

**PUSAT KOMPLIANS DAN KAWALAN KUALITI**

*CENTRE OF COMPLIANCE AND QUALITY CONTROL*

**BAHAGIAN REGULATORI FARMASI NEGARA**

*NATIONAL PHARMACEUTICAL REGULATORY AGENCY*

**KEMENTERIAN KESIHATAN MALAYSIA**

*MINISTRY OF HEALTH MALAYSIA*

**PENILAIAN PENENTUAN KEPERLUAN PEMERIKSAAN KAJIAN BIOEKUIVALENS (BE)**

*EVALUATION ON THE NEED FOR*

*BIOEQUIVALENCE (BE) STUDY INSPECTION*

**ARAHAN:**

*INSTRUCTION:*

1. **Permohonan hendaklah dibuat melalui ejen tempatan (Malaysia) yang dilantik bagi tujuan pendaftaran produk sahaja.**

*Application needs to be submitted only through a local (Malaysia) agent that has been appointed for product registration.*

1. **Hanya borang permohonan asal yang lengkap sahaja diterima. Setiap permohonan hanya untuk kajian BE yang melibatkan satu kekuatan (*strength*) produk sahaja.**

*Only the original and complete application forms will be accepted. Only BE study(ies) involving one product strength shall be submitted in each application form.*

1. **Hanya borang permohonan yang dicetak atas kertas A4 putih (depan dan belakang) sahaja diterima.**

*Only application forms printed on both sides of white A4 size paper will be accepted.*

1. **Borang yang telah lengkap bersama versi terkini BEDE Submission Checklist (N3-FR-56) hendaklah dihantar kepada Ketua Seksyen Pusat Kajian BE dan Jawatankuasa Etika, Pusat Komplians dan Kawalan Kualiti, Bahagian Regulatori Farmasi Negara, Kementerian Kesihatan Malaysia, Lot 36, Jalan Profesor Diraja Ungku Aziz, 46200 Petaling Jaya, Malaysia.**

*Please submit the completed form together with the latest version of the BEDE submission checklist* (N3-FR-56) *to: Head of Section, BE Centre & Ethics Committee, Centre of Compliance and Quality Control, National Pharmaceutical Regulatory Agency, Lot 36, Jalan Profesor Diraja Ungku Aziz, 46200 Petaling Jaya, Malaysia.*

1. **Versi terkini Manual Permohonan Penilaian Penentuan Keperluan Pemeriksaan Kajian BE (N3-FR-52) boleh diperolehi di dalam laman sesawang NPRA.**

*The latest version of the Application Manual for Assessment to Determine the Need of BE Study Inspection (N3-FR-52) can be found on the official NPRA website.*

1. **Jika terdapat sebarang pertanyaan, sila hubungi pegawai Seksyen Bioekuivalens dan Jawantankuasa Etika, Pusat Komplians & Kawalan Kualiti di alamat emel: beec@npra.gov.my**

*Kindly contact the officers of the Bioequivalence Centre & Ethics Committee Section, Centre of Compliance & Quality Control at beec@npra.gov.my for any queries.*

1. **Bagi semua koresponden melalui emel, sila gunakan awalan seperti di bawah pada permulaan tajuk di ruang ”PERKARA” emel.**

*Please use the following prefixes in the ”SUBJECT” for all correspondence through email.*

|  |  |
| --- | --- |
| **Awalan***Prefixes* | **Tujuan***Purpose* |
| BEDN | Berkaitan dengan permohonan pemeriksaan BE dalam negara*Related to inspection application for local BE*  |
| BELN | Berkaitan dengan permohonan pemeriksaan BE luar negara*Related to inspection application for foreign BE* |
| BEDE | Berkaitan dengan permohonan penilaian penentuan keperluan pemeriksaan kajian BE *Related to the application for evaluation to determine the need for BE study inspection* |
| ECU | Sebarang makluman terkini berkaitan jawatankuasa etika yang berdaftar dengan Pihak Berkuasa Kawalan Dadah (PBKD) seperti senarai ahli jawatankuasa yang telah dikemaskini atau laporan tahunan.*Any updates related to the ethics committees registered with the Drug Controlled Authority (DCA), such as an updated list of memberships or an annual report.* |
| ECI | Berkaitan dengan permohonan pendaftaran dan pemeriksaan jawatankuasa etika*Related to registration and inspection application for ethics committee* |
| QUERY | Sebarang pertanyaan umum*Any general enquiries* |

**Sebagai contoh:**

*As example:*

**BEDE - Permohonan penilaian keperluan pemeriksaan kajian BE - Produk ABC.**

*BEDE - Application for* *Evaluation on the Need for BE Study Inspection - Product ABC.*

**BAHAGIAN 1: ALIRAN PROSES PERMOHONAN**

*PART 1: APPLICATION PROCESS FLOW*

i. Penghantaran Permohonan

*i. Submission of Application*

ii. Saringan awal di kaunter

*ii. Preliminary Screening*

iii. Saringan & Permintaan Dokumen

*iii. Screening & Document Request*

iv. Penghantaran Dokumen

iv. *Submission of document*

v. Penilaian

*v. Assessment*

v. Keputusan

*v. Decision*

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Deskripsi*****Description*** | **Tempoh masa*****Timeline*** | **Tanggungjawab*****Responsibility*** |
|  | Ejen tempatan yang dilantik bagi tujuan pendaftaran produk. *A local agent has been appointed to register the product.* |  | Pemohon*Applicant* |
|  | Pegawai akan membuat saringan dan memastikan maklumat administratif lengkap.*Administrative screening of the application form to ensure complete information.* |  | Pegawai*Officer* |
|  | Pegawai akan meminta dokumen seperti yang disenaraikan di dalam Manual dan FAQ Permohonan BEDE.*Officer will request documents as listed in the Manual and FAQ for BEDE application.* | 30 Hari Bekerja*30 Working Days* | Pemohon*Applicant* |
|  | Pemohon mengemukakan dokumen (dalam bentuk *softcopy*) berserta borang L1. *Applicant to submit (in softcopy) including L1 Form.* | 30 Hari Bekerja*30 Working Days* | Pegawai*Officer* |
|  | Pegawai akan menilai permohonan dan meminta dokumen tambahan jika perlu.*Officer will assess the application and request for additional documents, if needed.* | 45 Hari bekerja45 Working Days | Pegawai*Officer* |
|  | Pegawai akan memaklumkan keputusan kepada pemohon*Officer will inform the decision to the applicant.* |  | Pegawai*Officer* |

**BAHAGIAN 2: MAKLUMAT PEMOHON**

*PART 2: DETAILS OF APPLICANT*

|  |  |  |
| --- | --- | --- |
| **1.** | **Nama Penuh (Huruf Besar)** *Full Name (Block Letter)* |  |
| **2.** | **No. Kad Pengenalan***Identity Card Number* |  |
| **3.** | **Jawatan** *Position* |  |
| **4.** | **Nama dan Alamat Syarikat Pemohon***Name and Address of the Applicant’s Company* |  |
| **5.** | **E-mel***Email address* |  |
| **6.** | **No. Telefon***Contact Number* |  |

**BAHAGIAN 3: MAKLUMAT PRODUK**

*PART 3: DETAILS OF PRODUCT*

|  |  |  |
| --- | --- | --- |
| **1.** | **Nama, Kekuatan Produk dan Bentuk Dosej untuk Didaftar***Name, Strength and Dosage Form of Product to be Registered* |  |
| **2.** | **Bahan Aktif***Active Ingredient* |  |
| **3.** | **Jumlah Kajian BE yang diperlukan untuk menyokong pendaftaran produk di Malaysia***Total number of BE study(ies) required to support the product registration in Malaysia* |  |
| **4.** | **Status Pendaftaran di Negara Lain/** *Registration Status in Other Countries* |
| 1. **Hanya Badan Regulatori dari negara rujukan NPRA yang akan diberi keutamaan semasa penilaian.**

*Only Regulatory Authorities from NPRA’s reference countries will be given priority during assessment.***Negara Rujukan NPRA/** *NPRA’s Reference Countries***:**  **United Kingdom, Sweden, France, United States of America, Australia, Canada, Japan, Switzerland, WHO and EMA centralised registration pathway.**1. **Laporan penilaian hanya perlu dihantar selepas diminta oleh pegawai saringan**

*Assessment report only needs to be submitted after being requested by the screening officer.* |
| **Negara/** *Country* | **Status/** *Status* | **Laporan Penilaian/** *Assessment Report* |
|  |  | **[ ] Ada/** *Available* **[ ] Tiada/** *None* |
|  |  | **[ ] Ada/** *Available* **[ ] Tiada/** *None* |

**BAHAGIAN 4: MAKLUMAT KAJIAN BE**

*PART 4: DETAILS BE STUDY (IES)*

**Jika terdapat lebih daripada satu kajian BE yang akan digunakan untuk menyokong pendaftaran produk tersebut, sila ulangi bahagian 4 untuk setiap kajian tersebut.**

*If there are more than one BE study to be used to support the registration of the same product, please repeat section 4 for each individual study.*

|  |  |  |
| --- | --- | --- |
| **1.** | **Tajuk Kajian BE***Title of BE Study* |  |
| **2.** | **Produk Kajian BE***BE study test product* |  |
| **3.** | **Produk Perbandingan***Comparator Product* |  |
| **4.** | **Nombor Protokol***Protocol Number* |  |
| **5.** | **Tarikh Kajian BE dijalankan****Contoh: 1 Januari 2022 - 10 Januari 2022***Date of BE Study conducted.**E.g.:* 1 January 2022 - 10 January 2022 | **Klinikal**/*Clinical*: **Bioanalitikal**/*Bioanalytical*: **Tarikh Laporan**/*Date of Report:*  |
| **6.** | **Nama Tapak Klinikal** *Name of Clinical Site*  |  |
| **7.** | **Alamat Tapak Klinikal** *Address of Clinical Site* |  |
| **8.** | **Nama Tapak Bioanalitikal**  *Name of Bioanalytical Site* |  |
| **9.** | **Alamat Tapak Bioanalitikal** *Address of Bioanalytical Site* |  |
| **10.** | **Penaja BE Kajian***Sponsor of the BE Study* |  |
| **11.** | **Penyelidik Utama***Principal Investigator* |  |
| **12.** | **Kelulusan Menjalankan Kajian BE***Approval for the BE Study Conduct* | **Jawatankuasa Etika (EC) /** *Ethics Committee (EC):***Status Pendaftaran** **EC**/ *Registration status of* *EC:***Badan Regulatori /** *Regulatory Authority:* |
| **13.** | **Status kepatuhan Kajian BE terhadap garis panduan** **Nota: Sila nyatakan garis panduan yang digunakan***Compliance status of the BE study to Guidelines* *Note: Please state the guidance referred to in the study* | **\*United States Food and Drug Administration (USFDA), European Medicines Agency (EMA), Association of Southeast Asian Nations (ASEAN) atau lain-lain.** *USFDA, EMA, ASEAN or others.* |
| **14.** | **Status pemeriksaan ke atas Kajian BE yang sama (Jika ada)***Inspection status of the same BE study (If any)* | **[ ] Ada/** *Available.* **Sila isi maklumat di bawah/** *Please include the details below.***[ ] Tiada/** *None***Badan Regulatori /** *Regulatory Authority:***Tarikh Pemeriksaan/** *Inspection Date:***Status Pemeriksaan/***Inspection Status:* |
| **Status penerimaan Kajian BE yang sama (Jika ada)***Acceptance status of the same BE study (If any)* | **[ ] Diterima/** *Accepted.* **Sila isi maklumat di bawah/** *Please include the details below.***[ ] Tidak diterima/** *Not accepted***[ ] Tidak berkaitan/** *Not applicable***Badan Regulatori /** *Regulatory Authority:***Tarikh Penerimaan/** *Submission Date:***Status Penerimaan/***Submission Status:* |
| **15.** | **Pemantauan ke atas pelaksanaan Kajian BE oleh Sponsor, Contract Research Organisation (CRO) atau lain-lain***Monitoring of the BE study conducted by Sponsor, CRO or others* | **[ ] Ada/** *Available*  **Sila isi maklumat di bawah/** *Please include the details below.***[ ] Tiada/** *None***Syarikat Pemantau/** *Monitoring Company***:****Kekerapan pemantauan/** *Monitoring frequency:* |
| **16.** | **Ringkasan Kajian BE/** *Summary of the BE Study* |
| ***Design* Kajian/** *Study Design:***Jumlah Subjek/** *Subject No.:***Deviasi dari Protokol/** *Protocol Deviation:* **[ ] Ada/** *Available* **[ ] Tiada/** *None* |
| **Validasi Tatacara Analisa*/*** *Method Validation:*1. **Tarikh Mula & Akhir Validasi Tatacara Analisa/** *Method Validation Start & End*

**(\*Termasuk P*artial Validation/*** *Include partial validation***)***Date: (e.g. dd/mm/yyyy - dd/mm/yyyy)* |
| **Analisis Sampel Subjek/** *Subject Sample Analysis:*1. **Deviasi dari *Method* Analisis@SOP/** *Method@SOP Deviation:*

**[ ] Ada/** *Available* **[ ] Tiada/** *None*1. **Analisis Semula@*Reinjection* Sampel/** *Sample Reanalysis@Reinjection:*

**[ ] Ada/** *Available* **[ ] Tiada/** *None*1. **Integrasi Semula@ Integrasi Secara Manual/** *Reintegration@Manual Integration:*

**[ ] Ada/** *Available* **[ ] Tiada/** *None* |
| **Analisis farmakokinetik dan Statistik/** *Pharmacokinetics and Statistical Analysis:*1. **Tarikh Analisis/** *Date of Analysis:*
2. **Pengecualian Subjek/** *Subject Exclusion:*

**[ ] Ada/** *Available* **[ ] Tiada/** *None* |
| **Audit oleh *Quality Assurance*/** *Quality Assurance Audit:***[ ] Ada/** *Available* **[ ] Tiada/** *None* |

**BAHAGIAN 5: MAKLUMAT PUSAT KAJIAN**

*PART 5: DETAILS OF STUDY CENTRE*

**Jika Tapak Klinikal dan Bioanalitkal merupakan entiti yang berbeza, sila ulangi bahagian 5 untuk setiap tapak.**

*If the Clinical and Bioanalytical sites are different entities, please repeat section 5 for each site.*

|  |
| --- |
| **[ ] Tapak Klinikal/**  *Clinical Site* **[ ] Tapak Bioanalitikal/** *Bioanalytical Site* |
| **1.** | **Nama Tapak** *Facility Name* |  |
| **2.** | **Alamat Tapak** *Facility Address* |  |
| **3.** | **Senarai Pemeriksaan ke atas Tapak Kajian oleh Badan Regulatori***List of Regulatory Inspections on the Facility*  |
| **Arahan/** *Instruction:*1. **Hanya senaraikan pemeriksaan yang dilalui dalam tempoh 5 tahun sebelum dan selepas kajian BE dijalankan.**

*Only list down the inspection conducted at the site within 5 years before and after the BE study was conducted.* 1. **Maklumat pemeriksaan hendaklah dimasukkan di dalam jadual di bawah.** *Inspection history has to be filled in according to the format below.*
2. **Laporan pemeriksaan, surat penutupan pemeriksaan bersama laporan tindakan pembetulan dan pencegahan hanya perlu dihantar selepas diminta oleh pegawai saringan**

*Inspection reports and closure letters, together with the corrective and preventive action (CAPA) report, only need to be submitted upon request by the screening officer.*1. **Semua maklumat di dalam laporan pemeriksaan tidak boleh ditapis. Dalam keadaan di mana maklumat tidak boleh didedahkan kepada pemohon, laporan tersebut boleh dilindungi dengan kata laluan sebelum dimuatnaik ke pautan yang dikongsikan semasa proses penyaringan/ penilaian. Kata laluan tersebut boleh dikongsikan kepada NPRA secara terus.**

*All information in the BE centre inspection report must not be redacted. In the event that confidentiality clauses prevent the disclosure of certain information to the applicant, the inspection report can be protected with a password before the same document is uploaded to the link shared during the screening/evaluation process. The password can be shared directly with NPRA.*1. **Semua dokumen hanya perlu dihantar di dalam format *softcopy (OCR pdf).***

*All documents need to be submitted in softcopy format (OCR pdf).* |
| **No./** *No.* | **Badan Regulatori/** *Regulatory Authority* | **Skop/** *Scope (e.g. Clinical/ Bioanalytical)* | **Tarikh/** *Date* | **Status/** *Status* | **Laporan/** *Report* |
|  |  |  |  |  | **[ ] Ada/** *Available* **[ ] Tiada/** *None* |
|  |  |  |  |  | **[ ] Ada/** *Available* **[ ] Tiada/** *None* |
|  |  |  |  |  | **[ ] Ada/** *Available* **[ ] Tiada/** *None* |
|  |  |  |  |  | **[ ] Ada/** *Available* **[ ] Tiada/** *None* |
|  |  |  |  |  | **[ ] Ada/** *Available* **[ ] Tiada/** *None* |
|  |  |  |  |  | **[ ] Ada/** *Available* **[ ] Tiada/** *None* |
|  |  |  |  |  | **[ ] Ada/** *Available* **[ ] Tiada/** *None* |
|  |  |  |  |  | **[ ] Ada/** *Available* **[ ] Tiada/** *None* |

|  |  |
| --- | --- |
|  | **Saya dengan ini mengisytiharkan bahawa sejarah pemeriksaan yang disenaraikan di atas adalah LENGKAP bagi kedua-dua tapak CL dan BA dari 5 tahun sebelum dan 5 tahun selepas kajian BE dijalankan.***I hereby declare that this is the COMPLETE inspection history for both the CL and BA sites from 5 years before and 5 years after the BE study was conducted.* |

**BAHAGIAN 6: PERAKUAN PEMOHON**

*PART 6: APPLICANT’S DECLARATION*

**Saya dengan ini, mengaku bahawa semua kenyataan di dalam borang ini dan dalam lampiran yang disertakan adalah benar.**

*I hereby confirm that all information provided in this form and the attached documents is correct.*

|  |  |  |
| --- | --- | --- |
| **1.** | **Tandatangan Pemohon***Signature of Applicant* |  |
| **2.** | **Nama Pemohon***Name of Applicant* |  |
| **3.** | **Cop Rasmi Syarikat***Official Stamp of the Company* |  |
| **4.** | **Tarikh (HH/BB/TT)***Date (DD/MM/YY)* |  |