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# The CDISC Trial Design Model (TDM), the EPOCH variable, and the Treatment Emergent Flag: How to Leverage these to Improve Review.

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## ABSTRACT

Many of us view the SDTM TDM (Trial Design Model), addition of the EPOCH variable to General-Observation-Class domains and potentially adding the AETRTEM Supplemental Qualifier as eSubmission overhead. Essentially something we must do to check-off that our eSubmission is compliant. We create them because CDISC and/or regulatory guidance requests them, and we put some time into designing their values, but unfortunately we don't look at them from a reviewers/consumers perspective and design the values to facilitate the review.

This paper reviews some of the rationale for deciding the appropriate granularity of the TDM, EPOCH and AETRTEM to provide reviewers/consumers with information that should facilitate the review.

## SCOPE

The TDM TA and TE domains describe the protocol plan for study treatment/procedures in a data matrix.

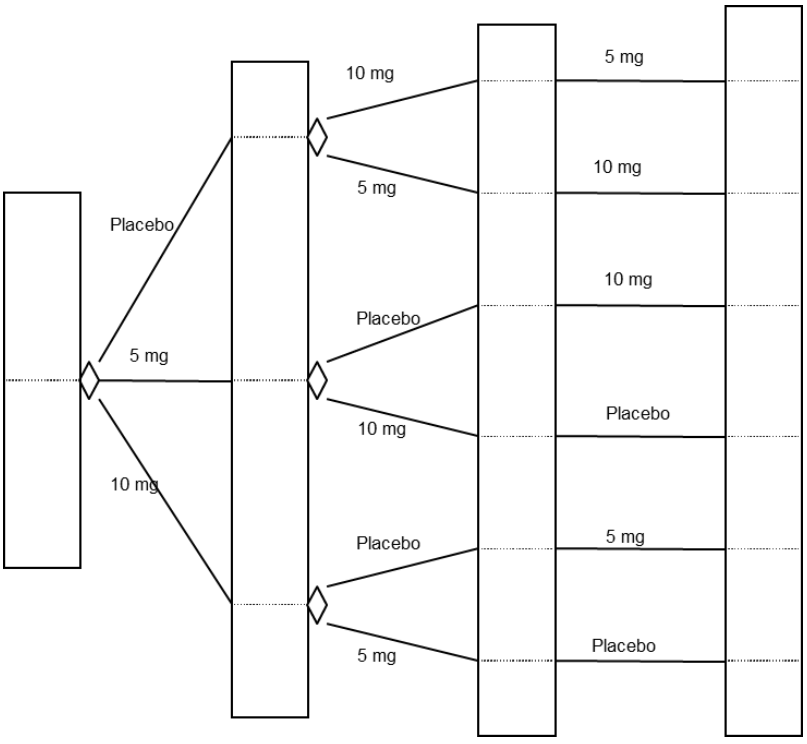
The treatment plans (Arms) defined in the TA and TE domains are assigned to subjects in the DM (Demographics) special purpose domain.

The EPOCH variable's values defined in TA are expected to be assigned to collected data in the General-Observation-Class domains to identify which Epoch the collected data began in, or was collected in.

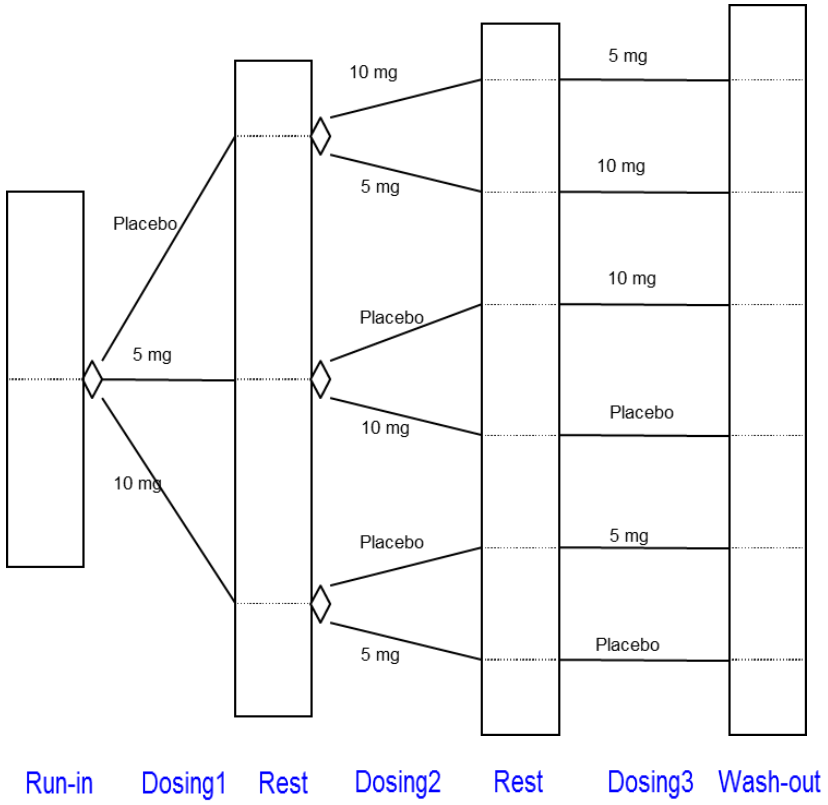
Adverse Events are expected to be identified as Treatment Emergent or not, using the AETRTEM Supplemental Qualifier.

## SAMPLE STUDY DESIGN

A picture tells a thousand words…



Let's add definitions:




## SAMPLE STUDY MAPPED TO TE

Let's assume each of the administrations is once-a-day for two weeks, and the Run-in, Rests and Wash-out are somehow different from each other.

| STUDYID | DOMAIN | ETCD | ELEMENT |
|---|---|---|---|
| ABC123 | TE | RUNIN | Run In |
| ABC123 | TE | PLA | Placebo |
| ABC123 | TE | 5MG | 5 Milligram |
| ABC123 | TE | 10MG | 10 Milligram |
| ABC123 | TE | REST | Rest |
| ABC123 | TE | WO | Wash Out |

The easy/straightforward part is done. Most would agree each of these are Elements.

## SAMPLE STUDY MAPPED TO TA

This is where all the decisions are made, or at least should be.

Many would map Run-in and Wash-out to separate Epochs, but many would map the Dosing1-Rest-Dosing2-Rest-Dosing3 to a single Treatment Epoch. Let's think about this is relationship to the AE Treatment Emergent flag. If the entire Dosing1-Dosing3 period of time is one Epoch, then how is this

different from Treatment Emergent? And how valuable would it be to a reviewer when we assign Epoch in the General-Observation-Class domains to know that data records started or were collected somewhere in the Treatment period of time?

Mapping this more granularly would likely aid the review, and in this example we should probably have an Epoch for each of the Elements. Generally the Elements should be more granular, but in this example since we assumed the treatments were all once-a-day for two weeks the granularity of the Elements and Epochs should be the same.

TA Example for the first two Arms:

| STUDYID | DOMAIN | ARMCD | ARM | TAETORD | ETCD | ELEMENT | EPOCH |
|---|---|---|---|---|---|---|---|
| ABC123 | TA | P-10-5 | Pla / 10mg / 5mg | 1 | RUNIN | Run In | Run-In |
| ABC123 | TA | P-10-5 | Pla / 10mg / 5mg | 2 | PLA | Placebo | Dosing1 |
| ABC123 | TA | P-10-5 | Pla / 10mg / 5mg | 3 | REST | Rest | Rest |
| ABC123 | TA | P-10-5 | Pla / 10mg / 5mg | 4 | 10MG | 10 Milligram | Dosing2 |
| ABC123 | TA | P-10-5 | Pla / 10mg / 5mg | 5 | REST | Rest | Rest |
| ABC123 | TA | P-10-5 | Pla / 10mg / 5mg | 6 | 5MG | 5 Milligram | Dosing3 |
| ABC123 | TA | P-10-5 | Pla / 10mg / 5mg | 7 | WO | Wash Out | Wash-Out |
| ABC123 | TA | P-5-10 | Pla / 5mg / 10mg | 1 | RUNIN | Run In | Run-In |
| ABC123 | TA | P-5-10 | Pla / 5mg / 10mg | 2 | PLA | Placebo | Dosing1 |
| ABC123 | TA | P-5-10 | Pla / 5mg / 10mg | 3 | REST | Rest | Rest |
| ABC123 | TA | P-5-10 | Pla / 5mg / 10mg | 4 | 5MG | 5 Milligram | Dosing2 |
| ABC123 | TA | P-5-10 | Pla / 5mg / 10mg | 5 | REST | Rest | Rest |
| ABC123 | TA | P-5-10 | Pla / 5mg / 10mg | 6 | 10MG | 10 Milligram | Dosing3 |
| ABC123 | TA | P-5-10 | Pla / 5mg / 10mg | 7 | WO | Wash Out | Wash-Out |

The Epochs are defined in TA, then used to identify the boundaries and values for assigning EPOCH in the General-Observation-Class domains. The granularity beyond “Treatment” provides value to reviewers to identify the study-period at a more granular level.

## SUMMARY

Per the FDA SDTCG (Study Data Technical Conformance Guide), the goal of standardizing data is to make the data more useful and to support semantically interoperable data exchange such that it is commonly understood by all parties.

In-order to make the data more useful, the agency has asked industry to identify the Epoch that collected General-Observation-Class data starts in or is collected in. Doing this at a more granular level than a single Treatment Epoch should help the reviewer/consumer understand when things happened relative to discrete study activities more easily, which should facilitate review.

Hope you agree.

Thanks. ☺

## REFERENCES

CDISC Study Data Tabulation Model (SDTM) v1.4 and Study Data Tabulation Model Implementation Guide (SDTMIG) v3.2. http://www.cdisc.org/sdtm

FDA STUDY DATA TECHNICAL CONFORMANCE GUIDE. Guidance for Industry Providing Regulatory Submissions in Electronic Format – Standardized Study Data. FDA CDER, CBER

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