1.0 INTRODUCTION:

1.1 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)	
Strength(s)	
Date of Submission <for official use only>	
Name of first Evaluator <for official use only>	
Date of first Evaluation <for official use only>	
Name of Second Evaluator <for official use only>	
Date of second Evaluation <for official use only>	
Date of evaluation Additional Information-Q1 <for official use only>	
Date of Evaluation Additional Information-Q2 <for official use only>	
Variation History	
Number of Binders	
Product Registration receipt number <for official use only>	

Application Number <for official use only>	
ATC code/ Pharmacological Classification	
Dosage form	
Route of administration	
Proposed Category of Distribution	
Proposed indication(s)	
Applicant name and address	
Applicant's contact information	Name: Phone: Fax: Email:
Name and complete address of the manufacturing site (s) for the FPP	
GMP status of the manufacturing site(s)	
Name and complete address of the manufacturing site (s) for the Drug Substance	
Country of origin	
Local Responsible Person	
Laboratory Analysis Status	
Conclusion of the evaluation <for official use only>	

SUMMARY OF QUALITY EVALUATION OF LABELLING AND SAMPLES:
<for official use only>

Discussion/comments on the quality components of:
(i) Summary of product characteristics (SmPC) <insert assessment observations, comments, etc.>
(ii) Labelling (outer and inner labels) <insert assessment observations, comments, etc.>
(iii) Package inserts <insert assessment observations, comments, etc.>
(iv) Samples (e.g. FPP, device) <insert assessment observations, comments, etc.>

Identify available literature references for the API and FPP:

Publication(s)	**Most recent edition/ volume i 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):		

DRUG SUBSTANCE (or ACTIVE PHARMACEUTICAL INGREDIENT (API)):

Name of API:	
Name of API manufacturer:	
□	*Confirmation of API Prequalification document (CPQ).* • Complete copy of the WHO Confirmation of API Prequalification document should be provided in *Module 1*, together with the duly filled out authorisation box in the name of th FPP manufacturer or applicant. • Discussion are provided on additional applicable physicochemical and other relevant API properties that are not controlled by the API manufacturer's specifications e.g. solubilities and polymorphs as per guidance in this section. ○ □ yes, □ no; • If the sterility of the FPP is based upon the sterile manufacture of the API then data on the sterilization process together with full validation data should be provided. • Elucidation of structure and other characteristics - studies to identify polymorphs and particle size distribution as per guidance in this section. • Specification - the specifications of the FPP manufacturer including all tests and limits of the API manufacturer's specifications and any additional tests and acceptance criteria

	that are not controlled by the API manufacturer's specifications such as polymorphs and/o particle size distribution. • Analytical procedures and validation – for any methods used by the FPP manufacturer in addition to those in the API manufacturer's specifications. • Batch analysis - results from two batches of at least pilot scale, demonstrating compliance with the FPP manufacturer's API specifications. • Reference standards or materials – information on the FPP manufacturer's reference standards. • Stability - data to support the retest period if either the proposed retest period is longer or the proposed storage conditions are at a lower temperature or humidity to that of the Prequalified API.
□	Certificate of suitability to the European Pharmacopoeia (CEP): • is a written commitment provided that the applicant will inform ZAMRA 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 provide in *Module 1*; • the declaration of access should be filled out by the CEP holder on behalf of the FPP manufacturer or applicant to ZAMRA who refers to the CEP; and • summaries of the relevant information should be provided under the appropriate sections.
□	Drug master file (DMF) procedure: • DMF number assigned by ZAMRA (if known):_____; version number (and/or date) o the open part:_____; version number (and/or date) of the closed part:_____; • a copy of the letter of access should be provided in *Module 1*; and • summaries of the relevant information from the Open part should be provided under the appropriate sections of the registration guidelines.
□	Full details in the PD: • summaries of the full information should be provided under the appropriate sections in the registration guidelines.

2.3.S DRUG SUBSTANCE -

2.3.S.1 General Information

2.3.S.1.1 Nomenclature of API

(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 of API

(a) Description of the Structure

(b) Schematic of amino acid sequence, including indication of any glycosylation sites, or other post-translational modifications, as appropriate.

(c) Relative molecular mass:

2.3.S.1.2 General Properties of API
Reference ICH: ICH Q6B

(a) Physico-Chemical properties

(b) Biological Activity
the specific ability or capacity of a product to achieve a defined biological effect

(c) Other relevant properties
e.g immunological properties, glycoforms

2.3.S.2 Manufacture

2.3.S.2.1 Manufacturer(s)

(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 and 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*):

(c) A summary of facility information, SMF, GMP classification of manufacturing rooms (2.3.A.1)

2.3.S.2.2 Description of Manufacturing Process and Process Controls

(a) Batch(es) and scale definition

(b) Cell Culture and Harvest (Upstream Processing)

i. Flow diagram of the synthesis process (es):

ii. Brief narrative description of the manufacturing process (es):

(c) Purification and modification reactions (Downstream Processing

i. Flow diagram of the synthesis process (es):

ii. Brief narrative description of the manufacturing process (es):

(d) Filling, storage and transportation (shipping)

(e) Reprocessing steps and justification

Reference ICH Guidelines: Q5A, Q5B, and Q6B, ICHQ11

2.3.S.2.3 Control of Materials

(a) Raw and starting materials

i) **Summary of the quality and controls of the raw materials and starting materials used in the manufacture of the API:**

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

ii) **Name and manufacturing site address of starting material manufacturer(s), including vendors for raw materials:**

iii) **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:**

(b) Control of source and starting material of biologic origin
e.g., Applicable to hormones harvested from human urine; viral seeds such as rabies virus, polio virus, etc Summaries of viral safety information for biologically-sourced materials should be provided. (Details in 3.2.A.2.)

Source, history, and generation of the cell substrate
Refer to ICH Q5D

Cell banking system, characterisation and testing
Refer to ICH Q5D

Cell bank stability
Refer to ICH Q5D, Q5C

Analysis of expression construct
Refer to ICH Q5B

Viral safety evaluation
Refer to ICH Q5A. This data may also be located in sections 3.2.A.2 and 3.2.S.2.5

2.3.S.2.4 Controls of Critical Steps and Intermediates

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

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

(b) Stability data supporting storage conditions of intermediates/ hold time data should be provided.
Reference ICH Guideline: Q5C

2.3.S.2.5 Process Validation and/or Evaluation

(a) Description of process validation and/or evaluation studies of Upstream and Downstream Processes

(b) Process validation and/or evaluation studies for Aseptic Processing and Sterilization
Sufficient information should be provided. Including process validation protocols and Reports attached in relevant modules.

(c) Viral reduction studies
For manufacturing steps intended to remove or inactivate viral contaminants, the information from evaluation studies should be provided in 3.2.A.2.

2.3.S.2.6 Manufacturing Process Development

(a) The developmental history of the manufacturing process, as described in 3.2.S.2.2, should be provided

(b) Description and discussion of the significant changes made to the manufacturing process and/or manufacturing site of the drug substance used in producing nonclinical, clinical, scale-up, pilot, and, if available, production scale batches:

(c) Selection criteria of critical process controls and acceptance criteria

2.3.S.3 Characterisation

2.3.S.3.1 Elucidation of Structure and other Characteristics

Summary of Studies performed

(a) Primary Structure

(b) Secondary and higher order structure

(c) Post-translational forms (e.g., glycoforms)

(d) Physicochemical properties (e.g molecular weight, isoform patterns, extinction coefficient,etc)

(e) Biological activity

(f) Immunochemical properties (where relevant)

(g) Purity

(h) Other characteristics

2.3.S.3.2 Impurities

Detailed Identification and Quantification Evaluation of Product Related and Process related Impurities

New analytical technology and modifications to existing technology are continuously being developed, and should be applied when appropriate. Methods of product – and process – related impurities should be suitable for accurate detection and quantification of impurities …ICH Q6B,(compared to the RBP for biosimilars only)

(a) Process-related impurities and contaminants
Discuss:
Cell substrate-derived impurities
Cell culture-derived impurities
Downstream-derived impurities
Other process related impurities

(b) Product-related impurities including degradation products
Discuss:
Truncated forms
Other modified forms

Aggregates
Other product related impurities

(c) Justification of proposed acceptance criteria for impurities (Basis for setting the acceptance criteria for impurities and maximum amount for the highest clinical dose)

(d) Data on observed impurities for relevant batches (e.g. pre-clinical and clinical batches, consistency batches, stability batches):

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

(e) Potential risks related to these identified impurities (e.g. potential impact on efficacy and safety, including immunogenicity, i) will have to be appropriately documented and justified:

2.3.S.4 Control of the API

2.S.4.1 Specification

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

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

See *3.R Regional Information* for summaries of the analytical procedures and validation information (i.e. *3.R.2 Analytical Procedures and Validation Information*).

2.3.S.4.3 Validation of Analytical Procedures

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

See *3.R Regional Information* for summaries of the analytical procedures and validation information (i.e. *3.R.2 Analytical Procedures and Validation Information*).

2.3.S.4.4 Batch Analyses

(a) Description of the batches:

Batch number	Batch size	Date and site of production	Use (e.g. pre-clinical, clinical, stability)

(b) Summary of batch analyses release results for relevant batches (e.g., pre-clinical, clinical, 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 2.2.8.2 and 2.2.8.3 (e.g. historical analytical procedures):

2.3.S.4.5 Justification of Specification

(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.4.6 Reference Standards or Materials
Reference ICH Q6A, ICH Q6B

Official/ Compendial Reference Standards

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

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

Non-official/ Non compendial standards

(a) Establishment of the reference standard
prepared from lot(s) representative of production and clinical materials.

(b) Qualification history

(c) 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):
performed with reliable state-of-the-art analytical methods

(d) Qualification procedure of future reference batches

(e) Storage conditions and stability of the reference standard

2.3.S.6 Container Closure System

(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. compatibility/ suitability studies):

2.3.S.7 Stability

2.3.S.7.1 Stability Summary and Conclusions

(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

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

Test	Results

(d) Proposed storage statement (or shelf-life, as appropriate): *No retest period for biologicals*

Container closure system	Storage statement	Shelf life

* 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.	
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	

Parameter	Details	
	Moisture	
	Impurities	
	Assay	
	etc.	
Testing frequency		
Container closure system(s)		

2.3.S.7.3 Stability Data

(d) The actual stability results should be provided.

(e) Summary of analytical procedures and validation information for those procedures not previously summarized in *2.2.8.2* (e.g. analytical procedures used only for stability studies):

2.3.P DRUG PRODUCT

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 (most recent	**Function**	**Strength (label claim)**	

edition/volume), and grade, if applicable		**Quant. per unit**	**%**	**Quant. per Batch**	**%**
<complete with appropriate title e.g., Powder for injection, Solution for Injection, etc>					
Subtotal 1					
<complete with appropriate title >					
Subtotal 2					
Total					

(c) Composition of all *components purchased as mixtures* (e.g. colourants, lipid/ nano particles):

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

(e) 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 3.1:

(ii) key physicochemical characteristics 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 3.1 (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) Identification of those attributes that are critical to the quality of the drug product, taking into consideration intended usage and route of administration.

(c) Information on primary (submission, registration, exhibit) batches including comparative pre-clinical and clinical, stability, commercial:

i. A summary of formulations used in clinical safety and efficacy

ii. Summary of batch numbers:

Batch number(s) of the FPPs used in			
Clinical			
Non-clinical batches			
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 consecuti production batches) or code(s)/version(s) for process validati protocol(s)			

iii. Summary of formulations and discussion of any differences:

Component and quali 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. Powder for injection>								
Subtotal 1								
<complete with appropriate title >								
Subtotal 2								
Total								

(d) **The differences between clinical formulations and the formulation (i.e. composition) described in 3.2.P.1 should be discussed.**
Any changes between the proposed commercial formulation ICH guideline Q8 (R2) on pharmaceutical development EMA/CHMP/ICH/167068/2004 Page 8/24 and those formulations used in pivotal clinical batches and primary stability batches should be clearly described and the rationale for the changes provided.

(e) Evolution of the formulation design from initial concept up to the final design.

2.3.P.2.2.2 Overages

(a) Justification of overages in the formulation(s) described in 3.1:

2.3.P.2.2.3 Physicochemical and Biological Properties

(a) Discussion of the parameters relevant to the safety, performance or manufacturability of the FPP

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,):

(b) **Discussion of the differences in the manufacturing process(es) for the batches used in the pre-clinical and clinical studies and the commercial process described in *3.3.3***

2.3.P.2.4 Container Closure System

(a) The choice and rationale for selection of the container closure system for the commercial product (described in 3.2.P.7) should be discussed. *Similar to next point*

(b) Discussion of the suitability of the container closure system (described in 3.7) 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):

(c) For a device accompanying a multi-dose container or dosing device, a summary of the study results demonstrating the reproducibility and accuracy 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):

(b) Integrity of the container closure system as it relates to preventing microbial contamination.

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 Module1):

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 standa (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. Powder for injection>			
Subtotal 1			
<complete with appropriate title>			
Subtotal 2			
Total			

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

2.3.P.3.3.1 **Flow diagram of the manufacturing process:**

2.3.P.3.3.2 **Narrative description of the manufacturing process, including equipment type and working capacity, process parameters:**

2.3.P.3.3.3 **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	Controls

(b) If holding times are foreseen for process intermediates, periods and storage conditions should be provided and justified by data in terms of physicochemical, biological and microbiological properties.

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):

(b) Aseptic Process Validation

i. *Product/filter compatibility / filter validation tests should be conducted, tests such as bubble point variation determination, flow rate variation, membrane mass determination, bacterial challenge test/ microbial retention efficacy tests and tests for extractables/leachables, product adsorption*
ii. *The processes of depyrogenation of stoppers, seals and accessories should be validated. Details of the sterilisation of the container closure system including heat distribution and penetration studies.*
iii. *Validation data for the cleaning procedure of equipment should be provided*
iv. *Simulation process trials should be conducted, and these should include media fill tests to verify the effectiveness of the aseptic filling process and to determine the longest filling time)*

(c) Lyophilization validation (if applicable)

2.3.P.4 Control of Excipients

2.3.P.4.1 Specifications
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
Summary of the analytical procedures for supplementary tests:

2.3.P.4.3 Validation of Analytical Procedures
Summary of the validation information for the analytical procedures for supplementary tests (where applicable):

2.3.P.4.4 Justification of Specifications
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) TSE-compliance certification

2.3.P.4.5 Novel Excipients

2.3.P.5 Control of FPP

2.3.P.5.1 Specification(s)

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 *3.R Regional Information* for summaries of the analytical procedures and validation information (i.e. *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 *3.R Regional Information* for summaries of the analytical procedures and validation information (i.e. *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. pre-clinical, clinical, commercial, stability)

(b) Summary of batch analyses release results for relevant batches (e.g. pre-clinical, clinical, stability):

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

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

etc.				

(c) Summary of analytical procedures and validation information for those procedures not previously summarized in 3.5.2 and 3.5.3 (e.g. historical analytical procedures):

2.3.P.5.5 Characterization of Impurities

(b) Summary of 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) Process-related impurities and contaminants

(c) Product-related impurities including degradation products

(d) Justification/basis of proposed acceptance criteria for impurities (Basis for setting the acceptance criteria for impurities and maximum amount for the highest clinical dose)

(e) Data on observed impurities for relevant batches (e.g. pre-clinical and clinical batches, consistency batches, stability batches):

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

(f) Potential risks related to these identified impurities (e.g. potential impact on efficacy and safety, including immunogenicity will have to be appropriately documented and justified):

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	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)
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, 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

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

Test	Results
Description	

Test	Results
Moisture	
Impurities	
Assay	
etc.	

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

Container closure syste	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.	

Parameter	Details
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.8.1 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 3.5 (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:

3 APPENDICES

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:

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

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

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:

3.R REGIONAL INFORMATION

3.R.1 Production Documentation

3.R.1.1 Executed Production Documents

(a) List of batches (including strengths) for which executed production documents have been provided (clinical batch):

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*.

3.R.2 Analytical Procedures and Validation Information

ANALYTICAL PROCEDURES AND VALIDATION INFORMATION SUMMARIES

ATTACHMENT NUMBER:	

Method Summary e.g. HPLC	**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 concentration Range (expressed as % "A"): Slope: Y-intercept: Correlation coefficient (r^2) :				
Accuracy:	Conc.(s) (expressed as % "A" Number of replicates: Perce recovery (avg/RSD):				
Precision **Repeatability:** (intra-assay precision)	Conc.(s) (expressed as % "A" Number of replicates: Res (avg/RSD):				
Precision / Intermedia **Precision:** (days/analysts/equipmer	Parameter(s) altered: Res (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):					

3.R.3 COMPARABILITY EXERCISE (Applicable to Biosimilar Products)

3.R.3.1 Consideration in Choice of the RBP

3.R.3.2 Details of Batches used in the comparability Exercise (batch no., source market, etc)

3.R.3.3 Summary of comparability exercise (*Quality, Non-clinical and Clinical)*

Submit comparability exercise protocols and reports

3.R.3.4 Statistical Analysis of the Comparability

3.R.3.5 Conclusion on comparability