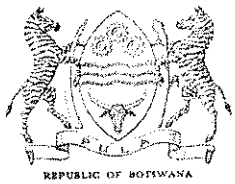
Biowaiver Application Form:
Biopharmaceutics Classification System (BCS)

First Edition



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DRUG ADVISORY BOARD
C/O Drugs Regulatory Units
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NOTE: This guideline has been adapted from the WHO Prequalification of Medicines Programme.

Biowaiver Application Form: Biopharmaceutics Classification System (BCS)

This application form is designed to facilitate information exchange between the Applicant and the Drugs Regulatory Unit if the Applicant seeks to waive bioequivalence studies, based on the Biopharmaceutics Classification System (BCS). For further information, please study the respective DRU biowaiver guidance documents. This form is not to be used, if a biowaiver is applied for additional strength(s) of the submitted product(s).

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 3.5 indicate in which Annex the Certificate of Analysis can be found.
- Please provide the document as part of application for registration, under page 6 of 7.
- 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 the DRU via e-mail dunit@gov.bw.

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:

Attention: Chief Pharmacist
Drugs Regulatory Unit
Department of Clinical Services
Floor 3, Block D
Ministry of Health Headquarters
Government Enclave
Gaborone

Administrative data

1. INN of active ingredient(s)
< *Please enter information here* >

2. Dosage form and strength
< *Please enter information here* >

3. Product WHO Reference number *(if product dossier has been accepted for PQ 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 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. Evidence of BCS Class

1.1 Information regarding solubility and permeability of the drug substance

- Determining drug substance permeability class.

Please provide literature supporting the permeability class and/or results of permeability studies

- Determining drug substance solubility class.

Please provide literature supporting the solubility class and/or results of solubility studies

<< Please enter information here>>

2. Test product

2.1 Tabulation of the composition of the formulation(s) proposed for marketing and those used for comparative dissolution studies

- Please state the location of the master formulae in the quality part of the submission.
- Tabulate the composition of each product strength using the table below.
- For solid oral dosage forms the table should contain only the ingredients in tablet core or contents of a capsule. A copy of the table should be filled in for the film coating/hard capsule, if any.
- Biowaiver batches should be at least of pilot scale (10% of production scale or 100,000 capsules or tablets whichever is greater) and manufacturing method should be the same as for production scale.

Please note: If the formulation proposed for marketing and those used for comparative dissolution studies are not identical, copies of this table should be filled in for each formulation with clear identification in which study the respective formulation was used

Composition of the batches used for comparative dissolution studies				
Batch number				
Batch size (number of unit doses)				
Date of manufacture				
Comments, if any				
Comparison of unit dose compositions and of clinical FPP batches (duplicate this table for each strength, if compositions are different)				
Ingredients (Quality standard)	Unit dose (mg)	Unit dose (%)	Biobatch (kg)	Biobatch (%)
Equivalence of the compositions or justified differences				

2.2 Potency (measured content) of test product as a percentage of label claim as per validated assay method

This information should be cross-referenced to the location of the Certificate of Analysis (CoA) in this biowaiver submission.

<< Please enter information here >>

2.0 COMMENTS FROM REVIEW OF SECTION 2.0 – *DRU USE ONLY*

3. Comparator product

3.1. Comparator product
Please enclose a copy of product labelling (summary of product characteristics), as authorized in country of purchase, and translation into English, if appropriate.

3.2. Name and manufacturer of the comparator product and official address

< Please enter information here >

3.3. Qualitative (and quantitative, if available) information on the composition of the comparator product
Please tabulate the composition of the comparator product based on available information and state the source of this information.

Composition of the comparator product used in dissolution studies		
Batch number		
Expiry date		
Comments, if any		
Ingredients	Unit dose (mg)	Unit dose (%)

3.4. Purchase, shipment and storage of the comparator product
Please attach relevant copies of documents (e.g. receipts) proving the stated conditions.

<< Please enter information here >>

3.5. Potency (measured content) of the comparator product as a percentage of label claim, as measured by the same laboratory under the same conditions as the test product.

This information should be cross-referenced to the location of the Certificate of Analysis (CoA) in this biowaiver submission.

<< Please enter information here >>

3.0 COMMENTS FROM REVIEW OF SECTION 3.0 – *DRU USE ONLY*

4. Comparison of test and comparator products

4.1. Formulation

4.1.1 Identify any excipients present in either product that are known to impact on *in vivo* absorption processes
A literature-based summary of the mechanism by which these effects are known to occur should be included and relevant full discussion enclosed, if applicable.

<< Please enter information here >>

4.1.2 Identify all qualitative (and quantitative, if available) differences between the compositions of the test and comparator products
The data obtained and methods used for the determination of the quantitative composition of the comparator product as required by the guidance documents should be summarized here for assessment.

<< Please enter information here >>

4.1.3 Provide a detailed comment on the impact of any differences between the compositions of the test and comparator products with respect to drug release and in vivo absorption

<< *Please enter information here* >>

4.1. COMMENTS FROM REVIEW OF SECTION 4.1 – *DRU USE ONLY*

4.2. Comparative in vitro dissolution

Information regarding the comparative dissolution studies should be included below to provide adequate evidence supporting the biowaiver request.

Please submit:

- the dissolution study protocol(s) in this biowaiver application
- the dissolution study report(s) in this biowaiver application
- the analytical method validation report in this biowaiver application

<< *Please enter information here* >>

4.3. Summary of the dissolution conditions and method described in the study report(s)

Summary provided below should include the composition, temperature, volume, and method of de-aeration of the dissolution media, the type of apparatus employed, the agitation speed(s) employed, the number of units employed, the method of sample collection including sampling times, sample handling, and sample storage. Deviations from the sampling protocol should also be reported.

4.3.1. Dissolution media: Composition, temperature, volume, and method of de-aeration

<< *Please enter information here* >>

4.3.2. Type of apparatus and agitation speed(s) employed

<< *Please enter information here* >>

4.3.3. Number of units employed

<< *Please enter information here* >>

4.3.4. Sample collection: method of collection, sampling times, sample handling and storage

<< *Please enter information here* >>

4.3.5. Deviations from sampling protocol

<< *Please enter information here* >>

4.4. Summarize the results of the dissolution study(s)
Please provide a tabulated summary of individual and mean results with %CV, graphic summary, and any calculations used to determine the similarity of profiles **for each set of experimental conditions**.

<< *Please enter information here* >>

4.5. Summarize conclusions taken from dissolution study(s)
Please provide a summary statement of the studies performed.

<< *Please enter information here* >>

4.2 – 4.5 COMMENTS FROM REVIEW OF SECTION 4.2 – 4.5: – *DRU USE ONLY*

5. Quality assurance

5.1. Internal quality assurance methods
Please state location in this biowaiver application where internal quality assurance methods and results are described for each of the study sites.

<< *Please enter information here* >>

5.2. Monitoring, Auditing, Inspections
Provide a list of all monitoring and auditing reports of the study, and of recent inspections of study sites by regulatory agencies. State locations in this biowaiver application of the respective reports for each of the study sites e.g., analytical laboratory, laboratory where dissolution studies were performed.

<< *Please enter information here* >>

5.0 COMMENTS FROM REVIEW OF SECTION 5.0 – *DRU USE ONLY*

CONCLUSIONS AND RECOMMENDATIONS – *DRU USE ONLY*