensible codelist	10 445	0	Medium	Warning	Open		Design, Mapping	Add an Explanation

Issue Details										
Manage Issues in Enterprise										
Dataset	Record	Count	Variables	Values	Rule ID	Message	Impact	Type		
ADEASI	2 331		STUDYID, PARAMCD, AVAL, AVALC	ABC123, XXXXX, 100, 100	AD0149B	Inconsistent value for AVALC	Medium	Error		
ADAE		10 445	ADURU	Days	CT2002	ADURU value not found in 'Unit' extensible codelist	Medium	Warning		

6.2 Issues Summary<<insert your text here and/or use following table>>

Dataset	Variable	Values	Rule ID	Type	Impact	Records/Count	P21 Message/CDISC rule description	Explanation
ADEASI	STUDYID, PARAMCD, AVAL, AVALC		AD0149B	Error	Medium	2	Inconsistent value for AVALC	For analysis purposes, values below the lower limit of quantification are treated as being equal to the lower limit of quantification. Hence, AVALC = "< 100" and AVALC="100" are both considered to have AVAL = 100.
ADAE	ADURU	Days	CT2002	Warning	Medium	10445	ADURU value not found in 'Unit' extensible codelist	Add an Explanation

ADRG Builder Python Application

Create final version of ADRG

- ☐ Select the ADRG to finalize
- ☐ Select the final ADaM define.xml and optionally the final Pinnacle 21 Enterprise report

The screenshot shows the 'Create final version of ADRG' tab selected in a four-tab interface. The tabs are: 'Create first ADRG version', 'Update existing ADRG version', 'Create final version of ADRG' (active), and 'Create PDF version of ADRG'. The main form area has a dark background. It contains three input fields with 'Browse' buttons: 'ADRG File to Finalize:' with 'adrg-final.docx', 'ADaM Define.xml File:' with 'define-final.xml', and 'P21E Report (Optional):' with 'ABC123-FDA-validation-report.xlsx'. There is also a 'Remove' button next to the P21E Report field. At the bottom left are 'Submit' and 'Reset Fields' buttons.

- ☐ ADRG checked against Define.xml/P21 Report and a check report produced if issues remain.
- ☐ The application perform operations and a final ADRG is generated if no issues remain.

Create final ADRG version

Sections 5.2.x

Original ADRG

5.2.1 ADSL - Subject-Level Analysis Dataset

ADSL contains variables to support baseline characteristics and disposition analyses. The population indicator variables and covariates are defined in ADSL and copied into other analysis datasets as needed.

All subjects in domain DM, except for screen failures were included.

5.2.2 ADAE - Adverse Events Analysis Dataset

ADAE contains variables to adverse events analyses.

All rows in domain AE were included in ADAE.

5.2.3 ADCM - Concomitant Medications Analysis Dataset

<<insert your text here>>

5.2.4 ADDE - Device Event Analysis Dataset

<<insert your text here>>

5.2.5 ADDL - Device-Level Analysis Dataset

ADDL contains variables to support medical devices disposition analyses.

All devices in DI were included in ADDL.

Empty
sections
removed

ADRG Final Version

5.2.1 ADSL - Subject-Level Analysis Dataset

ADSL contains variables to support baseline characteristics and disposition analyses. The population indicator variables and covariates are defined in ADSL and copied into other analysis datasets as needed.

All subjects in domain DM, except for screen failures were included.

5.2.2 ADAE - Adverse Events Analysis Dataset

ADAE contains variables to adverse events analyses.

All rows in domain AE were included in ADAE.

5.2.3 ADDL - Device-Level Analysis Dataset

ADDL contains variables to support medical devices disposition analyses.

All devices in DI were included in ADDL.

5.2.4 ADEASI - EASI Questionnaire Analysis Dataset

ADEASI is an Eczema Area and Severity Index (EASI) questionnaire dataset following the ADaM Basic Data Structure (BDS) that supports the Primary efficacy endpoint of the study.

Sections
renumbered

Create final ADRG version

Section 5.2

Original ADRG

5.2 Analysis Datasets

Dataset Dataset Label	Class	Efficacy	Safety	Baseline or other subject characteristics	PK/PD	Primary Objective	Structure
ADSL Subject-Level Analysis Dataset	ADSL			X			One record per subject
ADAE Adverse Events Analysis Dataset	OCCDS		X				One record per adverse event per subject
ADCM Concomitant Medications Analysis Dataset	OCCDS		X				One record per recorded medication occurrence or constant-dosing interval per subject
ADDE Device Event Analysis Dataset	MDOCCDS		X				One record per device event per subject
ADDL Device-Level Analysis Dataset	ADDL			X			One record per device per subject

ADRG Final Version

5.2 Analysis Datasets

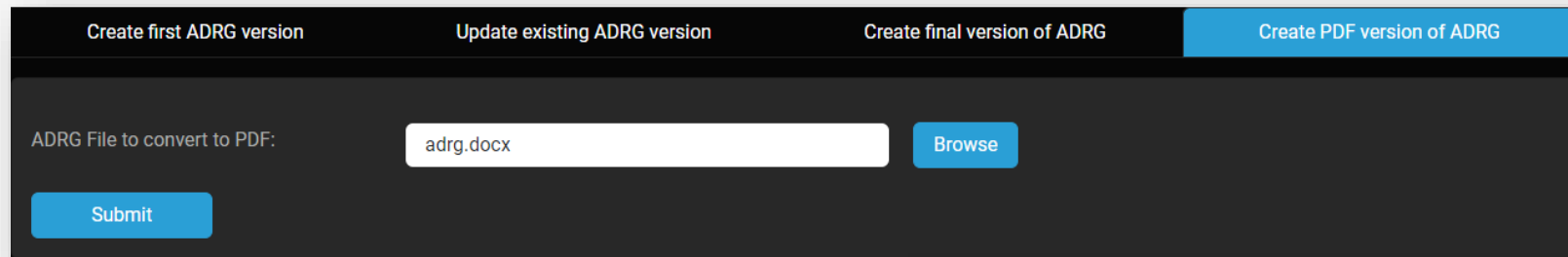
Dataset Dataset Label	Class	Efficacy	Safety	Baseline or other subject characteristics	PK/PD	Primary Objective	Structure
ADSL Subject-Level Analysis Dataset	ADSL			X			One record per subject
ADAE Adverse Events Analysis Dataset	OCCDS		X				One record per adverse event per subject
ADCM Concomitant Medications Analysis Dataset	OCCDS		X				One record per recorded medication occurrence or constant-dosing interval per subject
ADDE Device Event Analysis Dataset	MDOCCDS		X				One record per device event per subject
ADDL Device-Level Analysis Dataset	ADDL			X			One record per device per subject

Hyperlinks to
sections 5.2.x

ADRG Builder Python Application

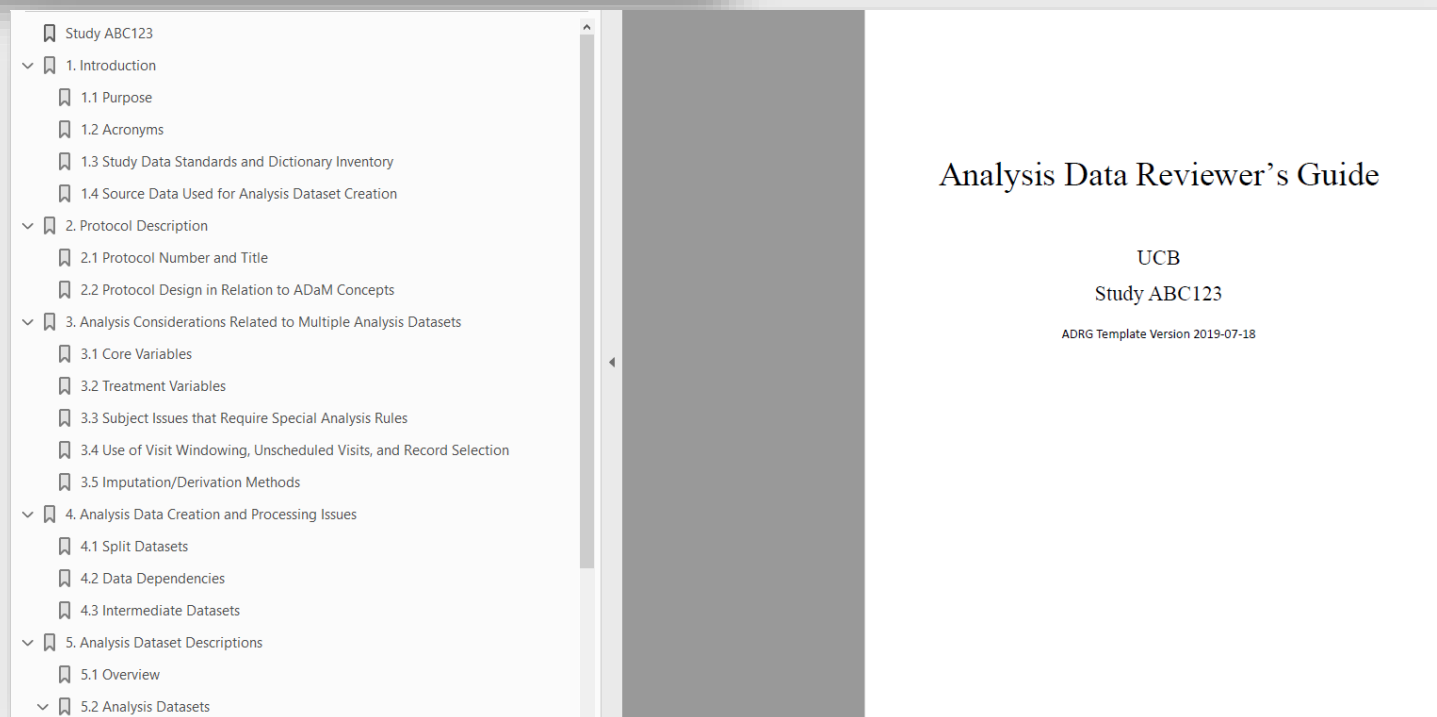
Create PDF version of ADRG

Finalization instructions from the ADRG Completion Guidelines document to a final ADRG:



The screenshot shows the 'Create PDF version of ADRG' tab selected. Below the tabs, there is a section labeled 'ADRG File to convert to PDF:' with a text input field containing 'adrg.docx' and a 'Browse' button. Below this, there is a 'Submit' button.

- ☐ Create bookmarks
- ☐ Delete information in the Title, Author, Subject and Keywords boxes
- ☐ PDF version



ADRG Builder Python Application

Check report

- ❑ Identify remaining issues and ensure consistency.
- ❑ Contains name/datetime creation of ADRG, define.xml and P21E report.
- ❑ Issues reported by sections and categorized as either “Error” or “Note”.
- ❑ Report need to be error free to proceed with creating a final version of ADRG.

Summary of Checks				
ADRG file: adrg-2024-08-08-09-53.docx Datetime ADRG file last saved: 2024-08-08 09:53:29 Define.xml file: define-second.xml Datetime Define.xml file last saved: 2024-08-06 10:29:22 P21 Enterprise file: ABC123-FDA-validation-report.xlsx Datetime P21 Enterprise file last saved: 2024-08-07 10:59:50				
Section	Issue	Current Value	Expected or Problematic Value	Category
1.1	Paragraph contains a placeholder.	This document provides context for the analysis datasets and terminology that benefit from additional explanation beyond the Data Definition document (define.xml) for an individual study. In addition, this document provides a summary of ADaM conformance findings. Also included are details regarding <<legacy analysis data conversion to ADaM>> << legacy tabulation data conversion to SDTM and then to ADaM>>.	<<legacy analysis data conversion to ADaM>>	Error
1.1	Paragraph contains a placeholder.	This document provides context for the analysis datasets and terminology that benefit from additional explanation beyond the Data Definition document (define.xml) for an individual study. In addition, this document provides a summary of ADaM conformance findings. Also included are details regarding <<legacy analysis data conversion to ADaM>> << legacy tabulation data conversion to SDTM and then to ADaM>>.	<< legacy tabulation data conversion to SDTM and then to ADaM>>	Error
1.2	Column Acronym in table contains a placeholder.	<<aCRF>>	<<aCRF>>	Error
1.2	Column Acronym in table contains a placeholder.	<<eCRF>>	<<eCRF>>	Error

Conclusion

- ❑ Part of standardization strategy.
- ❑ Saves time, ensures consistency and quality across documents.
- ❑ Improvements to the application are constantly performed, mostly based on users' feedback.
- ❑ Open-source technologies offer the chance to develop customized tools at a lower cost.

A woman with dark hair, wearing a black puffer vest over a dark sweater, a light blue scarf, and dark pants, stands on a paved path next to a wooden fence. Behind the fence is a river and trees with autumn foliage. A sign on the fence reads "DANGER DEEP WATER KEEP OUT".

Thanks. Any questions?