APPLICATION FOR BIOWAIVER - ADDITIONAL STRENGTH

(Medicines and Allied Substances Act [No. 3] of 2013 Part V Section 39)

The Guidelines on application for grant of Biowaiver on Additional Strength to be consulted in completing this form.

1.0 Particulars of the Product

Name of the Medicine
< *Please enter information here* >
INN of active ingredient(s)
< *Please enter information here* >
Dosage form and strengths
< *Please enter information here* >

2.0 Particulars of the Applicant

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

3.0 Manufacturer(s)

Name of manufacturer of finished product and official address
< *Please enter information here* >

4.0 Research facility(ies)

Name and address of the laboratory or Contract Research Organisation(s) where the biowaiver dissolution studies were conducted *(if applicable)*
< *Please enter information here* >

1. TEST PRODUCT

1.1 Tabulation of the composition of formulation proposed for marketing

- Please state the location of the master formulae in the quality part of the submission.
- 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 or 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.

Composition of the batch used for comparative dissolution studies				
Batch number for biowaiver batch				
Batch size (number of unit doses)				
Date of manufacture				
Expiry date				
Comments, if any				
Unit dose compositions and FPP batch composition				
Ingredients (Quality standard)	Unit dose (mg)	Unit dose (%)	Biowaiver batch (kg)	Biowaiver batch (%)

1.2 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 >>

1.3 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 >>

1.4 COMMENTS FROM REVIEW OF SECTION 1.1 - 1.3 – *OFFICIAL USE ONLY*

2. REFERENCE STRENGTH

2.1. Reference strength

In this context, the reference strength is the strength of the FPP that was compared to the comparator product in an *in vivo* bioequivalence study.

2.2. Tabulation of batch information for the reference strength

The biobatch of the reference strength (batch employed in the *in vivo* bioequivalence study) should be employed in the comparative dissolution studies.

Batch information for batch used for comparative dissolution studies				
Batch number				
Batch size (number of unit doses)				
Date of manufacture				
Expiry date				
Comments, if any				
Unit dose compositions and FPP batch composition				
Ingredients (Quality standard)	Unit dose (mg)	Unit dose (%)	Batch (kg)	Batch (%)

2.3. Batch confirmation

If the batch of reference strength employed in the comparative dissolution studies was not the biobatch of the reference strength (batch employed in the *in vivo* bioequivalence study), the following information should be provided:

- Batch number of biobatch
- Justification for use of a batch other than the biobatch
- Comparative dissolution data for batch employed vs. (historical data for) biobatch
- As an Appendix, executed batch manufacturing records (BMR) for batch employed in dissolution studies

<< Please enter information here >>

2.4 Potency (measured content) of reference 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 >>

2.5 COMMENTS FROM REVIEW OF SECTION 2.1 – 2.4 – *OFFICIAL USE ONLY*

3. COMPARISON OF TEST AND REFERENCE STRENGTHS

3.1. Tabulation of batch information for the test and reference strengths

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 or hard capsule, 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*

3.2. Confirmation of Proportionality

Applicant should confirm that the test and reference strength formulations are directly proportional. Any deviations from direct proportionality should be identified and justified in detail.

<< Please enter information here >>

3.3 COMMENTS FROM REVIEW OF SECTION 3.1 – 3.2 – *OFFICIAL USE ONLY*

4. 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.
- **As per the Quality guideline (*Guideline on Submission of Documentation for a Multi-source (Generic) Finished Pharmaceutical Product (FPP): Quality Part,* Appendix 1), comparative dissolution studies should be conducted in pH 1.2, 4.5, and 6.8 media. If the proposed dissolution medium for release of the products differs from these media, comparative dissolution data in the proposed release medium should also be provided.**
- Summary information regarding the comparative dissolution studies should be included below to provide a complete summary of the data supporting the biowaiver request.

4.1. 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 >>

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, method of filtration, 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 >>

4.5. COMMENTS FROM REVIEW OF SECTION 4.1 – 4.4 – *OFFICIAL USE ONLY*

5. COMPARATIVE *IN VITRO* DISSOLUTION:

STUDIES COMPARING EACH STRENGTH OF THE TEST PRODUCT TO EQUIVALENT STRENGTH OF COMPARATOR PRODUCT; ONLY TO BE SUBMITTED IN CASE *IN VITRO* DISSOLUTION DATA BETWEEN DIFFERENT STRENGTHS OF TEST PRODUCT (SEE SECTION 4) ARE NOT SIMILAR

- This section is applicable in cases where, due to low solubility of the API, similar comparative dissolution between differing strengths is difficult to achieve. The WHO comparator product as identified on the programme's website should be employed.
- Comparative dissolution data will be reviewed during the assessment of the Quality part of the dossier.
- **As per the Quality guideline (*Guideline on Submission of Documentation for a Multi-source (Generic) Finished Pharmaceutical Product (FPP): Quality Part*, Appendix 1), comparative dissolution studies should be conducted in pH 1.2, 4.5, and 6.8 media. If the proposed dissolution medium for release of the products differs from these media, comparative dissolution data in the proposed release medium should also be provided.**
- Summary information regarding the comparative dissolution studies should be included below to provide a complete summary of the data supporting the biowaiver request.

5.1. Purchase, shipment and storage of the comparator product

As per the documentation requirements for comparator products, please attach relevant copies of documents (e.g. receipts) proving the stated conditions.

<< Please enter information here >>

5.2. 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 >>

5.3. 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 >>

5.4. 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.

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

<< Please enter information here >>

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

<< Please enter information here >>

5.4.3. Number of units employed

<< *Please enter information here* >>

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

<< *Please enter information here* >>

5.4.5. Deviations from sampling protocol

<< *Please enter information here* >>

5.5. 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* >>

5.6. Summarize conclusions taken from dissolution study(s)

Please provide a summary statement of the studies performed.

<< *Please enter information here* >>

5.7. COMMENTS FROM REVIEW OF SECTION 5.1 – 5.6 – *OFFICIAL USE ONLY*

CONCLUSIONS AND RECOMMENDATIONS – *OFFICIAL USE ONLY*