MODULE 2.3
QUALITY OVERALL SUMMARY – PRODUCT DOSSIER (QOS –PD)

INTRODUCTION

The introduction should include proprietary name, non-proprietary name or common name of the drug substance, company name, dosage form(s), strength(s), route of administration, and proposed indication(s).

a) **Summary of product information:**

Non-proprietary name of the finished pharmaceutical product (FPP)			
Proprietary name of the finished pharmaceutical product (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			
Reference Number(s)			
Strength(s)			
Route of administration			
Proposed indication(s)			
Contact information	Name: Phone: Fax: Email:		

b) Other Introductory information:

Related dossiers (e.g. FPP(s) with the same API(s) submitted to the Namibia Medicines Regulatory Council (NMRC) by the applicant):

Reference number in MS	**Registered (Y/N)**	**API, strength, dosage form**	**API manufacturer** (including address)

Identify available literature references for the API and FPP:

Publication(s)	Most recent edition/volume in which API/FPP appears	Most recent edition/volume consulted
API status in pharmacopoeia and forum:		
Ph.Int.		
Ph.Int. monograph development (through www.who.int)	<e.g. monograph under development or draft/final published>	
USP		
Pharmacopeial Forum		
Ph.Eur.		
Pharmeuropa		
BP		
Other (e.g. JP)		
FPP status in pharmacopoeia and forum:		
Ph.Int.		
Ph.Int monograph development (through www.who.int)	<e.g. monograph under development or draft/final published>	
USP		
Pharmacopeial Forum		
BP		
Other (e.g. JP)		
Other reference texts (e.g. public access reports):		

SUMMARY OF QUALITY ASSESSMENT OF LABELLING AND SAMPLES *(NMRC 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 (NAME, MANUFACTURER)

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

Name of API:	
Name of API manufacturer:	
□	Certificate of suitability to the European Pharmacopoeia (CEP): • is a written commitment provided that the applicant will inform WHO in the event that the CEP is withdrawn and has 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 the Prequalification Programme who 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.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 Quality guideline.

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

Information from 3.2.S.1 should be included.

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 to 6.8):

Medium (e.g. pH 4.5 buffer)	Solubility (mg/ml)

Dose/solubility volume calculation:

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

Polymorphic form:

Solvate:

Hydrate:

d) Other:

Property	
pH	
pKa	
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)
Information from 3.2.S.2 should be included:

- Information on the 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	CEP number (if applicable)

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

- A brief description of the manufacturing process (including, for example, reference to starting materials, critical steps, and reprocessing) and the controls that are intended to result in the routine and consistent production of material(s) of appropriate quality;
- *A flow diagram, as provided in 3.2.S.2.2;*

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:

- A description of the Source and Starting Material and raw materials of biological origin used in the manufacture of the drug substance, as described in 3.2.S.2.3;

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

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

Step/starting material	Test(s)/method(s)	Acceptance criteria

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

(c) 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:

- A discussion of the selection and justification of critical manufacturing steps, process controls, and acceptance criteria. Highlight critical process intermediates, as described in 3.2.S.2.4;

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

- A description of process validation and/or evaluation, as described in 3.2.S.2.5.

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):

- A brief summary of major manufacturing changes made throughout development and conclusions from the assessment used to evaluate product consistency, as described in 3.2.S.2.6. The QOS should also cross-refer to the non-clinical and clinical studies that used batches affected by these manufacturing changes, as provided in the CTD-S and CTD-E modules of the dossier.

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)

For NCE: A summary of the interpretation of evidence of structure and isomerism, as described in 3.2.S.3.1, should be included.
When a drug substance is chiral, it should be specified whether specific stereoisomers or a mixture of stereoisomers have been used in the nonclinical and clinical studies, and information should be given as to the stereoisomer of the drug substance that is to be used in the final product intended for marketing.

For Biotech: A description of the desired product and product-related substances and a summary of general properties, characteristic features and characterisation data (for example, primary and higher order structure and biological activity), as described in 3.2.S.3.1, should be included.

For NCE and Biotech: The QOS should summarise the data on potential and actual impurities arising from the synthesis, manufacture and/or degradation, and should summarise the basis for setting the acceptance criteria for individual and total impurities. The QOS should also summarise the impurity levels in batches of the drug substance used in the non-clinical studies, in the clinical trials, and in typical batches manufactured by the proposed commercial process. The QOS should state how the proposed impurity limits are qualified. A tabulated summary of the data provided in 3.2.S.3.2, with graphical representation, where appropriate should be included.

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):

(d) Summary of studies performed to identify the particle size distribution of the API:

(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 (chemical name or descriptor)	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 API-

related 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 Drug Substance (name, manufacturer)
A brief summary of the justification of the specification(s), the analytical procedures, and validation should be included. Specification from 3.2.S.4.1 should be provided. A tabulated summary of the batch analyses from 3.2.S.4.4, with graphical representation where appropriate, should be provided.

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, 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 and validation information (i.e. *2.3.R.2 Analytical Procedures and Validation Information*).

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 analytical procedures and validation information (i.e. *2.3.R.2 Analytical Procedures and Validation Information*).

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)**

(b) 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.				

(c) 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)
Information from 3.2.S.5 (tabulated presentation, where appropriate) should be included.

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):

(b) 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 brief description and discussion of the information, from 3.2.S.6 should be included.

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)

This section should include a summary of the studies undertaken (conditions, batches, analytical procedures) and a brief discussion of the results and conclusions, the proposed storage conditions, retest date or shelf-life, where relevant, as described in 3.2.S.7.1.
The post-approval stability protocol, as described in 3.2.S.7.2, should be included.
A tabulated summary of the stability results from 3.2.S.7.3, with graphical representation where appropriate, should be provided.

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 is 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	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)		
Tests and acceptance criteria	Description	
	Moisture	
	Impurities	
	Assay	
	etc.	

Parameter	Details
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.	
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 (NAME, DOSAGE FORM)

2.3.P.1 Description and Composition of the Drug Product (name, dosage form)

Information from 3.2.P.1 should be provided. Composition from 3.2.P.1 should be provided.

2.3.P.1 Description and Composition of the FPP

(a) Description of the FPP:

(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	%	Quant. per unit	%	Quantity per unit	%
<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							

(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 (name, dosage form)
A discussion of the information and data from 3.2.P.2 should be presented.
A tabulated summary of the composition of the formulations used in clinical trials and a presentation of dissolution profiles should be provided, where relevant.

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			
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 >								

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	%
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):

(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):

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.3Manufacture (name, dosage form)
Information from 3.2.P.3 should include:

- Information on the manufacturer. •
- A brief description of the manufacturing process and the controls that are intended to result in the routine and consistent production of product of appropriate quality.
- *A flow diagram, as provided under 3.2.P.3.3.*
- A brief description of the process validation and/or evaluation, as described in 3.2.P.3.5.

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

(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/or 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 title e.g. Core tablet, 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

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):

2.3.P.4 Control of Excipients (name, dosage form)
A brief summary on the quality of excipients, as described in 3.2.P.4, should be included.

2.3.P.4 Control of Excipients

2.3.P.4.1 Specifications

(a) Summary of the specifications for officially recognized compendial excipients which include supplementary tests not included in the officially recognized compendial monograph(s):

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 the Prequalification Programme.

2.3.P.5 Control of Drug Product (name, dosage form)

A brief summary of the justification of the specification(s), a summary of the analytical procedures and validation, and characterisation of impurities should be provided. Specification(s) from 3.2.P.5.1 should be provided. A tabulated summary of the batch analyses provided under 3.2.P.5.4, with graphical representation where appropriate should be included.

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, 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 and validation information (i.e. *2.3.R.2 Analytical Procedures and Validation Information*).

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 analytical procedures and validation information (i.e. *2.3.R.2 Analytical Procedures and Validation Information*).

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 (chemical name or descriptor)	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	
	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.6Reference Standards or Materials (name, dosage form)
Information from 3.2.P.6 (tabulated presentation, where appropriate) should be included.

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 (name, dosage form)
A brief description and discussion of the information in 3.2.P.7 should be included.

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	Container size

(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 (name, dosage form)

A summary of the studies undertaken (conditions, batches, analytical procedures) and a brief discussion of the results and conclusions of the stability studies and analysis of data should be included. Conclusions with respect to storage conditions and shelf-life and, if applicable, in- use storage conditions and shelf-life should be given.

A tabulated summary of the stability results from 3.2.P.8.3, with graphical representation where appropriate, should be included. The post-approval stability protocol, as described in 3.2.P.8.2, should be provided.

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, freeze-thaw studies):

(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 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)		
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)

Biotech: A summary of facility information described under 3.2.A.1 should be included.

(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 and manufacturer)

A discussion on measures implemented to control endogenous and adventitious agents in production should be included.
A tabulated summary of the reduction factors for viral clearance from 3.2.A.2, should be provided.

Summary of the information assessing the risk with respect to potential contamination with adventitious agents:

2.3.A.3 Excipients

Summary of the details of manufacture, characterization and controls, with cross references to supporting safety data (nonclinical and/or clinical) for the novel excipients:

2.3.R REGIONAL INFORMATION

A brief description of the information specific for the region, as provided under "3.2.R" should be included, where appropriate.

2.3.R.7 Production Documentation

2.3.R.7.1 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.7.2 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*.

2.3.R.8 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 concentration (expressed as mg/ml, let this be termed "A"):			
Reference solution 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): :				

ATTACHMENT NUMBER:				
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):				