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.*

Commercialisation history: *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 name	*PhEur impurity*	*Applicant's specifications*	*PhEur specifications*	*Origin*	*Levels found*	*LOD of the method*	*LOQ of the method*

(b) Justify the specification based on data observed for impurities in relevant batches.

(c) Discuss briefly about the suitability of the monograph to control the potential in-house impurities present in the substance (starting materials, intermediates, by-products, 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 step x/y*	*Applicant's limit*	*ICH class / limit*	*Levels (ppm)*	*LOD of the method*	*LOQ of the 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 impurity/Metal	*Used in step x/y*	*Applicant's limit*	*ICH/EMA class / limit*	*Levels (ppm)*	*LOD of the method*	*LOQ of the 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 AND 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.