IPRP
International Pharmaceutical Regulators Programme

ASMF/DMF Quality Assessment Report (QAR)

QualityWorking Group for Generics (QWGG)

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
v 2.0	Revision	Quality WG	June 7, 2017
V 2.1	Change to QWGG	QWGG	Sep 20, 2018

Disclaimer

This document reflects the views of subject matter experts participating in the IPRP Quality Working Group for Generics (QWGG) and should not be construed to represent the official views of any given regulatory authority participating in the IPRP.

Foreword

In order to achieve the QWGG's objective to promote collaboration and convergence in the area of generic drug regulation, the QWGG has developed a series of reference documents covering a number of technical and procedural aspects of assessment.

These documents were developed among participating QWGG members and observers as model documents. These QWGG documents have been made available for use by any interested party.

The implementation of these documents by a given QWGG member or observer, either as a whole or in part, is not mandatory. Each QWGG member or observer 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 QWGG member or observer may for practical reasons choose to revise the format or written language of a model document.

ASMF/DMF
Quality Assessment Report

Version 2.0 (dated: 2017-06-07)

ADMINISTRATIVE INFORMATION

Regulatory Agency/Organisation:	
ASMF/DMF Reference Number:	
Active Pharmaceutical Ingredient (API) Name: *(INN, salts/counter ion, solvated state)*	
Applicant's Part version number and date:	Version: XX, dated: YYYY-MM-DD
Restricted Part version number and date:	Version: XX, dated: YYYY-MM-DD
ASMF/DMF Holder: *Company Name:* *Contact Person:* *Corporate Address:* *Phone:* *Fax:* *Email:*	
Contact person for the ASMF/DMF (if different than the ASMF/DMF Holder): *Company Name:* *Contact Person:* *Address:* *Phone:* *Fax:* *Email:*	
API Manufacturer(s) and manufacturing site(s): *Manufacturer's name:* *Site address:*	

This ASMF/DMF is being assessed in conjunction with an application with the following characteristics:

Maximum daily dose (MDD) for the drug product:	>2 g/day OR <2g/day
Dosage form:	
Route(s) of administration:	
Target patient population(s):	neonates/infants/children, adults
API manufactured as sterile or non-sterile?	☐ Sterile, ☐ Non-sterile
Other:	

Appendices:	1. Final Active/drug substance specification, Re-test period (or Shelf-life, if appropriate), and Storage conditions accepted by the Regulatory Agency *(to be appended only when the information is considered acceptable by the Regulatory Agency)*

REGIONAL INFORMATION (to be amended, as needed)

Assessment history of this ASMF/DMF:	This ASMF/DMF <has/has not> been previously assessed. It <was/was not> found to be acceptable in connection with an application with the above characteristics (e.g., MDD, route of administration). This ASMF/DMF was previously assessed and a List of Questions (LOQ) was sent to the ASMF/DMF Holder on <date>. This report includes the original assessment and an assessment of the ASMF/DMF Holder's responses to the LOQ.
International regulatory information and the status of this ASMF/DMF (e.g., foreign assessment reports):	<discuss, if available>

Recommendation:	This version of the ASMF/DMF **<is/is not>** considered acceptable to support the proposed application with the characteristics above.
Date of ASMF/DMF Quality Assessment Report:	2017-MM-DD (specify: Original QAR, QAR of Responses to LOQ)

Declarations:

Materials of risk of transmitting BSE/TSE agents:

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

QUALITY ASSESSOR'S INTRODUCTION

Summary of available literature references on the active/drug substance:

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

Other introductory information:

MODULE 3 – QUALITY

APPLICANT'S PART (AP) of the ASMF/DMF

ORIGINAL ASSESSMENT (AP)

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:	

3.2.S.2 Manufacture

3.2.S.2.1 Manufacturer(s)

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

Name and Address	Responsibility
	manufacturing
	sterilisation
	testing

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

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

It has been confirmed by the Assessor that the flow diagram 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) including a brief summary of results and conclusion:

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)	Acceptance Criteria (if applicable)

Applicable thresholds for drug-related impurities as per ICH Q3A guideline:

Maximum daily dose (mg/day):	
Identification Threshold:	
Qualification Threshold:	

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)	Acceptance Criteria (if applicable)

Discussion of potential mutagenic impurities:

Note: The justification for the proposed acceptance criteria for the drug-related and process-related impurities (and mutagenic impurities, if applicable) is discussed in 3.2.S.4.5.

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) (e.g., HPLC/House/ver. 1.0)	Acceptance Criteria

3.2.S.4.2 Analytical procedures

Discussion of in-house analytical procedures (e.g., analytical conditions, methods of quantification, 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

Summary of batch analyses results and conformance to proposed specifications:

3.2.S.4.5 Justification of specification

Discussion on the justification and acceptability of the proposed specification and the claimed standard (e.g., including the tests that are omitted or not routinely performed and the controls for impurities, polymorphs, particle size distribution, as applicable):

3.2.S.5 Reference Standards or Materials

Source of reference standards or reference materials (e.g., in-house, USP, BP, Ph.Eur.) for drug substance and impurity(ies):

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

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

3.2.S.6 Container Closure System

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

Discussion of the suitability of the container closure system (e.g., choice of materials, protection from moisture and light, compatibility of the materials of construction with the drug substance):

3.2.S.7 Stability

3.2.S.7.1 Stability summary and conclusions

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 described in 3.2.S.6

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

Discussion of the stability-indicating ability of the applicable analytical procedures(s) (e.g., observance of mass balance):

Proposed re-test period (or shelf-life, as appropriate) and storage conditions: XX months

The proposed re-test period and storage conditions <are/are not> supported by the stability data.

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

Summary of post-approval stability protocol and stability commitment:

3.2.S.7.3 Stability data

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 acceptance criteria as described in 3.2.S.4.1. 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 to be stability indicating. The container closure system <simulates/does not simulate> that described in section 3.2.S.6.

Overall Conclusions on the Applicant's Part of the ASMF/DMF:

<Include a brief summary of the main conclusions>

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

<Collate the LOQ on the Applicant's Part>

ASSESSMENT OF RESPONSES TO THE LIST OF QUESTIONS ON THE APPLICANT'S PART OF THE ASMF/DMF

For LOQ dated 2017-MM-DD:

<Include for assessment of responses to the LOQ. Delete this section if not applicable>

Question 1:

<…>

Summary of the ASMF/DMF Holder's Response:

<…>

Assessment of the ASMF/DMF Holder's Response and Conclusion:

<…>

Confidential

NB: THIS SECTION SHOULD NOT BE DISCLOSED TO THE APPLICANT

RESTRICTED PART (RP) of the ASMF/DMF

[NB: This section 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.]

ORIGINAL ASSESSMENT (RP)

3.2.S.2 Manufacture

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

Summary and discussion on the detailed manufacturing process and process controls:

This summary should include a flow diagram of the synthetic process(es), short summary of the narrative of the manufacturing process and process controls, other manufacturing procedures (if any, e.g., alternative processes, reprocessing, recovery, blending of batches), proposed production scale batch size(s)).

Discussion of milling or micronization details (e.g., operating principles and controls), when particle size distribution is a critical quality attribute:

3.2.S.2.3 Control of materials

Summary and discussion of the acceptability of the declared API starting material(s):

This summary should include the name, chemical structure, name and address of manufacturer(s), flow diagram of the synthetic route, specification, analytical methods (provided/not provided), justification of the API starting material.

Other materials (e.g., raw materials, reagents, catalysts, solvents):

Discussion on the quality and control of materials used in the manufacture of the drug substance (e.g., API starting material(s), raw materials, solvents (including those solvents known to be potentially contaminated with ICH Class 1 solvents such as benzene), reagents, catalysts):

3.2.S.2.4 Control of critical steps and intermediates

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

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

3.2.S.2.5 Process validation and/or evaluation

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

3.2.S.2.6 Manufacturing process development

Discussion on significant changes (if any) made to the manufacturing process and/or manufacturing site of the drug substance used in the bioavailability, clinical, scale up and production batches:

Discussion of manufacturing process development to support a design space and/or real time release (if proposed):

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):

3.2.S.4 Control of the Drug Substance

3.2.S.4.5 Justification of specification

Discussion on justification that has not been previously discussed in the assessment of the Applicant's Part of the ASMF/DMF (e.g., impurities not disclosed or discussed in the Applicant's Part):

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

Overall Conclusions on the Restricted Part of the ASMF/DMF:

<Include a brief summary of the main conclusions>

List of Questions (LOQ) on the Restricted Part of the ASMF/DMF:

<Collate the LOQ on the Restricted Part>

ASSESSMENT OF RESPONSES TO THE LIST OF QUESTIONS ON THE RESTRICTED PART OF THE ASMF/DMF

For LOQ dated 2017-MM-DD:

<Include for assessment of responses to the LOQ. Delete this section if not applicable>

Question 1:

<…>

Summary of the ASMF/DMF Holder's Response:

<…>

Assessment of the ASMF/DMF Holder's Response and Conclusion:

<…>

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:

Container Closure System	Storage Conditions	Re-test Period (or Shelf-life, as appropriate)