Kendle Implementation of CDASH

PhUSE October 2009

Dr Elke Sennewald, 19 October 2009

Outline

- Formation of CDASH Team
- Theoretical Development of Kendle's CDASH Standard
- Practical Implementation
- Mapping to SDTM and Data Validation Plan
- Progress to Date and Future Plans
- Repeating the Rewards

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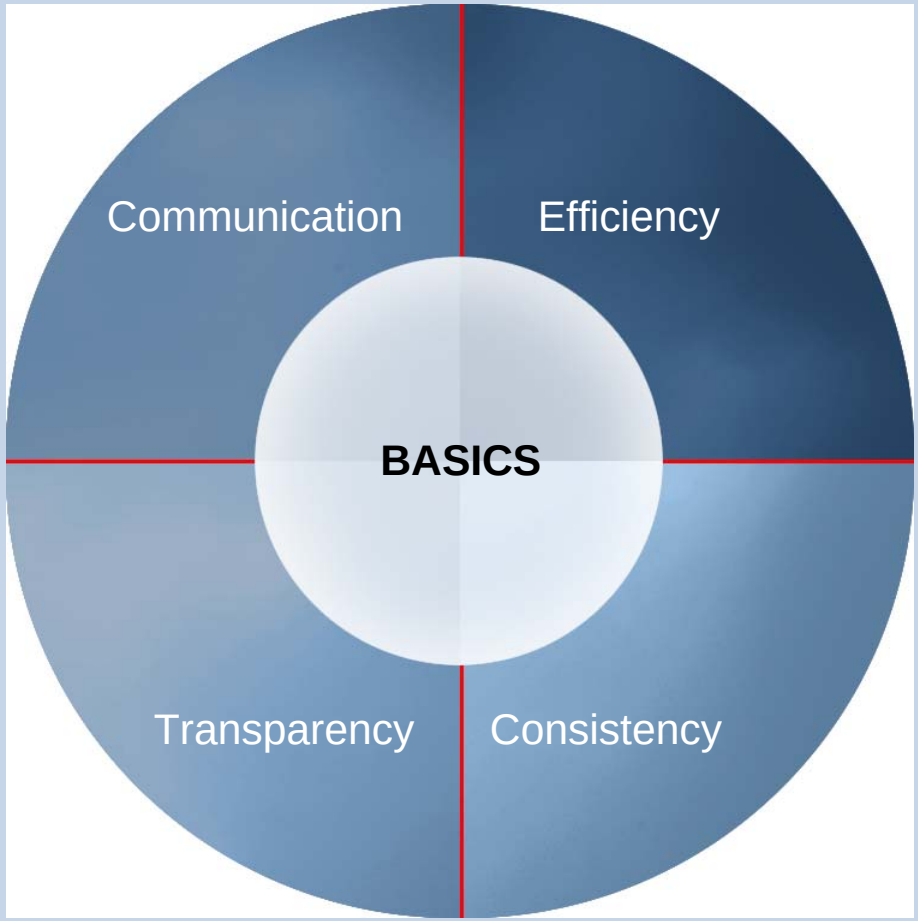
Formation of CDASH Team

CDASH Draft Published

- *April 2008* - CDISC put the draft of the CDASH (clinical data acquisition standards harmonization) documents out for public review
- Draft consisted of:
  - Introduction
  - List of CDASH domains with recommendations on variables to be collected, why and how
- Primary goal was “the development of ‘content standards’ for a basic set of global data collection variables that will support clinical research studies“
- Kendle decided to take the risk that this draft was near final and commence design of eCRF modules compliant with CDASH

Implementation Principles



Kendle's CDASH Team Formation

- *June 2008* – Kendle's CDASH team was formed with members from around the world representing CDM, Biostatistics, Programming and Clinical Development
- Each team member took on responsibility for one or more CDASH domains with the objective to:
  - review and understand the intention of CDASH re the domain
  - transfer the CDASH specs into Kendle's Study Definition Specification spreadsheet
  - cross reference as necessary to the CDISC SDTM controlled terminology list
- We thought this would be easy….

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Theoretical Development of Kendle's CDASH Standard

First CDASH Considerations

- *July 2008* – we found it was not so easy….
- CDASH, although reflecting the needs of SDTM, is not necessarily conducive to a database design
  - some domains can be collected once per study, once per visit or many times per visit
  - several domains have a very “vertical” structure – which is not immediately transferable to a database specification
- We discovered that we needed to supplement CDASH standards with our own Kendle standards
- Clinical input at this stage was vital – in order to define what were the most likely real-life scenarios we would encounter in the use of our standard eCRFs

CDASH Form Specification Template (1)

CDISC Domain	Form Label (to be Displayed)	Order	Kendle Question Prompt	Instructions to be Printed on CRF	CDASH CRF Label / Question

CDASH Form Specification Template (2)

Kendle Database Variable Name	CDASH Variable Name	CDASH Core	Conditional Rule	Data Type	Kendle Codelist Name

CDASH Form Specification Template (3)

CDISC SDTM Codelist Name	Min Precision	Max Precision	Min Length	Max Length	Display Question within table?	Table Details	Table Heading

CDASH Form Specification Template (4)

Dictionary Name/ Version	Loaded Electroni-cally?	Question Hidden?	Data Derived?	Derivation Description	Comment	Mapping Specification

Kendle Specification Examples

- Conditional Rule
  - **CMENDTC**: Yes - if CMONGO is NULL
- Comment
  - **AETOXGR**: Either AESEV or AETOXGR must appear on the CRF. Some studies may mandate the collection of both.
    Note: Completion of CTCAE grade is a mandatory field for cancer studies. In all other types of studies this is an optional field.
  - **AEREL**: It may be necessary to collect Relationship Type (e.g. Study Treatment Only, Device Only, Both Study Treatment and Device, or other types). If so, the variable AERELTP should be included on the CRF, with a codelist of AERELTP

Selection of Standard Variables

- *July 2008* – the CDASH document identifies the level of requirement to include each variable:
  - Highly Recommended = A data collection field that should be on the CRF
  - Recommended/Conditional = A data collection field that should be collected on the CRF for specific cases
  - Optional = A data collection variable that is available for use if need
- We needed to decide which level of variable we would always collect and, if not all variables at every level, which we would omit

CDASH Domain: Vital Signs

- Date of Measurements
- Time of Vital Sign Measurements
- Sponsor-Defined Identifier
- Planned Time Point
- Vital Sign Test Name
- Vitals Status
- Vital Sign Test Result or Finding
- Original Units
- Clinical Significance
- Location of Vital Signs Measurement
- Position of Subject

Highly recommended

Recommended / Conditional

Optional

Codelists and CDASH

- *August 2008* – we started to investigate the SDTM terminology list
- We needed to utilise this list to create “pick-lists” for categorical questions on the eCRF
- Whilst on the one hand the SDTM list is extremely useful…
  - it does did not cover all CDASH variables we needed to code
  - codelists for some CDASH variables are more than extensive and do not facilitate an eCRF pick-list
- We created our own “Kendle Codelists” as needed – either:
  - New codelists where none existed within the SDTM terminology lists or
  - Subsets of a codelist that does exist in SDTM terminology to make the list more manageable and appropriate as an eCRF pick-list
- Future version control will be vital as revised SDTM terminology lists are released

Helptext

- *August 2008* – the CDASH document also includes “Instructions to Clinical Site” for each variable
- We realised we could use this text to formulate our eCRF Helptext for each variable

- Examples implemented:
  - **AEYN:** Indicate if the subject experienced any adverse event. If yes, include the appropriate details where indicated
  - **AEONGO**: If the adverse event has not stopped at the time of data collection, check the ongoing box and leave the end/stop date blank

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Practical Implementation

Building and Testing the Draft eCRFs

- *September 2008* – we had now started to build our first eCRFs, but not without resolving a few more issues along the way, for example:
  - Our EDC system has its own limitations – which in some cases we needed to work around
  - It also has functionality which we needed to utilise to best advantage
- Testing the eCRFs began with peer review by another database programmer and a feedback/review cycle until the peer review passed to the next level

User Acceptance Testing (UAT)

- *October 2008* – once peer review of our draft eCRFS was completed, we commenced a full UAT process, undertaken by worldwide Kendle associates representing:
  - Clinical Data Management
  - Clinical Development
  - Coding
  - Programming
  - Statistics
- We needed to ensure our standard eCRFS covered the requirements of all departments who would directly use them whilst at the same time still adhered to the CDASH standards and so would map easily to SDTM
- CDASH version 1.0 was now published – we needed to ensure we incorporated any changes from the draft version

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Mapping to SDTM and Data Validation Plan

Mapping to SDTM

- *October 2008* – at the same time as UAT was undertaken, our programming representatives added a new field to our eCRF specification document – “Mapping Specification”
- This field defines the precise details of how each listed variable maps to SDTM
- Undertaking this further step also highlighted that in some cases it would not be easy to map to SDTM – and resulted in further changes to the way in which we had decided to collect some data items

Mapping Specification

- AESTM
  - Concatenate AESTD, AESTM, AESTY, and AESTTM to created AE:AESTDTC
    Date must be ISO8601 compliant.
    3 character month abbreviation must be converted to a 2 digit code (i.e. "MAR" -> "03").
- AEONGO
  - Use AEONGO as a component of the derivation for AE:AEENRF or as the sole component of derivation of AE:AEENRF.
  - If AEONGO only is to be used, then: If AEONGO = 'Y' then set AE:AEENRF = "AFTER", else set AE:AEENRF = "BEFORE/DURING".
    ** Suggested approach due to partial dates being allowed.**
  - IF AEONGO is to be used for the component of a derivation for AE:AEENRF,
    then: If AEONGO = "Y" then set AE:AENRF = "AFTER".
    The remaining components of AE:AEENRF will need to be derived based on AE:AESTDTC, AE:AEENDTC, DM:RFSTDTC, and DM:RFENDTC.
    Suggested values of AE:AEENRF are: "BEFORE", "DURING", and "AFTER".

Data Validation Plan (DVP)

- *November 2008* – we now commenced defining DVP modules to match our standard eCRFs
- This was a relatively easy process given the fact that we already had some standard DVP modules in place that just needed to be adapted to the new standard eCRFs
- Draft DVPs were created by a Data Manager and reviewed by:
  - Clinical Data Management (peer review)
  - Clinical Development
  - Programming
  - Statistics
- DVPs were finalised and now accompany each standard eCRF

Status End 2008

- *December 2008* – by the end of 2008 we had:
  - Defined, programmed and tested standard eCRFS which comply with the CDASH domains
  - Created “Kendle” coding lists to accompany and supplement SDTM controlled terminology
  - Defined the mapping process from our standard eCRFs to SDTM
  - Created Data Validation Plan modules to accompany our standard eCRFs

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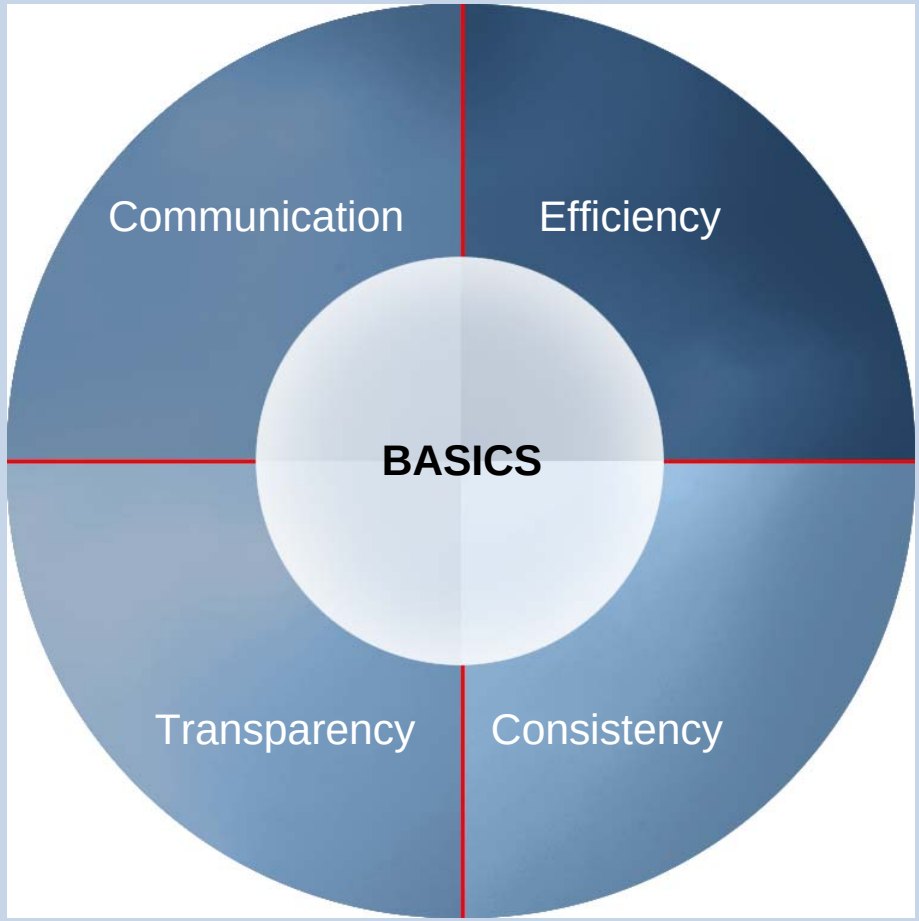
Progress to Date and Future Plans

Progress to Date

- *2009* – whilst we decided to focus initially on developing CDASH compliant eCRFs, like most companies we still process a lot of paper CRFs
- Therefore our focus was shifting to developing CDASH standards for a paper CRF process, including:
  - Development of CRF modules compliant with CDASH
  - Development of corresponding database modules within the database management system we use for processing paper CRFs
  - Development of corresponding mapping specifications to SDTM
  - Development of corresponding Data Validation Plan modules
- Finally, we developed program code which corresponds to our DVP specifications for both our EDC and paper CRF systems

Future Plans

- Create Job Aid
- Enhance / adopt specifications
- Increase efficiency
  - Promote CDASH
  - Minimize deviations from CDASH standards
  - Implement “modular” approach



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Repeating the Rewards

Reaping the Rewards

- *Here and now* – we are already finding the set up of our (EDC) study databases much simpler and quicker:
  - Data Managers are using and adapting our CDASH Study Design Specifications to define study specific database designs
  - Database Programmers are able to pull our eCRF modules and utilise for study specific database builds
  - Data Managers are using and adapting the standard DVP modules to develop study specific DVPs
  - Statistical Programmers are able to use the mapping specifications in our CDASH Study Design Specifications to write mapping programs more effectively
- The overall result to date is quicker and more cost effective study database builds with a reduction in the time from final protocol to database “go-live”

Questions?

Please contact

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