# **QUALITY OVERALL SUMMARY**

Reference: EDQM guideline PA/PH/CEP (04) 1 (as revised) Content of the dossier for chemical purity and microbiological quality

Substance name	
Monograph n°	
Subtitle (if any)	
Intended Holder of the CEP	
Written by	
Qualification*	
Date	

(\*): APPEND CV OF THE EXPERT

#### 2.3.S SUBSTANCE

# 2.3.S.1 General Information

Use of the substance: Route(s) of administration, maximum daily dose.

<u>Commercialisation history:</u> Summarise the history based on the table in the application form).

#### 2.3.S.1.1 Nomenclature

- (a) Recommended International Non-proprietary name (INN):
- (b) Chemical name(s):
- (c) Company or laboratory code:
- (d) Other non-proprietary name(s) (e.g., national name, USAN, BAN etc.):
- (e) CAS No., Molecular Formula, MW:

# 2.3.S.1.3 General Properties

Give summarised data on:

- (a) Physical description (e.g., appearance, colour, physical state...).
- (b) Physical form (e.g., polymorphic form, solvate, hydrate): to be commented especially if requested as grade.
- (c) Solubility and other properties as necessary.
- (d) Particle size: e.g. "non-micronised", "micronised" or any grade claimed as subtitle.

# 2.3.S.2 Manufacture

# 2.3.S.2.1 Manufacturer(s) (name, manufacturer) and sites involved in the entire process

Give the name, address and responsibility of each manufacturer, including contractors, intermediate manufacturers and other proposed production sites or facilities involved in process.

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

- (a) Give a brief narrative step-by-step description of the manufacturing process(es) and provide reference to detailed description in the documentation. Confirm the maximum batch size.
- (b) If applicable summarise alternate processes and give a short explanation of their use.
- (c) Comment shortly on recovery of materials (solvents, reagents, and mother liquor), on any reprocessing steps and give a brief justification.

# 2.3.S.2.3 Control of Materials

# I) Starting material(s)

Provide the name and address of each manufacturer / supplier and the routes of syntheses for each starting material and summarise differences between routes if more than one manufacturer/supplier is used for each starting material. Summarise the specification (including impurities profile) including their justification based on studies of carry-over.

NB: If starting material is obtained by fermentation or is from herbal origin, summarise the information related to the nature of this material.

#### II) Reagents and solvents

Summarise the quality and controls of the materials (e.g., raw materials, solvents pure and/or recovered, reagents, catalysts) used in the manufacture of the final substance.

# 2.3.S.2.4 Controls of Critical Steps and Intermediates

Summarise the controls performed at critical steps of the manufacturing process and on intermediates, compare analytical procedures used for intermediates and final substance.

#### 2.3.S.2.5 Process Validation and/or Evaluation

For aseptic processing and sterilization only give the summary of process validation and/or evaluation studies.

# 2.3.S.3 Characterisation

# 2.3.S.3.2 Impurities

- (I) Related substances
- (a) Fill in the following table identifying related substances, their origin and distinguishing between potential and actual impurities and comparing with impurity section of the monograph:

Chemical	PhEur	Applicant's	PhEur	Origin	Levels	LOD	LOQ
name	impurity	specifications	specifications		found	of the	of the
						method	method

- (b) Justify the specification based on data observed for impurities in relevant batches.
- (c) Discuss briefly about the <u>suitability of the monograph</u> to control the potential inhouse impurities present in the substance (starting materials, intermediates, byproducts, etc.).
- (d) Genotoxic impurities: Give a brief discussion on potential genotoxic or mutagenic impurities following current EU guidance.
- II. Residual solvents/metal impurities/reagents etc.
- (a) Discuss briefly the control of residual solvents and fill in the following table:

Solvent	Used in	Applicant's	ICH class /	Levels	LOD of	LOQ of
	step	limit	limit	(ppm)	the	the
	x/y				method	method

- (b) Discuss briefly the basis for setting the specification for non-ICH solvents.
- (c) Discuss briefly the control of metal (elemental) impurities following current EU guidance and fill in the following table:

Elemental	Used	Applicant's	ICH/EMA	Levels	LOD of	LOQ of
impurity/Metal	in step	limit	class / limit	(ppm)	the	the
	x/y				method	method

(d) Discuss briefly control of residual reagents of the process.

# 2.3.S.4 Control of the Substance

# 2.3.S.4.1 Specification

Give a table summarising the proposed specifications.

## 2.3.S.4.2 Analytical Procedures

Summarise the analytical procedures.

## 2.3.S.4.3 Validation of Analytical Procedures

Give the summary of the validation information for any in-house tests and compare briefly with the method(s) described in the monograph (cross validation).

# 2.3.S.4.4 Batch Analyses

- (a) Give a short description of the batches: Batch Number Batch Size Date and Site of Production.
- (b) Summarise the results for relevant batches (according to specifications and showing equivalence of any alternative supplier, process etc.).

## 2.3.S.4.5 Justification of Specification

Justify the substance specification, especially for additional impurities that cannot be controlled by the tests of the monograph.

#### 2.3.S.5 Reference Standards or Materials

- (a) Give the source of primary reference standards or reference materials (e.g. Ph. Eur.) for the final substance and its impurities where relevant.
- (b) Summarise characterization and evaluation of in-house standards.

#### 2.3.S.6 Container Closure System

- (a) Describe shortly the container closure system(s) for the storage and shipment of the substance (i.e. in a clear and understandable manner).
- (b) Summarise the specification for each component (description + identification).
- (c) Summarise the declarations of compliance of packaging materials to current EU regulations/directives and appropriate Ph.Eur monographs.

# 2.3.S.7 Stability

State if a re-test period is claimed for the substance and storage recommendations if any:

# 2.3.S.7.1 Stability Summary and Conclusions

- (a) Summarise accelerated <u>AND</u> long term testing (e.g., studies conducted, protocols used, results obtained).
- (b) Justify the re-test period claimed based on data available.
- 2.3.S.7.2 Post-approval Stability Protocol and Stability Commitment Give the stability protocol for commitment batches.