Gray Areas of ADaM and Ways to Provide Color

Panel Discussion

The ADaM Standard

- **Yes!** The basic principles of ADaM are also best practice for our industry
- **Yes!** ADaM a standard with enforceable rules and recognized structures
- **Yes!** The ADaM documentation provides examples of many of the most common analysis situations – 85/15 rule
- **NO!** How to apply ADaM in every analysis situation is obvious and no thinking is required

Getting to YES!

- When faced with an implementation issue that does not have a documented solution, what is the thought process? How to move forward with developing the best solution?

- Our panel today is comprised of members of the ADaM Leadership Team and they will share examples of how they have approached implementation issues and reached a compliant solution

- Then time for your questions!

ADaM Leadership Team and Today's Panel

- Susan Kenny
- Sandra Minjoe
- Nate Freimark
- Jack Shostak
- John Troxell
- Deb Bauer (not present)

Sandra Minjoe

I Need a Variable For …

I need a variable for …

- What to do when I need a variable other than one specified in the ADaM documents?

- Examples:
  - In ADSL, I need variable for baseline Karnofsky Performance Status
  - In BDS, I need a variable for the character version of the lab test result, for ease in printing a listing
  - In BDS, I need a variable for a 2nd baseline
  - In OCCDS, I need a variable to flag AEs that continued past data collection
  - In OCCDS, I am combining AE and CE into one analysis dataset and need a single variable for reporting body system

I need a variable for ...

General Process I follow:
1. Is it legal to include this variable?
   ◦ There are rules describing when variables can be added
2. Does a variable already exist for this concept?
   ◦ Look not only in ADaMIG, but also other standards documents
3. Does a variable fragment exist for any of this concept?
   ◦ Example: if a flag, use suffix FL
4. Consider other conventions when creating a new name

I need an ADSL variable for Baseline Karnofsky Performance Status

- Is it legal to include this variable?
- Does a variable already exist for this concept?
- Does a fragment exist for any of this concept?
- Consider other conventions when creating a new name

- My solution: KPSBL
  - KPS is an industry standard abbreviation for Karnofsky Performance Status
  - BL is an ADaM fragment, and is used as a suffix in ADaMIG examples

I need a BDS variable containing character lab test results for a listing

- Is it legal to include this variable?
- Does a variable already exist for this concept?
- Does a fragment exist for any of this concept?
- Consider other conventions when creating a new name

- My solution: LBSTRESC
  ◦ This variable already exists in SDTM, and I can copy to BDS
  ◦ If I did some imputation and can't use LBSTRESC, another option might be TESTRESL (test result for listing)

I need a BDS variable for more than one baseline

- ▸ Is it legal to include this variable?
- ▸ Does a variable already exist for this concept?
- ▸ Does a fragment exist for any of this concept?
- ▸ Consider other conventions when creating a new name

- ▸ My solution: Don't do it!
  - ◦ It is <u>not</u> legal to include more than one baseline variable
  - ◦ When more than one baseline is needed, that must be done by creating additional rows (alternately another dataset)

I need an OCCDS variable to flag continuing AEs

▸ Is it legal to include this variable?

▸ Does a variable already exist for this concept?

▸ Does a fragment exist for any of this concept?

▸ Consider other conventions when creating a new name

▸ My solution: CONTFL
  ◦ CONT is a reasonable abbreviation for continuing
  ◦ FL is the standard fragment for flags

I need an OCCDS variable to contain Body System for both AE and CE data

- ▸ Is it legal to include this variable?
- ▸ Does a variable already exist for this concept?
- ▸ Does a fragment exist for any of this concept?
- ▸ Consider other conventions when creating a new name

- ▸ My solution: ABODSYS
  - ◦ A is a common ADaM prefix, rather than SDTM's AE or CE
  - ◦ BODSYS is the root of both input variables AEBODSYS and CEBODSYS

I need a variable for …

General Process I follow:

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Use the standards, other documentation, and common sense

Nate Freimark

Original Discussion – What Should ADaM Look Like?

- AVAL vs –STRESN for analysis
  - ADaM-focused variables vs SDTM-plus
- Decision – have ADaM specific variables
  - AVAL/AVALC
  - PARAM/PARAMCD
  - AVISIT/AVISITN
  - ATPT/ATPTN

SDTM in ADaM – Good Uses

- Traceability
- Contrast
- Listings
- Variables not covered in ADaMIG

SDTM in ADaM – Good Uses

- Traceability
  - --SEQ from source SDTM should be included for traceability at a minimum if record comes directly from SDTM
    - Generally for ADaM created from a single SDTM domain
  - SRC* triplets may also sometimes be used
    - ADaMIG states "Table 3.3.9.1 defines additional variables useful in certain situations to facilitate data point traceability."
  - VISIT/VISITNUM and ARM might also be useful for traceability

SDTM in ADaM – Good Uses

- **Contrast**
  - When date/time imputation are needed it is a good idea to keep the SDTM variable that contains the partial value
  - AVISIT/AVISITN/ATPT/ATPN should be the timing variables that are in datasets – VISIT/VISITNUM/--TPT/--TPTNUM should also be kept if the values/algorithms differ
- **Listings**
  - Keeping SDTM variables for listing purposes is perfectly fine
- **Variables not covered in ADaMIG**
  - --CLSIG
  - --TOX

SDTM in ADaM – Not Good Uses

- ▸ Referencing SDTM in metadata instead of ADaM variables
- ▸ Creating/Changing SDTM values in ADaM
- ▸ Copying SDTM variables into every ADaM dataset
  - ▸ Creating analysis versions of SDTM concepts

SDTM in ADaM – Not Good Uses

- Referencing SDTM in metadata instead of ADaM variables
  - ADxx.AVALCAT1/AVALCAT2 should not reference XXSTRESC – it should reference AVALC
- Creating SDTM values in ADaM
  - VISIT/VISITNUM have to come from SDTM and cannot be derived
- Copying SDTM variables into every ADaM dataset
  - TCG does mention some SDTM variables to keep in each ADaM but that is a discrete list
  - ARM/ARMCD do not have to be included in every dataset – ADaM variables should be used (TRTSEQP)
- Creating analysis versions of SDTM concepts
  - ARMN- ARM/ARMCD are brought over from SDTM for traceability and not use in analysis.
  - There is no variable ARMGR1 in ADaM – ARM is not an analysis variable and therefore there should be no "grouping" of ARM.

OCCDS – SDTM Abuses

- ADAE – Populating AETERM with None for ANYAE=N records is not allowed
- ADAE – AEDUR is an SDTM variable that is character and IS8601 – it cannot be changed to numeric in ADaM – it is defined as character in the ADAE appendix – correct variable is ADURN
- ADCM – CMDOSU/CMDOSFRQ/CMROUTE changes from SDTM values – this is not allowed
- ADAE – AESEV – you cannot change values from SDTM – this includes changing case and label – this is supposed to be done in ASEV

Jack Shostak

Multiple ADSL's?
Versioning?
CDISC at all?

Need ADSL-like variables after ADSL

Need a single record per patient dataset that contains data content that is typically (and painstakingly) derived in BDS datasets.
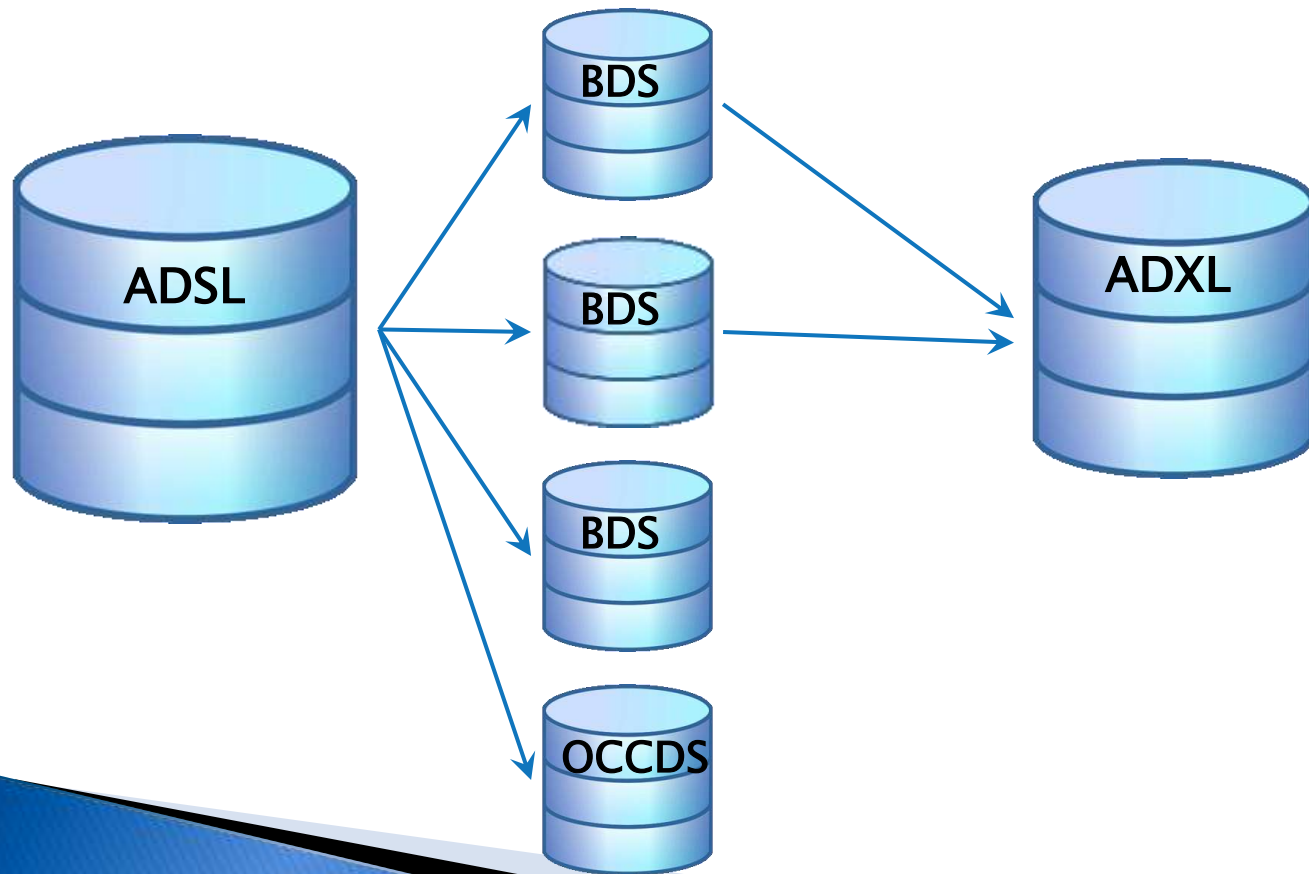
- ▶ For modelling reasons
- ▶ For population determination

No appetite for deriving the same thing two times in two different places.

Outright hatred for circularity.

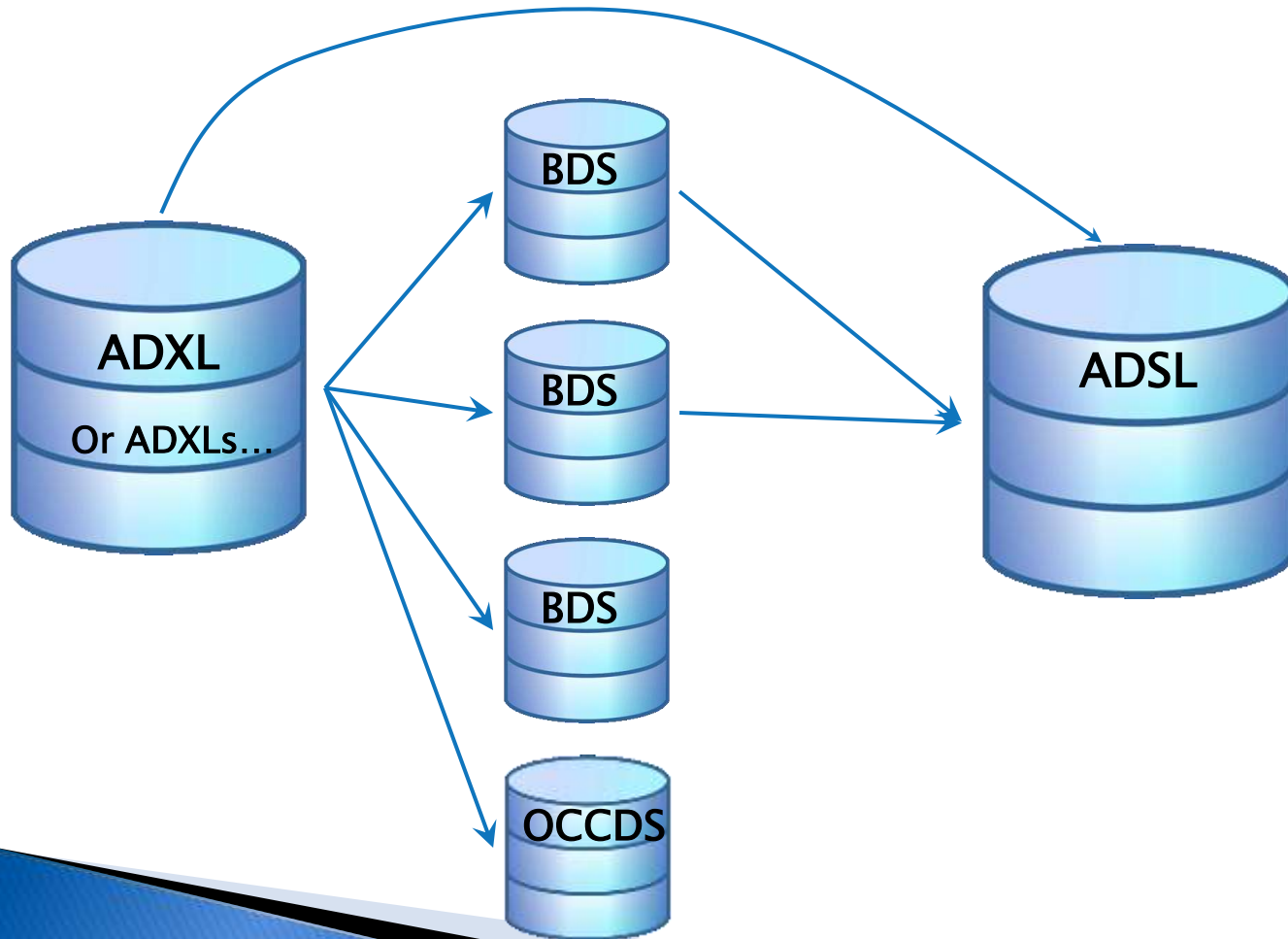# Need ADSL-like variables after ADSL

Approach #1

PROS:
- Linear process
- Each derivation in one place

CONS:
- You likely need both ADSL and ADXL for a full true ADSL dataset.
- BDS datasets that need ADXL content would be created downstream of ADXL creating complexity.

Need ADSL-like variables after ADSL

Approach #2

PROS:
- Each derivation in one place
- Just one ADSL file at the end

CONS:
- Could be multi-path linear, so dependencies can be tricky

ADaM Version Acceptance

FDA accepts ADaM IG 1.0.

OCCDS finalized January 13, 2015.

ADaM IG 1.1 finalized February 12, 2016.

Pinnacle follows FDA lead.

ADaM Version Acceptance

Practically, we follow the latest ADaM IG and adapt to the version adoption lag. That means:

▸ Using OCCDS, but being forced to dub it as class of ADAM OTHER.

▸ Pinnacle checks being behind the times and having to explain away warnings. Also no checks around new variables (e.g., DOSExxP, ASEQ, ASPER).

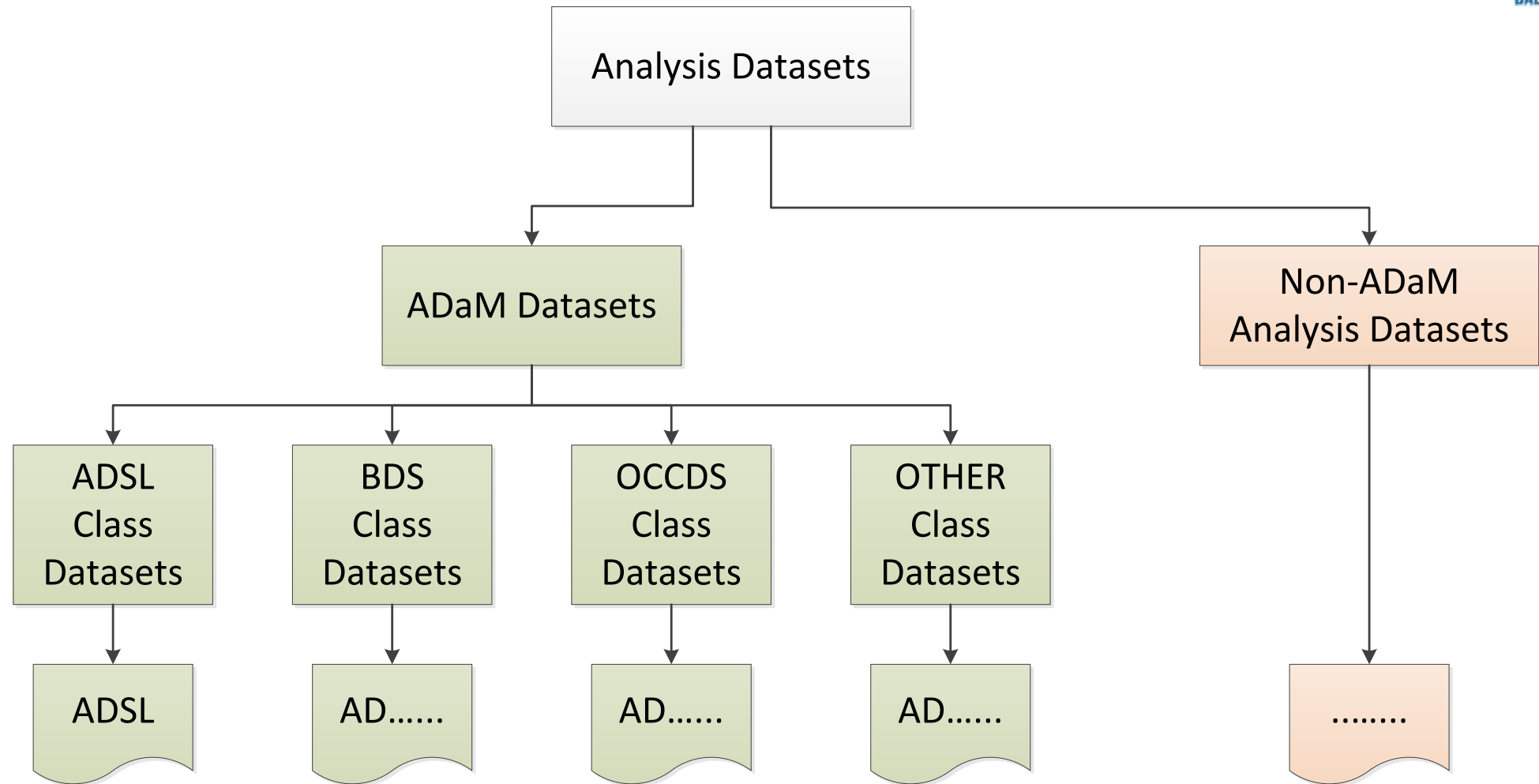This issue will become more pronounced as we publish IG 1.2 and ADaM v3.

When to ADaM....or CDISC in General

- Is ADaM/CDISC always the best idea?
- Investigator funded research
- Early phase studies
- There is no FDA exemption for Phase 1 studies. They carry a similar cost load for CDISC implementation.

- We consult on these on a case by case basis as to whether to ADaM/CDISC or not.

John Troxell

When Not to Use ADAM OTHER

The Universe of Analysis Datasets

Analysis Datasets and ADaM Datasets

- ADaM datasets
  - ◦ Follow ADaM fundamental principles – IMPORTANT in a practical way
  - ◦ Follow naming and other conventions
- ADAM OTHER class datasets are ADaM datasets
  - ◦ But do not follow one of the standard structures defined to date
- Non-ADaM analysis datasets
  - ◦ Do not follow ADaM fundamental principles and conventions
- Non-ADaM analysis dataset is *not* in the ADAM OTHER class
- No guidance provided about when it is <u>not</u> acceptable to use ADaM OTHER vs. a standard structure (BDS, OCCDS, …)

Use ADAM OTHER because I feel like it?

▸ *"I really don't like the BDS vertical dataset structure. I prefer a horizontal structure. Can I make a horizontal dataset like I am used to and call it an ADAM OTHER class dataset?"*

▸ ADaMIG has no opinion!

▸ But I advise (here is the color part):

▸ ADAM OTHER is not a loophole to drive a truck through

▸ ADaM is a data standard; we all benefit – don't degrade it

▸ FDA wants sponsors to use the ADaM data standard

▸ Use an ADaM standard structure when a standard structure is capable of enabling the analysis

Some Valid Reasons for ADAM OTHER

- No standard ADaM structure can enable the analysis
  - Use an ADaM OTHER Class dataset for analysis
- "Listing" view
  - But don't use for analysis
- Pre-ADSL dataset
  - Like BDS but without treatment and ADSL variables
  - But don't use for analysis
- Intermediate dataset; example:
  - EX-plus needed for statistician review; EX + ADSL + derived columns
  - If it follows ADaM fundamental principles etc., can be ADAM OTHER
  - But don't use for analysis; derive a BDS? dataset from it for analysis

Audience Q&A and Discussion