Bioanalytical Methods Templates

Guidance for Industry

Technical Specifications Document

For questions regarding this technical specifications document, contact CDER at cder-edata@fda.hhs.gov.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

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Technical Specifications

Revision History

Date	Version	Summary of Revisions
September 2019	1.0	Initial Version

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Contains Nonbinding Recommendations

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This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA office responsible for this guidance as listed on the title page.

1.0 INTRODUCTION

This guidance provides ready-to-use templates that sponsors can use to submit summaries of bioanalytical methods used in clinical pharmacology studies that involve pharmacokinetic concentration evaluation. The templates in this guidance are applicable to bioanalytical procedures such as chromatographic assays (CCs) and ligand-binding assays (LBAs) that quantitatively determine the levels of drugs and their metabolites and therapeutic proteins in biological matrices such as blood, serum, plasma, urine, and tissue such as skin.

These templates can be used for new drug applications (NDAs), biologics license applications (BLAs), and supplements to these applications.[2] General recommendations regarding bioanalytical method validation can be found in the May 2018 guidance entitled *Bioanalytical Method Validation*[3] and the June 2018 draft guidance entitled *M10 Bioanalytical Method Validation*.[4]

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of

[1] This technical specifications document has been prepared by the Office of Clinical Pharmacology in the Center for Drug Evaluation and Research at the Food and Drug Administration. You may submit comments on this guidance at any time. Submit comments to Docket No. FDA-2018-D-1216 (available at https://www.regulations.gov/docket?D=FDA-2018-D-1216) (see the instructions for submitting comments in the docket).

[2] Use of these templates is voluntary and invokes no new burden of data collection on the sponsor. All data are currently submitted in NDAs and BLAs as outlined in 21 CFR 314.50(d)(3)(i).

[3] We update guidances periodically. For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

[4] When final, this guidance will represent the Agency's current thinking on this topic.

the word *should* in Agency guidances means that something is suggested or recommended, but not required.

2.0 SUMMARY TABLES

The following tables can be included in your submission to provide information regarding the bioanalytical methods for pharmacokinetic assessments:

- **Table 1. Bioanalytical Method Life Cycle Information**: We recommend that you prepare Table 1 in landscape format for your submission.

- **Table 2a. Summary Method Performance**: Table 2a can be used to provide information for each bioanalytical method used to evaluate pharmacokinetic concentrations, using one method per analyte per table.

- **Table 2b. Summary of Method Modifications and Cross-Validation Results**: If the method described in Table 2a was modified, describe the modifications and cross-validation results can be described in Table 2b.

We recommend against deleting any rows or columns from the tables. You can state *not applicable* in rows or columns as appropriate. We recommend that when providing these tables, you include them as an Appendix in the Summary of Biopharmaceutics located in eCTD 2.7.1. In addition to including these tables in the Appendix, we request you also submit both tables, when they are provided, in docx format in eCTD 2.7.1. Finally, you can include any additional bioanalytical information that might be relevant for the review of your submission.

Table 1. Bioanalytical Method Life Cycle Information

	Method validation #1	Method validation #2	Clinical study #1	Clinical study #2
Analyte	Analyte name	Analyte name	Analyte name	Analyte name
Validation type	E.g., Full, partial, cross-validation	E.g., Full, partial, cross-validation	E.g., In-study	E.g., In-study
eCTD reference number	If available: x0000.0xxxxxxx	If available: x0000.0xxxxxxx	If available: x0000.0xxxxxxx	If available: x0000.0xxxxxxx
Method ID	E.g., SOP x or Method y (version)	E.g., SOP x or Method y (version)	E.g., SOP x or Method y (version)	E.g., SOP x or Method y (version)
Duration of time method is in use	E.g., 01/2000-12/2009	E.g., 12/2010-12/2015	E.g., 01/2000-12/2009	E.g., 12/2010-12/2015
Bioanalytical site	Name of test site and address, including city and country	Name of test site and address, including city and country	Name of test site and address, including city and country	Name of test site and address, including city and country
Matrix	E.g., Serum, plasma, whole blood, urine			
Platform	E.g., gas chromatography (GC), liquid chromatography/mass spectrometry (LC/MS), enzyme-linked immunosorbent assay (ELISA), enhanced chemiluminescence (ECL)			
Format	E.g., For ELISA or ECL: A validated sandwich format using x as capture and y as detection, a bridging format using z as both capture and detection, competitive assay using x as a capture and b as a competitor			
Stock reference, lot number, expiration date	Reference drug x, lot x, expiration date xx/xx/xxxx	Reference drug x, lot x, expiration date xx/xx/xxxx	Reference drug x, lot x, expiration date xx/xx/xxxx	Reference drug x, lot x, expiration date xx/xx/xxxx
Calibration range from the lower limit of quantitation (LLOQ) to the upper limit of quantitation (ULOQ)	E.g., x ng/mL to y ng/mL	E.g., x ng/mL to y ng/mL	E.g., x ng/mL to y ng/mL	E.g., x ng/mL to y ng/mL
Matrix study population	E.g., Normal, diseased	E.g., Normal, diseased	E.g., Normal, diseased	E.g., Normal, diseased
Link to reports and applicable amendments	Add hyperlink	Add hyperlink	Add hyperlink	Add hyperlink
Synopsis of amendment history	E.g., Reagent qualification, long-term storage stability	E.g., Reagent qualification, long-term storage stability	E.g., Reagent qualification, incurred sample re-analysis	E.g., Reagent qualification, incurred sample re-analysis

Table 2a. Summary Method Performance

For each '*'add additional products as needed; additional products are usually more applicable for 351(k) products

Bioanalytical method validation report name, amendments, and hyperlinks			
Method description			
Materials used for standard calibration curve and concentration			
Validated assay range			
Material used for quality controls (QCs) and concentration			
Minimum required dilutions (MRDs)			
Source and lot of reagents			
Regression model and weighting			
Validation parameters	**Method validation summary**		**Source location**
Standard calibration curve performance during accuracy and precision runs	Number of standard calibrators from LLOQ to ULOQ	x	E.g., Table x of report x
	Cumulative accuracy (%bias) from LLOQ to ULOQ Product A *	x to y% x to y%	E.g., Table x of report x
	Cumulative precision (%CV) from LLOQ to ULOQ Product A *	≤ x% ≤ x%	E.g., Table x of report x
Performance of QCs during accuracy and precision runs	**<u>Cumulative accuracy (%bias) in 5 QCs</u>** QCs for product A: Please list *	x to y% x to y%	E.g., Table x of report x
	<u>Inter-batch %CV</u> QCs for Product A: Please list *	≤ x% ≤ x%	E.g., Table x of report x
	<u>Total Error (TE)</u> QCs for Product A: Please list *	≤ x% ≤ x%	E.g., Table x of report x

Table 2a continued

Table 2a. Summary Method Performance continued

For each '*'add additional products as needed; additional products are usually more applicable for 351(k) products

Selectivity & matrix effect	Include number of total lots tested, the range of observed bias, and state any issues.	E.g., Table x of report x
Interference & specificity	Include number of total lots tested, the range of observed bias, and state any issues.	E.g., Table x of report x
Hemolysis effect	Include number of total lots tested, the range of observed bias, and state any issues.	E.g., Table x of report x
Lipemic effect	Include number of total lots tested, the range of observed bias, and state any issues.	E.g., Table x of report x
Dilution linearity & hook effect	Include the highest concentration tested and the number of dilution factors. Provide the range of observed bias.	E.g., Table x of report x
Bench-top/process stability	Describe summary data here for each product. Product A *	E.g., Table x of report x
Freeze-Thaw stability	Describe summary data here. Product A *	E.g., Table x of report x
Long-term storage	Describe summary data here. Product A *	E.g., Table x of report x
Parallelism	Describe summary data here.	E.g., Table x of report x
Carry over	Describe summary data here.	E.g., Table x of report x
Method performance in study # (Copy table and fill in for *each* study) (Provide report name and hyperlink to the report)		
Assay passing rate	Include incurred sample re-analysis passing rate.	E.g., Table x of report x
Standard curve performance	• Cumulative bias range: x to y% • Cumulative precision: ≤ x% CV	E.g., Table x of report x
QC performance	• Cumulative bias range: x to y% • Cumulative precision: ≤ x% CV • TE: ≤ x% (LBA only)	E.g., Table x of report x
Method reproducibility	E.g., Incurred sample re-analysis was performed in x% of study samples, and x% of the samples met the pre-specified criteria.	E.g., Table x of report x
Study sample analysis/ stability	Describe the length of storage stability for standard/QCs and study samples and the coverage.	E.g., Table x of report x
Standard calibration curve performance during accuracy and precision runs	Provide the number of standard calibrators from LLOQ to ULOQ.	

Table 2b. Summary of Method Modifications and Cross-Validation Results

Bioanalytical method validation report name and hyperlink			
Changes in method			
New validated assay range if any			
Validation parameters	**Cross-validation performance**		**Source location**
Standard calibration curve performance during accuracy and precision runs	Cumulative accuracy (% bias) in standard calibrators from LLOQ to ULOQ	x to y%	E.g., Table x of report x
	Cumulative precision (% CV) from LLOQ to ULOQ	≤ x%	E.g., Table x of report x
Performance of QCs during accuracy and precision runs	Cumulative accuracy (% bias) in 5 QCs	x to y%	E.g., Table x of report x
	Inter-batch % CV	≤ x%	E.g., Table x of report x
	Percent TE	≤ x%	E.g., Table x of report x
Cross-validation	If applicable, provide the number of spiked or incurred samples analyzed and results.		E.g., Table x of report x
List other parameters			E.g., Table x of report x