FREQUENTLY ASKED QUESTION (FAQ): DESKTOP EVALUATION ON THE NEED FOR BIOEQUIVALENCE STUDY SPECIFIC INSPECTION

The questions were collected prior and during the *Virtual Q&A Session: Evaluation on The Need for Bioequivalence Study Specific Inspection* which was held on 10 August 2020.

	Application Process / Form
Q1	Should the application be submitted in softcopy via email or in hardcopy?
A1	The application form (BEEC/F-017) should be submitted in hardcopy. Supporting documents are to be submitted in softcopy along with form BEEC/F-017-L1. A link will be provided for each application for the purpose of document submission and additional supporting documents may be requested.
Q2	Since each application will be for only one product, how should the application be submitted if the products for registration have different strengths or studies involving different states such as fed, fasting and/or steady states?
A2	This will depend on the requirements set by the Centre of Product & Cosmetic Evaluation. Applicants are expected to be aware of the studies required to support the products for product registration and assess on which mechanism would enable those studies to be accepted for review. In the event that more than 1 BE study is required, Part 4 should be repeated for each BE study in the application.
Q3	What are the differences between Form BEEC/F-017 and Form BEEC/F-017-L1?
A3	Form BEEC/F017 contains information that is declared by the applicant for the application to proceed. Note that no supporting documents will be submitted with the application form apart from the official receipt as proof of payment. The receipt is only applicable once the fee has been approved. Form BEEC/F-017-L1 will request for specific documents declared in the application form in addition to some additional information for the evaluation process. These documents should be submitted to the NPRA for review along with Form BEEC/F-017-L1 in softcopy via the link provided.
Q4	In Form BEEC/F-017 under *Bahagian 4: Maklumat Kajian BE, No. 12,* can this row be repeated if there are more than two (2) inspection statuses for the BE study?
A4	Yes, the row can be repeated.
Q5	Assuming that the application for desktop evaluation to determine the need for study-specific inspection is done on August 2020 and the BE study was conducted in 2013, what would be the range of years the list of inspections conducted at the site should be declared?
A5	List of inspections 3-5 years from the date of application: Inspection conducted from between 2015 to 2020.

	List of inspections 3-5 years before and after BE study: Inspection conducted between 2008 to 2018.
Q6	Since there is no procedure for appeal, can the application be submitted for re-evaluation if the desktop evaluation was rejected?
A6	Yes, the application may be submitted for re-evaluation. However, it is strongly recommended that the resubmitted application should include additional documents or information so that a different outcome may be expected.
Q7	Does the assessment reports requested under Part 2, No. 4 of the BEEC/F-017-L1 form refer to the Product Assessment Reports such as the reports under the decentralised submission procedure of the EMA?
A7	The assessment reports are issued by the regulatory authorities which reviewed the BE study for product registration in their respective country/region. Public Assessment Reports may be submitted as one of the main information sought from these reports is the status of GCP compliance in the studies evaluated by the assessors.
Q8	Can the application for both desktop evaluation (on the need for study-specific inspection) and product screening (for product registration evaluation) be done concurrently?
A8	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.
Q9	Based on the Application Process Flow, is it possible to skip the initial submission and directly proceed with the submission of Form BEEC/F-017-L1 along with supporting documents in hardcopy to the NPRA? NPRA can then proceed to request for the selected documents and the BEEC/F-017-L1 form in softcopy.
A9	The initial application form is required for the applicant to declare what are the available documents to support the evaluation. Applicants will also need to submit a copy of the official payment receipt along with the application form once approval has been granted for the application fee. Once accepted, the NPRA will request a list of documents from the information declared in the initial submission form. Since the information is already available, applicants may submit the documents in softcopy when requested via the link provided in the notification email.
Q10	Is there a limit on the number of studies to be included in an application?
A10	There is no limit to the number of studies to be submitted in one application form. However, each application will be for one product only. The request for documents to be submitted in Form BEEC/F-017-L1 will be for each of the studies submitted in the initial application form.
Q11	Some assessment reports by regulators such as the US FDA are only available in redacted versions. Under such circumstances, are these redacted documents acceptable by the NPRA with justification?

A11	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.
Q12	Is the OCR document format compulsory in the submission?
A12	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. Although not preferred, documents submitted without the search function or in OCR format will still be accepted for evaluation.

	Technical Evaluation
Q1	Are inspections from all regulatory authorities accepted? Should inspection reports from all regulatory agencies be submitted during the application process?
A1	During the initial submission, all regulatory inspections within the stipulated timeframe should be declared in the BEEC/F-017 form. Base on the declaration in the initial submission, specific inspection reports will be requested to be submitted in softcopy along with form BEEC/F-017-L1 in the notification email. Inspection reports from our reference authorities listed under *Lampiran 1* of BEEC/F-018 Submission Manual will be given priority in the request.
Q2	Will all the BE studies conducted before 2012 at BE Centres listed under the NPRA BE Centre Compliance Programme receive exemptions from this requirement?
A2	This requirement extends to all BE studies as long as it is conducted at BE centres before listing or outside the listing period on the NPRA programme. This includes BE studies conducted before 1 January 2012.
Q3	If the BE centre is located in Europe and inspected by the EMA or any of the agencies from the reference countries, does this evaluation still apply for BE studies conducted at this centre?
A3	Yes. Application for desktop evaluation is still required as long as the site is not listed in NPRA BE Centre Compliance Programme or the study is not conducted within the listing period. This evaluation also replaces the Bioequivalence Inspection Report Review (BEIR) process.
Q4	Is this desktop evaluation applicable for the following products? i. Generic products, ii. Generic products with no innovators registered in Malaysia, iii. Innovator products iv. “Hybrid” innovator products If this evaluation can be applied to innovator and hybrid innovator products, will there be an exemption or abridged route with a shorter timeline if the BE centre has been inspected by the agency from the reference countries?
A4	This desktop evaluation is applicable only for generic products and generic products in which the innovator is not registered in Malaysia. 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. There is no abridged/expedited pathway and the speed of the evaluation will depend on the speed and completeness of documents submitted.
Q5	Is this application compulsory before every generic product registration submission or it may be skipped if the applicant is sure that an NPRA inspection is required?
A5	Based on the information in the manual published, applicants should assess if they have the necessary documents to support the desktop evaluation application. If you deemed that there are insufficient documents to support the application, you may instead opt to apply for an inspection by the NPRA.
Q6	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?
A6	Acceptance of the BEIR approval will depend on whether the letter indicated a validity to the approval. If the letter has no validity stated i.e. for study-specific inspection reports or studies that were conducted within 3 years of the inspection date, the BEIR approval can still be accepted.
Q7	Can the desktop evaluation be applied for BE centres that are no longer in operation? All inspection reports and other required documents are available for BE studies that were conducted before the facility closed down.
A7	Yes. An application can be submitted for studies conducted at the BE centre before it was closed down along with valid supporting documents. The outcome of the evaluation will be based on the overall documents submitted.
Q8	Are GCP and GLP certificates sufficient? Some BE centres located in Europe do not have inspection reports but do have GCP and GLP certificates.
A8	GCP and GLP certificates can be submitted just as supporting documents along with other relevant documents. However, at least an inspection report from Regulatory Authorities is required before evaluation can proceed. The outcome of the evaluation will depend on the overall documents submitted.
Q9	Is this desktop evaluation applicable for BE studies conducted in BE centres located in any country?
A9	Yes. It applies to any BE studies conducted at centres not listed in the NPRA BE Centre Compliance Programme and/or not within the listing validity.
Q10	Is there a requirement that BE studies must be conducted within a certain time frame e.g. within the last 5 years?

A10	There is no specific requirement on the time frame to conduct the BE study. However, the risk when evaluating the component on Study Site will be perceived to be higher if there were no inspections conducted within 3 years of the study conduct.
Q11	Does Section 2 on page 1 of the BEEC/F-018 manual refer to CROs that are already registered with NPRA BE Centre Compliance Programme but the BE study was not being conducted within the validity period?
A11	Yes.
Q12	BE Study X is done at Site A which is not on the NPRA compliance programme. Study X has not been inspected by any of the reference agencies but Site A had been inspected by the reference agencies for other BE studies. Since there is no study-specific inspection report for BE Study X, is BE Study X eligible for the desktop evaluation?
A12	Yes, BE Study X may be submitted for desk evaluation to determine whether a study-specific inspection is required or not. In accordance to the BEEC/F-018 manual, the evaluation will be done by assessing the risk based on 3 components: Study, Site & Product.
Q13	Is the desktop evaluation only applicable for BE studies that required study-specific inspection?
A13	Yes, this mechanism is to evaluate the need for study-specific inspections on BE studies that were conducted at facilities that were not listed on the NPRA BE Centre Compliance Programme or conducted outside of valid listing on the programme.
Q14	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?
A14	This mechanism replaces and expands on the previous BEIR process. In the desktop evaluation, inspection reports conducted at the site in the last 3-5 years and 3-5 years before and after BE study was conducted may be submitted. However, submission of a product-specific inspection report will increase the confidence during evaluation.
Q15	If one of the studies in an application fails the evaluation, will the outcome of the application be considered as fail/rejected, even though other studies evaluated are satisfactory?
A15	Evaluation decisions will be explicit in stating the study requiring a study-specific inspection and the study being exempted from an inspection if more than one study is submitted in an application.
Q16	If a BE study was conducted at a listed BE centre on the NPRA BE Centre Compliance Programme and it is still within the validity period, is the submission of Form BEEC/F-017 required in order to get clearance prior to submission for product registration?

A16	Application for desktop evaluation is not required for studies conducted at BE centres that are listed under NPRA BE Centre Compliance Programme and/or conducted within the valid listing.

	Miscellaneous
Q1	How much is the application fee and when will it come into effect?
A1	The application fee will be RM2,000.00 for each application. NPRA is still in the process of obtaining Finance approval to implement the charges and potential applicants will be notified before charges will come into effect.
Q2	If an application has been made for a study-specific inspection, what is the procedure to withdraw the inspection application and request for a refund on the inspection cost and application fee before applying for the desktop evaluation?
A2	Applicants are suggested to apply for desktop assessment and wait until the result is known before withdrawing the inspection application. If the decision to withdraw the 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 to the cost of inspection contributions. The application fee of RM5,000.00 is not refundable.
Q3	With the new directive, there is a need to wait for results of the desktop evaluation before submission can be made for product registration evaluation. Previously, an application fee of RM5,000 can be made first and submission for product registration evaluation can be made concurrently. Is it possible for that mechanism to be implemented with this new directive?
A3	This desktop evaluation is replacing the BEIR process and will be processed in accordance to similar timelines as the BEIR process. Despite expanding the scope of evaluation to cover the Study, Site and Product compared to only evaluating study-specific inspection reports in the BEIR process, the existing timeline has been preserved. The sequence of events leading to submission for product registration evaluation is similar to those in place when BEIR was in effect.
Q4	If the desktop 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 so that an applicant can project the time required ahead of a product registration submission into Quest 3+?
A4	The following timeline estimation before submission for product registration evaluation is calculated under the assumption that each stage will take the maximum number of working days allotted for the respective stages. 1) Desktop Evaluation - 30 Working days (Screening) + 30 Working days (Applicant to respond) + 45 Working days (Evaluation) + 30 Working days (Applicant to respond during evaluation) = 135 Working days to get a decision. 2) Applicant to submit for Study Specific Inspection - 10 Working days after get the decision = 10 Working days 3) Submission to QUEST 3+ can be made once the applicant has received the official payment receipt from the study-specific inspection application.

	145 Working days is required starting from submission of the desktop evaluation application until the submission to Quest 3+ for product registration evaluation if a study-specific inspection is required. Product registration evaluation will start while waiting for the inspection to be conducted. However, said product will only be registered after a satisfactory result of the inspection is obtained. The timeline for inspection is subject to the queue for inspection, Trust Fund Meetings and during this pandemic period when travel restrictions are lifted and inspections can be resumed safely.
Q5	The NPRA BE report checklist requires the BEIR verification letter issued by the NPRA. Can the email of successful BE desktop evaluation application be used to replace this verification letter?
A5	Upon reaching a decision, a formal letter will be issued stating if the BE study requires a study-specific inspection or maybe accepted to support product registration evaluation. This letter will replace the BEIR verification letter. However, if a BEIR verification letter was issued before July 2020 and does not contain any restrictions on its validity, the BEIR letter may still be used to support product registration evaluation submissions.
Q6	In the event that a study-specific inspection is required, should form BEEC/F-003 or BEEC/F-004 be used in the application process?
A6	The form used will depend on where the BE centre is located. Form BEEC/F-003 is for centres located in Malaysia and Form BEEC/F-004 is for facilities located outside of Malaysia.
Q7	Will NPRA provide priority review for applications involving products that have been accepted for product registration evaluation on the basis that a study-specific inspection had been applied? Instead of proceeding with the planned inspection, the applicant would like to apply for desktop evaluation to determine the need for a study-specific inspection.
A7	Priority review will be considered for studies that have been planned for study-specific inspections but are disrupted by the COVID-19 pandemic. However, desktop evaluation decision on the need for study-specific inspections is still subject to relevant documents provided.
Q8	For BE studies of products planned to be covered under full inspections for BE centre accreditation but disrupted by the COVID-19 pandemic, would the product evaluation be rejected? Could special consideration/special exemption be given for these products if a desktop evaluation is applied but a decision has not been obtained before the first product registration evaluation correspondence?
A8	In the event the planned inspection has been disrupted by the pandemic, the applicant may apply for desktop evaluation for the BE studies that would have been covered in the inspection. If a favourable decision is obtained from the desktop evaluation, you may use the approval to support the product registration process. Please notify the NPRA during

	the application of the Desktop evaluation if the BE study fits into the situation mentioned above. The product registration evaluation will continue in parallel with the desktop evaluation.
Q9	Under normal circumstances, what is the lead time required for a study-specific inspection to be completed?
A9	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. The date of the inspection will be after the Trust Fund Meeting approval has been obtained and subject to the inspection queue.
Q10	Is there a mechanism in which the inspection application fee of RM5,000.00 can be refunded and/or be used for the application for the desktop evaluation?
A10	The application fee of RM5,000.00 is the processing fee for the inspection application and is stated in the Terms & Conditions as non-refundable. This Terms & Conditions must be agreed upon and completed by applicants prior to submission of the inspection application. Should you wish to file for an appeal on the refund, kindly email to beec@npra.gov.my
Q11	An application for a full inspection was submitted to list a BE centre on the compliance programme. However, the inspection was delayed by the COVID-19 pandemic. May the desktop evaluation be used to qualify the BE centre for listing on the programme?
A11	The desktop evaluation application is to determine if a BE study may be exempted from a study-specific inspection before being accepted for product registration evaluation. This application is not for accreditation of the BE centre to be listed in NPRA BE Centre Compliance Programme.
Q12	If an applicant had applied for a study-specific inspection and then a desktop evaluation, does the applicant need to reapply for the study-specific inspection and pay a new processing fee of RM5,000.00 if the desktop evaluation determines that a study-specific inspection is required?
A12	There is no need to apply and pay the processing fee for a study-specific inspection again provided that the applicant didn't withdraw the initial inspection application. Applicants are advised to wait for the desktop evaluation decision before deciding on withdrawing or maintaining the application for study-specific inspections.
Q13	Is the applicant for a desktop evaluation still required to pay the application fee of RM2,000.00 if the application was found to be unsuccessful/have insufficient documents during screening?
A13	Once finance approval has been obtained, payment of the application fee of RM2,000.00 must be made during the submission of each desktop evaluation application. Applicants are strongly advised to refer to the published manual (BEEC/F-018) for details on the minimum documents required for an application before a submission is made. The manual

	can be obtained from the NPRA website and in addition to that, applicants may submit any enquiries via email to beec@npra.gov.my.
Q14	With the COVID-19 pandemic limiting international travels to conduct foreign BE inspections, does the NPRA recommend going for a desktop evaluation instead of a formal audit at the BE facility?
A14	The desktop evaluation does not replace full and surveillance inspections for the listing of BE centres on the NPRA programme. List of facilities on the programme still requires an on-site inspection which is on hold due to the pandemic. The desktop evaluation only provides a potential alternative to study specific inspections to allow potential product registration holders to proceed with the submission for product registration evaluation.
Q15	Are there any MoU/Harmonization with ASEAN/PICS/ for Joint Assessment on the Desktop Evaluation?
A15	Currently, no.
Q16	A planned surveillance inspection on a listed BE centre had been delayed until further notice due to the COVID-19 pandemic and the listing validity on the NPRA programme had expired. Will BE studies conducted between the expired validity and relisting of the BE centre after the surveillance inspection be accepted by the NPRA?
A16	To determine if the BE studies conducted at BE centres outside of valid listing on the programme, a desktop evaluation application may be submitted. Extension of the BE centre's validity may be considered during the pandemic if an application for surveillance inspection had been submitted 15 months before the expiry of the latest accreditation status. For more information, kindly contact our officers at beec@npra.gov.my
Q17	In the event that the desktop evaluation finds that an inspection is required, will the BE centre be listed in the NPRA programme once the inspection is completed?
A17	The desktop evaluation is to determine if a study-specific inspection is required on the BE study. Kindly declare in the BE inspection application form if there is an intent to list the BE centre under the NPRA BE Centre Compliance Programme.

Last updated: 31st December 2020