PUBLIC CONSULTATION ON IMPLEMENTATION OF BIOEQUIVALENCE (BE) STUDY REQUIREMENTS FOR NEW DRUG PRODUCTS CONTAINING SCHEDULED POISON

NPRA, 16 April 2019

PROPOSED IMPLEMENTATION OF BE STUDY REQUIREMENTS

DATE OF IMPLEMENTATION	ALL NEW DRUG PRODUCT REGISTRATION APPLICATIONS RECEIVED ON OR AFTER **1 JANUARY 2021**
TYPE OF PRODUCT	HYBRID NCE GENERIC PRODUCT CONTAINING SCHEDULED POISON (REFER SLIDE NOS. 4 & 5)
TYPE OF APPLICATION	NEW DRUG PRODUCT REGISTRATION ONLY (RENEWAL IS EXEMPTED)
REFERENCE FOR PROPOSED PROCESS AND REQUIREMENTS	CURRENT PRACTICE AT GENERIC MEDICINE SECTION, NPRA

OBJECTIVES OF THIS CONSULTATION

TO DETERMINE:

1. SCOPE OF IMPLEMENTATION OF BE STUDY REQUIREMENTS FOR NEW DRUG PRODUCTS
2. REQUIREMENTS OF BE STUDY DESIGN
3. REQUIREMENTS OF BE STUDY CENTRE ACCREDITATION

BACKGROUND: ASSESSMENT ON GENERIC PRODUCTS AT CENTRE FOR PRODUCT REGISTRATION, NPRA

	GENERIC MEDICINE SECTION	NEW DRUG SECTION
TYPE OF GENERIC PRODUCT ASSESSED	A generic product* defined as a product that is essentially similar to a **currently registered** product (**innovator**) in Malaysia *The generic product must be of the same dosage form and must contain the same active ingredient as the registered innovator	A generic product# for which its **innovator has never been registered** in Malaysia #All other generic products which do not fall within the scope of Generic Medicine Section
SCOPE OF APPLICATION	Generic products containing poisons as listed in the First Schedule under Poisons Act 1952 (**scheduled poison**)	Generic products containing poisons as listed in the First Schedule under Poisons Act 1952 (**scheduled poison**)
DOCUMENTS REQUIRED	Based on ACTD module: Part I (administrative) Part II (quality) Bioequivalence study report	Based on ACTD module: Part I (administrative) Part II (quality) Part III (nonclinical – can refer to published studies of the innovator) Part IV (clinical – can refer to published studies of the innovator) Bioequivalence study report Risk management plan (RMP)
ASSESSMENT TIMELINE	210 working days	210 working days

PROPOSED SCOPE OF IMPLEMENTATION ON BE STUDY REQUIREMENTS FOR NEW DRUG PRODUCTS

TYPE OF NEW DRUG PRODUCT	BE STUDY REQUIREMENTS
NEW NCE PRODUCT	This category concerns products containing new active moieties never before registered in Malaysia and is not being considered in the scope of implementation on BE study requirements
HYBRID NCE PRODUCT	This category concerns all other products which do not fall under New NCE Product classification. They include: (a) New Drug Products containing registered chemical entities in new chemical/dosage forms; and (b) a generic product for which its innovator (in the same chemical/dosage form) has never been registered in Malaysia. Products in (a) are considered innovator line extension products, i.e. developed by the same innovator company through in-house pharmacokinetic/pharmacodynamics/bioavailability comparison studies. They are <u>outside the scope</u> of this proposed implementation. The proposed scope of implementation on BE study requirements will only include (b), i.e. a **Hybrid NCE Generic Product.**

PROPOSED REQUIREMENTS ON BE STUDY DESIGN

CHOICE OF COMPARATOR PRODUCT:

- List of comparator products for BE studies as published on NPRA website https://www.npra.gov.my/easyarticles/images/users/1071/List-of-Comparator-Products-For-Bioequivalence-Studies-March-2019.pdf
- A innovator / reference listed product at the country in which the generic product is registered/manufactured

REFERENCE DOCUMENTS FOR BE STUDY DESIGN REQUREMENTS:

- ASEAN Guideline for the Conduct of Bioequivalence Studies – most current version
- Malaysian Guidance on Biopharmaceutics Classification System (BCS)-based Biowaiver – most current version
- Current updates, directives, circulars and guidelines as can be found on NPRA website https://www.npra.gov.my/index.php/en/bioequivalence-be-2.html?highlight=WyJiaW9lcXVpdmFsZW5jZSIsImNvbXBhcmF0b3IiXQ==

PROPOSED REQUIREMENTS ON BE STUDY CENTRE ACCEPTANCE

NPRA'S COMPLIANCE PROGRAMME FOR BE CENTRE:

- BE study centre inspection team is based at NPRA's Centre of Investigational New Product
- Reference document: https://www.npra.gov.my/images/Guidelines_Central/Guidelines_on_Clinical_Trial/Malaysia%20Guideline%20for%20BE%20Inspection%20(5-9-14)%20-%20Final.pdf

BE STUDY CENTRE ACCEPTANCE BASED ON CURRENT PRACTICE:

- BE studies to support product registration at NPRA must be conducted at centres listed in NPRA's Compliance Programme or at centres inspected by regulatory authorities recognised by NPRA
- An assessment on BE centre inspection report may be conducted by NPRA in these cases:
  1. BE study centres in the USA and Canada inspected by the US FDA
  2. BE study centres in Europe and Canada inspected by the EMA, MHRA, ANSM, BfArM, AGES and other European regulatory agencies, subject to scope of inspection
  3. BE study centres outside the USA, Canada and Europe inspected by EMA, MHRA, ANSM, BfArM, AGES and other European regulatory agencies, subject to scope of inspection
- In case of any doubt on the adherence to GCP and GLP principles at the BE study centre:
  1. The BE study centre inspection report can be rejected
  2. An inspection visit to the BE study centre by the NPRA team can be called
  3. A refusal for inspection visit by the BE study centre can lead to product registration rejection

THANK YOU

Please email all enquiries and comments to Dr Yvonne Khoo, yvonne@npra.gov.my by 15 May 2019