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| Health Santé  Canada Canada  Therapeutic Products Directorate  Direction des produits thérapeutiques |

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| --- | --- | --- |
| To/À: |  | Security Classification/  Classification de sécurité: |
| From/De: | Date: |

|  |  |  |
| --- | --- | --- |
| **Subject /**  **Objet:** | **BCS-Based Biowaiver Evaluation** | |
|  | | |
| **Brand (Proprietary) Name of Drug Product** | |  |
| **Proper, Common or Non-proprietary Name of Drug Substance** | |  |
| **Manufacturer / Sponsor** | |  |
| **Therapeutic Classification** | |  |
| **Dosage Form(s) and Strength(s)** | |  |
| **Route(s) of Administration** | |  |
| **Type of Submission** | |  |
| **TPD Target Date / Review Target Date** | |  |
| **Control Number / File Number** | |  |

|  |  |
| --- | --- |
|  | |
| **Lead Review Bureau / Division** |  |
| **Biopharmaceutics Evaluator** |  |
| **Review References** |  |
| **Consultations** |  |
| **Notes to Other Review Units** |  |
| **Review Recommendation** |  |
| **Sponsor's Contact Information** |  |

1. **WAIVER REQUEST**

*Provide a brief description of the waiver request. For Abbreviated New Drug Submissions (ANDS) and Supplemental Abbreviated New Drug Submissions (SANDS), state the Canadian reference product for the submission.*

1. **DRUG SUBSTANCE**
   1. Solubility

*Summarise the solubility assessment for the drug substance. Identify the lowest measured solubility over the pH range of 1.2 – 6.8, used to classify the drug substance.*

* 1. Permeability

*Provide an assessment of permeability based on the extent of absorption derived from human pharmacokinetic studies, e.g., absolute bioavailability or mass balance studies, or permeability studies using Caco-2 cell assays.*

* + 1. Absolute Bioavailability and Mass Balance Studies
    2. Caco-2 cell permeability studies
    3. Supportive Evidence

1. Gastrointestinal Stability
2. Dose Proportional Pharmacokinetics
   1. BCS Classification – *TPD use only*
3. **TEST PRODUCT** 
   1. Formulation

Tabulate the composition of each product strength using the table below. For solid oral dosage forms the table should contain only the ingredients in the product core. A copy of the table should be filled in for the coating ingredients, if any.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Component and Quality Standard | Function | Strength (label claim) | | | |
| XX mg | | XX mg | |
| Quantity per unit | %\* | Quantity per unit | %\* |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
| TOTAL |  |  |  |  |  |

*\*each ingredient expressed as a percentage of the total core or coating weight*

* 1. Batches

*State the location of the certificate(s) of analysis in the submission, indicate the scale of the batch(es), and whether it is representative of that for market production.*

**Batches Employed in Dissolution Tests**

|  |  |  |
| --- | --- | --- |
| Drug Product |  |  |
| Strength |  |  |
| Batch number |  |  |
| Assay (% label claim) |  |  |
| Site of manufacture, batch size |  |  |
| Date of manufacture |  |  |

1. **REFERENCE PRODUCT** 
   1. Formulation

*Provide a qualitative description of the reference product formulation. For waiver requests for products containing BCS Class III drug substances, also provide quantitative compositional information.*

* 1. Batches

*State the location of the certificate(s) of analysis.*

**Batches Employed in Dissolution Tests**

|  |  |  |
| --- | --- | --- |
| Drug Product  Manufacturer/ Sponsor |  |  |
| Strength |  |  |
| DIN |  |  |
| Batch number |  |  |
| Assay (% label claim) |  |  |
| Expiry Date |  |  |

*DIN: Drug Identification Number, if applicable.*

1. **DISSOLUTION METHOD**

*Provide a summary of the dissolution method employed for the comparative dissolution studies in the table below:*

**Summary of Dissolution Test Method Parameters**

|  |  |
| --- | --- |
| Apparatus |  |
| Rate of Operation |  |
| Dissolution Media |  |
| Volume |  |
| Temperature |  |
| Sampling times |  |
| Number of Dosage Units |  |

1. **COMPARISION OF TEST AND REFERENCE PRODUCTS**
   1. Comparison of Formulations

*For waiver requests for products containing BCS Class I drug substances, identify any differences in excipients between test and reference products. The potential for differences in excipients to affect in vivo absorption should be assessed.*

*For waiver requests for products containing BCS Class III drug substances, provide a tabular summary of a quantitative comparison of excipients between test and reference products. All excipients should be qualitatively the same and quantitatively similar (except for film coating or capsule shell excipients), per recommendations in the ICH M9 guidance: Biopharmaceutics Classification System-Based biowaivers.*

* 1. Comparative *In Vitro* Dissolution

*Provide a tabular summary of dissolution data, including the range, means, and % relative standard deviations, for each pH, at each time point assessed, for the test and reference batches. For comparison of dissolution profiles, the similarity factor (f2) should be estimated per the ICH M9 guidance: Biopharmaceutics Classification System-Based biowaivers, where applicable.*

* + 1. Dissolution Profiles for Test Batches
    2. Dissolution Profiles for Reference Batches

1. **CLARIFAX/ CLARIMAIL REQUESTS – *TPD use only***
2. **CONCLUSIONS AND RECOMMENDATIONS – *TPD use only***
3. **REFERENCES**