IGDRP
International Generic Drug Regulators Programme

ASMF/DMF Quality Assessment Report (QAR)

ASMF/DMF Working Group

Version 1.2 – Nov 26, 2015

Version	Description of Change	Author	Effective Date
v 1.0	Original publication	ASMF/DMF WG	May 26, 2015
v 1.1	Watermark added	ASMF/DMF WG	Nov 17, 2015
V 1.2	Disclaimer added to page 2	ASMF/DMF WG	Nov 26, 2015

Disclaimer

In order to achieve the IGDRP's objective to promote collaboration and convergence in generic drug regulation, the ASMF/DMF working group has developed a series of reference documents covering a number of technical and procedural aspects of ASMF/DMF assessment.

These documents were developed among participating IGDRP members as model documents.

The implementation of these documents by a given IGDRP member, either as a whole or in part, is not mandatory. Each IGDRP member works within their own specific regulatory setting and some or all aspects of a document may, for a variety of reasons, not be applicable. Equally, a given IGDRP member may for practical reasons choose to revise the format or written language of a model document.

ASMF/DMF
Quality Assessment Report

Version 1.1 (final, 2015-11-19)

ADMINISTRATIVE INFORMATION

Regulatory Agency:	
National ASMF/DMF Reference Number:	
Active Pharmaceutical Ingredient (API) Name: *INN, salts/counter ion, solvated state*	
Applicant's Part version number and date (yyyy-mm-dd):	
Restricted Part version number and date (yyyy-mm-dd):	
ASMF/DMF Holder: *Company Name* *Corporate Address* *Phone* *Fax* *Email*	
Contact person for the ASMF/DMF: *Name* *Company Name* *Address* *Phone* *Fax* *Email*	
API Manufacturer(s) and manufacturing site(s): *Manufacturer's name* *Site address* *Country*	

Appendices:	1. Final Active/drug substance specification, Re-test period (or Shelf-life, if appropriate), and Storage conditions accepted by the Regulatory Agency

REGIONAL INFORMATION (to be amended, as needed)

Recommendation:	This version of the ASMF/DMF <is/is not> considered acceptable to support the proposed drug product application.
Date of ASMF/DMF Assessment Report:	

ASMF/DMF assessed in conjunction with: *Drug product name* *Dosage form* *Application reference number* *Applicant*	

Assessment history and status of ASMF/DMF:	<This ASMF/DMF <has/has not> been previously assessed. It was found to be acceptable in connection with an application for <dosage form X>>.
International regulatory information for the ASMF/DMF (e.g., foreign assessment reports):	<discuss, if available>

Good Manufacturing Practices (GMP) information for the facilities relevant to this ASMF/DMF:

Name and Address	Responsibility	GMP Status
	manufacturing	
	sterilisation	
	testing	

Declarations (e.g., BSE/TSE status):

It has been declared that no materials of animal or human origin are used in this manufacturing process.
OR
It has been declared that ..... is used in this manufacturing process.

QUALITY ASSESSOR'S INTRODUCTION

Summary of available literature references on the drug substance:

Literature Reference	Present (yes/no)?
USP	
Pharmacopeial Forum	
Ph.Eur.	
Pharmeuropa	
BP	
Ph.Int.	
Other References (specify)	

Other noteworthy information:

Maximum daily dose for the drug product (mg/day):	
Route(s) of administration for the drug product:	
Target patient population(s) (e.g., neonates, infants, children, adults)	
API manufactured as sterile (yes/no)?	
Other:	

MODULE 3 – QUALITY

APPLICANT'S PART of the ASMF/DMF

3.2.S.1 General Information

3.2.S.1.1 Nomenclature

International non-proprietary name (INN):	
Compendial name or other relevant names or codes (e.g., company code):	
Chemical Abstracts Service (CAS) Number:	

3.2.S.1.2 Structure

Structural formula (including relative and absolute stereochemistry, salt form and solvate moieties):	
Molecular formula:	
Molecular mass:	

3.2.S.1.3 General properties

Physical characteristics:	
Solubility over the physiological pH range (e.g., pH 1.2-6.8):	
Solubilities in relevant solvents:	
Hygroscopicity:	
Polymorphism:	
Other:	

Assessor's comments on 3.2.S.1 General Information:

3.2.S.2 Manufacture

3.2.S.2.1 Manufacturer(s)

Name, address, and responsibility of each manufacturing facility(ies) (including manufacturer(s) of the intermediates, if sourced from a third party):

3.2.S.2.2 Description of manufacturing process and process controls

Brief outline of the synthetic process(es) from the Applicant's part of the ASMF/DMF (if lengthy, include as an appendix):

Maximum proposed production scale batch size(s):

Assessor's comments on 3.2.S.2 Manufacture:

It has been confirmed by the Assessor that the outline of the synthetic process provided in the Applicant's Part of the ASMF/DMF contains sufficient information for the Applicant of the drug product dossier and is consistent with the information provided in the Restricted Part of the ASMF/DMF.

See the assessment included under the Restricted Part of this report for a discussion on the detailed manufacturing process and process controls.

3.2.S.3 Characterisation

3.2.S.3.1 Elucidation of structure and other characteristics

Studies performed to elucidate the structure (e.g., IR, UV, NMR, MS, elemental analysis):

Discussion relating to the characterisation of the drug substance (e.g., potential isomerism and identification of stereochemistry, polymorphism, particle size distribution):

3.2.S.3.2 Impurities

Drug-related impurities (e.g., starting materials, by-products, intermediates, chiral impurities, degradation products):

Descriptor*	Structure and Origin	Maximum Observed Levels	LOQ (if applicable)	Proposed Limits (if applicable)

* Chemical names of drug-related impurities:

Process-related impurities (e.g., residual solvents, reagents, elemental impurities):

Process-related impurity	ICH Q3C/Q3D Class and Concentration Limit	Step Used	Maximum Observed Levels	LOQ (if applicable)	Proposed Limits (if applicable)

Discussion of potential genotoxic impurities:

Justification for the proposed acceptance criteria for impurities:

Assessor's comments on 3.2.S.3 Characterisation:

3.2.S.4 Control of the Drug Substance

3.2.S.4.1 Specification

Standard Claimed (e.g., USP, BP, Ph.Eur., in-house)	
Specification Reference Number and/or Version	

Test Parameter	Analytical Procedure (type/source/version)	Acceptance Criteria

3.2.S.4.2 Analytical procedures

Discussion of in-house analytical procedures (e.g., analytical conditions, methods of quantification, acceptability of System Suitability Tests (SSTs)):

3.2.S.4.3 Validation of analytical procedures

Validation Parameter	Analytical Procedure			
	Assay	Impurities	Residual Solvents	
Method Type:	HPLC	HPLC	GC	
Method Number:	No. X	No. Y	No. Z	
Accuracy				
Precision: - Repeatability - Intermediate precision				
Specificity				
Detection limit (specify)				
Quantitation limit (specify)				
Linearity				
Range (specify)				
Robustness				
Solution stability				

+ indicates that the parameter is acceptably tested and validated
- indicates that the parameter is not tested
? indicates that questions remain before the parameter is judged to be acceptable

3.2.S.4.4 Batch analyses

Summary of batches:

Batch Number	Batch Size	Manufacturing Site	Manufacturing Date

3.2.S.4.5 Justification of specification

Assessor's comments on 3.2.S.4 Control of Drug Substance:

3.2.S.5 Reference Standards or Materials

Source of reference standards or reference materials (e.g., in-house, USP, BP, Ph.Eur.):

Discussion of the characterisation of any primary or secondary reference standards (if applicable):

Description of reference standards or materials for impurities (when applicable):

Assessor's comments on 3.2.S.5 Reference Standards or Materials:

3.2.S.6 Container Closure System

Description of the container closure system(s) for the storage of the drug substance:

Assessor's comments on 3.2.S.6 Container Closure System:

3.2.S.7 Stability

3.2.S.7.1 Stability summary and conclusions

Summary of forced degradation studies / stress testing (e.g., heat, humidity, oxidation, photolysis, acid/base) conducted:

Summary of long-term, intermediate (if applicable), and accelerated studies conducted:

Storage Conditions (Temp °C, % RH)	Number of Batches / Months	Batch Size(s)	Manufacturing Date	Container Closure System
				same as intended for commercial purposes (or specify, if different)

Proposed re-test period (or shelf-life, as appropriate):

This re-test period <is supported/is not supported> by the stability data.

3.2.S.7.2 Post-approval stability protocol and stability commitment

3.2.S.7.3 Stability data

Assessor's comments on 3.2.S.7 Stability:

Discussion of key stability data:

Test	Acceptance Criterion	Notable Results, Observations and Trends

The stability specification includes tests for assay, impurities, etc, with the same limits as described in 3.2.S.4.1. The stability specification <is acceptable/is not acceptable>. The <same/different> analytical methods described in 3.2.S.4.2 are used (where different, validation should be discussed). The analytical methods are considered stability indicating. The container closure system <simulates/does not simulate> that described in section 3.2.S.7.

CONCLUSION – APPLICANT'S PART

List of Questions on the Applicant's Part of the ASMF/DMF:

Major objections:

Other concerns:

ASSESSMENT OF RESPONSES TO DEFICIENCY COMMENTS ON APPLICANT'S PART

Comment 1:

<…>

Assessor's comments of ASMF/DMF Holder's response:

<…>

Comment 2:

<…>

Assessor's comments of ASMF/DMF Holder's response:

Confidential Annex

NB: THIS ANNEX SHOULD NOT BE DISCLOSED TO THE APPLICANT

RESTRICTED PART of the ASMF/DMF

[NB: This annex should not be disclosed to the Applicant. It should also be noted that this section should only include an assessment of information that has *not* been previously discussed in the Applicant's Part of the ASMF/DMF (e.g., only proprietary or detailed information on the manufacturing process, impurities not disclosed in the Applicant's Part). If applicable, those section(s) that are fully discussed/assessed in the Applicant's Part of the ASMF/DMF should be deleted.]

3.2.S.2 Manufacture

3.2.S.2.2 Description of manufacturing process and process controls

Discussion on the detailed manufacturing process and process controls and, if applicable, any proposed reprocessing procedures:

3.2.S.2.3 Control of materials

Discussion of the acceptability of the declared starting material(s):

Summary of the specification of the starting material(s):

Discussion on the quality and control of materials used in the manufacture of the drug substance (e.g., raw materials, starting material(s), solvents, reagents, catalysts):

List of reagents, solvents and raw materials:

3.2.S.2.4 Control of critical steps and intermediates

Discussion on the quality and controls performed at the critical steps and on intermediates isolated during the manufacturing process:

Lists of critical process and critical process parameters, intermediate specifications, and in-process control acceptance criteria:

3.2.S.2.5 Process validation and/or evaluation

Discussion of process validation and/or evaluation studies (e.g., for aseptic processing and sterilisation):

3.2.S.2.6 Manufacturing process development

Discussion of manufacturing process development to support a design space (if proposed):

Assessor's comments on 3.2.S.2 Manufacture:

3.2.S.3 Characterisation

3.2.S.3.2 Impurities

Impurities that have not been previously discussed in the assessment of the Applicant's Part of the ASMF/DMF (e.g., related to the detailed description of the manufacturing process):

Discussion of the ASMF/DMF Owner's justification for not routinely controlling potential impurities in the final active/drug substance:

Assessor's comments on 3.2.S.3 Characterisation:

3.2.S.4 Control of the Drug Substance

3.2.S.4.5 Justification of specification

Justification that has not been previously discussed in the assessment of the Applicant's Part of the ASMF/DMF or in 3.2.S.3.2 Impurities of the Restricted Part (e.g., related to the detailed description of the manufacturing process, control of materials and process validation):

Assessor's comments on 3.2.S.4 Control of the Drug Substance:

CONCLUSION – RESTRICTED PART

List of Questions on the Restricted Part of the ASMF/DMF:

Major objections:

Other concerns:

ASSESSMENT OF RESPONSES TO DEFICIENCY COMMENTS ON RESTRICTED PART

Comment 1:

<…>

Assessor's comments of ASMF/DMF Holder's response:

<…>

Comment 2:

<…>

Assessor's comments of ASMF/DMF Holder's response:

APPENDIX 1 - Final Active/drug substance specification, Re-test period, and Storage conditions accepted by the Regulatory Agency

Active/drug substance specification:

Re-test period (or Shelf-life, as appropriate) and Storage conditions: