Health Canada Santé Canada

QUALITY OVERALL SUMMARY - CHEMICAL ENTITIES
(Applications for Drug Identification Number Submissions)
(QOS-CE (DINA))

(version: 2004-04-01)

FOREWORD

The *Quality Overall Summary (QOS)* is a summary of the Quality Body of Data. This *QOS-CE (DINA)* template can be used by sponsors to summarize the Quality information for Applications for Drug Identification Number Submissions (DINAs) containing drug substances and their corresponding products of synthetic or semi-synthetic origin that are filed with Health Canada pursuant to Part C, Division 1 (C.01.014) of the *Food and Drug Regulations*, that are not subject to Part C, Division 8 of the *Regulations*. This would exclude submissions for Biotechnological/Biological (Schedule D) and Radiopharmaceutical (Schedule C) drugs.

Complete those sections and fields that apply. It is understood that certain sections and fields may not apply and should be indicated as such by reporting "Not applicable" in the appropriate area with an *accompanying explanatory note*. The use of tables to summarize the information is encouraged, where possible. The tables included in this template may need to be expanded, as necessary. These tables are included as illustrative examples of how to summarize information. Other approaches to summarize the information can be used if they fulfill the same purpose. If scanned images are incorporated into the document (e.g., synthetic schemes, molecular structures), sponsors should ensure that a low resolution is used to avoid files that are excessively large. Sponsors should consult the relevant Health Canada guidance documents for further details (e.g., *Quality Guidance: Applications for Drug Identification Number Submissions (DINAs) for Pharmaceuticals*).

It is acknowledged that the numbering of the sections may not entirely be sequential. Those sections that do not apply to DINAs have been removed (e.g., *S.5 Reference Standards or Materials*) and the remaining sections have retained their numbering to be consistent with submissions and guidance documents in other stages of drug development (e.g., New Drug Submissions, Abbreviated New Drug Submissions).

When completing the QOS-CE (DINA) template, this covering *Foreword* should be deleted.

QUALITY OVERALL SUMMARY (QOS)

INTRODUCTION

(a) Summary of product information:

Proprietary (Brand) Name of Drug Product	
Non-proprietary or Common Name of Drug Product	
Non-proprietary or Common Name of Drug Substance (Medicinal Ingredient)	
Company (Manufacturer/Sponsor) Name	
Dosage Form	
Strength	
Route of Administration	
Proposed Indication(s)	

(b) Other Introductory information:

S DRUG SUBSTANCE (NAME, MANUFACTURER)

S.2 Manufacture (name, manufacturer)

S.2.1 Manufacturer(s) (name, manufacturer)

(a) Name, address, and responsibility of each manufacturer, including contractors, and each proposed production site or facility involved in manufacturing and testing:

(b) List of referenced Drug Master Files (DMFs) and DMF Numbers:

S.2.3 Control of Materials (name, manufacturer)

(a) For drug substances or drug substance manufactured with reagents obtained from sources that are at risk of transmitting Bovine Spongiform Encephalopathy (BSE)/Transmissible Spongiform Encephalopathy (TSE) agents (e.g., ruminant origin), a letter of attestation (with supporting documentation) should be provided confirming that the material is not from a BSE/TSE affected country/area. A copy of the letter may be found in:

S.2.5 Process Validation and/or Evaluation (name, manufacturer)

(a) Description of process validation and/or evaluation studies (e.g., for aseptic processing and sterilization):

S.4 Control of the Drug Substance (name, manufacturer)

S.4.1 Specification (name, manufacturer)

(a) Standard claimed (e.g., Professed, House, USP, BP, Ph.Eur.):

(b) Specification for the drug substance (*complete either (i) or (ii)*):

(i) For drug substances claiming Schedule B compendial standard, provide attestation that the specification for the drug substance complies with the above stated Schedule B monograph:

(ii) For drug substances not claiming a Schedule B compendial standard, or for specifications that include supplementary tests to the Schedule B monograph, provide a summary of the specification:

Specification Reference Number and/or Version		
Test	**Acceptance Criteria**	**Analytical Procedure (Type/Source/Version)**

(c) For drug substances or drug substance manufactured with reagents obtained from sources that are at risk of transmitting Bovine Spongiform Encephalopathy (BSE)/Transmissible Spongiform Encephalopathy (TSE) agents (e.g., ruminant origin), a letter of attestation (with supporting documentation) should be provided confirming that the material is not from a BSE/TSE affected country/area. A copy of the letter may be found in:

S.4.2 Analytical Procedures (name, manufacturer)

(a) Summary of the non-compendial analytical procedures (e.g., key method parameters, conditions, system suitability testing):

S.4.3 Validation of Analytical Procedures (name, manufacturer)

(a) Summary of the validation information for non-compendial analytical procedures (e.g., validation parameters and results):

S.4.4 Batch Analyses (name, manufacturer)

(a) Copies of the certificates of analyses (e.g., by the manufacturer/supplier and by the company responsible for release testing) may be found in:

(b) Summary of results for relevant batches:

S.7 Stability (name, manufacturer)

S.7.1 Stability Summary and Conclusions (name, manufacturer)

(a) Confirmation that stability data in the proposed container closure system is available upon request:

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

P DRUG PRODUCT (NAME, DOSAGE FORM)

P.1 Description and Composition of the Drug Product (name, dosage form)

(a) Description of the dosage form:

(b) Composition of the dosage form:

(i) Composition, i.e., list of all components of the dosage form, and their amounts on a per unit basis (including overages, if any):

Component and Quality Standard (and Grade, if applicable)	Function	Strength (label claim)	
		Quantity per unit	%
Total			

(ii) Composition of all *components that are mixtures* (e.g., colourants, coatings, capsule shells, imprinting inks):

(c) Description of accompanying reconstitution diluent(s), if applicable:

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

P.2 Pharmaceutical Development (name, dosage form)

(a) For drug submissions containing *in vivo* studies (e.g., pivotal clinical, comparative bioequivalence), provide a discussion of any differences in the formulations and manufacturing process for the batches used in these studies and the formulation and manufacturing process described in P.3:

Use of Formulation	Summary of Differences

(b) For drug submissions containing comparative *in-vitro* studies (e.g., dissolution for solid oral products) and/or physicochemical testing (e.g., to support the absence of a comparative bioequivalence study for an aqueous solution subsequent entry product), provide a discussion of the results:

P.3 Manufacture (name, dosage form)

P.3.1 Manufacturer(s) (name, dosage form)

(a) Name, address, and responsibility of each manufacturer, including contractors, and each proposed production site or facility involved in manufacturing and testing:

(b) List of referenced Drug Master Files (DMFs) and DMF Numbers:

(c) Confirmation that all facilities involved in the production have a Good Manufacturing Practices (GMP) compliance rating and/or an Establishment License (EL):

(d) GMP and/or EL information can be found in:

P.3.2 Batch Formula (name, dosage form)

(a) List of all components of the dosage form to be used in the manufacturing process, and their amounts on a per batch basis (including overages, if any):

Strength (label claim)	
Master Production Document Reference Number and/or Version	
Batch Size(s) (number of dosage units)	
Component and Quality Standard (and Grade, if applicable)	**Quantity per batch**
Total	

P.3.3 Description of Manufacturing Process and Process Controls (name, dosage form)

(a) Narrative description of the manufacturing process, including equipment type and working capacity, process parameters:

(b) Reprocessing steps and justification, if applicable:

(c) Copies of the drug product master production documents for the proposed strength, each commercial batch size, and each manufacturing site may be found in:

(d) Copies of the executed production documents may be found in:

P.3.4 Controls of Critical Steps and Intermediates (name, dosage form)

(a) Summary of controls performed at the critical steps of the manufacturing process and on isolated intermediates:

P.3.5 Process Validation and/or Evaluation (name, dosage form)

(a) Summary of the process validation and/or evaluation studies conducted or a summary of the proposed validation protocol for the critical steps or critical assays used in the manufacturing process (e.g., description, results):

P.4 Control of Excipients (name, dosage form)

P.4.1 Specifications (name, dosage form)

(a) Summary of the specifications for non-compendial excipients and for compendial excipients which include supplementary tests not included in the monograph(s):

(b) Confirmation that none of the excipients which appear in the drug product are prohibited for use in drugs by the Canadian *Food and Drug Regulations*:

(c) List of referenced Drug Master Files (DMFs) and DMF Numbers:

P.4.2 Analytical Procedures (name, dosage form)

(a) Summary of the non-compendial analytical procedures:

P.4.3 Validation of Analytical Procedures (name, dosage form)

(a) Summary of the validation information for the non-compendial analytical procedures:

P.4.5 Excipients of Human or Animal Origin (name, dosage form)

(a) List of excipients that are of human or animal origin (including country of origin):

(b) Summary of the information (e.g., sources, specifications, description of the testing performed, viral safety data) regarding adventitious agents for excipients of human or animal origin:

(c) For excipients obtained from sources that are at risk of transmitting Bovine Spongiform Encephalopathy (BSE)/Transmissible Spongiform Encephalopathy (TSE) agents (e.g., ruminant origin), a letter of attestation (with supporting documentation) should be provided confirming that the material is not from a BSE/TSE affected country/area. A copy of the letter may be found in:

P.4.6 Novel Excipients (name, dosage form)

(a) Summary of the details on the manufacture, characterization, and controls, with cross references to supporting safety data (nonclinical and/or clinical) on novel excipients (i.e., those used for the first time in a drug product or by a new route of administration):

P.5 Control of Drug Product (name, dosage form)

P.5.1 Specification(s) (name, dosage form)

(a) Specification(s) for the drug product:

Standard Claimed (e.g., Professed, House, USP, BP)		
Specification Reference Number and/or Version		
Test	**Acceptance Criteria (release and stability)**	**Analytical Procedure (Type/Source/Version)**

P.5.2 Analytical Procedures (name, dosage form)

(a) Summary of the non-compendial analytical procedures (e.g., key method parameters, conditions, system suitability testing):

P.5.3 Validation of Analytical Procedures (name, dosage form)

(a) Summary of the validation information for non-compendial analytical procedures (e.g., validation parameters and results):

P.5.4 Batch Analyses (name, dosage form)

(a) Description of the batches:

Strength and Batch Number	Batch Size	Date and Site of Production	Use (e.g., nonclinical, clinical, comparative)

(b) Summary of results for relevant batches (e.g., nonclinical, clinical, comparative):

P.5.5 Characterisation of Impurities (name, dosage form)

(a) Identification of potential and actual impurities:

(i) List of drug-related impurities (e.g., degradation products), including chemical name, structure, and origin:

Drug-related Impurity (chemical name or descriptor)	Structure	Origin

(ii) List of process-related impurities (e.g., residual solvents, reagents), including compound name:

(b) Basis for setting the acceptance criteria for impurities:

(i) Maximum daily dose (i.e., the amount of drug substance administered per day), ICH Reporting/Identification/Qualification Thresholds for drug-related impurities, and Concentration Limits (ppm) for process-related impurities (e.g., residual solvents):

(ii) Data on observed impurities for relevant batches (e.g., nonclinical, clinical, and comparative):

Impurity (drug-related and process-related)	Acceptance Criteria	Results (include batch number and use) (e.g., nonclinical, clinical, comparative)		

(iii) Justification of proposed acceptance criteria for impurities:

P.7 Container Closure System (name, dosage form)

(a) Description of the container closure systems, including unit count or fill size, container size or volume:

(b) Materials of construction of each primary packaging component:

(c) Summary of specifications of each primary and functional secondary (e.g., foil pouches) packaging components:

(d) List of referenced Drug Master Files (DMFs) and DMF Numbers:

P.8 Stability (name, dosage form)

P.8.1 Stability Summary and Conclusions (name, dosage form)

(a) Summary of stress testing and results (e.g., photostability studies, cyclic studies for semi-solids, freeze-thaw studies):

(b) Summary of accelerated and long term testing (e.g., studies conducted, protocols used, results obtained):

(i) Description of stability study details:

Storage Conditions (°C, % RH, light)	Strength and Batch Number	Batch Size	Container Closure System	Completed (and Proposed) Test Intervals

(ii) Summary and discussion of stability study results:

(c) Proposed storage conditions and shelf life (and in-use storage conditions and in-use period, if applicable):

P.8.2 Post-approval Stability Protocol and Stability Commitment (name, dosage form)

(b) Stability protocol for continuing (i.e., ongoing) batches:

Protocol Parameter	Description
Storage conditions (including tolerances)	
Testing frequency	
Number of batches per strength and batch sizes	
Container closure system(s)	
Tests and acceptance criteria	
Other	

P.8.3 Stability Data (name, dosage form)

(a) The actual stability results (i.e., raw data) may be found in:

(b) Bracketing and matrixing design and justification for commitment and/or continuing (i.e., ongoing) batches, if applicable:

M MISCELLANEOUS

M.1 Labelling

(a) Copies of the container label(s) (and prescribing information or a package insert, where applicable) may be found in: