**APPENDIX A**

**MANUFACTURER SUBMISSION CHECKLIST**

**Appendix A**

**Nova Scotia Criteria for Interchangeability**

**Manufacturer Submission Check List**

**Summary of Product Information:**

|  |  |
| --- | --- |
| **Submission Received Date *(For Office Use):*** |  |

|  |  |  |  |
| --- | --- | --- | --- |
| **Generic Name:** |  | | |
| **Dosage Form:** |  | | |
| **Manufacturer:** |  | | |
| **ATC Code:** |  | | |
| **Submitted Product :** | | **Strength(s):** | **DIN Number(s):** |
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|  | |  |  |
| **Submitted Product has a Declaration of Bioequivalence to a Canadian Innovator Reference Product:**  **Yes**  **No** | | | |
| **Comparator Innovator Reference Product (for all submitted strengths) is in the Nova Scotia Formulary:**  **Yes**  **No** | | | |
| **Comparator Innovator Reference Product:** | | **Strength(s):** | **DIN Number(s):** |
|  | |  |  |
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| **Submitted Product is subject to a Cross-Licensing Agreement:**  **Yes**  **No** | | | |
| **Submitted Product is an UItrageneric:**  **Yes**  **No** | | | |
| **Cross-Licensed Comparator Product (for all submitted strengths) is in the Nova Scotia Formulary:**  **Yes**  **No** | | | |
| **Cross-Licensed Comparator Product:** | | **Strength(s):** | **DIN Number(s):** |
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**All correspondence and submissions should be addressed to:**

|  |  |  |
| --- | --- | --- |
| Pharmacist Consultant  Nova Scotia Pharmacare Programs  P.O. Box 500  Halifax, N.S. B3J 2S1  **(MAIL)** | or | Pharmacist Consultant  Nova Scotia Pharmacare Programs  230 Brownlow Ave  Dartmouth, N.S. B3B 0G5  **(COURIER)** |

**Bioequivalence is supported by which guideline(s) (check all that apply):**

|  |
| --- |
| [Conduct and analysis of bioavailability and bioequivalence studies Part A: Oral Dosage Formulations Used for Systemic Effects](http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/guide-ld/bio/bio-a-eng.php) |
| [Conduct and Analysis of Bioavailability and Bioequivalence Studies - Part B: Oral Modified Release Formulations](http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/guide-ld/bio/bio-b-eng.php) |
| Critical Dose Drugs |
| Other (e.g. liquids, inhalers, topicals)  Explain: |
| Exceptions (e.g. waivers to recognized study design, requirements and standards.)  Explain (include copy of waiver): |
| Other Relevant Comments: |

**Please complete the following regarding the submitted product monograph:**

|  |  |
| --- | --- |
| Date of Health Canada Approval for the submitted product monograph: | **Date:** |
| Are there differences from the innovator product monograph (e.g. stability and storage, etc.)?  Explain: | **Yes**  **No** |
| Does the product description in the monograph match the product pictures submitted?  Explain: | **Yes**  **No** |

**Please indicate if the product(s) demonstrate any of the following characteristics.**

|  |  |
| --- | --- |
| Declared bioequivalent with a non-Canadian Reference Product. | **Yes**  **No** |
| Declared bioequivalent with a non-innovator Canadian Reference Product. | **Yes**  **No** |
| Is an **oral** dosage formulation for which standard bioequivalence studies (e.g., Health Canada’s Conduct and Analysis of Bioavailability and Bioequivalence Studies: Part A: Oral Dosage Formulations Used for Systemic Effects, Part B: Oral Modified Release Formulations and Bioequivalence Requirements, Critical Dose Drugs) were not the basis of the bioequivalence determination. | **Yes  No** |
| Is a Critical Dose Drug [e.g. highly toxic drugs, drugs with a narrow therapeutic range (e.g., cyclosporine, digoxin, flecanide, lithium, phenytoin, sirolimus, tacrolimus, theophylline, warfarin), etc.]. | **Yes**  **No** |
| Has non-linear pharmacokinetics. | **Yes**  **No** |
| An early time of onset or rapid rate of absorption is important. | **Yes**  **No** |
| Is an “Old Drug” as defined by the Therapeutic Products Directorate, Health Canada. | **Yes**  **No** |

Note: Products which demonstrate any of the above characteristics will be ineligible for expedited review (including those with a declaration of bioequivalence to a Health Canada Innovator Reference Product). Products which are cross-licensed with products already deemed interchangeable in the Nova Scotia Formulary will be eligible for expedited review.

**The following submission requirements apply to both expedited and full reviews. Please provide a single copy of the following documents for expedited submissions and three copies for full submissions.**

|  |
| --- |
| Cover Letter (description of the submission, Table of Contents, and pagination for the complete submission) |
| Notice of Compliance (NOC) or DIN form for Old Drugs  For an NOC with Conditions (NOC/c), please include the *Request for Letter of Undertaking* and the *Letter of Undertaking*. |
| Health Canada approved product monograph or patient information for Old Drugs. |
| Letter authorizing **unrestricted communication** regarding the drug product between Nova Scotia and:   * Other federal, provincial and territorial (F/P/T) drug programs * F/P/T health authorities and related facilities * Health Canada * Patented Medicine Prices Review Board (PMPRB) * Canadian Agency for Drugs and Technologies in Health (CADTH) * other provincial interchangeability committees and their administrators |
| Letter indicating the product is available in sufficient quantity to meet demand and is available to all pharmacies in Nova Scotia. |
| Pricing information |
| Colour pictures of the oral solid dosage form (front and back view with ruler to provide a scale for size) for all strengths, clearly showing the product identification features. Hard copies must be submitted; electronic files will not be accepted. |
| Original market-ready product labeling (inner and outer packaging) for all marketed package sizes. Submission of actual drug material is not permitted. |
| **Additional documentation required for Cross-Referenced/Ultrageneric Submissions:**  Letters from both the manufacturer of the cross-referenced product and the manufacturer of the product being reviewed:  Authorizing **unrestricted communication** regarding the drug product (as noted above)  Identifying the manufacturer for both the cross-referenced product and the product being reviewed  Confirming a cross licensing agreement exists between the manufacturers  Confirming that the product being reviewed is identical to the cross-referenced product in all aspects *including* strength and dosage form, formulation including both active and inactive ingredients and their quantities, raw materials and finished product specifications, manufacturing processes, **manufacturing site** and basic packaging (excluding embossing and labels). |

**The following are the additional submission requirements for full submissions.**

|  |
| --- |
| Evidence of bioequivalence in the **fasting** state(Clinical Study Report Synopsis and graphs of mean plasma concentrations comparing the two products (regular and semi-log) including an estimate of the variability at each time point.)  Evidence of bioequivalence in the **fed** state (Clinical Study Report Synopsis and graphs of mean plasma concentrations comparing the two products (regular and semi-log) including an estimate of the variability at each time point.) |
| Completed Pharmacokinetic / Statistical Worksheet (**fasting**) (see Appendix C, Nova Scotia Criteria for Interchangeability)  Completed Pharmacokinetic / Statistical Worksheet (**fed**) |
| Comparative dissolution data with innovator product |
| Proportionality (if applicable) |
| Health Canada Approved Comprehensive Summary: Bioequivalence (CS-BE) |
| CPID – including master formula |

**For full submissions with physiochemical data used to support bioequivalence please include:**

|  |
| --- |
| Physiochemical Comparison Table. |
| Waiver of bioequivalence (explanation) |

**By signing this form, you are affirming that** the information provided is accurate **as of the date entered. Changes to the above information must be submitted in writing.**

|  |  |
| --- | --- |
| Signature: | Date: |
| Name / Title: | |