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Implementation of ADaM standards NOT driven by a submission

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Agenda

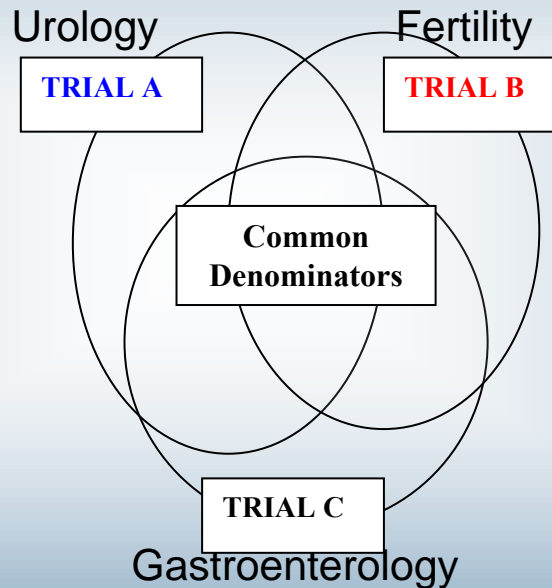
- Introduction
- Ferring ADaM
- The implementation
- Conclusion
- What is next?

Introduction

- Standardized analysis datasets to support regular trial reporting – NOT a submission! (but with a submission in mind)
- Implementation of SDTM and CRF standards
- Efficiency gain
- Two of the metadata components
 - Analysis dataset metadata
 - Analysis variable metadata

Introduction

- Maximum of what can be standardized across the therapeutic areas



- No ADaM without SDTM!

Ferring ADaM



- Standardized and very operational
(combine vertical/horizontal structure)

<u>VISITNUM</u>	<u>VSTESTCD</u>	<u>VSSTRESN</u>	<u>VSSTBASE</u>	<u>VSSTCHG</u>
1	DIABP	90	90	.
1	HEIGHT	180	180	.
1	PULSE	75	75	.
1	SYSBP	170	170	.
1	WEIGHT	90	90	.
2	DIABP	90	90	0
2	PULSE	74	75	-1
2	SYSBP	170	170	0
3	DIABP	81	90	-9
3	PULSE	82	75	7
3	SYSBP	149	170	-21
4	DIABP	74	90	-16
4	PULSE	73	75	-2
4	SYSBP	123	170	-47
5	DIABP	79	90	-11
5	PULSE	79	75	4
5	SYSBP	146	170	-24

Ferring ADaM



- No Supplemental Qualifiers included in Ferring-SDTM (SUPPQUAL)
- No “right” number of analysis datasets to submit. Define all analysis datasets/variables needed for the various analyses stated in the SAP

Implementation - *a succes!*



- ✓ *Resources/support*
- ✓ *Documentation and implementation guidelines for SDTM & ADaM*
- ✓ *Brainstorming/discussion with colleagues*
- ✓ *A linear strategy:*

Raw Data → Ferring-SDTM → Ferring-ADaM

- ✓ *Conduct a pilot study in parallel*

Implementation

- Types of standardization



1) Most standardized

Fully defined for (almost) all trial designs and therapeutic areas. Not necessary to add/remove variables.

(ADRD, ADDV, ADXP, ADAE, ADLB, ADSL, ADSLSF)

2) Partly standardized

Defines most common variables which are always present in the domains. Most variables are defined as in Ferring-SDTM and it may be necessary to add a few domain specific variables.

(ADVS, ADPE, ADEG, ADCM, ADSV)

Implementation

- Types of standardization



3) Least standardized

Very trial specific analysis datasets with very few (required) variables defined up front.

(*ADEX, ADEF/ADEF_n*)

4) Pure trial specific analysis datasets

Not specified, only a description of how to define these datasets.

(*AD--*)

Implementation

- ADSL (Subject Level)



- Contains all variables from DS and DM domains
- Excluding screening failures (ADSLSF)
- TRTxP is NOT present, only first and last exposure of treatment dates (TRTSTDT, TRTENDT)

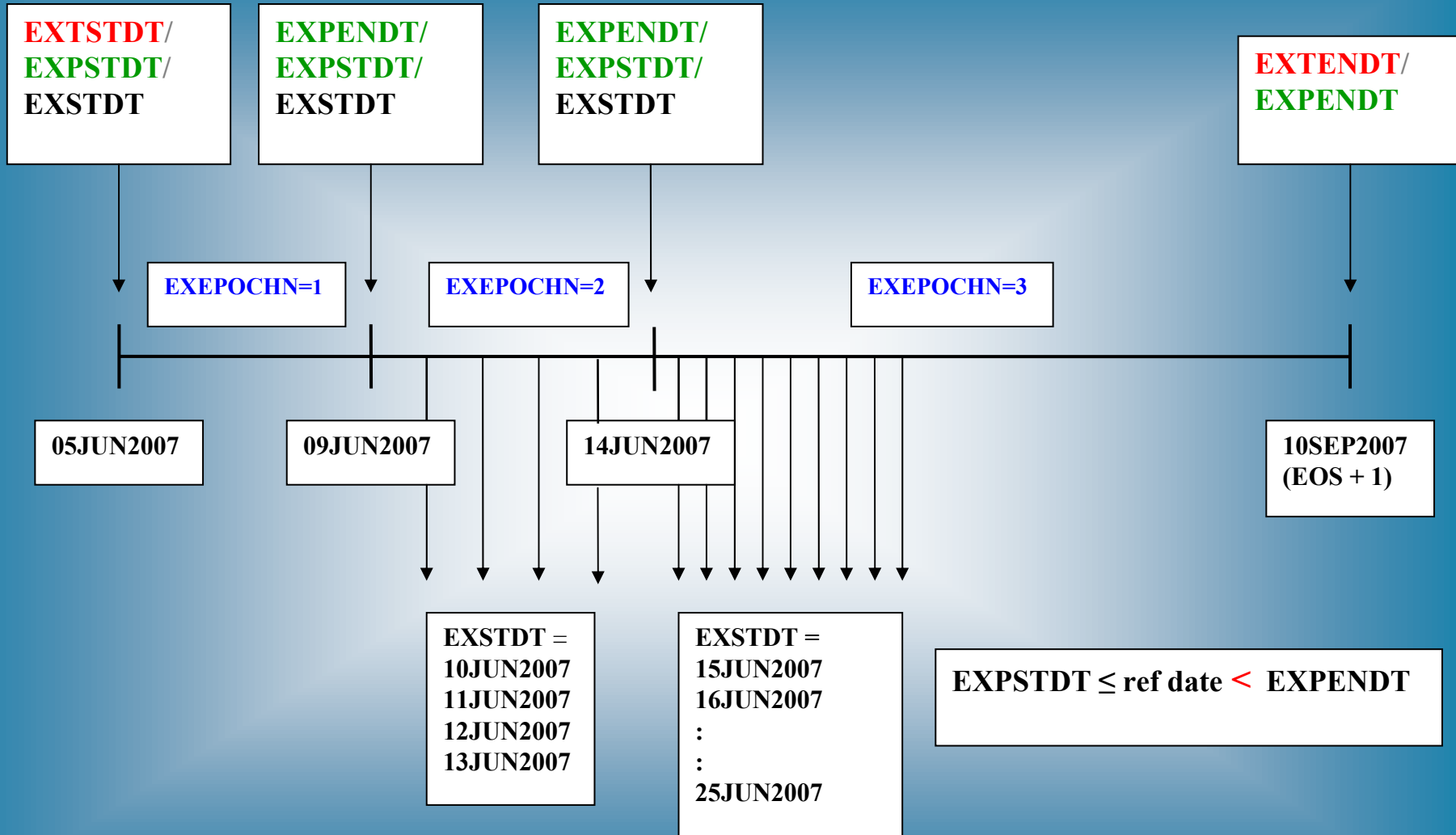
Implementation - TRTxP (ADEX)



Exposure Analysis Dataset (ADEX)

<u>EXTRT</u>	<u>TRTP</u>	<u>EXEPOCH</u>	<u>EXTSTD</u>	<u>EXTEND</u>	<u>EXPSTD</u>	<u>EXPEND</u>	<u>EXSTD</u>
BL INDED	Degarelix	Treatment (1)	05JUN2007	10SEP2007	05JUN2007	09JUN2007	05JUN2007
BL INDED	Placebo	Treatment (2)	05JUN2007	10SEP2007	09JUN2007	14JUN2007	09JUN2007
HP-hMG	HP-hMG	Treatment (2)	05JUN2007	10SEP2007	09JUN2007	14JUN2007	09JUN2007
HP-hMG	HP-hMG	Treatment (2)	05JUN2007	10SEP2007	09JUN2007	14JUN2007	09JUN2007
HP-hMG	HP-hMG	Treatment (2)	05JUN2007	10SEP2007	09JUN2007	14JUN2007	10JUN2007
HP-hMG	HP-hMG	Treatment (2)	05JUN2007	10SEP2007	09JUN2007	14JUN2007	11JUN2007
HP-hMG	HP-hMG	Treatment (2)	05JUN2007	10SEP2007	09JUN2007	14JUN2007	12JUN2007
HP-hMG	HP-hMG	Treatment (2)	05JUN2007	10SEP2007	09JUN2007	14JUN2007	13JUN2007
BL INDED	Degarelix	Treatment (3)	05JUN2007	10SEP2007	14JUN2007	10SEP2007	14JUN2007
HP-hMG	HP-hMG	Treatment (3)	05JUN2007	10SEP2007	14JUN2007	10SEP2007	14JUN2007
HP-hMG	HP-hMG	Treatment (3)	05JUN2007	10SEP2007	14JUN2007	10SEP2007	15JUN2007
HP-hMG	HP-hMG	Treatment (3)	05JUN2007	10SEP2007	14JUN2007	10SEP2007	16JUN2007
HP-hMG	HP-hMG	Treatment (3)	05JUN2007	10SEP2007	14JUN2007	10SEP2007	17JUN2007
HCG	HCG	Treatment (3)	05JUN2007	10SEP2007	14JUN2007	10SEP2007	18JUN2007
UTROGESTAN	UTROGESTAN	Treatment (3)	05JUN2007	10SEP2007	14JUN2007	10SEP2007	21JUN2007
UTROGESTAN	UTROGESTAN	Treatment (3)	05JUN2007	10SEP2007	14JUN2007	10SEP2007	22JUN2007
UTROGESTAN	UTROGESTAN	Treatment (3)	05JUN2007	10SEP2007	14JUN2007	10SEP2007	23JUN2007
UTROGESTAN	UTROGESTAN	Treatment (3)	05JUN2007	10SEP2007	14JUN2007	10SEP2007	24JUN2007
UTROGESTAN	UTROGESTAN	Treatment (3)	05JUN2007	10SEP2007	14JUN2007	10SEP2007	25JUN2007

Implementation - ADEX example



Implementation - Traceability



- The supportive variable --SEQ is not included in Ferring-SDTM

- VISITNUM is used to support traceability
 - Meaningful variable, which reflects the protocol and trial design
 - Expected/required variable in a submission

Discrepancies - What to do?



- SDTM: Study day variable --**DY** not allowed to contain 0,
ADaM: Analysis study day variable, ANL**DY**, contains 0
Ferring: Study day variable VISITDAY (contains 0)
- Duration variables --**DU** = ("**ref. date**" - **ADEX.EXTSTDT**)
The fragment --DUR is a reserved name in SDTM
- EXEPOCH ⇔ EPOCH
- **LBSTCHG** = **LBSTRESN** – **LBSTBASE**
(change from baseline=standard result - standard baseline result)
- Flags: *FL (char)/*FN (num) (exceptions: *DTF, *TMF)

Conclusion

- Time consuming process – but very important, educational and necessary!
- A standard in place for the every day work with trials
- New tasks:
 - Standardization of trial specific variables/datasets
 - More metadata
 - Analysis value level metadata (Code/Description)
 - Analysis result metadata (TLF's)

What is next?

- Use ADaM standards on many different trials
- Long term: Submission ready
- Standard programs
- Updates on Ferring-SDTM and Ferring-ADaM
 - Yes/No?
 - When?
 - How?

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Questions ?