BEDE Frequently Asked Questions 2023

A) Preliminary Requirements	
Q1	**Will all BE studies conducted before 2012 at BE Centres listed under the NPRA BE Centre Compliance Programme receive exemptions from this requirement?** The requirement to submit BEDE application extends to all BE studies conducted in BE centres before listing or outside the listing period on the NPRA programme which includes BE studies conducted before 1 January 2012.
Q2	**Is BEDE applicable for the following products?** **i. Generic products,** **ii. Generic products with no innovators registered in Malaysia,** **iii. Innovator products** **iv. "Hybrid" innovator products** **v. Non-innovator "Hybrid" products** This desktop evaluation is applicable only for generic products and generic products in which the innovator is not registered in Malaysia and non-innovator hybrid products. Applicants are advised to apply for product classification by the NPRA before deciding on the registration pathway. Products categorised above may utilise the desktop evaluation as an option to allow for BE studies conducted at BE Centres not on the NPRA compliance programme or not during valid listing to be accepted for product registration evaluation.
Q3	**Which dosage form of the above class of products requires BEDE evaluation?** Currently BE studies is required for the following dosage form. i. immediate release, oral solid dosage [effective 1 January 2012] ii. modified release (extended, prolonged, sustained release, etc.) [effective 12 June 2013] iii. effervescent, dispersible, orodispersible, sublingual, buccal and chewable [effective 1 January 2018]
Q4	**If the applicant is certain that a study specific inspection by NPRA is required, can the applicant apply for a study specific inspection instead of BEDE?** Applicants are advised to use the BEDE Submission Checklist published on the NPRA website. If applicants find that there are insufficient documents to support BEDE applications, applicants may instead opt to apply for an inspection by the NPRA. Please state on your inspection submission cover letter that the study does not qualify for BEDE application.
Q5	**If there has been a BEIR approval issued for the BE study of a product that has yet to be submitted for product registration evaluation, is the BEIR still valid or an application for desktop evaluation is required?** Acceptance of the BEIR approval depends on whether the letter indicated a validity to the approval. If the letter has no validity stated then the BEIR approval can still be accepted.

Q6	**Is BEDE applicable for BE studies conducted in BE centres located in any country?** Yes, it applies to any BE studies conducted at BE centres not listed in the NPRA BE Centre Compliance Programme and/or not within the listing validity.
Q7	**Previously, an application for BEIR evaluation was rejected due to the inspection report not being product - specific. Will this desktop evaluation also require product - specific inspection reports?** This mechanism replaces and expands on the previous BEIR process. In BEDE, inspection reports conducted within 5 years before and after the BE study conduct may be submitted. However, submission of a product-specific inspection report will increase the confidence during evaluation.
Q8	**Can the desktop evaluation be applied for BE centres that are no longer in operation?** Yes, an application can be submitted for studies conducted at these BE centres if valid supporting documents and information as per BEDE Submission Checklist can be submitted. The outcome of the evaluation will be based on the overall documents submitted.
Q9	**How many and which BE study/studies should be submitted for BEDE application?** It is recommended that only one BE study required to support the registration of one product for the purpose of product registration should be submitted for each BEDE application. Applicants may submit more than one BE study for one product, however, delays in the evaluation of the application should be expected.
Q10	**Which guidelines are referred to by the Generic Section, Centre for Product and Cosmetic Evaluation?** The following guidance is referred to: • ASEAN Guideline for Conduct of Bioequivalence Studies, March 2015 • EMA Product-specific Bioequivalence Guidance • Appendix 16 of Drug Registration Guidance Document (DRGD), Third Edition, Third Revision July 2022 • Guidelines on Bioequivalence from Centre for Product and Cosmetic Evaluation: Bioequivalence (BE) Main Page (npra.gov.my)
Q11	**Which guidelines are referred to by the New Chemical Entity Section, Centre for Product and Cosmetic Evaluation?** The following guidance is referred to: • ASEAN Guideline for Conduct of Bioequivalence Studies, March 2015 • EMA Product-specific Bioequivalence Guidance • Appendix 16 of Drug Registration Guidance Document (DRGD), Third Edition, Third Revision July 2022 • Guidelines on Bioequivalence from Centre for Product and Cosmetic Evaluation: Bioequivalence (BE) Main Page (npra.gov.my)

Q12	**Can I submit BEDE application if one/ both clinical/ bioanalytical sites have never been inspected by any Drug Regulatory Authority (DRA)?** Inspection reports issued by the DRA is required to qualify for acceptance of BEDE screening and evaluation. The application will be administratively rejected upon submission if there are no inspection reports can be provided for clinical and/ or bioanalytical sites.
Q13	**I would like to submit BE study which was conducted at clinical/ bioanalytical sites that have never been inspected by any Drug Regulatory Authority (DRA). What should I do?** Kindly submit study specific foreign inspection application for further consideration. Please state on your inspection submission cover letter that the BEDE was administratively rejected due to the unavailability of the DRA inspection history & reports to be submitted.
Q14	**Can the application for both BEDE and product screening (for product registration evaluation) be done concurrently?** Applicants are suggested to submit for product registration screening once applicants are certain on the outcome of the desktop evaluation. This is because the timeline for both product screening and desktop evaluation is independent of one another.

B) Application Form/ Submission	
Q15	**Where do I find BEDE application form (NPRA/434/12-1), BEDE submission checklist (NPRA-434-17-1) and the L1 form (NPRA/434/12-1-L1)?** The documents are available in the following link: https://www.npra.gov.my/index.php/en/application-forms-and-checklist.html
Q16	**What are the documents required during BEDE application submission?** For new BEDE submission, the hardcopy of BEDE application form (NPRA/434/12-1) printed double-sided along with the BEDE submission checklist (NPRA-434-17-1) are required.
Q17	**Should I submit other supporting documents in addition to the above hard copy documents?** No. Other supporting documents as listed in the BEDE submission checklist should be submitted (in softcopy) following request by the screening officer. A link will be provided for each BEDE application for the purpose of document submission.
Q18	**Should I submit my BEDE application at BEEC counter or via postage?** Administrative screening will be done during BEDE application submission. Therefore, the PRH is encouraged to submit application at the counter. However, we do understand that submission via postage is the only option for some applicants due to logistics issues. In situations where an incomplete application is received via postage, an administrative rejection email will be issued during screening.
Q19	**What are the documents required during BEDE application resubmission?**

	A letter explaining the gap between previous BEDE application and the resubmitted BEDE application must be provided in addition to the hardcopy of the application form and the BEDE Submission Checklist. The PRH is required to quote the BEDE reference number of the previous BEDE application in the BEDE Submission Checklist.
	i) Part 3: Details of Product
Q20	**I have one modified release products to be submitted for BEDE evaluation whereby both fasted and fed BE studies is required for product registration. How many BEDE applications should I submit?** The applicant is required to submit one BEDE application. Information of both BE studies shall be included in the same application whereby Part 4 should be repeated for each BE study.
Q21	**I would like to submit two BE studies with different strength of comparator product used during BE study conduct. For example, Rivaroxaban 10mg (BE Study A) and Rivaroxaban 20mg (BE Study B) How many BEDE applications should I submit?** BEDE application shall be submitted for each strength of comparator product. In this case, two BEDE applications should be submitted.
Q22	**What should I declare under *Registration Status in Other Countries* under No.4?** The Product Registration Holder (PRH) is required to confirm with the sponsor and CRO whether the test product have been registered with any of NPRA's reference agencies (as listed in the application form). Evidence is required to be submitted during submission of BEDE supporting documents. This information is vital as a different internal evaluation pathway will be determined if this verifiable evidence is available.
Q23	**What is the *Assessment Report* as stated under No. 4?** Assessment reports are reports issued by DRA which reviewed the BE study for product registration in their respective country/region. An example of assessment report is the Public Assessment Reports issued under the decentralised submission procedure of EMA. These documents shall be submitted as Appendix 2b following request from the screening officers.
	ii) Part 4: Details of BE Study(ies)
Q24	**How should I declare the date of Clinical, Bioanalytical in the application form (No. 5)?** The start and end date of Clinical, Bioanalytical and all Method Validation conducted shall be declared in the format of DD/MMM/YYYY – DD/MMM/YYYY. For example: • Clinical Date: 01 JAN 2013 – 20 JAN 2013 • Bioanalytical Date: 25 JAN 2013 – 10 JAN 2013
Q25	**What is the information required in *Inspection Status of the BE study and Acceptance Status of the BE Study (No. 14)?***

	The applicant is required to declare whether the BE study of interest (as submitted in the BEDE application) has been inspected and/or accepted for evaluation by any of NPRA's reference agencies (UKMHRA, United Kingdom; Sweden Medical Products Agency, Sweden; ANSM, France; USFDA, US; TGA, Australia; Health Canada, Canada; PMDA, Japan; Swissmedic, Switzerland and EMA through Centralised Procedure). The status of the inspection and evaluation should be declared under this section. Inspection and evaluation report shall be submitted during screening process as Appendix 6. (Refer to BEDE Submission Checklist and L1 form)
Q26	**How should I declare the date of Method Validation in the application form (No. 16)?** The start and end date of all Method Validation conducted shall be declared in the format of DD/MMM/YYYY – DD/MMM/YYYY. For example; • Full Validation (Report No.:…….) 01 JAN 2012 – 20 JAN 2012 • Partial Validation (Report No.:…….) 01 MAC 2012 – 20 MAC 2012
	iii) Part 5: Details of Study Centre(s)
Q27	**How should I fill up the *Details of Study Centre* under Part 5 of the application form?** The applicant should list out all Drug Regulatory Agency (DRA) inspection conducted at each clinical and bioanalytical site. A separate table should be prepared for each clinical and bioanalytical site of the BE Centre. For example, if the study is conducted at 3 clinical sites and 1 bioanalytical site, 4 separate tables shall be prepared.
Q28	**If the BE study was conducted in June 2018, how many years shall I declare the history of inspection conducted by DRA on those sites?** The history of inspection that should be listed is between June 2013 - June 2023. (5 years before and after the date of BE study conduct).
Q29	**One of the clinical/ bioanalytical sites have been inspected by the sponsor and/ or the 3rd party certification company such as the ISO. Shall I declare these inspections in the application form and submit those reports/ certificates to support BEDE application?** NPRA only recognize inspection reports issued by the DRA. These inspections (ISO etc) are not required to be declared in the application form.
Q30	**The clinical/ bioanalytical site has been inspected by a DRA. However, the inspection report could not be shared due to confidentiality issues. What should I do?** The applicant may reconfirm with the CRO and the sponsor if the inspection report can be shared with NPRA. NPRA would not be able to proceed with screening and evaluation if the reports are not available as it is one of the primary areas where risk assessment will be performed during BEDE evaluation.
Q31	**The BE studies I intend to submit were conducted on patients instead of healthy individuals The clinical site consists of multiple healthcare facilities such as hospitals**

	whereby some of the healthcare facilities does not have any inspection history. Can I still submit BEDE application? SBEEC may consider acceptance of BEDE application based on case-to-case basis. Kindly contact SBEEC, NPRA for further confirmation.

C) Screening Process	
Q32	**What are the supporting documents required during screening of BEDE application?** Appendix 1-14 as listed under the BEDE submission checklist shall be submitted following a request by screener during BEDE application will be requested. The details/ specific inspection reports (Appendix 15) will be requested by the screener via email during the screening stage.
Q33	**Which format shall I upload my documents?** Appendix 1 (L1 form) shall be submitted in MS Word format. Other documents as listed in BEDE Submission Checklist shall be submitted in searchable (OCR) PDF format.
Q34	**Is the OCR document format compulsory in the submission?** Documents submitted in the OCR format is preferred to allow the evaluation to take place in a fast and efficient manner. Documents in this format will allow for key information to be located and evaluated much quicker during the evaluation process.
Q35	**Some of the supporting documents for my BEDE application are not in English language. What should I do?** Kindly ensure all supporting documents are translated to English by a certified translator prior to application submission. The translated documents should be verified by the Quality Assurance Department of the relevant CRO. The applicant will only be given 30 working days to upload all supporting documents. Failure to do so may cause rejection of the application.
Q36	**Who is responsible to upload all relevant documents and correspondences for screening and evaluation of BEDE application?** The PRH is responsible to ensure all documents and correspondences is completely uploaded in the link provided during screening and evaluation of BEDE application.
Q37	**I could not upload documents using the link provided by NPRA. The website giving me errors such as '*File Not Found*'. What should I do?** NPRA performs periodic maintenance on our server which may cause the above errors. The PRH may share a link for the screening officers to download the files. Kindly ensure that the link provided is valid for at least 1 month for the screeners/ evaluators to download all the documents.
Q38	**How many correspondences are allowed between the applicant and the screener during the screening process?**

	Starting from 1st April 2023, only one correspondence is allowed during the screening process. If documents requested by the screener are not submitted within 30 working days, the application will be rejected.
Q39	**Can the applicant request for extension for document submission during screening?** All documents requested by the screener need to be submitted to NPRA within 30 working days. However, applicants are encouraged to submit all required documents within 10 working days to allow for second submission if the first set of documents was incomplete. Extension may be granted during the first document submission, however, kindly take note that all required documents need to be submitted to BEEC Section within 30 working days. Failure to do so will lead to screening rejection.
Q40	**How many inspection reports will be requested by the screener during screening?** Typically, the screener will request two inspection reports from each clinical and bioanalytical site. However, if the inspection reports shared is insufficient to support BEDE evaluation, the screeners and/ or evaluator may request more inspection reports for screening/ evaluation.
Q41	**BE centre inspection reports are confidential. I do not want the PRH to be able to view these documents. What should I do?** A The CRO is advised to encrypt the inspection reports with password and request the PRH to upload all the documents. The password should be forwarded directly to the screening/ evaluation officers email address. The CRO is advised to quote the BEDE application number in the email for traceability purposes.
Q42	**Some inspection reports by regulators such as the USFDA are only available in redacted versions. Under such circumstances, are these redacted documents acceptable by the NPRA?** Redacted documents can be submitted provided that the redaction is made by the regulators instead of BE centre and/or applicant. The redacted information should not involve information that is required for the evaluation process such as (but not limited to) name of sites, name of product etc.

D) Evaluation	
Q43	**Should inspection reports from all regulatory agencies be submitted during the application process?** All regulatory inspections within the stipulated timeframe should be declared in the NPRA/434/12-1 form. Specific inspection reports will be requested to be submitted in softcopy along with the form NPRA/434/12-1-L1 and priorities are given to inspection reports by NPRA reference agencies.

Q44	**Some BE centres located in Europe do not have inspection reports but do have GCP and GLP certificates. Can these certificates replace the inspection reports?** GCP and GLP certificates can be submitted just as supporting documents along with other relevant documents. However, inspection reports from regulatory authorities are required before evaluation can proceed. The outcome of the evaluation will depend on the overall documents submitted.
Q45	**How many correspondences are allowed between the applicant and the evaluator during the evaluation process?** Starting from 1st April 2023, only one correspondence is allowed during the evaluation process. If the queries by evaluator are not sufficiently addressed by the applicant during this correspondence, the application will be rejected. Applicants may submit a new application once all documents are available for submission.
Q46	**Is there any expedited review pathway for BE desktop evaluation?** Yes, applications for BE desktop evaluation can be considered for an expedited review if: a) The same BE study was submitted during product registration in NPRA's reference countries (United States, United Kingdom, France, Sweden, Switzerland, Japan and Australia). b) The BE study of interest has been inspected by NPRA's reference agencies (USFDA, UKMHRA, ANSM, EMA etc) Hence, it is crucial for applicants to declare the correct information on product registration status in Part 3 No. 4 and inspection and acceptance status of the BE study by NPRA's reference agencies in Part 4 No. 14 of the application form NPRA/434/12-1. Applicants should also ensure that verifiable supporting documents are submitted for evaluation.
Q47	**What are the documents required during screening in an expedited review pathway?** The screening process for an expedited review is similar to the conventional pathway. In an expedited review, the applicant is required to provide all documents listed in the BEDE Submission Checklist.
Q48	**Which marketing authorisation should be submitted along with the PAR?** The latest marketing authorisation should be submitted and applicants are required to declare if the marketing authorisation has expired and not renewed. The procedure number stated on the marketing authorization should be similar to the PAR procedure number submitted.
Q49	**What is the timeline for an expedited review pathway? How soon can the applicant expect a decision from BEEC?** The screening and evaluation timeline for an expedited review is similar to the conventional pathway (kindly refer to Part 1: Application Process Flow of the application form). However, the time for the evaluation process is expected to be shorter as fewer documents are reviewed and no correspondence is expected between the evaluator and the applicant.

E) Decision of BEDE Evaluation	
Q50	**What is the process of coming to a decision for BE desktop evaluation?** Review by first evaluator --> review by second evaluator (if applicable) --> review by the Head of Section --> table in *Mesyuarat Teknikal Pemeriksaan Klinikal dan Bukan Klinikal (MTekKBK)* However, if study specific inspection is required, the BEDE will be tabled in the next JKPPPK meeting *(Mesyuarat Jawatankuasa Penilaian Pemeriksaan Premis dan Kajian).*
Q51	**When can the applicant expect the decision letter from NPRA?** The decision letter will be emailed to the applicant within 14 working days of the technical meeting or the JKPPPK meeting depending whether your BEDE application is granted exemption from study specific inspection or not. The applicant is encouraged to collect the original letter at the BEEC Section, Level B3, NPRA within 30 days of the date of email.
Q52	**How long is the validity of the BEDE decision letter?** Kindly take note that the BEDE decision letter has no validity or expiry.
Q53	**What is next after receiving the BEDE decision letter?** Depending on the outcome of the BEDE application: a) If your BEDE application has a favourable outcome, it can be accepted for review by the Centre of Product and Cosmetic Evaluation, NPRA. b) If study specific inspection is required, the applicant may proceed to apply for study specific inspection. Applicants may liaise with BEEC officers for further information on the application process, inspection costs etc. However, if applicants decide to resubmit the BEDE application, please take note that resubmission is only accepted if new documents are available to support the evaluation process.

F) Miscellaneous	
Q54	**How much is the application fee?** The BEDE is currently free of charge until the implementation of the charges. Subject to approval, the fee is RM2,000.00 for each BEDE application.
Q55	**When is the implementation of the charges will come into effect?** The NPRA is still in the process of obtaining Finance Department approval to implement the charges. Potential applicants will be notified before charges will come into effect.
Q56	**Can I proceed for study specific inspection application concurrently with BEDE application?** The applicant is advised to apply for BEDE and wait for the outcome of BEDE evaluation before applying for a study specific inspection.
Q57	**How can I withdraw study specific inspection application following the satisfactory outcome of BEDE evaluation?**

	If the decision to withdraw the study specific inspection application is made, the applicant may request for a refund from the NPRA in writing. However, please be advised that the refund is only applicable for the cost of inspection contributions. The application fee of RM5,000.00 is not refundable.
Q58	**If BEDE evaluation determines that a study-specific inspection is required, what is the estimated timeline from the start of this evaluation process to the inspection outcome being known?** The timeline for inspection is subject to the queue for inspection, availability of the inspectors and decision from MOH Trust Fund Meetings. Kindly liaise with BEEC officers for further information.
Q59	**What is the lead time required for a study-specific inspection to be completed?** Under normal circumstances and assuming that the total allotted time required for each stage is taken, it will take 6 months for an inspection to be closed from the date of the inspection.
Q60	**Can BEDE be used to qualify the BE centre for listing on NPRA BE Centre Compliance Programme?** BEDE application is to determine if a BE study may be exempted from a study-specific inspection before being accepted for product registration evaluation. Therefore, BEDE cannot be used for accreditation of the BE centre to be listed in NPRA BE Centre Compliance Programme as the listings of BE centres still requires an on-site inspection.
Q61	**Are there any MoU or Harmonization with ASEAN / PICS / for Joint Assessment on BEDE evaluation?** Not at the moment.

Last updated: 28 February 2023