The Validation Template is used on receipt of an application to verify that all required information has been supplied to the South African Health Products Regulatory Authority (SAHPRA) in order to evaluate an application for the renewal of the certificate of registration of a medicinal product for human or veterinary use submitted in the eCTD format. The applicant must ensure that all relevant fields are completed.

**For products registered in the year 2017 and dating further back, a full eCTD baseline (0000) submission in line with the General Information Guideline (SAHPGL-HPA-07) for registration will be required (only if the dossier has not yet been converted to eCTD): Complete and submit only Sections A and C for the baseline sequence.**

**Follow-up sequences (related to the renewal application): Complete and submit only Sections A, B, D, and E.**

**A. ADMINISTRATIVE VALIDATION**

**COMPLIANCE CHECK**

*Applicant to fill in the table below as per the application M1.0.*

|  |  |
| --- | --- |
| **Product Information** | |
| **Applicant name** | [Licensed Name] |
| **Master product application number/s** |  |
| **Duplicate product application number/s** |  |
| **Clone/replica product application number/s** |  |
| **eCTD sequence number** |  |
| **Master product proprietary name/s** |  |
| **Duplicate product proprietary name/s** |  |
| **Clone/replica product proprietary name/s** |  |
| **Product strengths** |  |
| **Dosage form** |  |
| **API/s** |  |
| **Date of letter of application** |  |
| **Date of receipt *(SAHPRA use only)*** |  |

**BUSINESS VALIDATION**

*Applicant to indicate using a tick (✔) in the “YES” column if the required documents have been included or tick (✔) “No” if not required for a specific submission.* *Any question not ticked will be at risk of rejection.*

| **Dossier Information** | | **Yes** | **No** |
| --- | --- | --- | --- |
| 1 | **Are the following modules included in the eCTD?** |  |  |
| 1a | **Letter of Application (Module 1.0.1)** |  |  |
| Is the letter of application electronically rendered, or OCR (Optical Character Recognition) scanned? |  |  |
| 1b | **Correspondence from SAHPRA (Module 1.0.3)**  Are the variation approval letters included? |  |  |
| 1c | **Application Form (Module 1.2.1)** |  |  |
| Is the application form electronically rendered, or OCR scanned? |  |  |
| Has a separate Module 1.2.1 been submitted for each strength (and duplicates) if different strengths or duplicates are applied for? |  |  |
| Is/are copies of the application form(s) included in the working documents in MS Word format? |  |  |
| Application Form, inclusive of up-to-date *Variation History*:  Tabular summary of the types of variations notified to, approved by and still pending with SAHPRA for the product, together with the respective dates of approval, if applicable. |  |  |
| 1d | **Proof of payment (Module 1.2.2.1)**  *Note: Applicants to include a note that proof of payment will be submitted subject to publishing of fee in the Government Gazette.* |  |  |
| 1e | **Electronic copy declaration (Module 1.2.2.4)** |  |  |
| 1f | **Is the Renewal Validation template included in Module 1.2.5?**  *Note: Document should also be included in MS Word format.* |  |  |
| **For the renewal application, have sections B, C, D & E been**  **hyperlinked to the modules where relevant? (Hyperlinking to the word**  **“hyperlink”)**  ***NOTE: Section C will only be screened for the submission with new eCTD***  ***baseline.*** |  |  |
| 1g | **South African Product Information (Module 1.3)** |  |  |
| Is a copy of the current approved PI and PIL included in Modules 1.3.1.1.1 and 1.3.2.1 respectively?  *Note: Document should also be included in MS Word format.* |  |  |
| **Sample artwork (Module 1.3.6)** |  |  |
| Are the coloured mock-ups of the packaging of the product for all strengths, i.e., blister, label and unit carton in PDF format, included in Module 1.3.3.1?  *NOTE: Facsimile labels will be accepted for dormant products.* |  |  |
| 1h | **Additional Types of Applications Specific Requirements (Module 1.5.A)** |  |  |
| A declaration that:   * data related to any commitments/compliance with conditions which the product was registered under must be submitted. * the risk assessment for applications registered without nitrosamine risk assessment has been done and the necessary updates have been submitted to the Authority. |  |  |
| Is the Professional Information (PI) and Patient Information Leaflet (PIL) from 5 years prior to the renewal application included? |  |  |
| 1i | **Medicine Register Details (Module 1.5.2.2.1)** |  |  |
| Does the information in the “Current” column in the Medicine Register Details correspond with that on the current registration certificate or the old medicines letter? *Note that sites approved on the DVP should be in the Proposed column.* |  |  |
| Does the information in the “Proposed” column in the Medicine Register Details correspond with Module 1.2.1 and/or information on the variation summary (DVP) with all the approved sites included? |  |  |
| 1j | Medicine Registration Certificate/Old Medicines Letter (Module 1.5.2.2.2) |  |  |
| Is the current registration certificate included in Module 1.5.2.2.2? |  |  |
| Is the variation summary (DVP) appended to Module 1.5.2.2.2? If applicable |  |  |
| 1k | Is the Product Quality Review (PQR) report of the preceding 5 years included (1.7.14)? |  |  |
| 1l | Is an executive summary of the risk-benefit assessment report of the preceding 5 years included (1.8.2)? |  |  |
| 2 | **Module 3.2.R.8** |  |  |
| 2a | **QIS document in Module 3.2.R.8**  *NOTE: Document should also be included in MS Word format.* |  |  |
| 3 | **For follow-up sequences, is the operation attribute of the following documents reflected as “new”?** |  |  |
| 1.0.1 Letter of application |  |  |
| 1.2.1 Application form |  |  |
| 1.2.2.1 Proof of payment (when applicable) |  |  |
| 1.2.2.4 Electronic copy declaration |  |  |
| 1.5.2.1 Tabulated schedule of amendments (when relevant) |  |  |
| 4 | Are the leaf titles descriptive and logical, e.g., for applications with various strengths, and new documents in follow-up sequences? |  |  |

**Motivation for deviation from the validation requirements** (use the numbering in the checklist to link comments to specific questions):

**Applicant:**

**SCREENER**

**SAHPRA:**

|  |  |  |
| --- | --- | --- |
| ***SAHPRA Use Only***  ***Can the application proceed to technical screening?*** | ***Yes*** | ***No*** |
|  |  |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Full name** | **Title** | **Signature** | **Date** |
| **Screener** |  |  |  |  |
| **Approver** |  |  |  |  |

**B. TECHNICAL SCREENING (INSPECTORATE)**

*Applicant to indicate using a tick (✔) in the “YES” column if the required documents have been included.*

| **Good Manufacturing Practice (GMP)** | | **Yes** | **No** |
| --- | --- | --- | --- |
| 1a | Is there a Transfer of Applicant (TOA) in progress?  If yes, the Renewal Submission must be submitted by the new Holder of the Certificate of Registration (HCR) after the TOA is approved. |  |  |
| 1b | Are the GMP certificates/resolution letter or a copy of the appropriate licences of the manufacturers, packers and FPRCs included in 1.7.3? |  |  |
| 1c | Certificates of GMP of the Active Pharmaceutical Ingredient(s) manufacturing facilities, issued by Recognised Regulatory Authorities (RRAs) or by the National Competent Authority of the country of manufacture; |  |  |
| 1d | Certificates of GMP of the Final Pharmaceutical Product(s) manufacturing facilities\*\*, issued by RRAs.  *\*\* Includes all sites involved in the testing, manufacturing, and packaging of the*  *Finished Pharmaceutical Product (FPP).* |  |  |
| 1e | Is the date of last inspection within three (3) years of today’s date (1.7.3 or 1.7.1)? |  |  |
| 1f | Is the dosage form that is being applied for within the same dosage form grouping as the GMP certificate or licence (1.2.1 & 1.7.3)? *(Refer to Appendix 2 of the Guideline on Good Manufacturing Practice for Medicines GMP guideline (SAHPGL-INSP-02))* |  |  |
| 1g | Is the product type being manufactured in the application similar to the product on the GMP certificate or licence (1.2.1 & 1.7.3)? *(Refer to Appendix 2 of the Guideline on Good Manufacturing Practice for Medicines (SAHPGL-INSP-02))* |  |  |
| 1h | Are the activities that the manufacturer is approved for in the GMP certificate or licence the same as the activities being applied for? *(Refer to Appendix 2 of the Guideline on Good Manufacturing Practice for Medicines (SAHPGL-INSP-02))* |  |  |
| **Certificate of Pharmaceutical Product (CoPP – WHO Format):** | | **Yes** | **No** |
| 2 | Is CoPP issued by the relevant Health/Regulatory body in the country of manufacture of the product included (1.10.6)? |  |  |
| **Licensing of South African Holder of Certificate of Registration (HCR)** | | | |
| 3a | Has the licence of the South African Holder of Certificate of Registration (HCR) been included (1.7.3)? |  |  |
| 3b | Has proof of Registration of Pharmacy and Responsible Pharmacist with the South African Pharmacy Council been included and is valid at the time of submission (1.7.7)? |  |  |
| **Product Quality Review (PQR)** | | **Yes** | **No** |
| 4 | Product Quality Reviews (to be included in 1.7.14) should be conducted with no fewer than 10 consecutive batches manufactured over a period of the past 12 months or, where 10 batches were not manufactured in the past 12 months, no fewer than 25 consecutive batches manufactured over a period of the past 36 months and should include at least:  *NOTE: Product Quality Review reports of the preceding five (5) years should be provided.* |  |  |
| 4a | A review of starting and primary packaging materials used in the FPP, especially those from new sources (1.7.14) |  |  |
| 4b | A review of critical in-process controls and finished product results (1.7.14) |  |  |
| 4c | A review of all batches that failed to meet established specification(s) and their investigations (1.7.14) |  |  |
| 4d | A review of all significant deviations or non-conformances and related investigations (1.7.14) |  |  |
| 4e | A review of all changes carried out to the processes or analytical methods (1.7.14) |  |  |
| 4f | A review of the results of the stability-monitoring programme (1.7.14) |  |  |
| 4g | A review of all quality-related returns, complaints and recalls (1.7.14), including export-only medicinal products |  |  |
| 4h | A summary report of Post-Marketing Surveillance activities in the preceding five (5) years |  |  |
|  | **Further Notes:**  1. Reviews must include data from all batches manufactured during the review.  2. Data should be presented in tabular or graphical form, where applicable.  3. PQRs should not be summaries without data. |  |  |

**Comments if any answer is ‘NO’ (use the numbering in the checklist to link comments to specific questions):**

**Applicant:**

**SCREENER**

**SAHPRA:**

**C. TECHNICAL VERIFICATION (PHARMACEUTICAL EVALUATION MANAGEMENT – PEM)**

***This section is only for applications where the new eCTD baseline is submitted with the renewal application.***

**C.1** **QUALITY**

*Applicant to indicate using a tick (✔) in the “YES” column if the required documents have been included. If ticking “NO”, provide a motivation in the comments section, referencing the question number. Tick “N/A” if not applicable for this application.*

*Applicant to complete Section 1 for each API in the product you are applying for. Please replace <<API name>> with the name of the API. Additional table(s) for Section 1 can be duplicated, if necessary, by copying and pasting.*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Active Pharmaceutical Ingredient (API) (Module 3.2.S) <<API name>>** | | **Yes** | **No** | **N/A** |
| 1a | Is Module 3.2.S for each manufacturer of API included? |  |  |  |
| 1b | Is the API a mixture with other API(s) or Inactive Pharmaceutical Ingredient(s) (IPIs)? |  |  |  |
| 1c | Have signed, dated and version-controlled API specifications been provided for the API manufacturer and FPP manufacturer? (Module 3.2.S.4) |  |  |  |
| 1d | Have batch analysis and valid certificates of analysis (CoAs) of the API issued by the FPP manufacturer and API manufacturer(s), for at least two batches, been included? (Module 3.2.S.4) |  |  |  |
| 1e | Have stability data been included? (Module 3.2.S.7.3)  *Note: Storage conditions as defined in the stability guideline**[[1]](#footnote-1)* |  |  |  |
| i. NCE: At least 12 months long-term and six (6) months accelerated? |  |  |  |
| ii. Generics: At least 6 months long-term and three (3) months accelerated? |  |  |  |
| 1f | Is the API manufacturer identified in Module 3.2.S.2.1 (refer to Module 1.2.2.3) the same as that of: |  |  |  |
| i. The biostudy test batch? |  |  |  |
| ii. Development batches? |  |  |  |
| 1g | If the answer is **NO** to 1f(i) or 1f(ii), are pharmaceutical equivalence data of the API manufacturers included? (Module 3.2.R.4) |  |  |  |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **FPP (Module 3.2.P)** | | **Yes** | **No** | **N/A** |
| 2a | Is Module 1.2.2.3 completed according to the Module 1 guideline[[2]](#footnote-2) for all FPP batches? |  |  |  |
| 2b | Have signed, dated and version-controlled specifications been provided for the FPP? (Module 3.2.P.5) |  |  |  |
| 2c | Are validation data included for the method(s) used for assay and impurities? (Module 3.2.P.5.3) |  |  |  |
| 2d | Have stability data been included? (Module 3.2.P.8.3)  *Note: Storage conditions as defined in the stability guideline[[3]](#footnote-3)* |  |  |  |
| i. NCE: At least 12 months long-term and 6 months accelerated? |  |  |  |
| ii. Generics: At least 6 months long-term and three (3) months accelerated? |  |  |  |
| 2e | Is a tabulated summary of the batches, i.e. sizes, numbers, type, packaging material, conditions and period of testing, included for each FPP manufacturer? (Module 3.2.P.8.1) |  |  |  |
| 2f | Have stability data been generated from the FPP-containing API sourced from the manufacturer identified in Module 3.2.S.2.1? (Module 3.2.P.8) |  |  |  |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Regional information (Module 3.2.R)** | | **Yes** | **No** | **N/A** |
| 3a | For the API, where more than one site of the same parent company/API Master File (APIMF) holder is used, and an identical method of synthesis is used at these sites, has a statement to this effect been included? (Module 3.2.R.2) |  |  |  |
| 3b | Where more than one manufacturer of the API (not the same parent company/APIMF holder) is used, is Module 3.2.R.4 included? |  |  |  |
| 3c | If a CEP[[4]](#footnote-4) is submitted, is the declaration of access completed? **OR** If a CPQ[[5]](#footnote-5) is submitted, is the authorisation box completed and signed? (Module 3.2.R.3) |  |  |  |
| 3d | Has an executed batch manufacturing record been provided for the biobatch or developmental batch? (Module 3.2.R.7.1) |  |  |  |
| 3e | Have blank/master batch manufacturing records been included for each proposed batch size[[6]](#footnote-6) of the final product? (Module 3.2.R.7.2) |  |  |  |

**Comments if any answer is ‘NO’** (use the numbering in the checklist to link comments to specific questions):

Applicant:

**TECHNICAL SCREENER**

SAHPRA:

**D.** **TECHNICAL SCREENING (CLINICAL)**

*Applicant to indicate using a tick (✔) in the “YES” column if the required documents have been included, along with a hyperlink where relevant (hyperlink should be linked to the word “hyperlink” in the question). If ticking (✔) “NO”, provide a motivation in the comments section, referencing the question number.*

*Note: If any of sections 2 – 6 are not applicable, these sections should be left entirely blank.*

|  |  |  |  |
| --- | --- | --- | --- |
| **1** | **General Information** | **Yes** | **No** |
| 1a | Is the Professional Information (PI) and Patient Information Leaflet (PIL) from five (5) years prior to the renewal application included in Module 1.5.A? |  |  |
| 1b | Is a copy of the current approved PI and PIL included in Modules 1.3.1.1.1 and 1.3.2.1 respectively and in the working documents in MS Word format? |  |  |
| 1c | Is the PI and PIL variation approval included in Module 1.0.3 (if applicable)? |  |  |
| 1d | Is each page of the approved PI and PIL dated and paginated as page X of Y? |  |  |
| 1e | Is the format of the current approved PI completely aligned with the format indicated in the latest published PI guidelines? |  |  |

**Comments if any answer is ‘NO’ by the applicant** (use the numbering in the validation template to link comments to specific questions):

**Applicant:**

**TECHNICAL SCREENER**

**SAHPRA:**

**E. TECHNICAL SCREENING (PHARMACOVIGILANCE)**

*Applicant to indicate using a tick (✔) in the “YES” column if the required documents have been included, along with a hyperlink where relevant (hyperlink should be linked to the word “hyperlink” in the question). If ticking (✔) “NO”, provide a motivation in the comments section, referencing the question number.*

|  |  |  |  |
| --- | --- | --- | --- |
| **1** | **Risk-benefit Assessment Report** | **Yes** | **No** |
| 1a | A summary report of all adverse drug reactions observed in the preceding five (5) years and actions taken, including medication errors, potential medication errors, and including lack of efficacy, off-label use, misuse and abuse. |  |  |
| 1b | Is an executive summary report of the Periodic Risk-Benefit Evaluation Report (PBRER) or Periodic Safety Update Report (PSUR) included (1.8.2):  **The report should consist of the following sections:** |  |  |
| 1c | The Risk-benefit conclusions by the Holder of the Certificate of Registration, namely by the Clinical Expert or the HCR Responsible Pharmacist should contain the following: |  |  |
| 1d | Confirm that no new clinical data are available that change or result in a new benefit-risk balance evaluation. |  |  |
| 1e | Confirm that the product can be safely renewed for a 5-year period, or any action recommended or initiated should be specified and justified. |  |  |
| 1f | Confirm that the authorities have been kept informed of any additional data significant for the assessment of the benefit-risk balance of the product concerned. |  |  |
| 1g | Confirm that the product information is up to date with the current scientific knowledge including the conclusions of the assessments and the recommendations made.  *Note: In the event that the PI is outdated due to the pending variation, the applicant should submit proof of a variation submission and a cover letter of the variation application.* |  |  |

**Comments if any answer is ‘NO’ by the applicant** (use the numbering in the validation template to link comments to specific questions):

**Applicant:**

**TECHNICAL SCREENER**

**SAHPRA:**

|  |  |  |
| --- | --- | --- |
| ***SAHPRA Use Only***  ***Can the application proceed to evaluation?*** | ***Yes*** | ***No*** |
|  |  |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Full name** | **Title** | **Signature** | **Date** |
| **Screener** |  |  |  |  |
| **Approver** |  |  |  |  |

1. Latest implemented versions of EMA, ICH2.05 Stability Guideline and/or SADC Stability Guidelines [↑](#footnote-ref-1)
2. Latest implemented version of 2.24 Guidance General Module 1 [↑](#footnote-ref-2)
3. Latest implemented versions of 2.05 Stability Guideline EMA, ICH and/or SADC Stability Guidelines [↑](#footnote-ref-3)
4. Certificate of Suitability to the monographs of the European Pharmacopoeia [↑](#footnote-ref-4)
5. Confirmation of API Prequalification Document [↑](#footnote-ref-5)
6. Blank/master production documents for a pilot scale batch or bracketing for commercial batch sizes are permitted, provided the requirements in SAHPGL-PEM-02 2.02 Quality and Bioequivalence Guideline are satisfied [↑](#footnote-ref-6)