Bahagian Regulatori Farmasi Negara (NPRA)
National Pharmaceutical Regulatory Agency (NPRA)
Lot 36, Jalan Universiti, 46200 Petaling Jaya,Selangor.
No. Tel. *Tel. No.* : 03-78835400
No. Faks. *Fax No.* : 03-79571200
Laman Sesawang*Website* : http://npra.moh.gov.my

CENTRE OF PRODUCT AND COSMETIC EVALUATION

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).
- One form is only for the application of one strength. If there are several strengths requested for biowaiver, please fill in this form separately.
- Please submit this application form together with the relevant documents including bioequivalence (BE) submission checklist, BE report, comparative dissolution profile (CDP) report in QUEST 3+ system under section P9 for product screening and evaluation.
- Provide / fill in as much detailed, accurate and final information as possible.
- All the appended documents should be clearly identifiable by their location and tagging of the file names. Kindly refer to the 'Guide on how to upload the BE study report and other relevant documents in QUEST 3+ system under section P9'.
- 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

*Reminder:

i. Please be informed that all data submitted to support the registration application for this product will be subjected to further evaluation
ii. Please refrain from changing/removing all submitted data unless requested by NPRA or the data has been updated as per latest registration requirements.
iii. Kindly be reminded that decision whether the dossier is allowed for registration will be subjected to full evaluation and the final decision by the Drug Control Authority (DCA).
iv. Kindly also note that satisfactory and complete documentation must be submitted within 180 working days, after first evaluation remark is received to avoid rejection.

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

Signed on behalf of:

_____ (Product registration holder)

_____ (Date)

_____ (Name & title)

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)

Product name	
Active ingredient, strength and dosage form	
Batch number for biowaiver batch	
Batch size	
Date of manufacture	
Expiry date	
Potency (Assayed content)	
Name and full address of the drug substance manufacturing site	
Name and full address of the test product manufacturing site	

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.

Active ingredient, strength and dosage form	
Batch number	
Batch size (number of unit doses)	
Date of manufacture	
Expiry date	
Potency (Assayed content)	
Name and full address of the drug substance manufacturing site	
Name and full address of the test product manufacturing site	

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					

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 MANUFACTURING PROCESS

4.1 Tabulation of manufacturing process for the test product and reference strengths

Test Product	Reference Strength (BE test product)

4.2 Confirmation of manufacturing process

- Applicant should confirm whether the test product and reference strength are manufactured by the same manufacturing process.

5. 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

Name and address of laboratory or contract research organization(s) where the biowaiver dissolution studies were conducted	

5.1 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	

5.2 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.