# Biowaiver Application Form:

# Biopharmaceutics Classification System (BCS)

This application form is designed to facilitate information exchange between the Applicant and the PPB National Medicines Regulatory Authorities (PPBs) if the Applicant seeks to waive bioequivalence studies based on the Biopharmaceutics Classification System (BCS). For further information, please study the respective PPB biowaiver guidance documents. This form is not to be used if a biowaiver is requested for additional strength(s) of a submitted product(s), in which case a separate "*Biowaiver Application Form: Additional Strengths*" should be used.

*The PPB Prequalification Team - Medicines has identified some Active Pharmaceutical Ingredients (APIs) that are eligible for a BCS-based biowaiver application. For those APIs,it may not necessary to provide data to support the BCS classification of the respective API(s) in the application i.e., data supporting the drug substance solubility or absorption/permeability class.*

General Instructions:

Please review all the instructions thoroughly and carefully prior to completing the current Application Form.

* Provide as much detailed, accurate, and final information as possible.
* Please enter the data and information directly following the greyed areas.
* Please enclose the required documentation in full and state in the relevant sections of the Application Form the exact location (Annex number) of the appended documents. For example, in section 2.5 indicate in which Annex the Certificate of Analysis can be found.
* Please provide the document as an MS Word file.
* Do not paste snap-shots into the document.
* The appended electronic documents should be clearly identified in their file names, which should include the product name and Annex number.
* Before submitting the completed Application Form, kindly check that you have provided all requested information and enclosed all requested documents.
* Should you have any questions regarding this procedure, please contact pharmacy and Poisons Board).

The signed paper version of this Biowaiver Application Form together with Annexes (and their electronic copies on CD-ROM) should be included to the bioequivalence part of the submitted dossier and sent by surface mail to the following address:

CEO,

Pharmacy and Poisons Board

Kenya**Administrative data**

**1. INN of active ingredient(s)**

*<< Please enter information here >>*

**2. Dosage form and strength**

*<< Please enter information here >>*

**3. Product PPB Reference number** *(if product dossier has been accepted for PPB joint assessment)*

*<< Please enter information here >>*

**4. Name of applicant and official address**

*<< Please enter information here >>*

**5. Name of manufacturer of finished product and official address**

*<< Please enter information here >>*

**6. Name and address of the laboratory or Contract Research Organisation(s) where the BCS-based biowaiver solubility and dissolution studies were conducted**

*<< Please enter information here >>*

I, the undersigned, certify, that the information provided in this application and the attached documents is correct and true

Signed on behalf of

***<Company>***

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ (Date)

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ (Name and title)

1. **Justification for a BCS Biowaiver**

**1.1.Active Pharmaceutical Ingredient (API)**

Please confirm that the proposed product contains the same active substance (e.g. salt, ester, ether, isomer) as the comparator.

*<< Please enter information here >>*

**1.2. Therapeutic Index of the API**

Please enclose a copy of the comparator product labelling and literature references employed to support that the drug does not exhibit a narrow therapeutic index for all authorised indications

*<< Please enter information here >>*

**1.3. Pharmacokinetic properties of the API**

Please enclose a copy of the literature references employed to document the PK properties (PK linearity or reasons for non-linearity).

*<< Please enter information here >>*

**1.4.Dosage form**

Please confirm that:

* the dosage form is an immediate release product for systemic action
* the posology is limited to oral administration
* the administration without water is not included in the proposed posology

*<< Please enter information here >>*

1.0 COMMENTS FROM REVIEW OF SECTION 1 – *PPB USE ONLY*

1. **Solubility**

**(Completion of this section is not necessary if the API(s) are included on the list of biowaiver-eligible APIs in the PQTm document *General notes on Biopharmaceutics Classification System (BCS)-based biowaiver applications*.)**

**2.1. Maximum therapeutic dose of the API**

Please enclose a copy of the labelling of the comparator product to document the maximum single dose that can be administered in a single administration (e.g. two tablets together).

*<< Please enter information here >>*

**2.2.Stability of the drug in the physiological pH range**

Please discuss stability of the API in the pH range from 1.2 to 6.8 and in the gastrointestinal tract.

Please discuss the ability of the analytical method to distinguish the API from its degradation products.

*<< Please enter information here >>*

**2.3.Method of solubility determination**

Please describe method and conditions (e.g. shake flask method at 37±1ºC)

Please indicate also location of the solubility study protocol.

*<< Please enter information here >>*

**2.4.Solubility study dates**

Please indicate dates of study protocol, study conductance and study report

*<< Please enter information here >>*

**2.5. Analytical method validation**

Please summarise the results and indicate location in the documentation.

*<< Please enter information here >>*

**2.6. Results**

Please indicate location of the solubility study report.

Please fill in the following table for the necessary pH values. Add as many rows as necessary to create a solubility – pH profile

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Theoretical pH | Observed pH | Adjusted pH | Individual concentration at saturation (Cs) values | Cs (mean and CV(%)) | Amount that can be dissolved in 250 mL |
| pH 1.2 | Experiment 1Experiment 2Experiment 3 | Experiment 1Experiment 2Experiment 3 | Experiment 1Experiment 2Experiment 3 |  |  |
| IntermdiatepHs | Experiment 1Experiment 2Experiment 3 | Experiment 1Experiment 2Experiment 3 | Experiment 1Experiment 2Experiment 3 |  |  |
| pH 4.5 | Experiment 1Experiment 2Experiment 3 | Experiment 1Experiment 2Experiment 3 | Experiment 1Experiment 2Experiment 3 |  |  |
| Intermediate pHs | Experiment 1Experiment 2Experiment 3 | Experiment 1Experiment 2Experiment 3 | Experiment 1Experiment 2Experiment 3 |  |  |
| pH 6.8 | Experiment 1Experiment 2Experiment 3 | Experiment 1Experiment 2Experiment 3 | Experiment 1Experiment 2Experiment 3 |  |  |
| Other intermediate pH values (e.g. pKa, pKa-1, pKa+1) | Experiment 1Experiment 2Experiment 3 | Experiment 1Experiment 2Experiment 3 | Experiment 1Experiment 2Experiment 3 |  |  |

**2.7.Plot the Solubility – pH profile**

Please attach the plot of the pH-solubility profile based on the above data

*<< Please enter information here >>*

2.0 COMMENTS FROM REVIEW OF SECTION 2 – *PPB USE ONLY*