Medicines Control Authority of Zimbabwe

Form: ***EVF 07***

BIOWAIVER FOR ADDITIONAL STRENGTHS APPLICATION FORM

This application form is designed to facilitate information exchange between the Applicant and the MCAZ if the Applicant seeks for waiver of a biowaiver is applied for additional strength(s) of the submitted product(s). This form is not to be used, if the Applicant seeks to waive bioequivalence studies, based on the Biopharmaceutics Classification System (BCS), in which situation a separate "*Biowaiver Application Form"* should be used.

A request for a waiver from the requirement for conducting bioequivalence studies on additional strengths of the product submitted for registration can be made based on the proportionality of the formulations of the series of strengths. If additional strengths are proposed and a biowaiver for these strengths is sought, the following information should be provided

For further guidance, please consult:
MCAZ "***Guideline On Submission Of Documentation For Registration Of Multi-Source (Generic) Finished Pharmaceutical Products (Fpps)"***

Employing the dissolution conditions described in the guideline referenced above, *in vitro* dissolution data comparing the different strengths of the submitted (test) product to each other and data comparing each strength of the test product to the equivalent strength of the appropriate comparator product, if such a strength exists, must be provided.

The format of the dissolution study report(s) provided in support of this waiver request should be consistent with the format employed as a part of a BCS-based biowaiver application.

Final assessment of the proportionality of the proposed formulations and the acceptability of the comparative dissolution data will be made during the evaluation of Quality part of the dossier.

General Instructions:

1. Please review all the instructions thoroughly and carefully prior to completing the Application Form.
2. Provide as much detailed and accurate information as possible.
3. Please enter the data and information directly following the shaded areas.
4. 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.
5. The appended electronic documents should be clearly identified with their file names, which should include the product name and Annex number.
6. Before submitting the completed Application Form, ensure that you have provided all requested information and enclosed all requested documents.

Administrative data

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

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

3. Application number
< *Please enter information here* >

4. Name and address of applicant
< *Please enter information here* >

5. Name and address of manufacturer (s) of finished product
< *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)

_____ (Signature)

_____ (Name and title)

1. Test product

1.1 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 submitted dossier.
- Tabulate the composition of each product strength using the table below.
- For solid oral dosage forms the table should contain all the ingredients in tablet core or contents of a capsule and the film coating/hard capsule, if any. The recommended format for presentation of the formulation or schedule of ingredients of the FPP in **section 4.11** of the MCAZ "***Guidelines on submission of documentation for registration of multi-source (generic) pharmaceutical products (FPPS)"*** should be used.
- 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, primary stability and production FPP batches									
				Comparative dissolution studies batch		**Primary stability batch**		**Production batch**	
Batch number									
Batch size									
Date of manufacture									
Ingredients (Approved name)	**Reason for inclusion**	**Unit**		**Comparative dissolution studies**		**Primary stability batch**		**Production Batch**	
		Mg	**%**	**Kg**	**%**	**KG**	**%**	**KG**	**%**
Core tablet / capsule contents (*Please delete / change which does not apply*)									
API 1									
API 2									
API 3									
Please add / delete as many rows as necessary									
Excipient 1									
Excipient 2									
Excipient 3									
Excipient 4									
Please add / delete as many rows as necessary									
Subtotal 1									
Film coat / capsule shell (*Please delete / change which does not apply*)									
Proprietary film-coating mixture*									
Please add / delete as many rows as necessary									
Subtotal 2									
Grand total									
Equivalence of compositions or justified differences									
* All components (……..) of the proprietary mixture are described in the …….. Pharmacopoeia.									

1.2 Pharmacokinetics

- State whether the drug displays linear or non-linear pharmacokinetics
- Provide literature-based support for your response and append all references cited in the response and state the location of these references in the dossier.
- State concentrations at which non-linearity occurs and any known explanations. Particular attention should be paid to absorption and first-pass metabolism

<< Please enter information here >>

2. Comparator product

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

2.2. Name and manufacturer of the comparator product and official address
< *Please enter information here* >

2.3. 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 (%)

2.4. 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* >>

2.5. 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 the submitted dossier.

<< *Please enter information here* >>

3. Comparative *in vitro* dissolution:

Studies Comparing different strengths of the test product

Comparative dissolution data will be reviewed during the assessment of the Quality part of the dossier. Summary information regarding the comparative dissolution studies should be included below to provide a complete summary of the data supporting the biowaiver request.

3.1 Please state the location of:

- The dissolution study protocol(s) in the dossier
- The dissolution study report(s)in the dossier
- The analytical method validation report in the dossier

<< Please enter information here >>

3.2 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.

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

<< Please enter information here >>

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

<< Please enter information here >>

3.2.3 Number of units employed

<< Please enter information here >>

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

<< Please enter information here >>

3.2.5 Deviations from sampling protocol

<< Please enter information here >>

3.3 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 >>

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

4. Comparative *in vitro* dissolution:

Studies Comparing each strength of the test product to equivalent strength of comparator product

Comparative dissolution data will be reviewed during the assessment of the Quality part of the dossier. Summary information regarding the comparative dissolution studies should be included below to provide a complete summary of the data supporting the biowaiver request.

Please state the location of:

- the dissolution study protocol(s) in the dossier
- the dissolution study report(s) in the dossier
- the analytical method validation report in the dossier

4.2 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.

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

<< Please enter information here >>

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

<< Please enter information here >>

4.2.3 Number of units employed

<< Please enter information here >>

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

<< Please enter information here >>

4.2.5 Deviations from sampling protocol

<< Please enter information here >>

4.3 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 >>

4.4 Summarize conclusions taken from dissolution study(s)
Please provide a summary statement of the studies performed.
<< Please enter information here >>