IGDRP
International Generic Drug Regulators Programme

# ASMF/DMF Quality Assessment Report (QAR)

## ASMF/DMF Working Group

**Version 1.0 – May 26, 2015**

| Version | Description of Change | Author | Effective Date |
|---|---|---|---|
| v 1.0 | Original publication | ASMF/DMF WG | May 26, 2015 |

# ASMF/DMF
# Quality Assessment Report

*Version 1.0 (final, 2015-05-26)*

| ADMINISTRATIVE INFORMATION |
|---|

| | |
|---|---|
| Regulatory Agency: | |
| National ASMF/DMF Reference Number: | |
| Active Pharmaceutical Ingredient (API) Name:<br>*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:<br>*Company Name*<br>*Corporate Address*<br>*Phone*<br>*Fax*<br>*Email* | |
| Contact person for the ASMF/DMF:<br>*Name*<br>*Company Name*<br>*Address*<br>*Phone*<br>*Fax*<br>*Email* | |
| API Manufacturer(s) and manufacturing site(s):<br>*Manufacturer's name*<br>*Site address*<br>*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:<br>*Drug product name*<br>*Dosage form*<br>*Application reference number*<br>*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:<br>- Repeatability<br>- 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:**