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Sponsor Attestation Checklist for Abbreviated New Drug Submissions (ANDSs)

Health Canada use only

CR File Number	Control Number	Date/ Time of Receipt

Sponsors should address the points outlined below by answering **"Yes"**, **"No"**, or **"Not Applicable"**, providing a justification where required, and completing the requested information**.** This Sponsor Attestation Checklist is **not** required for Supplemental Abbreviated New Drug Submissions (SANDSs) or Labelling Only submissions.

Comment boxes have been provided to allow sponsors to add notes to reviewers where relevant. If the product includes more than one Drug Substance, sections S.1-S.7 should be answered for each Drug Substance.

Introduction

Do you wish to receive communications from Health Canada regarding this submission electronically (e.g. via email)?

◯ Yes ◯ No

Proposed Product:	**Canadian Reference Product (CRP):**
Brand Name:	Brand Name:
Drug Substance(s):	Drug Substance(s):
Company Name:	Company Name:
Dosage Form(s):	Dosage Form(s):
Strength(s):	Strength(s):

Module 1 – Administrative and Prescribing Information

Administrative Information		
1.2.5	**Compliance and Site Information** Have the filing requirements in Health Canada's February 10, 2017 Notice Submission Filing Requirements – Good Manufacturing Practices (GMP)/ Drug Establishment Licences (DEL)* been met, for all activities listed in the Notice? * http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/guide-ld/notice_gmp_el_avis_bpf_le-eng.php Comments:	◯ Yes ◉ No
1.2.6	**Authorization for Sharing Information** List Master File (MF) number(s) referenced in the submission (Type I–V):	☐ Not Applicable
	If there is no MF, is all information included in the submission	◯ Yes ◯ No
	Does a valid Certificate of Suitability (CEP) exist for this Active Pharmaceutical Ingredient (API) and manufacturing site/process?	◯ Yes ◯ No ◉ Not Applicable
	If "Yes" to the preceding question, has the CEP been filed following advice posted in the current Therapeutic Products Directorate (TPD) communiqué *? * http://www.hc-sc.gc.ca/dhp-mps/prodpharma/activit/int/edqm_2007-eng.php	◉ Yes ◯ No ◯ Not Applicable
	For the above MFs: 1. Have Letters of Authorization granting access to the DMFs on behalf of the submission sponsor been provided?	◯ Yes ◯ No
	2. Are the DMFs in order and up to date (e.g. fees paid)?	◉ Yes ◯ No
	Comments:	
1.2.7	**International Information** Provide information on the product application filing and marketing status of the proposed product in the following jurisdictions:	☐ Not Applicable
	☐ United States Food and Drug Administration (USFDA):	◯ Filed ◯ Mkd
	☐ European Union (EU):	◯ Filed ◯ Mkd
	If filed in the EU, indicate applicable procedure: ◯ Centralized ◯ De-Centralized ◯ Mutual Recognition ◯ National	
	☐ Switzerland's Swissmedic:	◯ Filed ◯ Mkd
	☐ Singapore's Health Sciences Authority (HSA) :	◯ Filed ◯ Mkd
	☐ Australia's Therapeutic Goods Administration (TGA):	◉ Filed ◉ Mkd
	Has Foreign Review Information for any of the above jurisdictions been provided? ☐ Review reports ☐ Other	◯ Yes ◯ No
	If Yes, has the Foreign Review Attestation and Summary of Quality Differences: Subsequent Market Entry Products (Human Drugs) * been provided? * http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/guide-ld/for_rev-exam_etr/foreign_rev_sdq_exam_etra_dtq-eng.php	◯ Yes ◯ No

Module 3 – Quality

Drug Substance		
S.1	**General Information** Does the proposed active pharmaceutical ingredient comply with the definition of Pharmaceutical Equivalent as per the Food and Drug Regulations and the Interpretation of "Identical Medicinal Ingredient" Policy?	◯ Yes ◯ No
S.4	**Control for the Drug Substance** a) Do any of the proposed limits for impurities exceed the applicable International Conference on Harmonisation (ICH) Qualification Threshold in Q3A?	◯ Yes ◯ No
	b) If "Yes" to a), have these impurities been qualified based on limits in an official compendial monograph?	◯ Yes ◯ No ◯ Not Applicable
	c) If "No" to b), have these limits been qualified based on levels of these impurities observed in the CRP?	◯ Yes ◯ No ◯ Not Applicable
	d) If "No" to c), have these limits been qualified based on safety (e.g. toxicological) data? Identify sections where complete safety (e.g. toxicological) data and justification for the limits have been provided (e.g. Module 4):	◯ Yes ◯ No ◯ Not Applicable
	Does the submission include a discussion of potential genotoxic impurities (e.g. including the identification of potential structural alerts)? Location of discussion:	◯ Yes ◯ No
S.7	**Stability** Has the minimum amount of stability data (2 batches, minimum pilot scale, 6 months long term, 6 months accelerated) been provided under ICH storage conditions? If No, provide justification:	◯ Yes ◯ No

Drug Product		
Proposed strength(s):		
Approved strength(s) for the Canadian Reference Product (CRP):		
Batches used in comparative bioavailability or physicochemical study/ studies	**Test Product**	**Canadian Reference Product (CRP)**
Strength(s):		
Batch number(s):		
Batch size:		Not applicable.
Largest proposed commercial batch size:		Not applicable.
Is the size of the biobatch at least "pilot scale" (i.e. manufactured by a procedure fully representative of and simulating that to be applied to a full production scale batch and, for solid oral dosage forms, one-tenth that of full production scale or 100,000 units, whichever is larger)? ◯ Yes ◯ No		

If No, provide justification:		
P.2	**Pharmaceutical Development**	
	Has a comparative in vivo bioequivalence study been provided on each of the proposed strengths?	◯ Yes ◯ No
	If 'No' to the above, has a request for waiver to perform the comparative *in vivo* bioequivalence study (e.g. for the product or a proposed strength) and justification been provided?	◯ Yes ◯ No
	For solid oral dosage forms: Have comparative dissolution profiles been provided for all generic strength(s) not used in a comparative bioavailability study against the generic strength for which bioequivalence was demonstrated?	◯ Yes ◯ No ◯ Not a solid oral dosage form
	Has justification of the choice of dissolution method including discussion of the discriminatory power of the dissolution method been provided?	◯ Yes ◯ No
	For liquid and semi-solid dosage forms: Have results of comparisons of the test and reference products been provided (e.g., formulations, physicochemical properties)?	◯ Yes ◯ No ◯ Not a liquid or semi-solid dosage form
	For dosage forms with delivery devices: Has a comparison of the physical and operating characteristics of the device attributes and performance of the delivery system been provided?	◯ Yes ◯ No ◯ No delivery device
	For solid oral products: Is the generic product identical to the CRP with respect to divisibility scoring configuration? If No, provide justification:	◯ Yes ◯ No ◯ Not a solid oral dosage form ◯ Not scored
	If both products are scored, have results of a divisibility study been provided for all strengths of the generic product? Location of results/study:	◯ Yes ◯ No ◯ Not Applicable
	For comparative bioavailability or physicochemical studies, was the reference product sourced from the Canadian market?	◯ Yes ◯ No ◯ No comparative studies
	If a foreign sourced reference product was used, have criteria outlined in the Canadian Reference Product policy been addressed*? * http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/pol/crp_prc_pol-eng.php Location of results/study:	◯ Yes ◯ No ◯ Not Applicable
	Was the same lot of the foreign sourced reference product used in the comparative bioavailability studies and/or all in vitro comparative studies? If No, provide justification:	◯ Yes ◯ No ◯ Not Applicable
P.2.4	**Container Closure System** **For liquids and semi-solid dosage forms:** Has a discussion or studies on Extractables/ Leachables been provided for the drug product during shelf-life? (e.g., Extractable compounds inherent to the primary components of the container-closure system (CCS) which may leach into the drug product (DP)	◯ Yes ◯ No ◯ Not a liquid or semi-solid dosage form

	during stability)? If No, provide justification: [ ]	
	Results provided for *: USP <381> Elastomeric Closures for Injections (includes USP <87>/<88> tests) USP <661> Containers USP <671> Containers – Performance Testing * Or the equivalent General Chapter of the Ph. Eur.	◯ Yes ◯ No ◯ Yes ◯ No ◯ Yes ◯ No
P.2.5	**Microbiological Attributes** Have the results of a Preservative Effectiveness Study been provided?	◯ Yes ◯ No There is no preservative in the formulation
P.2.6	**Compatibility** **For products to be diluted or reconstituted:** Have in-use stability data been provided for ALL diluents or reconstitution solutions over the concentration range, storage conditions, and storage times as specified in the Product Monograph for the CRP? If No, provide justification: [ ]	◯ Yes ◯ No ◯ Product does not require constitution or dilution
P.3.5	**Process Validation and/or Evaluation**	
	Has a process validation report been included with results performed on three consecutive, production-scale batches of the drug product?	◯ Yes ◯No
	If "No" to the preceding question, has a process validation protocol been submitted with a commitment that three consecutive, production-scale batches of the drug product will be subjected to prospective validation?	◯ Yes ◯No
	For sterile products: Has the following documentation been provided:	☐ Not a sterile product
	Drug substance Bacterial Endotoxin test validation Drug product Bacterial Endotoxin test validation Validation for sterile filters	◯ Yes ◯No ◯ Yes ◯No ◯ Yes ◯No
	Has a determination of extractables and leachables from process equipment (e.g. filters, tubing, coatings) or a commitment and study outline been provided? If Yes, specify report (e.g., Membrane Compatibility Test Report, Extractable Substances documentation): [ ]	◯ Yes ◯No ◯ Not applicable
	Has the validation of sterilization process been conducted?	◯ Yes ◯No
	For aseptic sterilisation techniques, has a justification been provided for the use of aseptic processes versus terminal sterilization? If No, provide justification: [ ]	◯ Yes ◯No ◯ Not aseptically processed

	Has the validation of sterilization of packaging materials been conducted and the validation report included in the submission?	◯ Yes ◯ No
	Has a study on the integrity of the container closure system been included?	◯ Yes ◯ No
P.5	**Control for the Drug Product**	
	a) Do any of the proposed limits for impurities exceed the applicable International Conference on Harmonisation (ICH) Qualification Threshold in Q3B?	◯ Yes ◯ No
	b) If "Yes" to a), have these impurities been qualified based on limits in an official compendial monograph?	◯ Yes ◯ No ◯ Not Applicable
	c) If "No" to b), have these limits been qualified based on levels of these impurities observed in the CRP?	◯ Yes ◯ No ◯ Not Applicable
	d) If "No" to c), have these limits been qualified based on safety (e.g. toxicological) data?	◯ Yes ◯ No ◯ Not Applicable
	Identify sections where complete safety (e.g. toxicological) data and justification for the limits have been provided (e.g. Module 4):	
	Has a Risk Assessment Summary for Elementary Impurities been included (to be in line with ICH Q3D)?	◯ Yes ◯ No
	If yes, indicate the location of this document (section P.2/P.5.5/P.5.6/other):	
P.8	**Stability**	
	Has the minimum amount of stability data (6 months long term, 6 months accelerated) been provided under ICH storage conditions?	◯ Yes ◯ No
	If No, provide justification:	
	Have stability data been provided on at least two unique batches of each strength at pilot scale?	◯ Yes ◯ No
	If No, provide justification:	
	Have stability data been provided in all types of container closure systems?	◯ Yes ◯ No
	If No, provide justification:	

	Have the results of stress testing (e.g., including Photostability studies of the drug product) been provided? Location of results/study: If No, provide justification:	◯ Yes ◯ No
Regional Information		
R.1.1	**Executed Production Documents** Have copies of the executed production documents been provided for each strength (including the test batches used in the pivotal clinical and/or comparative biostudies)? If the Executed Production Documents have not been provided in English or French, have translations into either English or French been provided? If multiple drug product manufacturing sites are proposed, has the above been provided for at least one batch from each proposed manufacturing site? If No, provide justification:	◯ Yes ◯ No ◯ Yes ◯ No ◯ Not Applicable ◯ Yes ◯ No
R 1.2	**Master Production Documents** Have copies of the drug product master production documents been provided for each proposed strength, commercial batch size, and manufacturing site? If the Master Production Documents have not been provided in English or French, have translations into either English or French been provided? For sterile products, have details of manufacturing processes (e.g., washing, treatment, sterilizing, and depyrogenating of containers, closures and equipment; filtration of solutions, final inspection of the product, and sterilization cycle) been provided, including referenced Standard Operating Procedures (SOPs) where applicable? If No, provide justification:	◯ Yes ◯ No ◯ Yes ◯ No ◯ Not Applicable ◯ Yes ◯ No ◯ Not a sterile product

Module 5 – Clinical Study Reports

Comparative Bioavailability Studies

Has a Module 5 been provided? ◯ Yes ◯ No
If "No", leave the below section blank.

List comparative bioavailability study or studies included in the submission:

The description should include study title, study number, study design, products administered, dose and conditions of administration (e.g., 1 x 100 milligrams, fasting/fed).

For each study – Has justification been provided for the use of non-standard conditions of administration (e.g., fed instead of fasting conditions, modifications to test meal composition for studies conducted under fed conditions)? ◯ Yes ◯ No ◯ Not Applicable

Location of justification:

For each study - If the study was conducted outside of Canada, provide a list of clinical and bioanalytical facilities employed:
The description should include the name and address of each facility.

For each study - Has documentation establishing the GCP compliance of the clinical and bioanalytical facilities to current FDA or ICH standards been provided? ◯ Yes ◯ No ◯ Not Applicable
Specifically, documentation should be provided to support the outcome(s) of inspection(s) of the sites by the FDA or an ICH Authority. Note that documentation from the FDA should include all 482 and 483 Forms that were issued, the responses to the deficiencies noted on Form 483, as well as the Establishment Inspection Report.

Comments:

Test Product

Are all strengths proportionally formulated to the strength administered in the comparative bioavailability study as per the criteria outlined in the Bioequivalence of Proportional Formulations policy? ◯ Yes ◯ No ◯ Not Applicable

Is a waiver of the requirement to provide comparative bioavailability data requested? ◯ Yes ◯ No

If "Yes" to the above, justification for the waiver request is based on:
- ☐ Proportionality Policy?
- ☐ In-vitro in-vivo correlation based data?
- ☐ Biopharmaceutics Classification System (BCS)?

Location of results/study:

If "Yes" to the BCS-based waiver: ☐ No BCS-based waiver

Is this an immediate-release product? ◯ Yes ◯ No

Have the elibility criteria been met as listed in the Guidance Document: Biopharmaceutics Classification System Based Biowaiver, section 2.2? ◯ Yes ◯ No

Have all criteria listed in the Guidance Document: Biopharmaceutics Classification System Based Biowaiver, Appendix 1, been addressed?	◯ Yes ◯ No
Has dissolution data for a minimum of two batches of the proposed product and one of the reference product been provided? If No, provide justification:	◯ Yes ◯ No
Reference Product Are reference product labels for the lot used in the comparative bioavailability studies provided, including expiry date and lot number?	◯ Yes ◯ No

Bioanalytical Method	
Analyte(s) measured: ☐ parent ☐ metabolite	
Has justification been provided for basing bioequivalence on metabolite data instead of parent? Location of justification if provided:	◯ Yes ◯ No ◯ Not Applicable
Has the bioanalytical report been provided?	◯ Yes ◯ No ◯ Not Applicable
Has the method validation report been provided?	◯ Yes ◯ No
Does the validation report include the following stability experiments with multiple (minimum three) replicates at each of the low quality control (QC) and high QC concentrations in the appropriate matrix (including the same anticoagulant used in the comparative bioavailability study), as per Health Canada's October 8, 2015 Notice for Industry: Clarification of bioanalytical method validation procedures? Long term stability data (frozen at the temperature used in the study) in spiked plasma to cover the maximum storage period for subject samples. Freeze-thaw stability data for the number of cycles that is considered to be reflective of the number of cycles experienced by subject samples from the study (frozen at - the temperature used in the study and thawed at room temperature) in spiked plasma. Bench top stability data in spiked plasma over a length of storage that is considered to be reflective of the processing period of the batches of the subject samples from the study	◯ Yes ◯ No
If no, has justification been provided? Location of justification if provided:	◯ Yes ◯ No

Sponsor Attestation

I, the undersigned, certify that:

1. The information and material included in this checklist is accurate and complete.
2. No information is false or misleading and no omissions have been made that may affect its accuracy and completeness.

Name of Authorized Signing Official	Signature	Date (YYYY/MM/DD)

Company Name and Address	Title

Telephone Number	Fax Number	E-mail Address