IPRP
International Pharmaceutical Regulators Programme

Quality Assessment Report (QAR) – Full Dossier template

Quality Working Group (QWG)

Version	Description of Change	Author	Effective Date
v 1.0	Original publication		2021-06-07

Disclaimer

This document reflects the views of subject matter experts participating in the IPRP Quality Working Group (QWG) 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 QWG's objective to promote collaboration and convergence in the area of drug regulation, the QWG has developed a series of reference documents covering a number of technical and procedural aspects of assessment.

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

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

Quality Assessment Report (QAR)
Full Dossier

Version 1.0 (dated: 2021-06-07)

1 APPLICATION INFORMATION

Application Information	
Brand (Trade) Name of Drug Product:	
Non-proprietary Name of Drug Product:	
Non-proprietary Name of Drug Substance (INN or modified INN):	
Name of Applicant:	
Therapeutic Classification (ATC Code):	
Dosage Form(s):	
Strength(s):	
Route(s) of Administration:	
Maximum Daily Dose (MDD) for the Drug Product:	
Applicant's Contact Information:	[Contact's Name] [Position Title] [Company Name] [Email Address]
Regional Regulatory Information	
Application Reference Number:	
Assessor's Recommendation:	This application Choose IS/IS NOT considered to be acceptable from a Quality perspective.
Date of Assessment Report:	
Appendices:	1. Final active/drug substance specification, re-test period (or shelf-life, if appropriate), and storage conditions 2. Final medicinal/drug product specification, shelf-life, and storage conditions

Note(s) to Programme Areas	
Clinical Division	
Labelling Division	

Project/Case Management	
Inspection/Compliance Programme	

Information on the Reference Product (i.e., for a generic drug product application)	
Brand Name of the Reference Product:	
Dosage Form(s):	
Strength(s):	
Marketing Authorisation Holder's Name:	
Country source of Reference Product Used in Bioequivalence Study(ies):	
Strength(s) Used in Bioequivalence Study(ies):	

2 ASSESSMENT OF THE APPLICATION

L Labelling

Assessment of the Quality information in the labelling (e.g., product labelling, prescribing information):

Labelling Section	Assessment/Discussion

S Drug Substance – Enter the international non-proprietary name of the drug substance

Indicate the approach used by the applicant for providing information on the drug substance:

Approach for providing information on the drug substance	Details
Choose an item.	Choose an item.

CERTIFICATE OF SUITABILITY (CEP) ASSESSMENT <delete this section if no CEP is provided>

The API is:

☐ not a polymeric complex and
☐ not an API that could be contaminated by adventitious agent(s) of human or animal origin.

Manufacturer (CEP holder): Click to enter text.

Manufacturing Site: Click to enter text.

1	Is CEP current & valid?	☐ Yes ☐ No
2	Is CEP information complete?	☐ Yes ☐ No
3	Use of animal sourced material declared in manufacturing covered by CEP?	☐ Yes ☐ No

Discuss any additional data that has been assessed in relation to the CEP:

CONCLUSION

☐ CEP is Acceptable

☐ CEP is Not Acceptable

S.4 Control of the Drug Substance

S.4.1 Specification

<include a summary of the currently proposed drug substance specifications from the drug product manufacturer>

Discussion on the acceptability of the proposed specification and claimed standard:

Discussion on how the drug substance is controlled by the drug product manufacturer:

Summary of risk assessment and discussion on the potential presence of Nitrosamine impurities, taking into consideration the manufacturing process and controls for the drug substance and the potential for degradation:

S.4.2 Analytical Procedures and (S.4.3) Validation of Analytical Procedures

<Complete the following table for any analytical methods that have not been previously assessed. Add additional columns as required. Delete the table if all methods have been reviewed as part of the CEP.>

Analytical Procedure	Insert Method Description or "N/A"
Method Type:	
Routine System Suitability Tests and Acceptance criteria	
Specificity	
Linearity	
Accuracy	
Precision:	
- Repeatability	
- Intermediate precision	
Range (specify)	
Detection limit (specify)	
Quantitation limit (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
<include any discussion below the table>

S.5 Reference Standards or Materials

Source of reference standards or reference materials for drug substance and impurity(ies):

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

S.7 Stability

S.7.1 Stability summary and conclusions

<include a summary of the currently proposed re-test period (or shelf life), container closure system, and storage conditions>

Container Closure System	Storage Conditions	Retest period

ASMF/DMF ASSESSMENT <delete this section if no ASMF/DMF is referenced>

Manufacturer (ASMF/DMF holder): Click to enter text.

Manufacturing Site: Site name and address from Section S.2.1 of Module 3 of the application and confirmed in the ASMF

Discussion:

<provide a brief summary of the status of the assessment of the ASMF/DMF at the time of initial assessment >

CONCLUSION

☐ ASMF/DMF is Acceptable at the time of initial assessment

☐ ASMF/DMF is Not Acceptable at the time of initial assessment

S.4 Control of the Drug Substance

S.4.1 Specification

<include a summary of the currently proposed drug substance specifications from the drug product manufacturer>

Discussion on the acceptability of the proposed specification and claimed standard:

Discussion on how the drug substance is controlled by the drug product manufacturer:

Summary of risk assessment and discussion on the potential presence of Nitrosamine impurities, taking into consideration the manufacturing process and controls for the drug substance and the potential for degradation:

S.4.2 Analytical Procedures and (S.4.3) Validation of Analytical Procedures

<Complete the following table for any analytical methods that have not been previously assessed (e.g., in the assessment of the ASMF/DMF). Add additional columns as required. Delete the table if all methods have been reviewed as part of the ASMF/DMF and cross-referenced to the ASMF/DMF.>

Analytical Procedure	Insert Method Description or "N/A"
Method Type:	
Routine System Suitability Tests and Acceptance criteria	
Specificity	
Linearity	
Accuracy	
Precision:	
- Repeatability	
- Intermediate precision	

Range (specify)	
Detection limit (specify)	
Quantitation limit (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
<include any discussion below the table>

S.5 Reference Standards or Materials

Source of reference standards or reference materials for drug substance and impurity(ies):

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

S.7 Stability

S.7.1 Stability summary and conclusions

<include a summary of the currently proposed re-test period (or shelf life), container closure system, and storage conditions>

Container Closure System	Storage Conditions	Retest period

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

<Only complete the table if stability is reviewed as part of the drug application (i.e., the checkbox below is NOT checked). Otherwise, delete the table.>

Test	Acceptance criteria	Pertinent stability results	Discussion

☐ N/A (the re-test period is supported by the referenced ASMF/DMF)

Discussion regarding the impact of processing not covered by the ASMF/DMF on drug substance stability (e.g., stability data for the micronized drug substance):

The proposed re-test period and storage conditions <are/are not> considered acceptable at this time.

FULL API ASSESSMENT <delete this section if an ASMF/DMF or CEP is referenced>

S.1 General Information

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:	

S.1.2 Structure

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

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:	

S.2 Manufacture

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>

S.2.2 Description of manufacturing process and process controls

Flow diagram of the synthetic process(es) (if lengthy, include as an appendix):

<It has been confirmed by the Assessor that the flow diagram of the synthetic process provided in the application contains sufficient information.>

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, critical process steps 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:

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):

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:

S.2.5 Process validation and/or evaluation

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

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):

S.3 Characterisation

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):

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)
<Ethanol>	<Class 3/NMT 5000>				
<Diethyl ether>	<Class 3/NMT 5000>				
<Acetone>	<Class 3/NMT 5000>				
<Ethyl acetate>	<Class 3/NMT 5000>				
<Isopropanol>	<Class 3/NMT 5000>				
<Methanol>	<Class 2 /NMT 3000>				
<Acetonitrile>	<Class 2/NMT 410>				
<Dichloromethane>	<Class 2/NMT 600>				
<Tetrahydrofuran>	<Class 2/NMT 720>				
<Toluene>	<Class 2/NMT 890>				
<Benzene>	<Class 1/NMT 2 >				
<delete or insert impurities as necessary>					

Discussion of potential mutagenic impurities and control strategy applied as per ICH M7 (including a summary of risk assessment for the potential presence of Nitrosamine impurities taking into consideration the manufacturing process and controls for the drug substance and the potential for degradation):

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.

S.4 Control of the Drug Substance

S.4.1 Specification

<include a summary of the currently proposed drug specifications from the drug product manufacturer>

Discussion on the acceptability of the proposed specification and claimed standard:

Discussion on how the drug substance is controlled by the drug product manufacturer:

S.4.2 Analytical Procedures and (S.4.3) Validation of Analytical Procedures

<add additional columns as required>

Analytical Procedure	Insert Method Description or "N/A"
Method Type:	
Routine System Suitability Tests and Acceptance criteria	
Specificity	
Linearity	
Accuracy	
Precision:	
- Repeatability	
- Intermediate precision	
Range (specify)	
Detection limit (specify)	
Quantitation limit (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
<include any discussion below the table>

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:

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):

S.5 Reference Standards or Materials

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

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

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 and in view of the API stability results):

S.7 Stability

S.7.1 Stability summary and conclusions

<include a summary of the currently proposed re-test period (or shelf life), container closure system, and storage conditions from Module 3>

Container Closure System	Storage Conditions	Retest period

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

Test	Acceptance criteria	Pertinent stability results	Discussion

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):

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

S.7.2 Post-approval stability protocol and stability commitment

Summary of post-approval stability protocol and stability commitment:

S.7.3 Stability data

P Drug Product

P.1 Description and Composition of the Drug Product

Description of the dosage form:

Composition of the dosage form:

<include a summary of the currently proposed formulation>

Type of container and closure used for the dosage form and accompanying reconstitution diluent, if applicable:

P.2 Pharmaceutical Development

P.2.1 Components of the Drug Product

P.2.1.1 Drug Substance

Discussion of the chemical form of the drug substance/active pharmaceutical ingredient, the form of the active substance in the proposed drug product, and the form for the active moiety:

Discussion of the relevant physicochemical characteristics of the drug substance:

Discussion on the compatibility of the drug substance with excipients listed in 3.2.P.1:

P.2.1.2 Excipients

Discussion on the critical functionality and acceptability of the choice of excipients:

P.2.2 Drug Product

Summary and discussion on Formulation Development:

P.2.3 Manufacturing Process Development

Summary and discussion on Manufacturing Process Development:

P.2.4 Container Closure System

Brief description of the container closure system (CCS):

Discussion of any compatibility, qualification, or performance studies for the CCS:

P.2.5 Microbiological Attributes

Brief summary and discussion of the microbiological control strategy and microbial testing:

P.2.6 Compatibility

Discussion of any compatibility studies (e.g., to support in-use periods with reconstitution diluents, co-administered drugs):

P.3 Manufacture

P.3.1 Manufacturer(s)

Name, address, and responsibility of each manufacturer:

<include a summary from section P.3.1>

P.3.2 Batch Formula

List of all components of the dosage form to be used in the manufacturing process and their amounts on a per batch basis:

<include a summary from section P.3.2>

P.3.3 Description of Manufacturing Process and Process Controls

Flow diagram and/or narrative description of the manufacturing process:

<include a summary from section P.3.3>

Discussion of the critical manufacturing process(es) and significant findings:

P.3.4 Controls of Critical Steps and Intermediates

Summary and discussion of controls performed at the critical steps and data used to support controls:

<include a summary from section P.3.4>

P.3.5 Process Validation and/or Evaluation

Summary and discussion of the process validation studies and/or process validation protocols:

P.4 Control of Excipients

Discussion regarding the control of excipients:

P.5 Control of Drug Product

P.5.1 Specification(s)

<include a summary of the currently proposed specifications>

P.5.2 Analytical Procedures and P.5.3 Validation of Analytical Procedures

<Complete the following table for analytical methods. Add additional columns as required.>

Analytical Procedure	Insert Method Description or "N/A"
Method Type:	
Routine System Suitability Tests and Acceptance criteria	
Specificity	
Linearity	
Accuracy	
Precision:	
- Repeatability	
- Intermediate precision	
Range (specify)	
Detection limit (specify)	
Quantitation limit (specify)	
Robustness	
Solution stability	
Other (specify and discuss)	

+ 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

P.5.4 Batch Analyses

Discussion on batch size, relevant results and notable observations:

P.5.5 Characterization of Impurities

Discussion of data for additional specified impurities in the drug product and not present in the drug substance:

Discussion of potential mutagenic impurities (including a summary of risk assessment for the potential presence of Nitrosamine impurities taking into consideration the manufacturing process and controls for the drug product, the excipients, the container closure system and the potential for degradation):

Discussion of the ICH Q3D risk assessment:

P.5.6 Justification of Specification

Discussion on the justification and acceptability of the proposed specification and the claimed standard

P.6 Reference Standards

Discussion of reference standards:

P.7 Container Closure System

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

Discussion of the specifications for the container closure system((s):

P.8 Stability

P.8.1 Stability Summary and Conclusions

Summary of batches placed on stability:

Batch Information (number of batches of each strength, batch size)	**Container Closure**	**Duration of Study and Storage Conditions**

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

Discussion of stress testing studies conducted:

Discussion of the stability-indicating ability of the applicable analytical procedures(s):

Proposed shelf-life and storage conditions:

Container Closure System	**Storage Conditions**	**Shelf-life**

This shelf-life <is supported/is not supported> by the stability data.

P.8.2 Post-Approval Stability Protocol and Stability Commitment

Discussion of post-approval stability protocol and stability commitment:

P.8.3 Stability Data

Stability data summary:

Test and Specification	Pertinent Results - Accelerated	Pertinent Results – Long-term	Notable Observations (e.g., trends and OOS results)

Discussion of key stability data and trends:

Discussion of the stability specification, analytical methods, container closure system used during the stability studies:

R Regional Information

R.1 <summary of any Regional Information>

<details>:

3 OVERALL CONCLUSIONS AND LIST OF QUESTIONS

< collate list of questions>

<Major Objections:>

1. <Level 1>
    a. <Level 2>
        i. <Level 3>
        ii. <etc.>

<Other Concerns:>

2. <Level 1>
    a. <Level 2>
        i. <Level 3>
        ii. <etc.>

4 ASSSESSMENT TO THE RESPONSES TO THE LIST OF QUESTIONS

For the list of questions issued on choose date:

Question 1:

1. <…>

Summary of Applicant's Response:

<…>

Assessment of the Applicant's Response and Conclusion:

<…>

Question 2:

2. <…>

Summary of Applicant's Response:

<…>

Assessment of the Applicant's Response and Conclusion:

<…>

For the list of questions issued on choose date:

Question 1:

1. <…>

Summary of Applicant's Response:

<…>

Assessment of the Applicant's Response and Conclusion:

<…>

Question 2:

2. <…>

Summary of Applicant's Response:

<…>

Assessment of the Applicant's Response and Conclusion:

<…>

5 APPENDICES

<Include a copy of the final specifications when recommending authorisation.>

APPENDIX 1 - Final Active/drug substance specification, re-test period (or shelf-life), and storage conditions authorized by the Regulatory Agency

Final active/drug substance specification:

Re-test period (or shelf-life, as appropriate) and storage conditions:

APPENDIX 2 - Final medicinal/drug product specification, shelf-life, and storage conditions authorized by the Regulatory Agency

Final medicinal/drug product specification:

Shelf-life and storage conditions: