The Validation Template is used on receipt of an application to verify that all required information has been supplied to SAHPRA in order to evaluate an application for the renewal of registration of a medicinal product for human or veterinary use submitted in 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 for registration will be required (only if the dossier has not yet been converted to eCTD): Complete and submit only Sections A.1; A.3 and C for the baseline sequence.**

**Follow-up sequences (related to the renewal application): Complete and submit only Sections A.1 A.3; B; D and E.**

**A ADMINISTRATIVE VALIDATION**

**A.1 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)* |  |

*Applicant to indicate using a tick (✔) in the YES column if the required documents have been included or tick (✔) N/A if not required for specific submission.* *Any question not ticked will be at risk of rejection.*

|  |  |  |  |
| --- | --- | --- | --- |
| **Dossier Information** | | **Yes** | **N/A** |
| 1a | Is the application submitted within the correct Phase and quarter as per the renewal roadmaps schedule? |  |  |
| 1b | Have the following documents in eCTD format been submitted? |  |  |
| 1c | Is the correct FTP file naming convention followed and unit clearly indicated? |  |  |
| 2a | Letter of Application (Module 1.0) |  |  |
| Has the virus check statement been included?  Does the virus check statement indicate that the submission is virus-free?  Does the letter of application clearly indicate different strengths and/or duplicates and/or clones/replicas? |  |  |
| 2b | Application Form (Module 1.2.1) |  |  |
| Is Module 1.2.1(c) signed by the authorised pharmacist and dated? |  |  |
| Has a separate Module 1.2.1 been submitted for each strength if different strengths are applied for? |  |  |
| Has a separate Module 1.2.1 been submitted for each duplicate? |  |  |
| Has a separate Module 1.2.1 been submitted for each clone/replica? |  |  |
| 2c | Electronic copy declaration (Module 1.2.2.4) |  |  |
| 2d | Validation template (Module 1.8)? |  |  |
| 2e | MD5 checksum – identifiable, signed and dated |  |  |
| 2f | Technical Validation Report (indicating valid submission and justification for any Best Practice criteria that are not met where relevant, attached to the report) |  |  |
| Validation tool used and version stated? |  |  |

**A.2 TECHNICAL VALIDATION**

*SAHPRA use only.*

*Approved Import into the reviewing system and notify applicant of successful technical validation.*

*Rejected Notify the applicant of rejection with the reasons*

**A.3 BUSINESS VALIDATION**

*Applicant to indicate using a tick (✔) in the YES column if the required documents have been included or tick (✔) N/A if not required for specific submission.* *Any question not ticked will be at risk of rejection.*

| **Dossier Information** | | **Yes** | **N/A** |
| --- | --- | --- | --- |
| 1 | Are the following modules included in the eCTD? |  |  |
| 1a | Letter of Application (Module 1.0) |  |  |
| Is the letter of application electronically rendered or OCR scanned? |  |  |
| 1b | 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? |  |  |
|  | 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. |  |  |
| 1c | Electronic copy declaration (Module 1.2.2.4) |  |  |
| 1d | PI and PIL (Module 1.3) |  |  |
|  | Is the Professional Information (PI) and Patient Information Leaflet (PIL)PI and PIL from 5 years prior to the renewal application included in Module 1.3? |  |  |
|  | Is a copy of the current approved PI and PIL included in the Module 1.3 and in the working documents in MS word format? |  |  |
|  | Is the PI and PIL variation approval included in the Module 1.3 (if applicable)? |  |  |
|  | Is the coloured mock-ups of packaging of the product, i.e., blister, label and unit carton in PDF format included in the Module 1.3?  Facsimile labels will be accepted for dormant dossiers. |  |  |
| 1e | Medicine Register Details (Module 1.5.2.2.1) |  |  |
|  | Does the information on 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 on the “Proposed” column in the Medicine Register Details correspond with all the sites to be included in the revised registration certificate? |  |  |
|  | Does the information on the “Proposed” column in the Medicine Register Details correspond with Module 1.2.1 and/or information on the variation summary? |  |  |
| 1f | 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 appended to Module 1.5.2.2.2? If applicable |  |  |
| 1g | Renewal Validation template (Module 1.8) and working documents 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 D will only be screened for the submission with new eCTD  baseline. |  |  |
| 1h | QOS and / or QIS document in 3.2.R.8 and working documents in MS Word format? |  |  |
|  | * A declaration that data related to any commitments/compliance with conditions which the product was registered under, must be submitted.   Note: The declaration can be included with the QIS and QOS in Module 3.2.R.8 or as an annexure to the cover letter in Module 1.0. |  |  |
|  | * A declaration that the risk assessment for applications registered without nitrosamine risk assessment has been done and the necessary updates.   Note: The declaration can be included with the QOS or in the SCoRE document in Module 3.2.R 8. |  |  |
| 2 | Check envelope for correctness of information: |  |  |
| Application number/s (stated separately) |  |  |
| Applicant |  |  |
| Proprietary name/s (stated separately) |  |  |
| Multiple / duplicate applications – name and application number/s |  |  |
| Dosage form |  |  |
| INN |  |  |
| eCTD sequence number |  |  |
| Related eCTD sequence number |  |  |
| Submission type |  |  |
| Submission data type – proof of efficacy |  |  |
| 3 | Module 3.2.R |  |  |
| Is it structured according to correct granularity? |  |  |
| Are the node extensions numbered according to the relevant section? |  |  |
| Are the node extensions named correctly? |  |  |
| 4 | For follow up sequences, is the operation attribute of the following documents reflected as “new”? |  |  |
| 1.0 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) |  |  |
| 5 | Are the leaf titles descriptive and logical, e.g.; for applications with various strengths, and new documents in follow-up sequences? |  |  |
| 6 | Is a risk-benefit assessment report of the preceding 5 years included (1.13)? |  |  |
| 7 | Is Product Quality Review (PQR) included (1.7.2) |  |  |

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

Applicant:

*SAHPRA use only*

*Compliant Continue with technical screening*

*Non-compliant Errors identified during the content check must be resolved by the applicant through the submission of a new eCTD sequence*

**SCREENER**

SAHPRA:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **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. If ticking (✔) NO, provide a motivation in the comments section, referencing the question number.*

| **Good Manufacturing Practice** | | **Yes** | **No** |
| --- | --- | --- | --- |
| 1a | Are the GMP certificates / resolution letter or a copy of the appropriate licences of the manufacturers, packers and FPRCs included in 1.7.3? |  |  |
| 1b | 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; |  |  |
| 1c | Certificates of GMP of the Final Pharmaceutical Product(s) manufacturing facilities\*\*, issued by Recognised Regulatory Authorities (RRAs).  \*\* Includes all sites involved in the testing, manufacturing, and packaging of the  FPP |  |  |
| 1d | Is the date of last inspection within 3 years of today’s date (1.7.3 or 1.7.1)? |  |  |
| 1e | 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 GMP guideline)*? |  |  |
| 1f | 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 GMP guideline)*? |  |  |
| 1g | Are the activities that the manufacturer is approved for in the GMP certificate or license the same as the activities being applied for *(Refer to appendix 2 of the GMP guideline)*? |  |  |
| **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 (1.7.6)? |  |  |
| **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 1.7.2) should be conducted with no fewer than 10 consecutive batches manufactured over the 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 the period of the past 36 months and should include at least: |  |  |
| 4a | A review of starting and primary packaging materials used in the FPP, especially those from new sources (1.7.2) |  |  |
| 4b | A review of critical in-process controls and finished product results (1.7.2); |  |  |
| 4c | A review of all batches that failed to meet established specification(s) and their investigations (1.7.2); |  |  |
| 4d | A review of all significant deviations or non-conformances and related investigations; (1.7.2) |  |  |
| 4e | A review of all changes carried out to the processes or analytical methods (1.7.2); |  |  |
| 4f | A review of the results of the stability-monitoring programme (1.7.2); |  |  |
| 4g | A review of all quality-related returns, complaints and recalls (1.7.2), including export-only medicinal products; |  |  |
| 4h | A summary report of Post-Marketing Surveillance activities in the preceding 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:

*SAHPRA use only*

*Can the application proceed with technical screening?*

**SCREENER**

SAHPRA:

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

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

*Applicant to indicate using a tick (✔) the proposed PEM evaluation pathway.*

***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 Finished Pharmaceutical Product (FPP) manufacturer? (Module 3.2.S.4) |  |  |  |
| 1d | Have batch analysis and valid certificates of analysis (CoAs) of the API issued by 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 6 months accelerated? |  |  |  |
| ii. Generics: At least 6 months long-term and 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 1fi or 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 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 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:

*SAHPRA use only*

*Can the application proceed to evaluation?*

**C.2** **FOREIGN REGULATORY STATUS**

Please see SAHPRA’s *2.02 Quality and Bioequivalence General information (SAHPGL-HPA-07) or Reliance (5.08) Guidelines* for the full list of recognised regulatory authorities, as well as for more information on reliance.

*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.*

| **Requirements[[7]](#footnote-7)** | | **Yes** | **No** | **N/A** |
| --- | --- | --- | --- | --- |
| 1 | Is the product registered using reliance? |  |  |  |
| 2 | If Yes to 1, please confirm the inclusion of the following documentation: |  |  |  |
| 2a | The applicant must provide an updated declaration of sameness |  |  |  |
| 2b | Or indicate what variations have been submitted which deviate from the RRA product |  |  |  |

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

**TECHNICAL SCREENER**

SAHPRA:

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

**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. Tick (✔) N/A if not applicable for this application.*

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

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **1** | **General Information** | **Yes** | | **No** | **N/A** |
| 1.1 | Is the Professional Information (PI) and Patient Information Leaflet (PIL) from 5 years prior to the renewal application included in Module 1.3? |  |  | |  |
| 1.2 | Is the current approved PI and PIL included in Module 1.3 and in the working folder in MS word format? |  |  | |  |
| 1.2.1 | Is the PI and PIL variation approval included in the Module 1.3 (if applicable)? |  |  | |  |
| 1.3 | Is each page of the approved PI and PIL dated and paginated as page X of Y? |  |  | |  |
| 1.4 | 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):

*SAHPRA use only*

Applicant:

*Can the application proceed to evaluation?*

**TECHNICAL SCREENER**

SAHPRA:

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

**E TECHNICAL SCREENING (PHAMACOVIGILANCE)**

*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. Tick (✔) N/A if not applicable for this application.*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **1** | **Risk-benefit assessment report** | **Yes** | **No** | **N/A** |
| 1.1 | Is an executive summary report of the latest Periodic Risk-Benefit Evaluation Report (PBRER) or Periodic Safety Update Report (PSUR) included (1.13):  The report should consist of the following sections: |  |  |  |
| 1.2 | Risk-benefit conclusions by the Holder of the Certificate of Registration, namely by the Clinical Expert or the HCR Responsible Pharmacist. The conclusion/statement should: |  |  |  |
| 1.2.1 | Confirm that the product can be safely renewed for a 5-year period, or any action recommended or initiated should be specified and justified. |  |  |  |
| 1.2.2 | 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. |  |  |  |
| 1.2.3 | 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 where the PI is outdated due to the pending variation, the applicant should submit proof of variation submission and 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:

*SAHPRA use only*

*Can the application proceed to evaluation?*

**TECHNICAL SCREENER**

SAHPRA:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **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 GuidelineEMA, 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)
7. [↑](#footnote-ref-7)