

# Challenges in Processing PK Data from ANDA Submissions for BE Assessment and Current Perspectives on Updating the PK Data Standard

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# Outline

- Background
- Challenge and issue
- Current solutions
  - BE Assessment Mate (BEAM) – an automation tool to mitigate the issue.
- Updating PK data standard

# Background

- Dating back to 2015 and earlier, generic drug applicants followed a simple format to prepare and submit PK data in ANDAs.

PK  
Concentration  
data

Subject ID	Sequence	Period	Treatment	Concentrations (1-n)	Time (1-n)
1	2	1	1	0...83.3	0...120
1	2	2	2	0...94.4	0...120
2	1	1	2	0...155.2	0...120

PK  
parameter  
data

Subject ID	Sequence	Period	Treatment	AUCt	AUCi	Cmax	Tmax
1	2	1	1	2577.78	2878.63	174.1	3.677
1	2	2	2	2734.63	2575.78	137.2	3.373
2	1	1	2	3677.39	3875.4	277.6	1.7

# Background

- As the CDISC (Clinical Data Interchange Standards Consortium) was implemented<sup>1-3</sup>, potential ambiguities existed for generic drug applicants to prepare PK data.
  - Inconsistent variables were used to report data
  - Data entry can be random, even wrong:
    - Drug name was used to fill out the variable of treatment, instead of using “T or R”
    - Text description were mixed in the reported time points and/or data values
    - And more random errors
  - Critical information were missing

1. Providing Regulatory Submissions In Electronic Format — Standardized Study Data Guidance for Industry

2. ANDA Submissions — Content and Format Guidance for Industry

3. STUDY DATA TECHNICAL CONFORMANCE GUIDE - Guidance for Industry Providing Regulatory Submissions in Electronic Format – Standardized Study Data

# Challenges and Issues

- Due to the ambiguities, applicants used their own interpretations to prepare PK data, which leads to:
  - Inconsistent PK data
  - Wrong use of variables or data entries
  - Missing information
  - OGD reviewers need to manually clean/curate submitted data (4-6 hours)
  - IR may be issued to delay the review process

# Current solutions

- BE reviewers can manually clean up submitted PK datasets for the downstream analysis (time consuming)
- **BEAM (BE Assessment Mate)** – a BE assessment tool developed to facilitate the good-quality and efficient BE assessment by streamlining labor-intensive work in BE assessment

#### Step 0

- REPORT WITH eCTD TABLE

#### Step 1

- PK DATA PROCESSING

#### Step 2

- BE STATISTICAL ANALYSIS

#### Step 3

- REPORT GENERATION

#### Step 4

- Publish to GDS A BE



## BE ASSESSMENT MATE

Making Assessment More Efficient

What is **BEAM**?

**BEAM** was developed to streamline the labor-intensive work during PK/BE data analysis to facilitate high-quality and efficient regulatory assessments.

## Integration

### Benefit:

- Data engine to supply data for internal BE information management system
- Enterprise-level solution to host other BE review tools
- Improving business intelligence for the BE assessment process

4

## PK data processing

### Benefit:

- BE reviewers often need a few hours to make the submitted PK data executable for downstream analysis
- With BEAM, this effort can be done within a few clicks

1

## BEAM's core functions

3

## Review documents generation

### Benefit:

- One click to auto-populate the BE review template from the submitted eCTD information tables and BE statistical analysis report
- ~70% tables/figures in the template can be auto-populated.

2

## Routine BE statistical analysis

### Benefit:

- BE reviewers click a few buttons to complete BE statistical analysis
- Flexible for different analysis needs (e.g., recalculating PK parameters)



# A Quick Look at the BEAM Tool

# Start BEAM

BE ASSESSMENT MATE  
The Default ANDA ID is: 214552  
BEAM v1.3 Navigation Menu

**Welcome**

[Manage My ANDAs](#)

**Step 0**  
[- REPORT WITH eCTD TABLE](#)

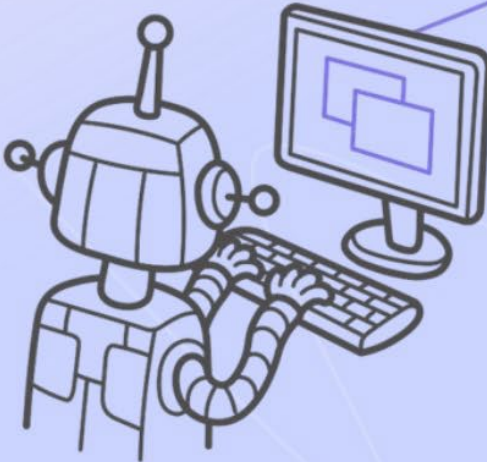
**Step 1**  
[- PK DATA PROCESSING](#)

**Step 2**  
[- BE STATISTICAL ANALYSIS](#)

**Step 3**  
[- REPORT GENERATION](#)

**Step 4**  
[- Publish to GDSA BE](#)

The BEAM tool now runs on a server so the 356h form (.pdf), summary biopharm table (.docx) and data (.xpt) will be uploaded to your folder on the server in step 0 or step 3.



## BE ASSESSMENT MATE

Making Assessment More Efficient

Welcome Page

# Step 1 – PK DATA PROCESSING

[Welcome](#)

[Manage My ANDAs](#)

**Step 0**  
[- REPORT WITH eCTD TABLE](#)

**Step 1**  
[- PK DATA PROCESSING](#)

**Step 2**  
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**Step 3**  
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**Step 4**  
[- Publish to GDSA BE](#)

### Loading Conc Data

☒ Upload Conc XPT Files

Fast:  

Choose Files

 fast-adpc.xpt

Fed:  

Choose Files

 fed-adpc.xpt

Sprinkle:  

Choose Files

 No file chosen

.....

Upload File(s)

Fast Conc Input

.....

Select options then submit processing for selected uploaded XPT file.

fast-adpc.xpt

 Select uploaded file to use

☐ Truncated AUC

☐ Multiple Strength

☐ Actual Time

Submit

Upload Conc Results

Fast 0.1 file1 of 1. name: fast-adpc.xpt size: 814560 bytes

Fed 0.2 file1 of 1. name: fed-adpc.xpt size: 1717760 bytes

XPT Upload Complete. if 2+ files uploaded, select file to process using dropdown list.

Fast Conc Results

.....

.....

# Step 1 – PK DATA PROCESSING

**Welcome**

[Manage My ANDAs](#)

**Step 0**  
[- REPORT WITH eCTD TABLE](#)

**Step 1**  
[- PK DATA PROCESSING](#)

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**Step 3**  
[- REPORT GENERATION](#)

**Step 4**  
[- Publish to GDSA BE](#)

Fast Conc Input

---

Select options then submit processing for selected uploaded XPT file.

Select uploaded file to use

☐ Truncated AUC

☐ Multiple Strength

☐ Actual Time

Fast Conc Results

Process Complete. [use links below to download.xlsx file(s) if needed]

Show  entries Search:

sub	seq	per	trt	c1	c2	c3	c4	c5	c6	c7
1	RT	1	R	0	118.869	270.646	249.111	314.631	330.298	346.065
1	RT	2	T	0	243.433	374.845	260.417	380.236	357.282	317.303
2	TR	1	T	0	257.328	257.346	248.131	255.083	272.988	371.042
2	TR	2	R	3.837	143.125	214.153	253.571	266.803	226.929	243.805
3	RT	1	R	0	457.207	501.709	483.644	752.815	833.751	890.58
3	RT	2	T	0	268.23	310.204	359.792	370.39	457.717	434.482
5	TR	1	T	0	95.084	153.135	213.561	233.02	265.72	225.008
5	TR	2	R	3.135	49.677	333.69	307.106	377.977	328.158	352.322
6	RT	1	R	0	175.199	201.981	231.463	256.208	267.056	280.312
6	RT	2	T	0	247.979	268.079	256.512	246.679	275.734	272.814

Showing 1 to 10 of 66 entries Previous  2 3 4 5 6 7 Next

[Click to download Fast\\_Conc.xlsx](#)

# Step 2 – BE STATISTICAL ANALYSIS

## Welcome

[Manage My ANDAs](#)

## Step 0

[- REPORT WITH eCTD TABLE](#)

## Step 1

[- PK DATA PROCESSING](#)

## Step 2

[- BE STATISTICAL ANALYSIS](#)

## Step 3

[- REPORT GENERATION](#)

## Step 4

[- Publish to GDSA BE](#)

### ☒ Change Type of Analysis

- ☒ Using Firm-Supplied KE and PK Data
- ☐ Using Firm-Supplied KE but Recalculating PK Data
- ☐ Recalculating KE and PK Data

☐ Upload the Modified XLSX files from Step 1 if needed (optional)

### Go4Fasting

Completed

### Go4Fed

Start

### Go4Sprinkle

Start

### Generate Statistical Analysis Report

☐ [Check to run Report without rerunning Go4 steps](#)

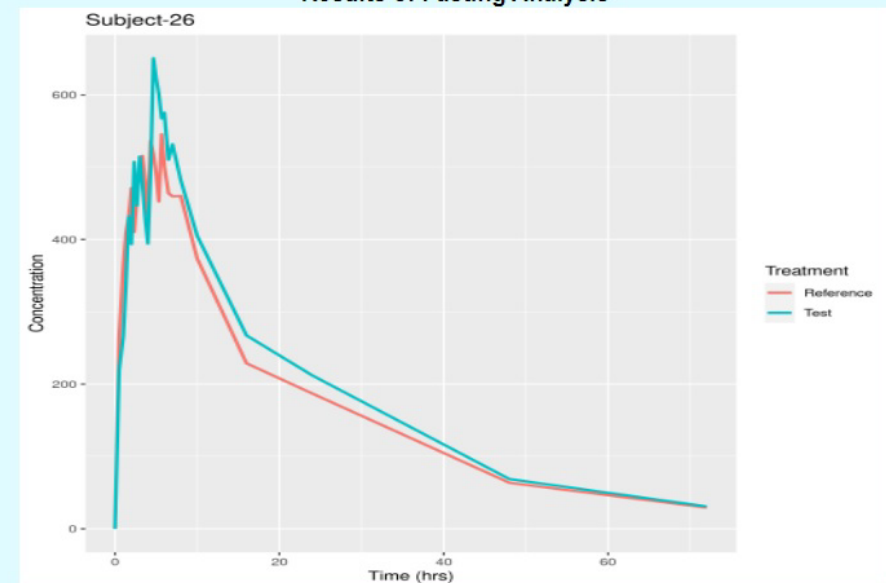
Start

Default ANDA Set.

### Time Concentration Plot of A Random Subject

Note: TimeConcPlot\_\*.docx in the working folder will contain the mean plots and all the individual plots.

### Results of Fasting Analysis



[Click to download example fasting.png](#)  
[Click to download TimeConcPlot\\_Fasting.docx](#)

[Click to download \\_Fasting\\_plot\\_.png](#)  
[Click to download \\_Fasting\\_Datasets\\_sas.doc](#)  
[Click to download \\_Fasting\\_stat\\_sas.doc](#)  
[Click to download \\_Fasting\\_table\\_sas.doc](#)

# Step 3 – REPORT GENERATION

BEAM v1.3 Navigation Menu

Welcome

Manage My ANDAs

Step 0

- REPORT WITH eCTD TABLE

Step 1

- PK DATA PROCESSING

Step 2

- BE STATISTICAL ANALYSIS

Step 3

- REPORT GENERATION

Step 4

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Generate BE Review and Full-Assessment Forms

Select the file(s) to upload to the Server

Upload One 356h form (.pdf)  
and  
One Summary Biopharm table (.docx)

Choose Files

2 files

Upload

Generate Assessment Form

Submit

Check Results

Default ANDA set.  
Select Files to upload and start BE Final Document process.

BEAM Uploaded 2 Files

filename	filesize
fda-form-356h-0001-01292020.pdf	2,650,431
summary-biopharm-summary-bio-word.docx	316,677



# Step 4 – Publish to GDSA BE

## BEAM v1.3 Navigation Menu

### Welcome

### Manage My ANDAs

### Step 0

- REPORT WITH eCTD TABLE

### Step 1

- PK DATA PROCESSING

### Step 2

- BE STATISTICAL ANALYSIS

### Step 3

- REPORT GENERATION

### Step 4

- Publish to GDSA BE

Please hit the publish button once you are ready to share either the Step 0 or Step 3 generated file(s) with the GDSA BE system for pickup to synch with:

☐ [Step 0 Generated File] ANDA#DB-Review.docx

or

☒ [Step 3 Generated File] ANDA#DB-Full-Assessment.docx

Publish

*Note: We will parse out the required data elements from the Word document above to produce a JSON file to share with the GDSA BE system.*

Default ANDA set.

Select Path of Files to upload and Transfer to GDSA BE.

# Resolving the issue at the source

- The functions of PK data processing in the BEAM tool were developed by studying hundreds in-house ANDAs.
- However, there are still issues for some new ANDA submissions, for new variations or errors are not fully predictable due to the nature of human error involved in this issue.
- Updating PK data standards by providing more instructive guideline would address the issue at the source.
  - STUDY DATA TECHNICAL CONFORMANCE GUIDE - Guidance for Industry Providing Regulatory Submissions in Electronic Format – Standardized Study Data



# Discussion

- Does your agency experience similar PK data-related issues? If so, what are your experience and suggestions on how to handle it?
- Could you share any experience/suggestion about updating data standard?

Thank you for your attention!