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CENTRE FOR PRODUCT REGISTRATION

APPLICATION FOR A BIOWAIVER: ADDITIONAL STRENGTH

Adopted from the:
"WHO/PQT: medicines; Application for a Biowaiver: Additional Strength (Application from 01 May 2010)".
With some adaptation for MALAYSIA application.

General Instructions

- Please review all the instructions thoroughly and carefully prior to completing the current application form.
- This form is not to be used other than biowaiver requested for additional strength(s) of the submitted product(s).
- Please submit this application form in hardcopy together with the relevant documents including bioequivalence (BE) submission checklist, BE report, comparative dissolution profile (CDP) report upon product screening approval.
- Provide / fill in as much detailed, accurate and final information as possible.
- All the appended documents (hardcopy and electronic format documents) should be clearly identifiable by their location and tagging of the file names, which should include the section name, annex number and document version.
- Kindly check that you have signed on the checklist, provided all requested information and enclosed all requested documents.
- Should you have any questions regarding this procedure or the checklist, kindly contact Generic Medicine Section (Bioequivalence Evaluation) via e-mail be_sug@npra.gov.my

Administrative data

(Please fill in the following information)

1.	Product name	
2.	Reference / MAL number (for all strengths of the product line, including the reference strength)	
3.	Active ingredient	
4.	Dosage form and strength	
5.	Name of applicant and official address	
6.	Name and address of manufacturer of finished product	
7.	Name and address of laboratory or contract research organization(s) where the biowaiver dissolution studies were conducted	

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

Signed on behalf of:

(Please state the company name)

_____ _____

(Name & title of product holder) (Date)

1. TEST PRODUCT

1.1 Information of the biowaiver batch

- Attach the certificate of analysis (COA) of biowaiver batch.
- Attach the formulation page and manufacturing process summary in the batch manufacturing records (BMRs) of biowaiver batch.
- Biowaiver batches should be at least of pilot scale
  (≥100 000s @ 1/10 X full production scale, whichever greater. In case of production batch smaller than 100 000s, a full production batch will be required)

Batch number for biowaiver batch	
Batch size	
Date of manufacture	
Expiry date	
Potency (Assayed content)	

Unit dose composition and batch manufacturing formula		
Ingredients	Unit Dose (mg)	Biowaiver batch (kg)

1.2 Pharmacokinetics

- State whether the drug displays linear or non-linear pharmacokinetics
- Provide literature-based support for your response

2. REFERENCE STRENGTH (test product used in the bioequivalence (BE) study)

2.1 Information of the reference strength

In this context, reference strength is referred to the strength of the BE test product that was used in the in vivo BE study.
The same batch of the test product used in the BE study should be used in the comparative dissolution profile (CDP) studies.

Batch number	
Batch size (number of unit doses)	
Date of manufacture	
Expiry date	
Potency (Assayed content)	

Unit dose composition and batch manufacturing formula		
Ingredients	Unit Dose (mg)	Biowaiver batch (kg)

2.2 Batch confirmation

If the batch of the product used in comparative dissolution studies was <u>not the same</u> batch as test product used in BE study, the following information should be provided:

- Justification on the use of different batch in comparative dissolution studies
- The certificate of analysis (COA) of reference strength used in comparative dissolution studies
- The formulation page and manufacturing process summary from BMRs of reference strength used in comparative dissolution studies

3. COMPARATIVE FORMULATION TABLE

3.1 Tabulation of batch information for the test and reference strengths

Ingredients	Function	Strength (label claim)			
		Reference Strength (should be same batch as BE test product)		Test Product (the additional strength test product used in CDP study)	
		……mg		……mg	
		Quantity per unit	% of total core	Quantity per unit	% of total core
Total					

Ingredients	Function	Strength (label claim)			
		Reference Strength (should be same batch as BE test product)		Test Product (the additional strength test product used in CDP study)	
		……mg		……mg	
		Quantity per unit	% of total core	Quantity per unit	% of total core
Total					

Ingredients	Function	Strength (label claim)			
		Reference Strength (should be same batch as BE test product)		**Test Product** (the additional strength test product used in CDP study)	
		…….mg		**…….mg**	
		Quantity per unit	**% of total core**	**Quantity per unit**	**% of total core**
Total					

3.2 Confirmation of proportionality

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

4. Comparative in vitro dissolution studies between test and reference strength

- 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 in vitro data in dissolution medium for release should also be provided.
- Attach the dissolution study protocol and dissolution study report

4.1 Summary of the dissolution conditions and method (please state for each medium used)

Composition of dissolution medium	
Temperature of dissolution medium	
Volume of dissolution medium	
Type of apparatus	
Agitation	
Detection method	
Number of units employed	

4.2 Summarize the results of the dissolution study

- 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.