Health Canada Santé Canada

GUIDANCE DOCUMENT

Certified Product Information Document - Chemical Entities (CPID-CE)

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Health Products and Food Branch

Canada

Our mission is to help the people of Canada maintain and improve their health. *Health Canada*	The Health Products and Food Branch's (HPFB) mandate is to take an integrated approach to managing the health-related risks and benefits of health products and food by: • minimizing health risk factors to Canadians while maximizing the safety provided by the regulatory system for health products and food; and, • promoting conditions that enable Canadians to make healthy choices and providing information so that they can make informed decisions about their health. *Health Products and Food Branch*

Également disponible en français sous le titre : Ligne directrice sur le document certifié d'information sur les produits - Entités chimiques (DCIP-EC)

FOREWORD

Guidance documents are meant to provide assistance to industry and health care professionals on **how** to comply with governing statutes and regulations. Guidance documents also provide assistance to staff on how Health Canada's mandates and objectives should be implemented in a manner that is fair, consistent and effective.

Guidance documents are administrative instruments not having force of law and, as such, allow for flexibility in approach. Alternate approaches to the principles and practices described in this document ***may be*** acceptable provided they are supported by adequate justification. Alternate approaches should be discussed in advance with the relevant programme area to avoid the possible finding that applicable statutory or regulatory requirements have not been met.

As a corollary to the above, it is equally important to note that Health Canada reserves the right to request information or material, or define conditions not specifically described in this document, in order to allow the Department to adequately assess the safety, efficacy or quality of a therapeutic product. Health Canada is committed to ensuring that such requests are justifiable and that decisions are clearly documented.

This document should be read in conjunction with the accompanying notice and the relevant sections of other applicable guidance documents.

Document Change Log

Version	Certified Product Information Document- Chemical Entities (CPID-CE) Guidance Document (2017)	**Replaces**	Certified Product Information Document - Chemical Entities (CPID-CE) Guidance Document (draft, 2014)
Date	January 31, 2017	**Date**	August 31, 2016

Change	August 31, 2016
Nature of and/or Reason for Change	Document finalized. 1. Clarification of site activities to be recorded in CPID. 2. Addition of site for drug substance intermediate manufacture. 3. Guidance on the CCS description. 4. Editorial changes.
Change	February 5, 2016 Updated in content to reflect comments received during consultation
Nature of and/or Reason for Change	Changes in the content of this draft revision include updates to add tables to further guide the sponsor in the preparation of the CPID-CE and to include additional sections for drug substance information.

INTRODUCTION

The *CPID-CE* template should be completed to provide a condensed summary of the key Quality information for New Drug Submissions (NDSs) and Abbreviated New Drug Submissions (ANDSs) containing drug substances and their corresponding products of synthetic or semi-synthetic origin that are filed with Health Canada pursuant to Part C, Division 8 of the *Food and Drug Regulations.* This would exclude submissions for Biotechnological / Biological (Schedule D) and Radiopharmaceutical (Schedule C) drugs.

The CPID-CE constitutes part of the Notice of Compliance (NOC) package. The CPID-CE provides an accurate record of key quality information for the product proposed for marketing at the time the NOC is issued, and thereafter serves as an official reference document during the course of post-approval inspections and post-approval change evaluations as performed by Health Canada. The CPID-CE is a condensed version of the Quality Overall Summary and represents the final, agreed upon key data from the drug submission review [for example (e.g.), identification of the manufacturer(s), drug substance / drug product manufacturing process and controls and specifications, stability conclusions, commitments]. Refer to the Quality (Chemistry and Manufacturing): NDS and ANDSs guidance document for more information on the type of information required when completing this document.

The CPID-CE template is structured to permit the rapid assembly of the CPID-CE by copying requisite information from the corresponding portions of the Quality Overall Summary filed with the original drug submission. Tables can be modified as necessary. It is acknowledged that the numbering of the sections may not entirely be sequential. Those sections not considered necessary to be included in the CPID-CE have been removed (e.g. *2.3.S.5 Reference Standards or Materials*) and the remaining sections have retained their numbering to be consistent with original submission. No information on executed batches should be included in the CPID.

The CPID-CE should be submitted as a clean document in Word format at the time of filing. An individual CPID should include information on all strengths of a single dosage form. For different dosage forms a separate CPID can be provided for each dosage form or each dosage form can be described in different P sections within a single CPID.

For Supplements to New Drug Submissions (SNDSs), Supplements to Abbreviated New Drug Submissions (SANDSs), the CPID-CE should be completed *in its entirety* (regardless of the proposed change). It is acknowledged that when filing a Supplement to a (Abbreviated) New Drug Submission, the updated CPID-CE could include changes that did not require prior approval by Health Canada (e.g. Annual Notifications or Record of Changes). All changes made subsequent to the last Health Canada approved CPID should be annotated, and changes submitted in the SNDS or SANDS should be differentiated from those made as Annual Notification or a Record of Changes.

When the CPID-CE is provided as part of a Type I Master File (MF), the sections related to the drug product information can be deleted.

CERTIFIED PRODUCT INFORMATION DOCUMENT - CHEMICAL ENTITIES (CPID-CE)

SUMMARY OF PRODUCT INFORMATION

Brand Name of Drug Product	As per 3011 form. Insert same brand name into footer of this document.
Non-proprietary (Proper or common name) Name of Drug Product	The Proper name is the name of an applicable drug product monograph in the Schedule B Pharmacopeia. If there is no Schedule B monograph for a drug product, refer to Health Canada Labelling guidance for appropriate terminology of the common name of drug product and drug substance
Non-proprietary or Common Name of Drug Substance (Medicinal Ingredient)	Include the name of the input drug substance specifying salt and solvated forms.
Company (Manufacturer/Sponsor) Name	Insert manufacturer and sponsor (if different) name as per 3011 form
Dosage Form(s)	
Strength(s)	It should be clear whether strength is declared in terms of free acid/base, salt form, anhydrous and/or solvent-free basis (e.g. X mg Moxifloxacin (as Moxifloxacin Hydrochloride)
Route of Administration	
Proposed Indication(s)	

(a) Sponsor's Date of CPID:

(b) Administrative Summary: *(Health Canada use only)*

DocuBridge Identifier	
Control Number	
Internal Version and/or Date of Acceptance	

2.3.S DRUG SUBSTANCE (NAME, MANUFACTURER)

2.3.S.1 General Information

2.3.S.1.2 Structure

(a) Structural formula, including relative and absolute stereochemistry:

If the active includes enantiomers, the ratio of enantiomers should be listed.

(b) Molecular formula:

Include salt form and hydrated/solvated form, if applicable. The molecular formula should be listed in a manner that separates the salt/solvent from the active moiety.

(c) Molecular mass:

List separate molecular masses for free acid/base and salt and hydrated/solvated forms, if applicable.

2.3.S.1.3 General Properties

(a) Physical form (for example [e.g.], polymorphic form, solvate, hydrate):

(b) Solubilities and Dose/Solubility Volume over the physiological pH range (1.2-6.8):

(c) pK_a:

2.3.S.2 Manufacture (name, manufacturer)

If more than 1 manufacturer of a drug substance is proposed, duplicate S.2 or add additional lines to the table in S.2.1 for each manufacturer and use subheadings for each manufacturing site. If the specifications are different for the drug substance from each manufacturer, the section S.4.1 can be duplicated. For S.6 and S.7, information from all sources can be consolidated in a single section.

2.3.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:

Name and Address	**Responsibility** (for example, manufacturing, packaging, labelling and testing)	**MF # or CEP #**

2.3.S.2.2 Description of Manufacturing Process and process controls (name, manufacturer)

(a) Flow diagram showing reactants, solvents and reagents:

The flow diagram should be sufficiently detailed to include reagents and control parameters Refer to the Quality (Chemistry and Manufacturing): NDS and ANDSs guidance document for more information on the level of detail required.

For micronized / milled or compacted drug substances, the type of equipment and critical process parameters (equipment setting and operating conditions) should be described.

If a design space has been approved, insert details of range of acceptable parameters/attributes for controls covered by design space.

Name and address of sites manufacturing the API starting material(s) and/or intermediates:

Name and chemical structure of API starting material/intermediate:
Manufacturer:
Manufacturing site address:

S.3.2 Impurities
<This section is only required in the CPID provided with the restricted information on the manufacture of the drug substance.>

Potential impurities not routinely controlled in the drug substance:

Include a list of impurities that may be present but are not proposed for routine testing but should be tested for change control purposes. These would include impurities tested during development but the testing was sufficient to support that routine control is not necessary, e.g. genotoxic impurities, catalysts, elemental impurities.

2.3.S.4 Control of the Drug Substance

2.3.S.4.1 Specification (name, manufacturer)

(a) Specification for the drug substance:

Standard Claimed [for example, House, United States Pharmacopeia (USP), British Pharmacopoeia (BP), European Pharmacopoeia (Ph.Eur.)]		
Specification Reference Number and/or Version		
Test	**Acceptance Criteria**	**Analytical Procedure (Type/Source/Version)**

Standard Claimed [for example, House, United States Pharmacopeia (USP), British Pharmacopoeia (BP), European Pharmacopoeia (Ph.Eur.)]		
Specification Reference Number and/or Version		
Test	**Acceptance Criteria**	**Analytical Procedure (Type/Source/Version)**

The assay should include the chemical formula so that it is clear as to how the dose is declared (i.e. free acid/base versus salt.)

Chemical or unambiguous names of impurities (e.g. USP or Ph.Eur. naming conventions) should be used in the table or included as a footnote.

Where reduced testing is proposed for individual tests, the testing schedule for these tests should be clearly marked as a footnote.

2.3.S.6 Container Closure System

(a) Description of the container closure system(s) for the storage and shipment of the drug substance:

Include whether the product is packaged under an inert atmosphere, if applicable.

2.3.S.7 Stability

2.3.S.7.1 Stability Summary and Conclusions

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

Container Closure System	Storage Conditions	Re-test Period

2.3.P DRUG PRODUCT (NAME, DOSAGE FORM)

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

(a) Composition of the dosage form:

(i) Composition, that is (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)	**Strength (label claim)**			
	Quantity per unit	**%**	**Quantity per unit**	**%**
Total				

For tablets with a non-functional film coating the percent weight should be expressed in terms of the weight of the tablet core. For hard capsules the percent weight should be expressed in terms of the fill weight. MF numbers for capsule shells, colourants, coatings or imprinting inks should be listed if applicable.

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

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

2.3.P.3 Manufacture (name, dosage form)

If more than one manufacturer of a drug substance is proposed, duplicate P.3 or use subheadings for each manufacturing site in P.3.3-3.5. If the specifications are different for the drug product from each manufacturer, the section P.5.1 can be duplicated. For P.7 and P.8, information from all sources can be consolidated in a single section.

2.3.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:

Name and Address	**Responsibility** (for example, manufacturing, packaging, and testing)	**MF #**

Each site responsible for manufacturing finished product or in-process drug should be identified. Each primary packaging site should be identified.

Sites involved in sterilization of packaging materials not subsequently exposed to terminal sterilization should be listed.

Importer/distributer can be listed when known.

2.3.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**	**Quantity per batch**
Total		

Commercial batch sizes should be listed. If there is a granulation step using intra and extra-granular excipients these should be listed separately.

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

(a) Flow diagram of the manufacturing process:

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

The narrative description should be based on the details listed in the master production documents for the commercial batch size.

If a design space has been approved, the narrative description should include both the normal operating ranges indicated in the master production documents and the design space ranges for those parameters/attributes.

For sterile products, details of validated sterilization parameters (e.g. load size, autoclave program, gamma radiation dose) and equipment (e.g. sterilizing filters, filling syringes) should be listed.

Approved hold times should be listed.

2.3.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:

All in-process controls routinely monitored for production batches should be listed. For products developed using QbD principles, non-critical controls can be designated as such.

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

(a) Summary of process validation information, including any commitments, for the critical steps in the manufacturing process (e.g. protocol number, parameters):

Validation Protocol # / Report #	**Description**	**Status** (Commitment / Completed**)**	**Filed with Submission Control No.**

The reference number (including version and/or date) of the process validation protocol should be listed. If process validation is complete, the process validation report reference number can be listed.

A tabulated summary of sampling, tests and acceptance criteria to be performed during process validation studies which are **additional to the routine tests** performed for production batches should be included in this section.

Process validation commitments should be listed e.g. prospective validation of 3 consecutive commercial scale batches of each strength, at each commercial manufacturing site.

Other validation commitments, such as additional hold time studies should be listed in this section. Protocol numbers, or other descriptors of the studies to be performed, should be listed.

This section should be lifecycle managed by maintaining a list of all commitments unless they are no longer relevant (e.g. the manufacturing site is no longer used), however if protocols are updated or replaced, the most recent protocol number should be listed.

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

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

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

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

The assay should include the chemical formula so that it is clear as to how the dose is declared (i.e. free acid/base vs. salt.)

Dissolution conditions should be listed as a footnote to the table.

Chemical or unambiguous names of impurities (e.g. USP or Ph.Eur. naming conventions) should be used in the table or included in as a footnote.

If specifications are different for sterile powders and their reconstituted solutions, this information should be clearly identified.

Where reduced testing is proposed for individual tests, the testing schedule for these tests should be clearly marked as a footnote.

2.3.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:

Strength	Unit Count or Fill Size	Container Size(s)	Description

The container should be described with sufficient detail to allow for adequate identification (e.g. materials of construction, child-resistant closures). Desiccants and the composition of primary packaging materials should be listed. Secondary packaging material should be listed if they provide additional protection for stability or serve to deliver the product (functional secondary packaging). Sample packs for physicians should also be included. MF numbers for container closure systems should be listed if applicable. Use of inert atmosphere should be identified, if applicable. The number of dosage units per packing format should be listed. Packaging materials should be unambiguously described (e.g. Type of glass, colour, thickness, container size). Reference code numbers should also be listed. Products co-packaged for administration should be included.

2.3.P.8 Stability (name, dosage form)

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

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

Container Closure System	Storage Conditions (and In-use Storage Conditions, if applicable)	Shelf Life (and In-use Period, if applicable)

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

(a) Stability protocol for commitment batches:

Commitment batches are an International Council for Harmonisation (ICH) requirement. Three (3) commercial scale batches or, if relevant, the number of batches as per the Post-Notice of Compliance NOC) Changes - Quality guidance should be included as commitment batches unless the stability studies have been completed. If batches are considered both commitment and ongoing stability they should be listed in the commitment section. Stability commitments do not need to be life-cycle managed and only the most recent commitments should be listed.

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	

Other stability commitments, such as transportation studies or one-time studies such as assessment of leachable components should be listed in this section. Protocol numbers, or other descriptors of the studies to be performed, should be listed.

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

Stability studies on ongoing batches (i.e. annual batches) are a GMP requirement. Where multiple strengths, packaging formats or manufacturing sites are proposed for commercial purposes, the commitment should clearly state how batches will be placed on stability.

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	

2.3.P.8.3 Stability Data (name, dosage form)

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