Why Are There So Many ADaM Documents, and How Do I Know Which to Use?

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ABSTRACT

As of this writing, the CDISC website has the following ADaM documents for download: a model document, three versions of the implementation guide, an adverse event data structure, an occurrence data structure, a time-to-event document, a document with examples in commonly used statistical analysis methods, an analysis result metadata document, conformance rules, and an important considerations document. Additionally, you can download three release packages, each containing a subset of these documents. This paper describes why there are so many documents, walks through basic information contained in each, and makes recommendations of which set of documents to use in which circumstances.

INTRODUCTION

Those new to the CDISC (Clinical Data Interchange Standards Consortium) Analysis Data Model (ADaM) can be overwhelmed by the list of documents available, and have questions. This paper will answer questions such as:

- How do I know which version of the implementation guide I should use?

- Which documents can be used together, and which should not be?

- Which documents are relevant to my needs?

- Do I need to read all of these documents?

- How will the ADaM team address this in the future?

Before getting into the details of each ADaM document, this paper first reviews ADaM history to explain how these documents came to be. Then it describes some regulatory and CDISC material that will help you decide which set of documents is best to use for your case. It then lists each ADaM document, with a summary and a description of which parts should be read. The paper wraps up by looking ahead to how things might evolve in the future.

HISTORY

According to Wikipedia, CDISC began as a volunteer group in late 1997. Its first documents, SDS v1.0 and ODM v0.8, were released in 1999.

In the year 2000, CDISC became a non-profit organization. It also followed up the prior SDS release with v1.1. During that year, the ADaM team began regular meetings to create a model document.

THE EARLY YEARS

In 2002, ADaM v1.0, the first ADaM model document, was released. This document focused on the fundamental principles of ADaM and the use of metadata. It described the now common task of separating data preparation from generation of analysis results.

At that time, the team could not agree on a standard structure. Some team members preferred a more horizontal structure with lots of analysis variables, while others preferred a more vertical structure, similar to the current Basic Data Structure (BDS). Instead of choosing one structure, the team created a set of "strawman" examples, demonstrating various ADaM-compliant structures that could be used for a variety of specific types of statistical analyses.

ADDING STANDARD STRUCTURES

Although the ADaM team continued to mostly disagree on standardizing the analysis dataset structures, one thing everyone seem to have in common was the need for a dataset that contained subject-level information in a one-record-per-subject structure. ADSL, the subject-level analysis dataset, became the first ADaM structure developed. It was released as part of ADaM v2.0. in 2006.

Meanwhile, the SDS team released SDTM v2.0, which included the more vertical Findings observation class that we still use today. With this standardized input data now taking hold across the industry, it was time for ADaM to choose a single structure for our common analysis needs. A structure similar to that SDTM Findings structure, with some improvements for analysis, had the advantage that it allowed for traceability back to SDTM data, and would meet that ADaM fundamental principle.

The BDS one-record-per-subject-per-parameter-per-optional-timepoint was developed and included in the 2009 release of both ADaM v2.1 and an ADaM Implementation Guide (ADaMIG). ADaMIG v1.0 described and provided examples of both ADSL and the Basic Data Structure (BDS). This combination of ADaM v2.1 and ADaMIG v1.0 covered many of the common analysis needs.

APPENDIX DOCUMENTS

By the time the ADaMIG v1.0 was finalized, the ADaM team was large enough to split up and work in sub-teams. Within a couple years, these sub-teams help produce and publish several "appendix documents".

- One ADaM sub-team combed through ADaM v2.1 and ADaMIG v1.0 to identify automatable checks that could be run to help determine compliance to ADaM. The first version of ADaM validation checks was released in 2010.

- A second ADaM sub-team created a set of examples that used the BDS structure for common statistical analysis methods. This examples document was published in 2011.

- A third ADaM sub-team focused on the time-to-event analysis need. This team started with the existing BDS structure, but found the need to create a few additional standard variables to supplement it. The ADaM time-to-event document was published in 2012.

- A fourth sub-team worked on one of the components missing from ADaMIG v1.0: adverse event summaries. After determining that BDS was definitely not the best structure to meet that analysis need, the team instead created a new structure just for standard adverse event analysis. The ADaM adverse event document was published in 2012.

ADaM v2.1, ADAMIG v1.0, and these four appendix documents now covered most of our analysis needs.

CONTINUED ADAM DEVELOPMENT

Because the appendix documents were created after ADaMIG v1.0 was published, that ADaMIG does not reference them. This was one of the main reasons to create a new version of the ADaMIG. ADaMIG v1.1 also clarified existing concepts, added several new variables, and included a table showing which documents to use with which ADaMIG version, which we'll see later.

At the same time as this update to the ADaMIG was being developed, an ADaM sub-team was working to expand the adverse event structure to other similar analysis needs. This new Occurrence Data Structure (OCCDS) was described in another document, and it included all the adverse event examples from the earlier adverse event document plus other similar analysis needs such as for concomitant medications and medical history. OCCDS v1.0 is like a mini ADaMIG, just for that one structure.

In 2016, ADaMIG v1.1 and OCCDS v1.0 were released together. ADaMIG v1.1 references the OCCDS document rather than including details about OCCDS.

EXTERNAL FORCES

The US FDA (United States Food and Drug Administration) had been involved in some CDISC developments, and reviewers were getting excited about the real possibility that standards could make it

easier and more efficient for them to do their jobs. In 2014, FDA released binding guidance documents stating that in most cases the data submitted to the Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER) would need to follow specific industry standards. Related documents, such as their Study Data Standards Catalog, provided more details about specific standards, including ADaM.

Additionally, updates were being made to CDISC Define-XML. Define v1.0 had been developed specifically for SDTM, without any ADaM involvement, for pdf creation. Define-XML v2.0, released in 2013, was a significant revamp, especially for value-level metadata. That team decided to release Define-XML v2.0 without analysis results metadata, since only ADaM needed it, and followed up the Define-XML 2.0 document with an extension to add Analysis Results Metadata (ARM). This extension was released in 2015, and for the first time CDISC had a way to represent all the metadata needed to support ADaM.

CLARIFYING CONTENT

In 2019, another new version of the ADaMIG was published. ADaMIG v1.2 added a few new ADSL and BDS variables, and made a lot of clarifications in the rest of the document.

Also in 2019, the ADaM team created a 1-page document titled "Important Considerations When Using ADaM v2.1". It focused on three key updates since the 2009 publication of ADaM v2.1:

- OCCDS was added, but is not referenced at all in the ADaM model document. It points the reader to the OCCDS document to learn more.

- The metadata within ADaM v2.1 uses features of Define-XML v1.0, some of which were modified with Define-XML v2.0. It points the reader to reference the metadata from the Define-XML version which will be used.

- There have been many other ADaM documents released since the ADaM model document. It points the reader to a table in ADaMIG v1.2 which describes which documents to use with which version of each ADaMIG.

Additionally, because of the way ADaM has evolved, with documents often being developed by sub-teams, these documents can be a little out-of-sync. ADaMIG v1.1 and 1.2 both include text "… documents with different release dates are often used together. If there are conflicts among the documents applicable to a particular version of the ADaMIG, the best practice is to use the content from the document with the latest date of final publication."

CHOOSING WHICH ADAMIG AND DEFINE-XML TO USE

Before trying to determine anything else, first decide which version of ADaMIG and Define-XML will be used. This choice is often made by considering whether data will be submitted to a regulatory agency.

REGULATORY AGENCIES

Are you creating ADaM for submission to a regulatory agency? If so, which agency(ies)?

Both the US FDA and Japan Pharmaceuticals and Medical Devices Agency (PMDA) publish a Data Standards Catalog that shows which version of which standards are accepted. US FDA has a formal process to request a different standard than the one(s) listed within the catalog. At the time of this writing:

- US FDA accepts only ADaM model v2.1, ADaMIG v1.1, and both Define-XML v1.0 and 2.0

- Japan PMDA accepts only ADaM model v2.1, ADaMIG v1.0, and Define-XML v2.0

If submitting to exactly one of these agencies, use the ADaMIG requested by that country. If submitting to both, you will need to decide whether to:

1. Create two different sets of data, one in each version of the ADaMIG that each country wants.

2. Submit a request to the USFDA to use ADaMIG v1.0 rather than ADaMIG v1.1. If allowed, then submit to both countries using ADaMIG v1.0.

3. Submit to both countries using the same data in the same standard ADaMIG. Because ADaMIG v1.0 and ADaMIG v1.1 are similar, it is possible to call the version a different number and still run automated checks on it. This will likely require a little more explanation in the Analysis Data Reviewers Guide (ADRG) section 7 to explain conformance rule messages.

It is my recommendation to go with option 3 above, but the decision is left to the submitter.

Because both agencies will accept Define-XML v2.0, and because Define-XML v2.0 is much better suited to ADaM data, it is my recommendation to use Define-XML v2.0.

In the future, it is likely that catalogs from these two countries will continue be reference different versions of documents. Each agency has their own processes in place, and proceeds at their own pace to update their documents. Always review the most recent version of the catalog from the country or countries where data will be submitted before making the decision on which versions of the ADaM model, ADaMIG, and Define-XML to use. Links to the US FDA and Japan PMDA websites are included in the References section at the end of this paper.

USING ADAM WITHOUT SUBMITTING TO ANY REGULATORY AGENCY

If not submitting to either agency, the choice of which ADaM model, ADaMIG, and Define-XML to use is less restricted. My recommendation is to make use of the most current versions of these documents whenever possible. Exceptions to consider are whether it is important be consistent with any prior studies using older standards, and if tools will be used that were designed for earlier versions of the standards.

ADAMIG AND RELATED DOCUMENTS

Once a version of the ADaMIG is chosen, the ADaM team provides some help to determine which other documents to use. ADaMIG v1.2 Table 1.3.1.1 includes a column for each ADaMIG version, rows for all the other ADaM documents, and shows which are applicable or not applicable. I used this content to create Table 1 below, adding coloring for clarity, where: green = applicable to this IG, pink = not applicable to this IG, and yellow = mostly applicable to this IG. Note that ADaMIG v1.1 has a similar table, without the column for ADaMIG v1.2.

Table 1: Other CDISC Documents and their Applicability to ADaMIG Versions

Document	ADaMIG v1.0	ADaMIG v1.1	ADaMIG v1.2
Analysis Data Model (ADaM) v2.1, December 2009	Foundational document for ADaMIG v1.0	Applicable	Applicable
ADaM Examples in Commonly Used Statistical Analysis Methods v1.0, December 2011	Written for ADaMIG v1.0	Applicable	Applicable
The ADaM Basic Data Structure for Time-to-Event Analyses v1.0, May 2012	Written for ADaMIG v1.0	Applicable	Applicable
Update to the first CDISC SDTM/ADaM Pilot Project, January 2013	Written for ADaMIG v1.0	Applicable	Applicable
ADaM Data Structure for Adverse Event Analysis v1.0, May 2012	Written for ADaMIG v1.0	Superseded by OCCDS v1.0	Superseded by OCCDS v1.0
ADaM Occurrence Data Structure (OCCDS) v1.0, February, 2016	Not written for ADaMIG v1.0	Written for ADaMIG v1.1	Applicable
CDISC ADaM Conformance Rules v2.0, March 2019	Applicable	Applicable	Mostly applicable
Define-XML v2.0, March 2013	Applicable	Applicable	Applicable

As you can see, most documents are applicable to most versions of the ADaMIG. The exceptions are:

- ADaM Data Structure for Adverse Event Analysis v1.0 is applicable to only ADaMIG v1.0 (not to ADaMIG v1.1 and 1.2).

- ADaM Occurrence Data Structure (OCCDS) v1.0 is applicable to only ADaMIG v1.1 and 1.2 (not to ADaMIG v1.0).

- CDISC ADaM Conformance Rules v2.0 has many rules that will apply to ADaMIG v1.2, even though it is not explicitly stated to cover that version. In other words, you could run ADaMIG v1.1 conformance rules on ADaMIG v1.2 data and still learn a lot.

RELEASE PACKAGES

For a different view, consider release packages from the ADaM page of CDISC website. A release package groups each IG with all other ADaM documents that can be used with it into a zip file. Once you know which version of the IG to use, you simply download the zip file to get that IG along with all related documents. Using the zip files prevents you from mismatching documents.

Screen shots of the CDISC ADaM website showing release packages for ADaMIG v1.0, v1.1, and v1.2 are in Figure 1, Figure 2, and Figure 3, respectively.

Figure 1: ADaMIG v1.0 Release Package
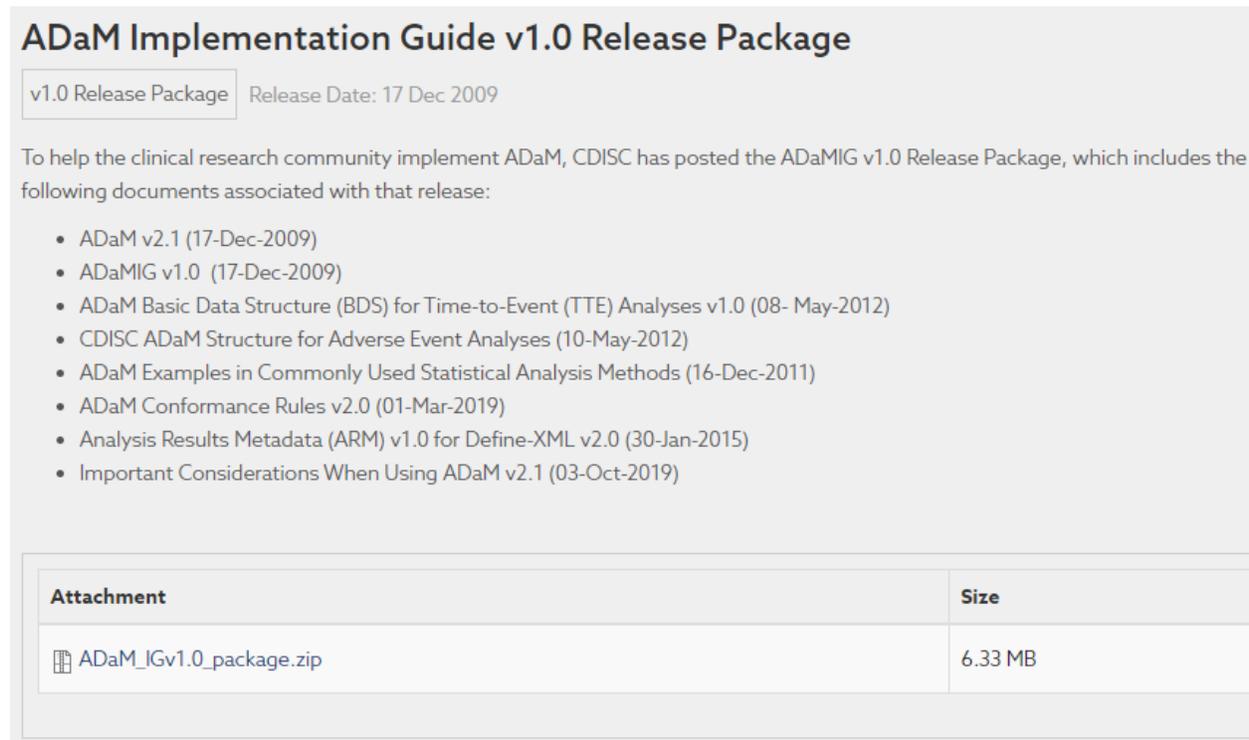
ADaM Implementation Guide v1.0 Release Package

v1.0 Release Package | Release Date: 17 Dec 2009

To help the clinical research community implement ADaM, CDISC has posted the ADaMIG v1.0 Release Package, which includes the following documents associated with that release:

- ADaM v2.1 (17-Dec-2009)
- ADaMIG v1.0 (17-Dec-2009)
- ADaM Basic Data Structure (BDS) for Time-to-Event (TTE) Analyses v1.0 (08- May-2012)
- CDISC ADaM Structure for Adverse Event Analyses (10-May-2012)
- ADaM Examples in Commonly Used Statistical Analysis Methods (16-Dec-2011)
- ADaM Conformance Rules v2.0 (01-Mar-2019)
- Analysis Results Metadata (ARM) v1.0 for Define-XML v2.0 (30-Jan-2015)
- Important Considerations When Using ADaM v2.1 (03-Oct-2019)

Attachment	Size
ADaM_IGv1.0_package.zip	6.33 MB

Figure 2: ADaMIG v1.1 Release Package

ADaM Implementation Guide v1.1 Release Package

v1.1 Release Package | Release Date: 10 Feb 2016

To help the clinical research community implement ADaM, CDISC has posted the ADaMIG v1.1 Release Package, which includes the following documents associated with that release:

- ADaM v2.1 (17-Dec-2009)
- ADaMIG v1.1 (12-Feb-2016)
- ADaM Basic Data Structure (BDS) for Time-to-Event (TTE) Analyses v1.0 (08-May-2012)
- ADaM Structure for Occurrence Data (OCCDS) v1.0 (12-Feb-2016)
- ADaM Examples in Commonly Used Statistical Analysis Methods (16-Dec-2011)
- ADaM Conformance Rules v2.0 (01-Mar-2019)
- Analysis Results Metadata (ARM) v1.0 for Define-XML v2.0 (30-Jan-2015)
- Important Considerations When Using ADaM v2.1 (03-Oct-2019)

Attachment	Size
ADaM_IGv1.1_package.zip	7.03 MB

Figure 3: ADaMIG v1.2 Release Package

ADaM Implementation Guide v1.2 Release Package

1.2 Release Package | Release Date: 3 Oct 2019

To help the clinical research community implement ADaM, CDISC has posted the ADaMIG v1.2 Release Package, which includes the following documents associated with that release:

- ADaM v2.1 (17-Dec-2009)
- Important Considerations When Using ADaM v2.1 (03-Oct-2019)
- ADaMIG v1.2 (03-Oct-2019)
- ADaM Basic Data Structure (BDS) for Time-to-Event (TTE) Analyses v1.0 (08-May-2012)
- ADaM Structure for Occurrence Data (OCCDS) v1.0 (12-Feb-2016)
- ADaM Examples in Commonly Used Statistical Analysis Methods (16-Dec-2011)
- ADaM Conformance Rules v2.0 (01-Mar-2019)
- Analysis Results Metadata (ARM) v1.0 for Define-XML v2.0 (30-Jan-2015)

Attachment	Size
ADaM_IGv1.2_package.zip	7.2 MB

ADAM DOCUMENT SUMMARIES

Because the list of documents shown in Table 1, and the release packages in Figure 1, Figure 2, and Figure 3, contain all the possible documents you might need, there might be some documents or sections of documents that fit with your version of the ADaMIG but don't apply to your study analysis needs. For

example, if you are not doing survival analysis, there is no need to read the ADaM Basic Data Structure for Time-to-Event Analyses v1.0 document. This section contains a summary of each document and when to use it. It also contains my recommends on what to read, skim, and reference. It can help you determine where best to spend your time.

MODEL DOCUMENT

ADaM v2.1

This document was released in December, 2009. It works with ADaMIG version 1.0, v1.1, v1.2.

Summary:

- Sections 1 and 2 provide a high-level overview of ADaM. They are short and worth reading.

- Section 3 covers the ADaM fundamental principles and is very important to read.

- Section 4.1 covers practical considerations when creating datasets, and is also an important section to read. Section 4.2 introduces the ADaM structures, which is covered in more detail in the ADaMIG.

- Section 5 describes metadata, and the examples apply only if using Define-XML v1.0. Otherwise, look at the ADaM examples from the Define-XML version you will be using.

- Section 6 gets into a little more detail on ADSL, and Section 6.1 is important to read if your study has screen fail subjects.

Note that the one-page **Important Considerations when Using the Analysis Data Model (ADaM) v2.1** document was designed to be read along with ADaM v2.1.

IMPLEMENTATION GUIDES AND OTHER NORMATIVE DOCUMENTS

This section includes the three implementation guide versions plus other documents that define standard variables.

ADaMIG v1.0

This document was released in December, 2009.

Summary:

- Sections 1 and 2 provide an introduction. They are short and worth reading.

- Section 3 contains all the standard variables for the ADSL and BDS structures, plus naming conventions and standard fragments for use when creating your own variables. This section is essential to using ADSL and BDS.

- Section 4 contains implementation issues, standard solutions, and examples. All eight sub-sections are worth at least a quick review, and be sure to read 4.2 to see when to derive rows vs. columns.

ADaMIG v1.1

This document was released in February, 2016.

Summary:

- Sections 1 and 2 provide an introduction. They are short and worth reading.

- Section 3 contains all the standard variables for the ADSL and BDS structures, plus naming conventions and standard fragments for use when creating your own variables. This section is essential to using ADSL and BDS, and some of the content also applies to OCCDS.

- Section 4 contains implementation issues, standard solutions, and examples. All nine sub-sections are worth at least a quick review, and be sure to read 4.2 to see when to derive rows vs. columns.

ADaMIG v1.2

This document was released in October, 2019.

Summary:

- Sections 1 and 2 provide an introduction. They are short and worth reading.
- Section 3 contains all the standard variables for the ADSL and BDS structures, plus naming conventions and standard fragments for use when creating your own variables. This section is essential to using ADSL and BDS, and some of the content also applies to OCCDS.
- Section 4 contains implementation issues, standard solutions, and examples. All ten sub-sections are worth at least a quick review, and be sure to read 4.2 to see when to derive rows vs. columns.

Analysis Data Model (ADaM) Data Structure for Adverse Event Analysis

This document was released in May, 2012. It is designed to work only with ADaMIG v1.0. Only read this if doing Adverse Event analysis. ***Do not use with ADaMIG v1.1 or v1.2***.

Summary:

- Sections 1-3 lay out the groundwork. They are short and worth reading.
- Section 4 contains all the standard variables for the structure. This section is essential to using the Adverse Event structure.
- Sections 5-8 are examples, applying the structure. Read through the introduction of each example, and then read the rest of the section if it applies to your study analysis needs.

ADaM Structure for Occurrence Data (OCCDS) v1.0

This document was released in February, 2016, as a more generalized version of the prior Adverse Event structure (above). It uses content available starting in ADaMIG v1.1, and is therefore designed to work with only with ADaMIG v1.1 and 1.2. ***Do not use with ADaMIG v1.0***.

Summary:

- Sections 1-2 lay out the groundwork. They are short and worth reading.
- Section 3 contains all the standard variables for the structure. This section is essential to using the OCCDS structure.
- Sections 4-11 are examples, applying the structure to adverse event, concomitant medication, and medical history data. Read through the introduction of each example, and then read the rest of the section if it applies to your study analysis needs.

EXAMPLE DOCUMENTS

ADaM has two documents that contain only examples, without normative content.

ADaM Examples in Commonly Used Statistical Analysis Methods v1.0

This document was released in December, 2011. It works with ADaMIG v1.0, 1.1, and 1.2.

Summary:

- Section 1 provides an introduction, including a nice chart that shows which of the document's examples support different types of statistical methods. This is worth reading.
- Section 2 provides eight examples. After reading Section 1, you can determine which of these examples to read in detail.

The ADaM Basic Data Structure for Time-to-Event Analyses v1.0

This document was released in May 2012. It includes a few variables not found in ADaMIG v1.0, but which are included in ADaMIG v1.1 and v1.2. ***Only read this document if doing survival analysis***.

Summary:

- Sections 1-3 lay out the groundwork. They are short and worth reading.

- Section 4 includes all the standard variables for the time-to-event application of BDS. If using ADaMIG v1.1 or v1.2, you will already have read about these variables and this will be a refresher. If using ADaMIG v1.0, this section is essential to using the time-to-event application of BDS.

- Sections 5-7 provide examples. It is worth reading all examples if doing survival analysis.

OTHER DOCUMENTS

Analysis Results Metadata (ARM) v1.0 for Define-XML v2.0

This document was released in January, 2015. It is a zip file with not only a pdf, but also many examples. It works with ADaMIG v1.0, 1.1, and 1.2. *Only read this document if using Define-XML v2.0 or later*.

Summary:

- Start by looking through the define2-0-0-example-adam.xml file for examples of all the types of metadata that can be provided.

- The pdf document provides a lot of technical detail. Read it if you will be creating the define.xml file. Otherwise, it is useful as a reference when you have questions about specific metadata.

ADaM Conformance Rules v2.0

This document was released in March, 2019. It is a zip file with not only a pdf, but also a filterable Excel file. Because all the rules are based on the contributing documents, there is nothing here that isn't also in one of the other documents mentioned above. It works with ADaMIG v1.0 and 1.1. Additionally, the ADaMIG v1.1 rules could be applied to ADaMIG v1.2 data, so it can also be useful with ADaMIG v1.2.

Summary:

- Sections 1-3 of the pdf lay out the groundwork. They are short and worth reading.

- Section 4 of the pdf contains all the same information as the Excel file. Use the Excel file because you can filter by ADaMIG version and other columns to look at just the material you need.

Important Considerations When Using ADaM v2.1

This document was released in October, 2019. It works with ADaMIG v1.0, 1.1, and 1.2.

Summary:

- This is a 1-page document and should be read in its entirety. Keep this content in mind whenever ADaM v2.1 is referenced.

WHAT TO EXPECT IN THE FUTURE

The ADaM team is currently preparing several documents for release in 2020 and 2021. These documents are tentatively titled:

- ADaM Conformance Rules vX.X (updates for ADaMIG v1.2 and many of the documents below)

- ADaM Data Structures for Integration v1.0

- ADaM for Oncology v1.0

- ADaMIG for Medical Devices v1.0

- ADaMIG for Non-Compartmental Analysis v1.0

- ADaM Traceability Examples v1.0

- OCCDS v1.1

As these documents are completed, the ADaM team is planning to begin consolidating the multiple ADaM documents into a smaller set of documents. This consolidation should remove redundancy and help make the content more consistent. Until then, we will need to manage even more separate documents.

CONCLUSION

Yes, there are a lot of ADaM documents, but you don't necessarily need to use all of them. Instead, follow this process:

1. Determine which ADaMIG you will use. If submitting to US or Japan regulatory agencies, choose the version that agency requests. If using ADaM for something other than submission, choose the most recent version that works with any tools that you need to use.

2. Once you know the ADaMIG, determine which other documents work with that IG by either

    a. Looking at the release packages on the CDISC ADaM website (at this website you can download a zip file containing all of these files)

    b. Reviewing Table 1.3.1.1 found in ADaMIG v1.2 or ADaMIG v1.1.

After you have this list of documents, review the document summaries provided within this paper to see which documents or portions of documents to read. You might be able to skip sections of documents or even entire documents.

Finally, keep up-to-date on any new ADaM documents by watching the CDISC ADaM website.

REFERENCES

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