QUALITY OVERALL SUMMARY: PRODUCT DOSSIER (QOS-PD)

DOCUMENT NO:	**FDA/DRI/DER/TP-QOS/2019/04**
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ACKNOWLEDGEMENT

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MODULE 2.3

INTRODUCTION

Summary of product information:

Non-proprietary name(s) of the finished pharmaceutical product(s) (FPP)	
Proprietary name(s) of the finished pharmaceutical product(s) (FPP)	
International non-proprietary name(s) of the active pharmaceutical ingredient(s) (API(s)), including form (salt, hydrate, polymorph)	
Applicant name and address	
Dosage form	
Application number	| |
Strength	| |
Route of administration	
Proposed indication(s)	
Primary Contact person responsible for this application[1]	Title: First name: Family Name:
Contact person's job title	
Contact person's postal address *(Complete only applicable fields)*	
Unit	
Building/PO Box number	
Road/Street	
Plant/Zone	
Village/suburb	
Town/City	
District	

[1] *Please note that the contact listed in this form will be the primary contact for email and mail communication for this specific application.*

Region / Province / State	
Postal code	
Country	
Contact person's email address	
Contact person's phone number	

If there are other contacts who should be routinely copied into correspondence for this application they should also be listed below.

Additional contact person	**Title:** **First name:** **Family name:**
Contact person's job title	
Contact person's postal address *(Complete only applicable fields)*	
Unit	
Building/PO Box number	
Road/Street	
Plant/Zone	
Village/suburb	
Town/City	
District	
Region / Province/State	
Postal code	
Country	
Contact person's email address	
Contact person's phone number	

Additional contact person	**Title:** **First name:** **Family name:**
Contact person's job title	
Contact person's postal address *(Complete only applicable fields)*	
Unit	
Building/PO Box number	
Road/Street	
Plant/Zone	
Village/suburb	
Town/City	
District and Mandal	
Region / Province / tate	
Postal code	
Country	
Contact person's email address	
Contact person's phone number	

Other Introductory information:

Related dossiers (e.g. FPP(s) with the same API(s) submitted to the FDA by the applicant):

Application number (eg AFH0001)	**Registered (Y/N)**	**API, strength, dosage form** (eg. Abacavir (as sulphate) 300 mg tablets)	**API manufacturer** (including address if same supplier as current dossier)

Identify available literature references for the API and FPP:

Publication(s)	Monograph exists/does not exist/exists in other combination only	Most recent edition/volume consulted
API status in pharmacopoeias and fora:		
Ph.Int.	<e.g. Monograph exists>	<e.g. Ph.Int. 4th Edition Suppl. 4>
Draft Ph.Int. monographs not yet published (through www.who.int)	<e.g. Draft monograph available> <e.g. No revised unpublished monograph>	<e.g. www.who.int as of June 2014>
USP	<e.g. Monograph exists>	<e.g. USP 38>
Pharmacopeial Forum	<e.g. API monograph in 34 (3), change to reference now reflected in current USP monograph>	<e.g. 40 (4) July-August 2014>
Ph.Eur.	<e.g. Monograph exists>	<e.g. Ph.Eur. 8.0>
Pharmeuropa	<e.g. 24.1; nothing postpublication of Ph.Eur. monograph above. Most recent changes are in Ph.Eur. 8.0, 2nd LC method introduced and addition of impurities V and W.>	<e.g. EDQM databases as of June 2014>
BP	<e.g. monograph exists>	<e.g. BP 2014>
Other (e.g. JP)	<e.g. Monograph exists>	<e.g. JP 16th Edition>
FPP status in pharmacopoeias and fora:		
Ph.Int.	<e.g. Monograph exists>	<e.g. Ph.Int. 4th Edition Suppl. 4>
Draft Ph.Int. monographs not yet published (through www.who.int)	< e.g. Draft monograph available> <e.g. No revised unpublished monograph >	<e.g. www.who.int as of June 2014>
USP	<e.g. Nothing for monocomponent tablets.>	<e.g. USP 38>
Pharmacopeial Forum	<e.g. Monograph does not exist>	<e.g. 40 (4) July-August 2014>
BP	<e.g. Monograph exists>	<e.g. BP 2014>
Other (e.g. JP)	<e.g. Monograph exists>	<e.g. JP 16th Edition>
Other reference texts (e.g. public access reports):		
<e.g. WHOPARs, EPARs>	<e.g. WHOPAR HAXXX>	<e.g. PQ website as of June 2014>

FDA/DRI/DER/TP-QOS/2019/04

SUMMARY OF QUALITY ASSESSMENT OF LABELLING AND SAMPLES (*FDA Use Only*)
Discussion/comments on the quality components of:
Summary of product characteristics <insert assessment observations, comments, etc.>
Labelling (outer and inner labels) <insert assessment observations, comments, etc.>
Package leaflet (patient information leaflet) <insert assessment observations, comments, etc.>
Samples (e.g. FPP, device) <insert assessment observations, comments, etc.>

2.3.S DRUG SUBSTANCE (or ACTIVE PHARMACEUTICAL INGREDIENT (API)) (NAME, MANUFACTURER)

Complete the following table for the option that applies for the submission of API information:

Name of API:	
Name of API manufacturer:	
□	Confirmation of API FDA document: • a copy of the confirmation of API FDA document should be provided in *Module 1*, and • summaries of the relevant information should be provided under the appropriate sections (e.g. S.1.3, S.2, S.3.1, S.4.1 through S.4.4, S.5 and S.7; see Quality guideline).
□	Certificate of suitability to the European Pharmacopoeia (CEP): • is a written commitment provided that the applicant will inform FDA in the event that the CEP is withdrawn and acknowledged that withdrawal of the CEP will require additional consideration of the API data requirements to support the dossier: □ yes, □ no; • a copy of the most current CEP (with annexes) and written commitment should be provided in *Module 1*; • the declaration of access should be filled out by the CEP holder on behalf of the FPP manufacturer or applicant to FDA refers to the CEP; and • summaries of the relevant information should be provided under the appropriate sections (e.g. S.1.3, S.3.1, S.4.1 through S.4.4, S.5, S.6 and S.7; see Quality guideline).
□	Full details in the PD: • Summaries of the full information should be provided under the appropriate sections; see Section 3.2.S in the FDA quality guideline. • Document version number/identifier of current module 3.2.S: _____ • If an earlier Module 3.2.S document was provided with a previous FPP submission: • a) list document number/identifier of the most recent submission to aid comparison: Document version:_____ submitted with FPP _____, and, • b) provide a summary of changes document comparing the current and most recent version of the Module 3.2.S. • If the API and FPP suppliers are not part of the same pharmaceutical company then for each API supplier the following declarations have been provided: • A declaration from the API manufacturer that they have provided to the FPP manufacturer all information pertaining to the manufacture, control and stability of the API: □ yes, □ no; • A declaration from the API manufacturer that they will inform the FPP manufacturer of all changes to the preparation, control and stability of the API: □ yes, □ no;

2.3.S.1 General Information (name, manufacturer)

2.3.S.1.1 Nomenclature (name, manufacturer)

(a) (Recommended) International Non-proprietary name (INN):

(b) Compendial name, if relevant:

(c) Chemical name(s):

(d) Company or laboratory code:

(e) Other non-proprietary name(s) (e.g. national name, USAN, BAN):

(f) Chemical Abstracts Service (CAS) registry number:

2.3.S.1.2 Structure (name, manufacturer)

(a) Structural formula, including relative and absolute stereochemistry:

(b) Molecular formula:

(c) Relative molecular mass:

2.3.S.1.3 General Properties (name, manufacturer)

(a) Physical description (e.g. appearance, colour, physical state):

(b) Solubilities:

In common solvents:

Quantitative aqueous pH solubility profile (pH 1.2 to 6.8) at 37°C:

Medium (e.g. pH 4.5 buffer)	Solubility (mg/ml)
<pH = pKa, if pKa is between 1.2 and 6.8>	<e.g. pKa = 13.1, therefore solubility result at this pH is not required>

Dose/solubility volume calculation:

(c) Physical form (e.g. polymorphic form(s), solvate, hydrate):

Polymorphic form:

Solvate:

Hydrate:

(d) Other:

Property	
pH	
pK	
Partition coefficients	
Melting/boiling points	
Specific optical rotation (specify solvent)	
Refractive index (liquids)	
Hygroscopicity	
UV absorption maxima/molar absorptivity	
Other	

2.3.S.2 Manufacture (name, manufacturer)

2.3.S.2.1 Manufacturer(s) (name, manufacturer)

(a) Name, address and responsibility (e.g. fabrication, packaging, labelling, testing, storage) of each manufacturer, including contractors and each proposed production site or facility involved in these activities:

Name and address (including block(s)/unit(s))	Responsibility	WHOAPI-PQ number/APIMF/CEP number (if applicable)

Note: In the absence of identified block numbers, all blocks producing the API at this site will be considered as part of the inspection.

(b) Manufacturing authorization for the production of API(s) and, where available, certificate of GMP compliance (GMP information should be provided in Module 1):

2.3.S.2.2 Description of Manufacturing Process and Process Controls (name, manufacturer)

(a) Flow diagram of the synthesis process(es):

(b) Brief narrative description of the manufacturing process(es):

(c) Alternate processes and explanation of their use:

(d) Reprocessing steps and justification:

2.3.S.2.3 Control of Materials (name, manufacturer)

(a) Name of starting material:

(b) Name and manufacturing site address of starting material manufacturer(s):

(c) Flow diagram of the starting material preparation:

(d) Summary of the quality and controls of the starting materials used in the manufacture of the API:

Test parameter	Test(s)/method(s)	Acceptance criteria

(e) Where the API(s) and the starting materials and reagents used to manufacture the API(s) are without risk of transmitting agents of animal spongiform encephalopathies, a letter of attestation confirming this can be found in:

2.3.S.2.4 Controls of Critical Steps and Intermediates (name, manufacturer)

(a) Summary of the controls performed at critical steps of the manufacturing process and on intermediates:

Step/materials	Test(s)/method(s)	Acceptance criteria

2.3.S.2.5 Process Validation and/or Evaluation (name, manufacturer)

(a) Description of process validation and/or evaluation studies (e.g. for aseptic processing and sterilization):

2.3.S.2.6 Manufacturing Process Development (name, manufacturer)

(a) Description and discussion of the significant changes made to the manufacturing process and/or manufacturing site of the API used in producing comparative bioavailability or biowaiver, stability, scale-up, pilot and, if available, production scale batches:

2.3.S.3 Characterisation (name, manufacturer)

2.3.S.3.1 Elucidation of Structure and other Characteristics (name, manufacturer)

(a) List of studies performed (e.g. IR, UV, NMR, MS, elemental analysis) and conclusion from the studies (e.g. whether results support the proposed structure):

(b) Discussion on the potential for isomerism and identification of stereochemistry (e.g. geometric isomerism, number of chiral centres and configurations) of the API batch(es) used in comparative bioavailability or biowaiver studies:

(c) Summary of studies performed to identify potential polymorphic forms (including solvates): <including identification of and data on the API lot used in bioavailability studies>

(d) Summary of studies performed to identify the particle size distribution of the API: <including identification of and data on the API lot used in bioavailability studies>

(e) Other characteristics:

2.3.S.3.2 Impurities (name, manufacturer)

(a) Identification of potential and actual impurities arising from the synthesis, manufacture and/or degradation:

i. List of API-related impurities (e.g. starting materials, by-products, intermediates, chiral impurities, degradation products), including chemical name, structure and origin:

API-related impurity (code name, chemical name and compendial name (e.g. USP RC A) if relevant)	Structure	Origin

ii. List of process-related impurities (e.g. residual solvents, reagents), including compound names and step used in synthesis:

Process-related impurity (compound name)	Step used in synthesis

(b) Basis for setting the acceptance criteria for impurities:

i. Maximum daily dose (i.e. the amount of API administered per day) for the API, corresponding to ICH Reporting/Identification/Qualification Thresholds for the APIrelated impurities and the concentration limits (ppm) for the process-related impurities (e.g. residual solvents):

Maximum daily dose for the API:	**<x mg/day>**	
Test	**Parameter**	**ICH threshold or concentration limit**
API-related impurities	Reporting Threshold	
	Identification Threshold	
	Qualification Threshold	
Process-related impurities	<solvent 1>	
	<solvent 2>, etc.	

ii. Data on observed impurities for relevant batches (e.g. comparative bioavailability or biowaiver, stability batches):

Impurity (API-related and process-related)	**Acceptance Criteria**	**Results (include batch number* and use**)**		

*** include strength, if reporting impurity levels found in the FPP (e.g. for comparative studies) ** e.g. comparative bioavailability or biowaiver studies, stability**

iii. **Justification of proposed acceptance criteria for impurities:**

2.3.S.4 Control of the API (name, manufacturer)

2.3.S.4.1 Specification (name, manufacturer)

(a) API specifications of the FPP manufacturer:

Standard (e.g. Ph.Int., Ph.Eur., BP, USP, in-house)		
Specification reference number and version		
Test	**Acceptance criteria**	**Analytical procedure (Type/Source/Version)**
Description		
Identification		
Impurities		
Assay		
etc.		

2.3.S.4.2 Analytical Procedures (name, manufacturer)

(a) Summary of the analytical procedures (e.g. key method parameters, conditions, system suitability testing):

See *2.3.R Regional Information* for summaries of the analytical procedures (i.e. *2.3.R.2 Analytical Procedures and Validation Information*).

Summarized tabulated methods and validation may be provided in a separate file <provide reference>.

2.3.S.4.3 Validation of Analytical Procedures (name, manufacturer)

(a) Summary of the validation information (e.g. validation parameters and results):

See *2.3.R Regional Information* for summaries of the validation information (i.e. *2.3.R.2 Analytical Procedures and Validation Information*).

Summarized tabulated methods and validation may be provided in a separate file <provide reference>.

2.3.S.4.4 Batch Analyses (name, manufacturer)

(a) Description of the batches:

Batch number	Batch size	Date and site of production	Use (e.g. comparative bioavailability or biowaiver, stability)

(a) Summary of batch analyses release results *of the FPP manufacturer* for relevant batches (e.g. comparative bioavailability or biowaiver, stability):

Test	Acceptance Criteria	Results		
		<batch x>	<batch y>	etc.
Description				
Identification				
Impurities				
Assay				
etc.				

(b) Summary of analytical procedures and validation information for those procedures not previously summarized in 2.3.S.4.2 and 2.3.S.4.3 (e.g. historical analytical procedures):

2.3.S.4.5 Justification of Specification (name, manufacturer)

(a) Justification of the API specification (e.g. evolution of tests, analytical procedures and acceptance criteria, differences from officially recognized compendial standard(s)):

2.3.S.5 Reference Standards or Materials (name, manufacturer)

(a) Source (including lot number) of primary reference standards or reference materials (e.g. Ph.Int., Ph.Eur., BP, USP, in-house):

(b) Characterization and evaluation of non-official (e.g. not from an officially recognized pharmacopoeia) primary reference standards or reference materials (e.g. elucidation of structure, certificate of analysis):

(c) Description of the process controls of the secondary reference standard (comparative certificate of analysis and IR spectra against primary standard):

2.3.S.6 Container Closure System (name, manufacturer)

(a) Description of the container closure system(s) for the shipment and storage of the API (including the identity of materials of construction of each primary packaging component and a brief summary of the specifications):

Packaging component	Materials of construction	Specifications (list parameters e.g. identification (IR))

(b) Other information on the container closure system(s) (e.g. suitability studies):

2.3.S.7 Stability (name, manufacturer)

2.3.S.7.1 Stability Summary and Conclusions (name, manufacturer)

(a) Summary of stress testing (e.g. heat, humidity, oxidation, photolysis, acid/base): and results:

Stress condition	Treatment	Results (e.g. including discussion whether mass balance and peak purity are observed)
Heat		
Humidity		
Oxidation		
Photolysis		
Acid		
Base		
Other		

(b) Summary of accelerated and long-term testing parameters (e.g. studies conducted):

Storage condition (◦C, % RH)	Batch number	Batch size	Container closure system	Completed (and proposed) testing intervals

Summary of the stability results observed for the above accelerated and long-term studies:

Test (limits)	Results
Description	
Moisture	
Impurities	
Assay	
etc.	

(c) Proposed storage statement and re-test period (or shelf-life, as appropriate):

Container closure system	Storage statement	Re-test period*

* indicate if a shelf-life is proposed in lieu of a re-test period (e.g. in the case of labile APIs)

2.3.S.7.2 Post-approval Stability Protocol and Stability Commitment (name, manufacturer)

(a) Stability protocol for *Primary stability batches* (e.g. storage conditions (including tolerances), batch numbers and batch sizes, tests and acceptance criteria, testing frequency, container closure system(s)):

Parameter	Details	
Storage condition(s) (◦C, % RH)		
Batch number(s) / batch size(s)	*<primary batches>*	
Tests and acceptance criteria	Description	
	Moisture	
	Impurities	
	Assay	
	etc.	
Testing frequency		
Container closure system(s)		

(b) Stability protocol for *Commitment batches* (e.g. storage conditions (including tolerances), batch numbers (if known) and batch sizes, tests and acceptance criteria, testing frequency, container closure system(s)):

Parameter	Details	
Storage condition(s) (◦C, % RH)		
Batch number(s) / batch size(s)	*<not less than three production batches>*	
Tests and acceptance criteria	Description	
	Moisture	
	Impurities	
	Assay	
	etc.	
Testing frequency		
Container closure system(s)		

(c) Stability protocol for *Ongoing batches* (e.g. storage conditions (including tolerances), batch sizes and annual allocation, tests and acceptance criteria, testing frequency, container closure system(s)):

Parameter	Details	
Storage condition(s) (◦C, % RH)		
Annual allocation	*<at least one production batch per year (unless none is produced that year) in each container closure system >*	
Tests and acceptance criteria	Description	
	Moisture	
	Impurities	
	Assay	
	etc.	
Parameter	**Details**	
Testing frequency		
Container closure system(s)		

2.3.S.7.3 Stability Data (name, manufacturer)

(a) The actual stability results should be provided in *Module 3*.

(b) Summary of analytical procedures and validation information for those procedures not previously summarized in 2.3.S.4 (e.g. analytical procedures used only for stability studies):

2.3.P DRUG PRODUCT (or FINISHED PHARMACEUTICAL PRODUCT (FPP))

2.3.P.1 Description and Composition of the FPP

(a) Description of the FPP (in signed specifications):

(b) Composition of the FPP:

i. Composition, i.e. list of all components of the FPP and their amounts on a per unit basis and percentage basis (including individual components of mixtures prepared in-house (e.g. coatings) and overages, if any):

Component and quality standard (and grade, if applicable)	**Function**	**Strength (label claim)**					
		Quant. per unit or per mL	**%**	**Quant. per unit or per mL**	**%**	**Quantity per unit or per mL**	**%**
<complete with appropriate titles e.g. Core tablet (Layer 1, Layer 2, etc. as applicable), Contents of capsule, Powder for injection>							
Subtotal 1							
Component and quality standard (and grade, if applicable)	**Function**	**Strength (label claim)**					
		Quant. per unit or per mL	**%**	**Quant. per unit or per mL**	**%**	**Quantity per unit or per mL**	**%**
<complete with appropriate title e.g. Film-coating >							
Subtotal 2							
Total							

ii. Composition of all *components purchased as mixtures* (e.g. colourants, coatings, capsule shells, imprinting inks):

(c) Description of accompanying reconstitution diluent(s), if applicable:

(d) Type of container closure system used for the FPP and accompanying reconstitution diluent, if applicable:

2.3.P.2 Pharmaceutical Development

2.3.P.2.1 Components of the FPP

2.3.P.2.1.1 Active Pharmaceutical Ingredient

(a) Discussion of the:

i. compatibility of the API(s) with excipients listed in 2.3.P.1:

ii. key physicochemical characteristics (e.g. water content, solubility, particle size distribution, polymorphic or solid-state form) of the API(s) that can influence the performance of the FPP:

iii. for fixed-dose combinations, compatibility of APIs with each other:

2.3.P.2.1.2 Excipients

(a) Discussion of the choice of excipients listed in 2.3.P.1 (e.g. their concentrations, their characteristics that can influence the FPP performance):

2.3.P.2.2 Finished Pharmaceutical Product

2.3.P.2.2.1 Formulation Development

(a) Summary describing the development of the FPP (e.g. route of administration, usage, optimization of the formulation, etc.):

(b) Information on primary (submission, registration, exhibit) batches including comparative bioavailability or biowaiver, stability, commercial:

i. **Summary of batch numbers:**

Batch number(s) of the FPPs used in			
Bioequivalence or biowaiver	**<e.g. bioequivalence batch A12345> <e.g. biowaiver batch X12345>**		
For proportional strength biowaiver: the bioequivalence batch of the reference strength			
Dissolution profile studies			
Stability studies (primary batches)			
‹packaging configuration I›			
‹ packaging configuration II›			
‹Add/delete as many rows as necessary›			

Stability studies (production batches)			
‹ packaging configuration I›			
‹ packaging configuration II›			
(Add/delete as many rows as necessary)			
Validation studies (primary batches) if available			
‹ packaging configuration I›			
‹ packaging configuration II›			
(Add/delete as many rows as necessary)			
Validation studies (at least the first three consecutive production batches) or code(s)/version(s) for process validation protocol(s)			

ii. **Summary of formulations and discussion of any differences:**

Component and quality standard (e.g. NF, BP, Ph.Eur, in-house)	**Relevant batches**							
	Comparative bioavailability or biowaiver		**Stability**		**Process validation**		**Commercial (2.3.P.1)**	
	<Batch nos. and sizes>		**<Batch nos. and sizes>**		**<Batch nos. and sizes>**		**<Batch nos. and sizes>**	
	Theor. quantity per batch	**%**	**Theor. quantity per batch**	**%**	**Theor. quantity per batch**	**%**	**Theor. quantity per batch**	**%**
<complete with appropriate title e.g. Core tablet, Contents of capsule, Powder for injection>								
Subtotal 1								
<complete with appropriate title e.g. Film-coating >								
Subtotal 2								
Total								

(c) Description of batches used in the comparative *in vitro* studies (e.g. dissolution) and in the *in vivo* studies (e.g. comparative bioavailability or biowaiver), including strength, batch number, type of study and reference to the data (volume, page):

(d) Summary of results for comparative *in vitro* studies (e.g. dissolution):

Summary of the multi-point dissolution profiles for the biobatch(es) in three BCS media across the physiological pH range and the proposed medium if different from the BCS media:

(e) Summary of any information on *in vitro-in vivo* correlation (IVIVC) studies (with cross-reference to the studies in *Module 5*):

(f) For scored tablets, provide the rationale/justification for scoring:

2.3.P.2.2.2 Overages

(a) Justification of overages in the formulation(s) described in 2.3.P.1:

2.3.P.2.2.3 Physicochemical and Biological Properties

(a) Discussion of the parameters relevant to the performance of the FPP (e.g. pH, ionic strength, dissolution, particle size distribution, polymorphism, rheological properties):

2.3.P.2.3 Manufacturing Process Development

(a) Discussion of the development of the manufacturing process of the FPP (e.g. optimization of the process, selection of the method of sterilization):

(b) Discussion of the differences in the manufacturing process(es) for the batches used in the comparative bioavailability or biowaiver studies and the process described in 2.3.P.3.3:

2.3.P.2.4 Container Closure System

(a) Discussion of the suitability of the container closure system (described in 2.3.P.7) used for the storage, transportation (shipping) and use of the FPP (e.g. choice of materials, protection from moisture and light, compatibility of the materials with the FPP):

(b) For a device accompanying a multi-dose container, a summary of the study results demonstrating the reproducibility of the device (e.g. consistent delivery of the intended volume for the lowest intended dose):

2.3.P.2.5 Microbiological Attributes

(a) Discussion of microbiological attributes of the FPP (e.g. preservative effectiveness studies):

2.3.P.2.6 Compatibility

(a) Discussion of the compatibility of the FPP (e.g. with reconstitution diluent(s) or dosage devices, co-administered FPPs):

2.3.P.3 Manufacture

2.3.P.3.1 Manufacturer(s)

(a) Name, address and responsibility (e.g. fabrication, packaging, labelling, testing) of each manufacturer, including contractors and each proposed production site or facility involved in manufacturing and testing:

Name and address (include block(s)/unit(s))	Responsibility

(b) Manufacturing authorization, marketing authorization and, where available, WHO-type certificate of GMP (GMP information should be provided in *Module 1*):

2.3.P.3.2 Batch Formula

Largest intended commercial batch size:
Other intended commercial batch sizes:
<information on all intended commercial batch sizes should be in the QOS-PD>

(a) List of all components of the FPP to be used in the manufacturing process and their amounts on a per batch basis (including individual components of mixtures prepared in-house (e.g. coatings) and overages, if any):

Strength (label claim)			
Master production document reference number and version			
Proposed commercial batch size(s) (e.g. number of dosage units)			
Component and quality standard (and grade, if applicable)	**Quantity per batch (e.g. kg/batch)**	**Quantity per batch (e.g. kg/batch)**	**Quantity per batch (e.g. kg/batch)**
<complete with appropriate titles e.g. Core tablet (Layer 1, Layer 2, etc. as applicable), Contents of capsule, Powder for injection>			
Subtotal 1			
<complete with appropriate title e.g. Film-coating >			
Subtotal 2			
Total			

2.3.P.3.3 Description of Manufacturing Process and Process Controls

(a) Flow diagram of the manufacturing process:

(b) Narrative description of the manufacturing process, including equipment type and working capacity, process parameters:

(c) Justification of reprocessing of materials:

2.3.P.3.4 Controls of Critical Steps and Intermediates

(a) Summary of controls performed at the critical steps of the manufacturing process and on isolated intermediates:

Step (e.g. granulation, compression, coating)	Controls (parameters/limits/frequency of testing)

Proposed/validated holding periods for intermediates (including bulk product):

2.3.P.3.5 Process Validation and/or Evaluation

(a) Summary of the process validation and/or evaluation studies conducted (including product quality review(s) where relevant) and/or a summary of the proposed process validation protocol for the critical steps or critical assays used in the manufacturing process (e.g. protocol number, parameters, results):

Document code(s) for the process validation protocol(s) and/or report(s) (including reference number/version/date):

2.3.P.4 Control of Excipients

2.3.P.4.1 Specifications

(a) Summary of the specifications for in-house standard specifications:

2.3.P.4.2 Analytical Procedures

(a) Summary of the analytical procedures for supplementary tests:

2.3.P.4.3 Validation of Analytical Procedures

(a) Summary of the validation information for the analytical procedures for supplementary tests (where applicable):

2.3.P.4.4 Justification of Specifications

(a) Justification of the specifications (e.g. evolution of tests, analytical procedures and acceptance criteria, exclusion of certain tests, differences from officially recognized compendial standard(s)):

2.3.P.4.5 Excipients of Human or Animal Origin

(a) For FPPs using excipients *without* risk of transmitting agents of animal spongiform encephalopathies, a letter of attestation confirming this can be found in:

(b) CEP(s) demonstrating TSE-compliance can be found in:

2.3.P.4.6 Novel Excipients

Novel excipients are not accepted in FDA. See quality guideline for definition.

2.3.P.5 Control of FPP

2.3.P.5.1 Specification(s)

(a) Specification(s) for the FPP:

Standard (e.g. Ph.Int., BP, USP, in-house)			
Specification reference number and version			
Test	**Acceptance criteria (release)**	**Acceptance criteria (shelf-life)**	**Analytical procedure (type/source/version)**
Description			
Identification			
Impurities			

Assay etc.			

2.3.P.5.2 Analytical Procedures

(a) Summary of the analytical procedures (e.g. key method parameters, conditions, system suitability testing):

See 2.3.R Regional Information for summaries of the analytical procedures (i.e. *2.3.R.2 Analytical Procedures and Validation Information*).

Summarized tabulated methods and validation may be provided in a separate file <provide reference>.

2.3.P.5.3 Validation of Analytical Procedures

(a) Summary of the validation information (e.g. validation parameters and results):

See 2.3.R Regional Information for summaries of the validation information (i.e. *2.3.R.2 Analytical Procedures and Validation Information*).

Summarized tabulated methods and validation may be provided in a separate file <provide reference>.

2.3.P.5.4 Batch Analyses

(a) Description of the batches:

Strength and batch number	Batch size	Date and site of production	Use (e.g. comparative bioavailability or biowaiver, stability)

(b) Summary of batch analyses release results for relevant batches (e.g. comparative bioavailability or biowaiver, stability):

Test	Acceptance criteria	Results		
		<batch x>	<batch y>	etc.
Description				
Identification				
Impurities				
Assay				
etc.				

(c) Summary of analytical procedures and validation information for those procedures not previously summarized in 2.3.P.5.2 and 2.3.P.5.3 (e.g. historical analytical procedures):

2.3.P.5.5 Characterisation of Impurities

(a) Identification of potential and actual impurities:

Degradation product (code name, chemical name and compendial name (e.g. USP RC A) if relevant)	Structure	Origin

Process-related impurity (compound name)	Step used in the FPP manufacturing process

(b) Basis for setting the acceptance criteria for impurities:

i. Maximum daily dose (i.e. the amount of API administered per day) for the API, corresponding ICH Reporting/Identification/Qualification Thresholds for the degradation products in the FPP and the concentration limits (ppm) for the process-related impurities (e.g. residual solvents):

Maximum daily dose for the API:	<x mg/day>	
Test	Parameter	ICH threshold or concentration limit
Degradation product	Reporting Threshold	
Maximum daily dose for the API:	<x mg/day>	
Test	Parameter	ICH threshold or concentration limit
	Identification Threshold	

	Qualification Threshold	
Process-related impurities	<solvent 1>	
	<solvent 2>, etc.	

ii. Data on observed impurities for relevant batches (e.g. comparative bioavailability or biowaiver):

Impurity (degradation product and process-related)	**Acceptance criteria**	**Results**		
		<batch no., strength, use>		

iii. **Justification of proposed acceptance criteria for impurities:**

2.3.P.5.6 Justification of Specification(s)

(a) Justification of the FPP specification(s) (e.g. evolution of tests, analytical procedures and acceptance criteria, differences from officially recognized compendial standard(s)):

2.3.P.6 Reference Standards or Materials

(a) Source (including lot number) of primary reference standards or reference materials (e.g. Ph.Int., Ph.Eur., BP, USP, in-house) *not* discussed in 3.2.S.5:

(b) Characterization and evaluation of non-official (e.g. not from an officially recognized pharmacopoeia) primary reference standards or reference materials (e.g. elucidation of structure, certificate of analysis) *not* discussed in 3.2.S.5:

(c) Description of the process controls of the secondary reference standard (comparative certificate of analysis and IR spectra against primary standard) *not* discussed in 3.2.S.5:

2.3.P.7 Container Closure System

(a) Description of the container closure systems, including unit count or fill size, container size or volume:

Description (including materials of construction)	Strength	Unit count or fill size (e.g. 60s, 100s etc.)	Container size (e.g. 5 ml, 100 ml etc.)

(b) Summary of specifications of each primary and functional secondary (e.g. foil pouches) packaging components:

Packaging component	Specifications (list parameters e.g. identification (IR))
HDPE bottle	
PP cap	
Induction sealed liners	
Blister films (PVC, etc)	
Aluminum foil backing	
etc.	

(c) Other information on the container closure system(s):

2.3.P.8 Stability

2.3.P.8.1 Stability Summary and Conclusions

(a) Summary of stress testing and results (e.g. photostability studies, cyclic studies, freezethaw studies, demonstration of stability-indication of purity/assay method(s)):

(b) Summary of accelerated and long-term testing parameters (e.g. studies conducted):

Storage conditions (◦C, % RH)	Strength and batch number	Batch size	Container closure system	Completed (and proposed) test intervals

Summary of additional stability studies, if applicable (with reference to data location) *<e.g. studies at intermediate conditions, holding period studies for intermediates and bulk product, transport studies, inuse studies>:*

Summary of the stability results observed for the above accelerated and long-term studies:

Test	Results
Description	
Moisture	
Impurities	
Assay	
etc.	

(c) Proposed storage statement and shelf-life (and in-use storage conditions and in-use period, if applicable):

Container closure system	Storage statement	Shelf-life

2.3.P.8.2 Post-approval Stability Protocol and Stability Commitment

(a) Stability protocol for *Primary stability batches* (e.g. storage conditions (including tolerances), batch numbers and batch sizes, tests and acceptance criteria, testing frequency, container closure system(s)):

Parameter	Details	
Storage condition(s) (◦C, % RH)		
Batch number(s) / batch size(s)	*<primary batches>*	
Tests and acceptance criteria	Description	
	Moisture	
	Impurities	
	Assay	
	etc.	
Testing frequency		
Container closure system(s)		

(b) Stability protocol for *Commitment batches* (e.g. storage conditions (including tolerances), batch numbers (if known) and batch sizes, tests and acceptance criteria, testing frequency, container closure system(s)):

Parameter	Details
Storage condition(s) (◦C, % RH)	

Batch number(s) / batch size(s)	*<not less than three production batches in each container closure system>*	
Tests and acceptance criteria	Description	
	Moisture	
	Impurities	
	Assay	
	etc.	
Testing Frequency		
Container Closure System(s)		

(c) Stability protocol for *Ongoing batches* (e.g. storage conditions (including tolerances), number of batches per strength and batch sizes, tests and acceptance criteria, testing frequency, container closure system(s)):

Parameter	Details	
Storage condition(s) (◦C, % RH)		
Batch size(s), annual allocation	*<at least one production batch per year (unless none is produced that year) in each container closure system >*	
Tests and acceptance criteria	Description	
	Moisture	
	Impurities	
	Assay	
	etc.	
Testing frequency		
Container closure system(s)		

2.3.P.8.3 Stability Data

(a) The actual stability results should be provided in *Module 3*.

(b) Summary of analytical procedures and validation information for those procedures *not* previously summarized in 2.3.P.5 (e.g. analytical procedures used only for stability studies):

(c) Bracketing and matrixing design and justification for *Commitment* and/or *Ongoing stability batches*, if applicable:

2.3.A APPENDICES

2.3.A.1 Facilities and Equipment (name, manufacturer)

(a) Summary of information on facilities and equipment, in addition to the information provided in other sections of the submission: Not applicable.

2.3.A.2 Adventitious Agents Safety Evaluation (name, dosage form, manufacturer)

(a) Summary of the information assessing the risk with respect to potential contamination with adventitious agents: Not applicable.

2.3.A.3 Excipients

(a) Summary of the details of manufacture, characterization and controls, with cross references to supporting safety data (nonclinical and/or clinical) for the novel excipients: Not applicable. Novel excipients are not accepted in FDA. See quality guideline for definition.

2.3.R REGIONAL INFORMATION

2.3.R.1 Production Documentation

2.3.R.1.1 Executed Production Documents

(a) List of batches (including strengths) for which executed production documents have been provided (e.g. comparative bioavailability or biowaiver batches):

2.3.R.1.2 Master Production Documents

(a) The blank master production documents for each strength, proposed commercial batch size and manufacturing facility should be provided in *Module 3*.

Discussion of differences between the proposed commercial batch size master production documents compared to the biostudy batch records with respect to the formulation (2.3.P.2.2.1 b) (ii)) and the manufacturing process (2.3.P.2.3 b)):

<include a tabulated discussion for all differences, including processes, equipment (model/make/capacity), settings and operating parameters >

Parameter (e.g. process, equipment, process parameter)	**Bioequivalence/biowaiver batch** **<indicate batch number>**	**Proposed production batches** **<indicate proposed batch size>**	**Discussion of the relevance of the differences**
<Main processes and associated equipment (make, model, capacity, settings)>			

2.3.R.2 Analytical Procedures and Validation Information

ANALYTICAL PROCEDURES AND VALIDATION INFORMATION SUMMARIES	
ATTACHMENT NUMBER:	
HPLC Method Summary	**Volume/Page:**
Method name:	
Method code:	**Version and/or Date:**
Column(s) / temperature (if other than ambient):	
Mobile phase (specify gradient program, if applicable):	
Detector (and wavelength, if applicable):	
Flow rate:	
Injection volume:	
Sample solution preparation and concentration (expressed as mg/ml, let this be termed “A”):	
Reference solution preparation and concentration (expressed as mg/ml and as % of “A”):	
System suitability solution concentration (expressed as mg/ml and as % of “A”):	
System suitability tests (tests and acceptance criteria):	
Method of quantification (e.g. against API or impurity reference standard(s)):	
Other information (specify):	

ATTACHMENT NUMBER:		
Validation Summary		**Volume/Page:**
Analytes:		
Typical retention times (RT)		
Relative retention times ($RT_{Imp.}/RT_{API\ or\ Int.\ Std.}$):		
Relative response factor ($RF_{Imp.}/RF_{API}$):		
Specificity:		
Linearity / Range:	Number of concentrations: Range (expressed as % “A”): Slope: Y-intercept: Correlation coefficient (r^2) :	

Accuracy:	Conc.(s) (expressed as % "A"): Number of replicates: Percent recovery (avg/RSD):				
Precision / Repeatability: (intra-assay precision)	Conc.(s) (expressed as % "A"): Number of replicates: Result (avg/RSD):				
Precision / Intermediate Precision: (days/analysts/equipment)	Parameter(s) altered: Result (avg/RSD):				
Limit of Detection (LOD): (expressed as % "A")					
Limit of Quantitation (LOQ): (expressed as % "A")					
Robustness:	Stability of solutions: Other variables/effects:				
Typical chromatograms or spectra may be found in:					
Company(s) responsible for method validation:					
Other information (specify):					