
# It's all About EPOCH

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PharmaSUG Single Day Event

# Agenda

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- EPOCH and the FDA
- A brief history of EPOCH
- Definition
- EPOCH as a Trial Design Model Tool
- EPOCH Controlled Terminology
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# Questions Around EPOCH

Dear Standards committee,

What are the policies around EPOCH for SDTM 3.1.2 or higher? It appears that the variable is only listed for SDTM 3.1.2 for the domain TA, AE, DS, DV, EX and SE, and except for TA they all 'Perm' or "Permissible". CDISC does not seem to want to add it to all the domains as a requirement. However, the recent FDA Technical Conformance Guide states to include EPOCH.

- Is it ok to include only the 6 above that are included in the SDTM specifications?
- Other schools of thought are to include in every possible domain. EPOCH is also available as an optional permissible variable for the Events, Interventions and Findings classes. Should we be including whenever possible?
- Are there programming conventions to add this variable at the record level into every allowable SDTM domain?

Regards,
Karin

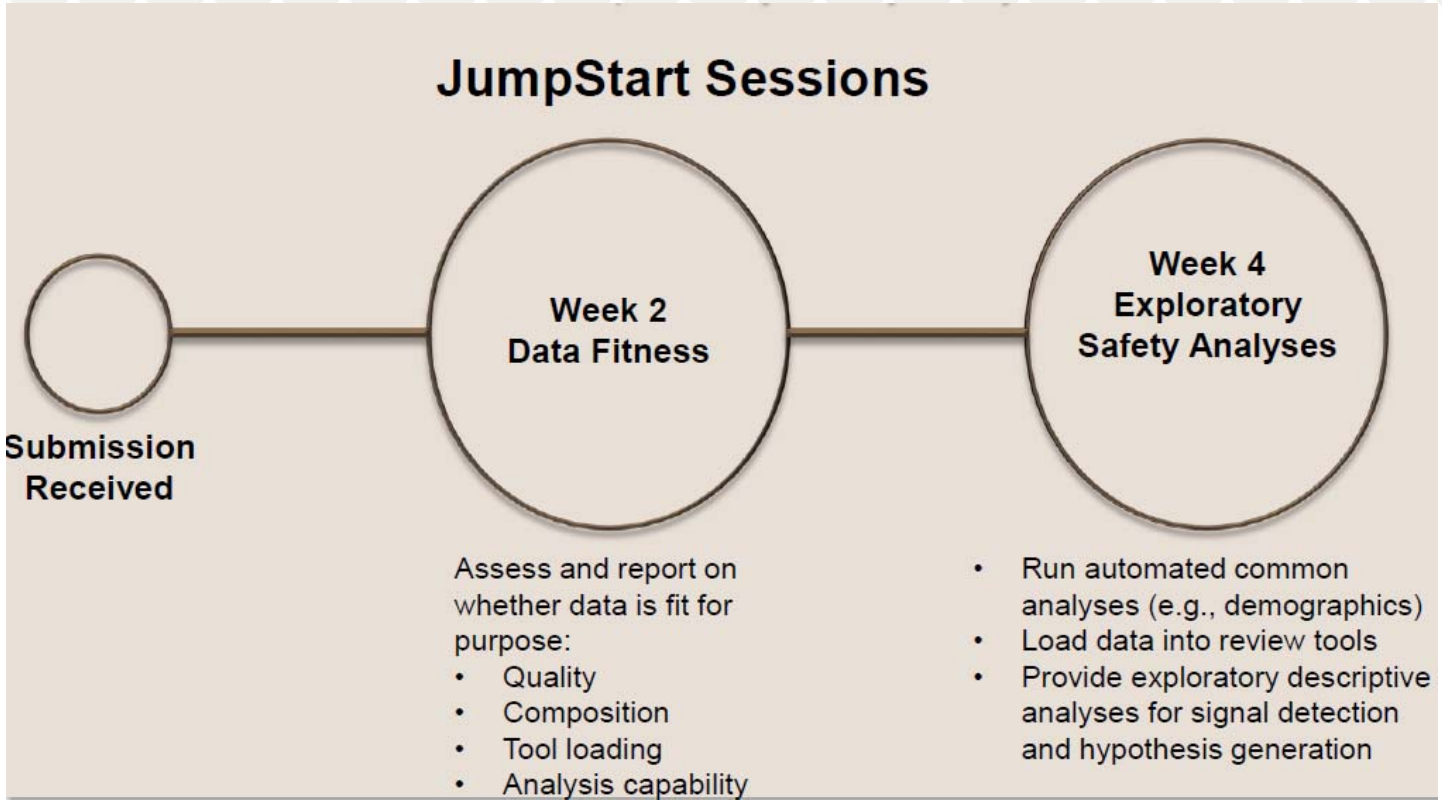
# EPOCH and the FDA

- PhUSE-CSS meeting of 2013 FDA presents about the DataFitness tool, requests EPOCH as a variable
- PhUSE-CSS meeting of 2015 FDA presents again, encourages EPOCH as important variable for use in Data Fitness Tool. Promotes faster review of submissions with EPOCH
- FDA Study Data Technical Conformance Guide, Version 2.2 (June 2015)
  - Guide recommends to add EPOCH to all possible domains on p.15

    "EPOCH designators. Please follow CDISC guidance for terminology.[26] The variable EPOCH should be included for clinical subject-level observation (e.g., adverse events, laboratory, concomitant medications, exposure, vital signs). This will allow the reviewer to easily determine during which phase of the trial the observation occurred (e.g., screening, on-therapy, follow-up), as well as the actual intervention the subject experienced during that phase. "

# EPOCH and the FDA

PhUSE CSS 2015 – Lilliam Rosario Presentation. FDA promotes new tools. Data Fitness tool requires EPOCH.



# EPOCH and the FDA

- FDA states that EPOCH variable is missing in 90% of applications for the domains AE, LB,CM, EX, VS, and DS
- JumpStart provides a systematic assessment of the data fitness and data quality
- Jumpstart identifies inconsistencies in the date that requires information request be sent to the Applicant for clarification/corrections
- Data validation step enables data to be loaded to the Data Warehouse
- High quality data enables regulatory reviewers to fully utilize Computational Science Center's tools to support decision making

# A Brief History of EPOCH in SDTM IG

- EPOCH concept originated in the Trial Design Domain as high level view
- 2009 – SDTM v.3.1.1 TA, DS, DV domains include EPOCH as ‘Perm’. Label is ‘Trial Epoch’.
- FDA requests EPOCH in a few key domains
- 2012 – SDTM v.3.1.2 EPOCH in the TA domain changed from ‘Perm’ to ‘Req’ . Also added to SE, EX domains in the tabulations specifications as ‘Perm’ variable. Label change from ‘Trial Epoch’ to ‘Epoch’..
- 2013 – SDTM V.3.1.3 same as above
- 2014 – SDTM v.3.2 Added (EPOCH) Controlled Terminology (CT) and updated examples to use same.

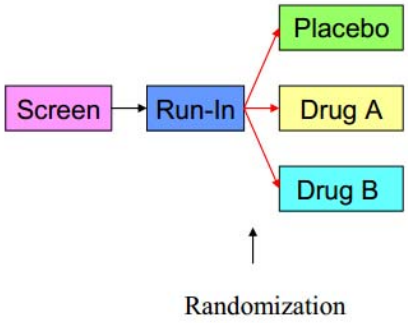
# EPOCH Definition

According to the SDTMIG 3.1.3 and higher, the definition of EPOCH

- Planned periods of time
- Each period of time serves a purpose in the trial as a whole
- High level – following primary objective of trial
- Examples – determine subject eligibility, treatments, and washout periods.
- Treatment is high level strategy, not individual dosing of drugs

# EPOCH as a Trial Design Concept

- Visualize the study




- Build a simple trial design matrix

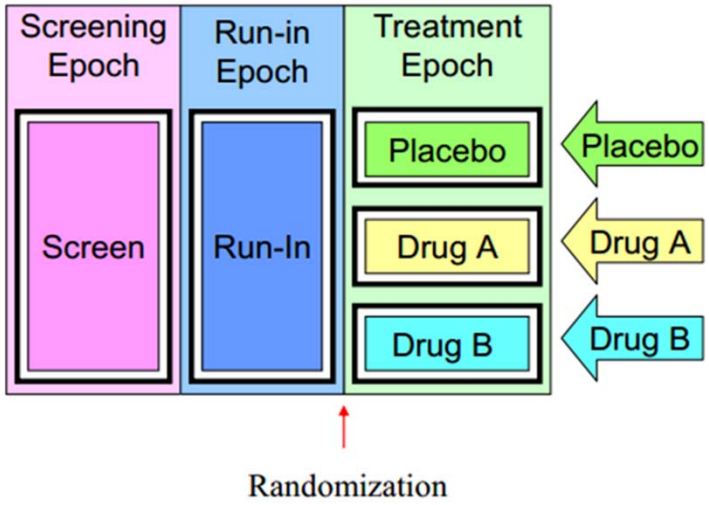
Trial Design Matrix for Example Trial 1

| | Screen | Run-in | Treatment |
|---|---|---|---|
| **Placebo** | Screen | Run-in | PLACEBO |
| **A** | Screen | Run-in | DRUG A |
| **B** | Screen | Run-in | DRUG B |

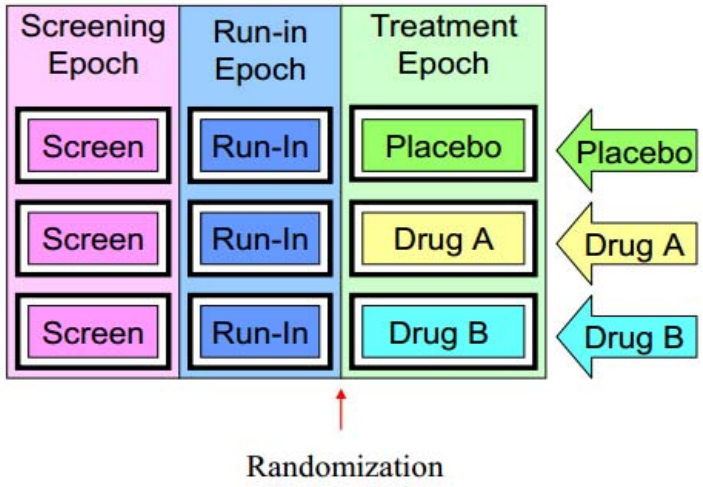
Source: SDTMIG v.3.1.3 section 7.2.3.1 example 1

# Example 1 – Parallel Design

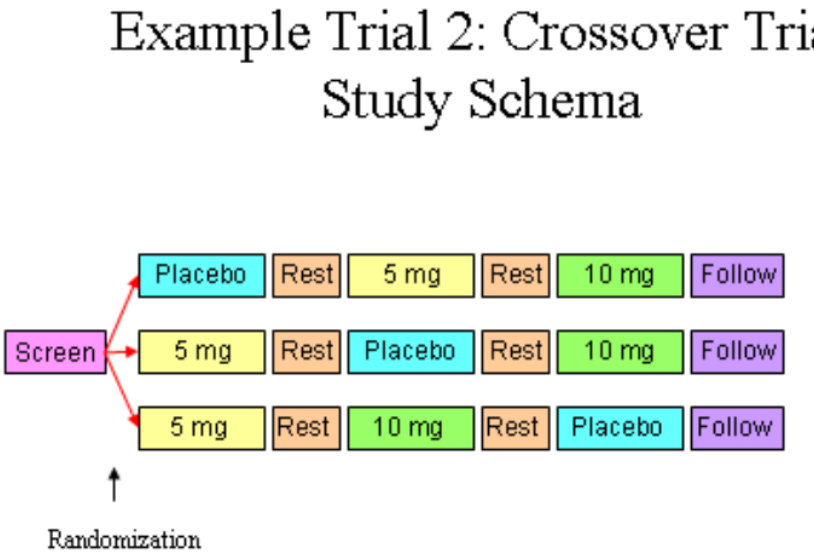
Example 1 – Prospective view

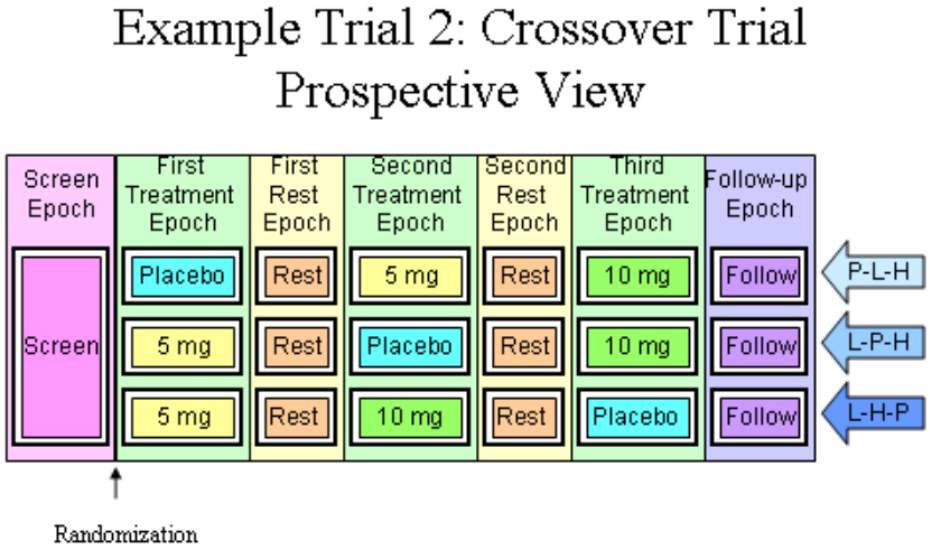



Example 1 – Retrospective view



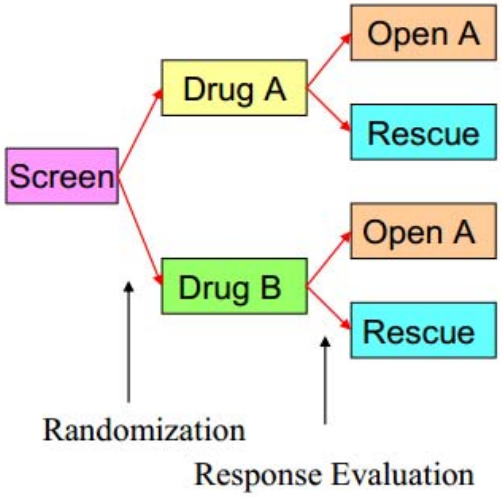
# Example 2 – Cross-over Trial

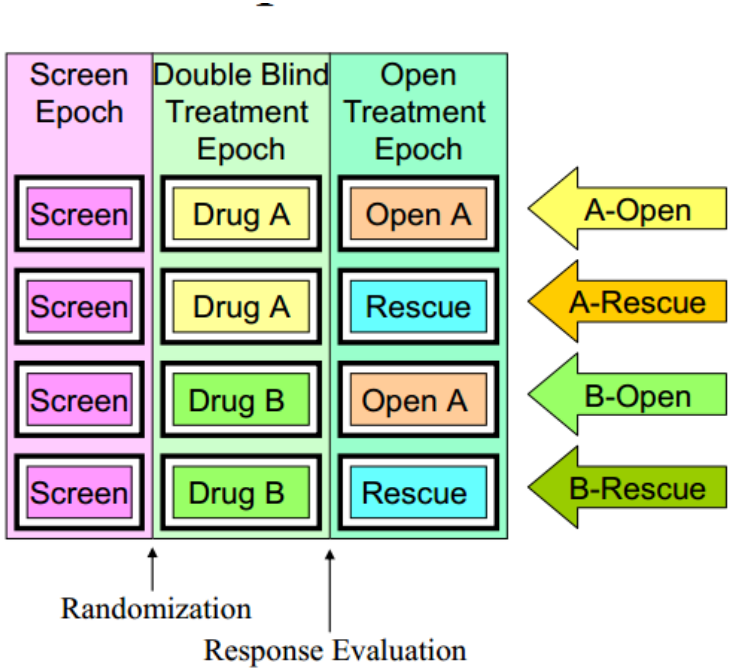



Source: SDTMIG v.3.1.3 section 7.2.3.2 example 2

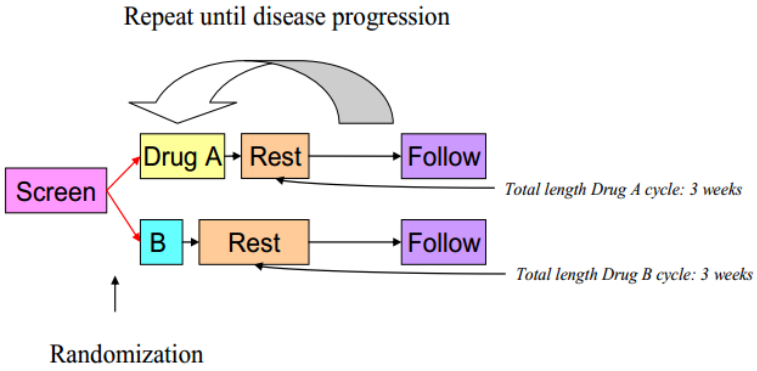
# Example 3: Multiple branches

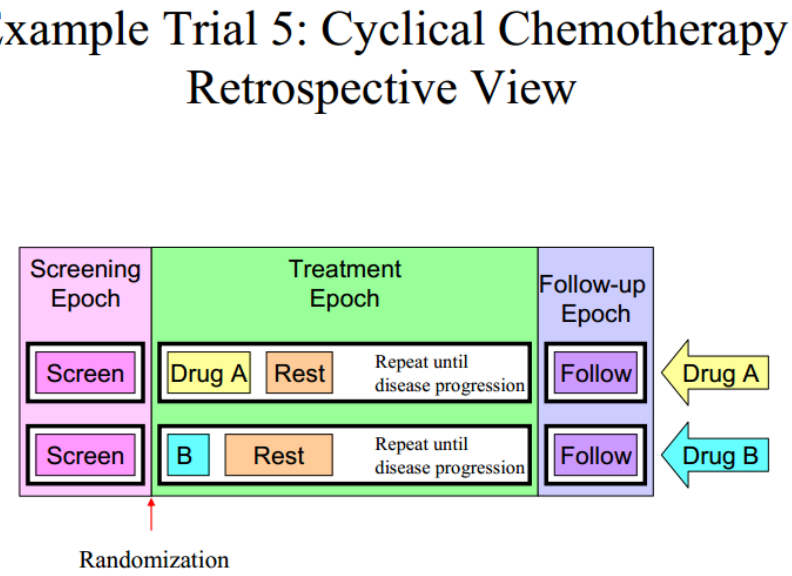



Source: SDTMIG v.3.1.3 section 7.2.3.3 example 3

# Example 5 – Cyclical Chemotherapy -Different Chemo Durations



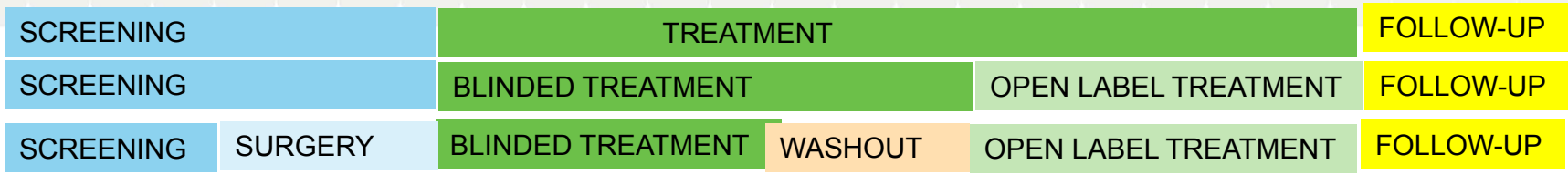

Source: SDTMIG v.3.1.3 section 7.2.3.5 example 5

# EPOCH Controlled Terminology (CT)

- The CT for EPOCH is (EPOCH) and has 10 registered categories as of 2015-09-25. The CT is extensible.

| Code | Codelist Code | Codelist Extensible (Yes/No) | EPOCH |
|---|---|---|---|
| C99079 | | Yes | BLINDED TREATMENT |
| C123452 | C99079 | | CONTINUATION TREATMENT |
| C102255 | C99079 | | FOLLOW-UP |
| C123453 | C99079 | | INDUCTION TREATMENT |
| C99158 | C99079 | | LONG-TERM FOLLOW-UP |
| C16032 | C99079 | | OPEN LABEL TREATMENT |
| C102256 | C99079 | | RUN-IN |
| C98779 | C99079 | | SCREENING |
| C48262 | C99079 | | TREATMENT |
| C101526 | C99079 | | WASHOUT |

# Mapping example




| Screen | Surgical Procedure | Blinded Treatment | Washout | Open-label Treatment | Follow-up |
|---|---|---|---|---|---|
| Screen | Surg | Placebo | Washout | Treat A | Follow-up |
| Screen | Surg | Treat A | Washout | Treat A | Follow-up |
| Screen | Surg | Treat B | Washout | Treat A | Follow-up |

Disposition event of enrollment

Disposition event of randomization

# EPOCH and OpenCDISC

- Keep the EPOCH categories at high level
- Follow CT whenever possible
- Order of EPOCH is before - - STDTC or - -DTC variables
- Add own CT as needed (will cause OpenCDISC Warning)
  - Example for Study 2 cross over trial – TREATMENT 1 , TREATMENT 2, TREATMENT 3
  - Other examples: BASELINE, SURGERY

| Domain | Record | Count | Variables | Values | OpenCDISC ID | Publisher ID | Message | Category | Severity |
|---|---|---|---|---|---|---|---|---|---|
| EG | | 1260 | EPOCH | BASELINE | CT2002 | FDAC341 | EPOCH value not found in 'Epoch' extensible codelist | Terminology | Warning |
| LB | | 4511 | EPOCH | BASELINE | CT2002 | FDAC341 | EPOCH value not found in 'Epoch' extensible codelist | Terminology | Warning |
| QS | | 1281 | EPOCH | BASELINE | CT2002 | FDAC341 | EPOCH value not found in 'Epoch' extensible codelist | Terminology | Warning |
| SE | | 74 | EPOCH | BASELINE | CT2002 | FDAC341 | EPOCH value not found in 'Epoch' extensible codelist | Terminology | Warning |
| TA | | 4 | EPOCH | BASELINE | CT2002 | FDAC341 | EPOCH value not found in 'Epoch' extensible codelist | Terminology | Warning |

# EPOCH in the TA Domain

- TA Domain – the *only* Trial Design Model (TDM) domain containing epoch
  - **EPOCH** only domain where it is 'Req' or Required variable. The origin of EPOCH on the define is assigned for TA.
  - Variables in TA:
    - STUDYID, DOMAIN, ARMCD, ARM
    - TAETORD – Number of the ELEMENT within ARM, considered a Timing variable
    - ETCD – Element code, limited to 8 char
    - ELEMENT- The name of an Element. May occur more than once within and ARM
    - TABRANCH – Condition met to be in this Element
    - TATRANS – If there is a transitional situation that could either be 'Proceed to next element or go to End of Study visit
    - **EPOCH** - Name of the Trial Epoch with which this Element of the Arm is associated.

# How to add to SDTM Domains
# General Observations Class

**Interventions**
**CM EX**
**SU**

- Compare – STDTC to RFXSTDTC, include highest common level of precision
- Compare - -STDTC to RFXENDTC, to the YYMMDD level

**Events**
**AE DS MH**

- Compare - -STDTC to RFXSTDTC, include highest common level of precision
- Start date of event determines the EPOCH at which it is assigned.

**Findings**
**EG IE QS**
**PE VS**

- Visit-based tests, can either use VISIT, or reference dates.
- Unscheduled requires comparing to reference dates

# General Observations Class Tips and Tricks

- DS Domain - Only assign EPOCH for DSCAT = 'DISPOSITION EVENT'
- Disposition events drive the addition of EPOCH, and not considered timing event.
- AE Domain - According to FDA Study Data TCG Assign AE to the EPOCH at start of event only. It should be based on AESTDTC, rather than AEENDTC
- CM Domain – If 'ONGOING' then assign to treatment EPOCH
- If Findings have unscheduled, then assign based on date ranges. Otherwise can assign based on VISIT
- If complex design will need additional treatment dates from EX other than RFXSTDTC and RFENDTC
- EPOCH is not required yet, so it can be omitted in a compliant submission from all except TA

# How to add Epoch in SDTM Domains Special Purpose

- SE Domain
  - Working with the TA domain, Subject Elements captures at the subject level the dates and times of changes in elements. One or more elements can be part of one EPOCH designation and be repeated.
  - SESTDTC – Datetime of start of element
  - SEENDTC – Datetime of end of element

- If carefully constructed, SE can drive the derivations for all EPOCH variables in the various domains using SESTDTC and SEENDTC.
- General practice is to specify instructions for deriving EPOCH in each domain.

# A word about EPOCH in ADaM

- Keep from SDTM to ADaM
- Does not included date derivations when created in SDTM
- Has limited usability in analysis
- Can be helpful in cross-over study or study with wash-out periods
- Can be useful in identifying study elements (cycles, periods)

# SUMMARY

- EPOCH is part of Study Design and Modeling activities
- High-level concept of Subject's progression through the study
- CDISC team has made EPOCH 'Perm' variable. It is not required for compliant submission other than TA domain
- FDA encourages to add to all allowable domains for potentially faster turnaround of review

# Contact Info

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