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| --- |
| eCTD VALIDATION and TECHNICAL SCREENING FOR NEW REGISTRATIONS |



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| --- |
| **VALIDATION TEMPLATE FOR eCTD APPLICATIONS** |

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 new registration of a medicinal product for human use submitted in eCTD format. It is also used for follow-up sequences that may be required for the new registration. The applicant must ensure that all relevant fields are completed.

**Sequence 0000 (new application for registration): Complete Sections A.1, A.3, B, C, D and E.**

**Follow-up sequences (related to the new registration): Complete and submit only Sections A.1 and A.3**

**Baseline sequence: Complete and submit only Sections A.1 and A.3**

# 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 |  |
| eCTD sequence number |  |
| Master product proprietary name/s |  |
| Duplicate 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** |
| 1 | Is each CD / DVD / USB clearly and correctly labelled *(refer 4.1 of Guideline 2.23),* and in an envelope? |  |  |
| 2 | Have the following documents in paper format been submitted? |  |  |
| 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? |  |  |
| * In the case of a line extension application, has the application number of the original application been indicated? |  |  |
| 2b | Application form (Module 1.2.1) |  |  |
| * Is Module 1.2.1(c) signed by the authorised pharmacist (original signature) 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? |  |  |
| 2c | ***First submission (sequence 0000):***  Validation and application fee (proof of payment, submitted in a separate envelope, with copy of the letter of application) (module 1.2.2.1) |  |  |
| 2d | ***Follow-up sequence:***  Validation fee (proof of payment, submitted in a separate envelope, with copy of the letter of application) (Module 1.2.2.1) |  |  |
| 2e | Electronic copy declaration (Module 1.2.2.4) |  |  |
| 2f | Validation template (Module 1.8) with declaration letter attached |  |  |
| 2g | MD5 checksum – identifiable, signed and dated |  |  |
| 2h | 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? |  |  |
| 3 | First submission (sequence 0000) |  |  |
| 3a | Is a sample included in an envelope (include motivation for sample not being included when relevant)? |  |  |

# 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 OCR scanned? |  |  |
| 1b | Application form (Module 1.2.1) |  |  |
| * Is the application form OCR scanned? |  |  |
| * Has a separate Module 1.2.1 been submitted for each strength (and duplicates) if different strengths or duplicates are applied for? |  |  |
| 1c | Proof of payment (Module 1.2.2.1) |  |  |
| 1d | Electronic copy declaration (Module 1.2.2.4) |  |  |
| 1e | Validation template (Module 1.8) |  |  |
| * For sequence 0000, have sections B, C, D & E been hyperlinked to the modules where relevant? (hyperlinking to the word “hyperlink”) |  |  |
|  | * Is the declaration letter attached to the validation template? |  |  |
| 1f | SCoRE document in 3.2.R.8 |  |  |
| 1g | Module 1.10 reliance documentation |  |  |
| 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 | PI and PIL |  |  |
| 3a | Is the PI hyperlinked to the references? |  |  |
| 3b | If sequence 0000, has the PI been included in Module 1.3.1.1? |  |  |
| 3c | If sequence 0000, has the PIL been included in Module 1.3.2? |  |  |
| 3d | Is the PIL hyperlinked to the PI? |  |  |
| 3e | For responses, have the annotated PI and PIL been included in Module 1.5.5? |  |  |
| 4 | Is Module 2 hyperlinked to Modules 3 / 4 / 5, when necessary? |  |  |
| 5 | Is the Tabulated Schedule of Amendments hyperlinked to the new / updated data? |  |  |
| 6 | 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? |  |  |
| 7 | 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) |  |  |
| 8 | 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:

*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

# 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.*

| **Proposed Holder of certificate registration** | | **Yes** | **No** |
| --- | --- | --- | --- |
| 1 | Has the licence of the Proposed Holder of Certificate of Registration been included in the submission? (1.7.3) |  |  |
| 2 | Is the declaration of who is authorised to conduct regulatory action included? |  |  |
| 2a | Has proof of the responsible pharmacist’s SAPC registration, certificate and proof of current registration (registration card), been included and is it valid at the time of submission? (1.7.7.1) |  |  |
| 3 | Is the proof of registration with the registrar of companies available? (1.7.8) |  |  |
| **Manufacturing** | | **Yes** | **No** |
| 4 | Are the GMP certificates or a copy of the appropriate licences of the manufacturers, packers and FPRCs included in 1.7.3? |  |  |
| 4a | Is the date of last inspection within 3 years of today’s date (1.7.3 or 1.7.1)? |  |  |
| 4b | 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)*? |  |  |
| 4c | 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)*? |  |  |
| 4d | 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)*? |  |  |
| 4e | If GMP certificates are not included or are not valid from last 3 years, is the site a South African site (1.2.1)? |  |  |
| 5 | Has the inspection flow diagram been attached (1.7.12)? |  |  |
| 6 | Is there a declaration from the site that further inspections conducted after the date on the GMP certificate did not indicate non-performance/negative review? |  |  |
| **Laboratory** | | **Yes** | **No** |
| 7 | Is there a declaration that the API has been received by a site that is approved by the EDQM (3.2.R)? |  |  |
| 7a | Is a certificate of analysis for the API present? |  |  |
| 7b | Has a Confirmation of sample been included (1.7.10)? |  |  |
| 7c | Is there a declaration that the batch manufacturing record of the sample is available for inspection at the request of the regulator? |  |  |
| 7d | Is there a declaration that the executed batch manufacturing record is available for inspection at the request of the regulator? |  |  |

**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?*

# C TECHNICAL VERIFICATION (MEDICINES EVALUATION AND RESEARCH – ME&R)

*Applicant to indicate using a tick (✔) the proposed ME&R evaluation pathway.*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Proposed ME&R[[1]](#footnote-1) evaluation pathway** (refer to 2.02 Quality and Bioequivalence Guideline for more information) | | | | | | | | |
| Full review |  | Abridged review | |  | Verified review |  | Recognition |  |
| Summary of motivation for proposed pathway (Relevant documents to be included in Module 1.10) | | | *<Application qualifies for an Abridged review because it is a generic product registered in 2015 through the EMA Centralised Procedure>* | | | | | |
| Note: The final evaluation pathway decision for an application is at the discretion of SAHPRA, and will depend on the quality of reliance documentation submitted. SAHPRA will share screening queries with applicants regarding insufficient reliance documentation to ensure that as many applications as possible qualify for abridged and verified reviews. | | | | | | | | |

**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[[2]](#footnote-2) |  |  |  |
| 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[[3]](#footnote-3) 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[[4]](#footnote-4) |  |  |  |
| 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[[5]](#footnote-5) is submitted, is the declaration of access completed? **OR** If a CPQ[[6]](#footnote-6) 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[[7]](#footnote-7) 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 BIOEQUIVALENCE**

*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.*

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **General information** | | | **Yes** | | **No** | | **N/A** | | |
| 1a | Has the completed Bioequivalence Trial Information Form (BTIF) (6.32) been included in MS Word format? (Working documents folder)? | |  | |  | |  | |
| 1b | Has the biowaiver template been included in MS Word format? (Working documents folder)? | |  | |  | |  | |
| i. BCS based biowaiver: IPRP[[8]](#footnote-8) template | |  | |  | |  | |
| ii. Additional strength biowaiver: WHO template? | |  | |  | |  | |
| 2 | Has the biostudy been granulated according to the ICH E3 requirements? | |  | |  | |  | | |
| 3 | Is/are the fasting and/or fed bioequivalence study(ies) included? | |  | |  | |  | | |
| 4 | Are the following components of the biostudy included? | |  | |  | |  | | |
| 4a | Date and place of study on the title page or the first page of the bioequivalence study report? | |  | |  | |  | | |
| 4b | The protocol? (E3, Appendix 16.1.1) | |  | |  | |  | | |
| 4c | Evidence of ethical approval? (E3, 5.2) | |  | |  | |  | | |
| 4d | Analytical report - All individual patient data? (E3, 11.4) | |  | |  | |  | | |
| 4e | Individual concentration data and pharmacokinetic parameters included? (E3, 11.2.3) | |  | |  | |  | | |
| 4f | Investigator’s curriculum vitae? (E3, 16.1.4) | |  | |  | |  | | |
| 4g | Quality assurance statement? (E3, 16.1.8) | |  | |  | |  | | |
| **Batch size of the test product** | | | **Yes** | | **No** | | **N/A** | | |
| 5a | Is the batch size a minimum of 100,000 units or at least 10% of the production batch, whichever is greater? (Modules 1.2.2.3 and 3.2.P.3.2) | |  | |  | |  | | |
| 5b | If the batch size is less than 100,000 units, has the use of a smaller batch size been motivated? (Module 3.2.R.1) | |  | |  | |  | | |
| **Analytical validation** | | | **Yes** | | **No** | | **N/A** | | |
| 6a | Is the bioanalytical report and the bioanalytical method validation report included? (Module 5.3.1.4) | |  | |  | |  | | |
| 6b | Are chromatograms included from analytical runs for at least 20% of the subjects, with quality control samples and calibration standards of the runs including these subjects[[9]](#footnote-9)? (Module 5.3 Appendix 16.2) | |  | |  | |  | | |
| 6c | CoAs (Module 3.2.R.1.3) and dissolution profiles (Module 3.2.R.1.4) of test and reference products and CoA of API of test product? | |  | |  | |  | | |
| **Regional requirements (Module 3.2.R)** | | | **Yes** | | **No** | | **N/A** | | |
| 7a | Has the country of procurement of the reference product and name and address of the relevant supplier been stated? (Module 3.2.R.1.2) | |  | |  | |  | | |
| 7b | Was the reference product procured in a country with which SAHPRA aligns itself? (Module 3.2.R.1.2) | |  | |  | |  | | |
| 7c | Is the biostudy reference product strength within the SAHPRA approved Professional Information (PI) dose range? (Module 1.3.1) | |  | |  | |  | | |
| 7d | If relevant, has a full report on comparative data to demonstrate equivalence of the foreign reference product to the South African reference product been submitted? (Module 3.2.R.1.4.1) | |  | |  | |  | | |
| **Biostudy test product** | | | | **Yes** | | **No** | | **N/A** | |
| 7a | | Is the biostudy test product manufactured by the same manufacturer, at the same site, as the product being applied for? | |  | |  | |  | |
| 7b | | If **NO** to 7a: | |  | |  | |  | |
| i. Has a comparison between the formulations, manufacturing process and a tabulated comparison of physico-chemical characteristics been provided? (Module 3.2.R.1.1.7) | |  | |  | |  | |
| ii. Have tabulated comparative data been provided to show essential similarity in physico-chemical characteristics? (Module 3.2.R.4.1) | |  | |  | |  | |
| 7c | | Is the API(s) used in the biostudy test product manufactured by the same API manufacturer being applied for? | |  | |  | |  | |
| 7d | | If **NO** to 7a and/or 7c, has a comparative dissolution report been provided (data in three media)? (Module 3.2.R.1.4.1) | |  | |  | |  | |
| **Biowaivers** | | | | **Yes** | | **No** | | **N/A** | |
| 8a | | Additional strengths | |  | |  | |  | |
| i. Are the additional strengths proportionally formulated? (Module 3.2.R.1 and/or Module 3.2.P.3.2) | |  | |  | |  | |
| ii. Has a comparative dissolution report been included for the additional strengths? (Module 3.2.R.1.4.1) | |  | |  | |  | |
| 8b | | If a BCS biowaiver is requested, are the following included: | |  | |  | |  | |
| i. A motivation and justification? (Module 3.2.R.1) | |  | |  | |  | |
| ii. A full report in accordance with the report format described in the dissolution guideline[[10]](#footnote-10) with the appropriate data comparing the test and reference products in the three dissolution media, pHs 1,2; 4,5 and 6,8? | |  | |  | |  | |

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

*SAHPRA use only*

Applicant:

*Can the application proceed to evaluation?*

**C.3 FOREIGN REGULATORY STATUS**

Please see SAHPRA’s *2.02 Quality and Bioequivalence Guideline* 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[[11]](#footnote-11)** | | **Yes** | **No** | **N/A** |
| --- | --- | --- | --- | --- |
| 1 | Is this product registered by a recognised regulatory authority (RRA)? |  |  |  |
| 2 | If Yes to 1, please confirm the inclusion of the following documentation: |  |  |  |
| 2a | Completed abridged review template (6.33) or verified review template (6.34) in MS Word format? (Working documents folder) |  |  |  |
| 2b | Registration / marketing authorisation certificate? (Module 1.10) |  |  |  |
| 2c | Full, unredacted assessment reports from the RRA? (Module 1.10)  Note*: Public assessment reports will not be accepted* |  |  |  |
| 2d | If **NO** to 2c, letter of access[[12]](#footnote-12) for SAHPRA to obtain full, unredacted assessment reports from the RRA? (Appended to validation template) |  |  |  |
| 2e | Sameness declaration[[13]](#footnote-13) (Appended to validation template) |  |  |  |
| 2f | Summary of Product Characteristics (SmPC)? (Module 1.10) |  |  |  |

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

Applicant:

# D TECHNICAL SCREENING (PRE CLINICAL AND CLINICAL)

*Applicant to fill in the tables below specific to the Clinical aspect of the application*

|  |  |
| --- | --- |
| **Clinical reference product A: Local innovator[[14]](#footnote-14)**[for Generics only] | |
| HCR |  |
| API(s) |  |
| Name of the medicine(s) |  |
| Dosage strength(s) |  |
| Method(s) of administration |  |
| Registration number(s) |  |
| Registration / revision date |  |
| **Clinical reference product B: Foreign innovator** [for an NCE, applicant to supply details of their own SmPC registered with a recognised regulatory authority (RRA)] | |
| MAH |  |
| API(s) |  |
| Name of the medicine(s) |  |
| Dosage strength(s) |  |
| Method(s) of administration |  |
| Registration number(s) |  |
| Authorisation / revision date |  |
| RRA |  |

*Applicant to indicate using a tick (✔) the proposed evaluation pathway, and provide a brief motivation.*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Proposed Clinical[[15]](#footnote-15) evaluation pathway** (refer to 2.09 Clinical Guideline for more information) | | | | | | | | |
| Full review |  | Abridged review | |  | Verified review |  | Recognition |  |
| Motivation for proposed pathway | | |  | | | | | |
| Note: The final evaluation pathway decision for an application is at the discretion of SAHPRA, and will depend on the quality of reliance documentation submitted. SAHPRA will share screening queries with applicants regarding insufficient reliance documentation to ensure that as many applications as possible qualify for abridged and verified reviews. | | | | | | | | |

*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 | Are MS word versions of the proposed PI and PIL included in the ‘working documents’ folder? |  |  |  |
| 1.2 | Are the cross-references in the PI written with the exact page/s and location on the page/s (i.e. column, and paragraph, and/or line numbers) of the document that is referenced?  *Note: Former MCC Standardised Package Insert (SPI), Monthly Index of Medical Specialities (MIMS), MIMS Desk Reference (MDR), South African Medicine Formulary (SAMF) and information on Micromedex are not acceptable references.* |  |  |  |
| 1.2.1 | Are the cross-references hyperlinked to exact page/s and location on the page/s? [Ensure no hyperlinks are broken] |  |  |  |
| 1.3 | Is each page of the proposed PI and PIL dated and paginated as page X of Y? |  |  |  |
| 1.4 | Are the proposed PI and PIL documents line numbered? |  |  |  |
| 1.5 | Are the standard references referred to in the proposed PI included in Module 1.3.1.2? |  |  |  |
| 1.6 | Is the format of the proposed PI completely aligned with the format indicated in the latest published PI guidelines? |  |  |  |
| 1.7 | Has the information in the proposed PIL been cross-referenced to the **proposed PI only**? (Including exact page/s and location on the page/s) E.g. Information in PIL on symptoms/action to be taken on severe allergic reaction should be referenced to immune system disorders in the PI. |  |  |  |
| 1.8 | Are the references legible and complete? |  |  |  |
| 1.9 | Do all **reference** PIs contain the following summary information upfront (either on the front page, a cover page or a header – whichever is practical):   * the reference HCR / MAH, * name of the medicine, * name of the RRA (if applicable), * date of registration / authorisation and / or revision? |  |  |  |
| 1.10 | Are all *scanned* references OCR-scanned (optical character recognition), such that the reviewer can search and copy text? |  |  |  |
| 1.11 | For any re-typed PIs, has a photocopy of the original printed PI been included (Module 1.3), along with a declaration of sameness attached at the end of the re-typed PI? The re-typed PI should be submitted in PDF format to allow hyperlinking from the proposed PI. Insert hyperlink(s). |  |  |  |
| 1.12 | Does the application comply with the requirements stipulated in the 2.40 Multiple Submissions guideline? (E.g. For duplicates only one PI and PIL is to be submitted with the Proprietary Name indicated as “Product Name”) |  |  |  |
| **2** | **Generics** | **Yes** | **No** | **N/A** |
| 2.1 | Is the most recently SAHPRA-approved[[16]](#footnote-16) innovator PI submitted? Insert hyperlink. |  |  |  |
| 2.1.1 | If not marketed any longer/de-registered, is the most recently SAHPRA-approved16 generic PI submitted? Insert hyperlink. |  |  |  |
| 2.1.2 | Are the THERAPEUTIC INDICATION(s) and POSOLOGY and METHOD OF ADMINISTRATION completely in line with the SA innovator? Note: if the SA innovator is no longer marketed or is deregistered, alignment must be to a generic. |  |  |  |
| 2.2 | Is a recently approved innovator SmPC/PI from a RRA submitted? Insert hyperlink. |  |  |  |
| 2.2.1 | Has the innovator SmPC/PI from a RRA been **used to update safety only?** (Any information, safety or other, not related to SAHPRA-approved therapeutic indications, posology and method of administration may not be added in the proposed PI.) |  |  |  |
| 2.2.2 | In addition to the local innovator, has only **one** foreign innovator PI (registered by a RRA) been referenced in the proposed PI (and included in Module 1.3.1.2)? Note that any other foreign PIs should still be included in Module 1.10, even if not referenced by the proposed PI. |  |  |  |
| 2.3 | Is the API the same as the reference/innovator product? |  |  |  |
| 2.3.1 | If not, does the product yield the same quantity of the API per dosage form as the reference/innovator product? |  |  |  |
| 2.3.2 | Is the proposed salt/hydrate/ester/pro-drug the same as that of the innovator/reference product? |  |  |  |
| 2.3.3 | If not, are there any safety concerns stemming from the different salt/hydrate/ester/pro-drug? E.g. potassium salt versus sodium salt for IV administration. |  |  |  |
| 2.4 | Do the formulations and dosage strengths make provision for the claimed THERAPEUTIC INDICATIONS, POSOLOGY AND METHOD OF ADMINISTRATION in the target population(s)? Ensure that the lowest/initial dose/titration dose is possible in the target population. |  |  |  |
| **3** | **NCEs and Generics with Clinical data** | **Yes** | **No** | **N/A** |
| 3.1 | Has the information in Modules 2.4, 2.5, 2.6 and 2.7 (Non-clinical and Clinical Overviews and Summaries) been included? Insert hyperlink(s). |  |  |  |
| 3.2 | Is the proposed PI primarily cross-referenced to the Overviews and Summaries submitted in Module 2? |  |  |  |
| 3.3 | Has the information of Modules 4 (Pre-clinical study reports) and 5 (Clinical study reports) been included and are the summaries in Module 2 cross-referenced to this information? |  |  |  |
| 3.4 | Is the NCE registered with one or more RRAs (as indicated in Module 1.10)? |  |  |  |
| 3.5 | Do the formulations and dosage strengths make provision for the claimed THERAPEUTIC INDICATIONS, POSOLOGY AND METHOD OF ADMINISTRATION in the target population(s)? |  |  |  |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **4** | **Extension applications (Clinical[[17]](#footnote-17))** | **Yes** | **No** | **N/A** |
| 4.1 | Is the extension application for a change of bioavailability? |  |  |  |
| 4.2 | Is the extension application for a change of pharmacokinetics (e.g., change in rate of release)? |  |  |  |
| 4.3 | Is the extension application for a change or addition of a new strength[[18]](#footnote-18)/potency? |  |  |  |
| 4.3.1 | Does the new strength follow the approved target population, approved route of administration and the approved dosage schedule? |  |  |  |
| 4.4 | Is the extension application for a change or addition of a new pharmaceutical form? |  |  |  |
| 4.5 | Is the extension application for a change or addition of a new route of administration? |  |  |  |
| **5** | **Clones** | **Yes** | **No** | **N/A** |
| 5.1 | Has the approved PI and PIL of the registered product been submitted? Include hyperlink(s). |  |  |  |
| 5.2 | Has the proposed PI been referenced and hyperlinked to the PI of the registered product only? |  |  |  |
| 5.3 | Are the THERAPEUTIC INDICATION(s) and POSOLOGY and METHOD OF ADMINISTRATION completely in line with the registered product? |  |  |  |
| **6** | **FDCs** | **Yes** | **No** | **N/A** |
| 6.1 | Has the contribution of each active to the therapeutic effect at the dosages proposed been established in a reference PI(s)? |  |  |  |
| 6.2 | Which FDC scenario is being applied? | *{Applicant to state the scenario here}* | | |
| 6.2.1 | Has the correct scenario according to FDC guidelines been used? |  |  |  |

**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?*

# E TECHNICAL SCREENING (NAMES AND SCHEDULING)

In evaluating the safety and efficacy of a medicine during the registration process, SAHPRA considers whether the proposed proprietary name of such a product could potentially pose public health or safety concerns or whether it may be misleading. It seeks to prevent, to the greatest extent possible, potential medication errors or medical misadventures that may occur because of look-alike or sound-alike proprietary names, or names which may imply an ingredient, benefit or use that may be misleading either in nature or in degree.

The applicant should use one or more of the following tools when compiling the application for the appropriateness of the proprietary name:

* The SAHPRA Registered Medicines Database
* The current Database of Medicine Prices, published by the Department of Health
* The current MIMS/ SAMF/ MDR

**A separate technical screening checklist should be submitted for master and duplicate submissions.**

**A separate technical screening checklist with alternate proprietary names should be submitted following a non-approval of a proprietary name. This should be linked to the original screening checklist and outcome of the evaluation.**

|  |  |
| --- | --- |
| **Proposed proprietary name** | {Proposed proprietary name} |
| **Type of submission** | {Master/Duplicate} |

This checklist is non-exhaustive and the completion of the checklist does not necessarily imply that the proposed proprietary name will be approved by SAHPRA, as each application is evaluated on its merits.

*Applicant to indicate using a tick (✔) to either YES or NO to the questions below.* *Ticking YES to any of the questions, without substantial motivation where required, indicates the high likelihood that the proposed proprietary name will be rejected by SAHPRA.*

| **Proposed proprietary name** | | **Yes** | **No** |
| --- | --- | --- | --- |
| 1 | Is the proposed proprietary name identical to the proprietary name of an existing registered medicine? |  |  |
| 1a | Is the proposed proprietary name identical to the proprietary names of medicines previously marketed, but subsequently withdrawn, discontinued or no longer marketed? |  |  |
| 1b | If YES, is adequate motivation supplied for use of the withdrawn / discontinued name? |  |  |
| 2 | Is the proposed proprietary name similar in print, handwriting (orthography) or speech to the proprietary name of an existing registered medicine? |  |  |
| 2a | Is the proposed proprietary name similar in print, handwriting (orthography) or speech to the proprietary name of medicines previously marketed, but subsequently withdrawn, discontinued or no longer marketed? |  |  |
| 2b | If YES, is adequate motivation supplied for use of the withdrawn/ discontinued name? |  |  |
| 3 | Is the proposed proprietary name confusing or similar to the WHO International Non-proprietary Name (INN) of the Active Pharmaceutical Ingredient (API)? |  |  |
| 3a | Does the proposed proprietary name contain 50 % or more of the approved WHO INN of the API? |  |  |
| 4 | Does the proposed proprietary name include elements from biochemical nomenclature, as specified in guideline *2.15 Proprietary Names for Medicines*?  e.g. feron from interferon; leukin from interleukin |  |  |
| 5 | Does the proposed proprietary name contain any of the following symbols:  +, &, #, @, =, [ ]. |  |  |
| 6 | Does the proposed proprietary name contain an unacceptable abbreviation, not in line with the guideline *2.15 Proprietary Names for Medicines*? |  |  |
| 7 | Does the proposed proprietary name include a qualifier comprising of letters or numerals that appropriately differentiates the medicine from other medicines? |  |  |
| 7a | If YES, is there adequate justification for the use of the qualifier or abbreviation? |  |  |
| 8 | Does the proposed proprietary name include promotional qualifications, abbreviations or manufacturers own codes? |  |  |
| 9 | Does the proposed proprietary name contain non-English names derived from local or international languages? |  |  |
| 9a | Does the application include an English interpretation, translation, transliteration, explanation, and motivation for the use of the word / phrase? |  |  |
| 9b | If YES, are these names misleading in any way? |  |  |
| 10 | Does the proposed proprietary name contain ordinary English words or phrases?  e.g. Whisper, Hello |  |  |
| 11 | Does the proposed proprietary name contain personal names of people, whether fictional or non-fictional?  e.g. Hippocrates, Diana |  |  |
| 12 | Does the proposed proprietary name comprise one or two letters, ciphers and/or acronyms? |  |  |
| 13 | Does the proposed proprietary name make reference to non-medicine products or the use of terms which imply that the product is not a medicine and trivialises its medicinal properties? |  |  |
| 14 | Does the proposed proprietary name create inappropriate impressions or implicit claims of superiority or greater potency, efficacy or speed of action? |  |  |
| 14a | If YES, is there adequate scientific evidence to support these claims? |  |  |
| 15 | Is the company identifier a company name other than that of the Holder of Certificate of Registration (HCR) or the registered applicant in South Africa? |  |  |
| 15a | If YES, has a declaration from the HCR been included, confirming that the PHCR is allowed to use their name in connection with the product being applied for? |  |  |
| 16 | Does the proposed proprietary name include the entire INN together with the company identifier/ house brand in the format – “Company Identifier *INN”?* |  |  |
| 16a | If YES, has a motivation to justify the use of the Company identifier as a prefix rather than a suffix been included? |  |  |
| 17 | Does the proposed proprietary name include the company identifier with an invented name? |  |  |
| 18 | Does the proposed proprietary name include a company identifier with a description of the indication, pharmacological action or therapeutic class? |  |  |
| 19 | If the proposed proprietary name includes an umbrella name, is sufficient motivation provided for the use of an umbrella name according to the guideline *2.15 Proprietary Names for Medicines*? |  |  |

**Comments if any answer is ‘YES’** (use the numbering in the checklist to link comments to specific questions):

Applicant:

*SAHPRA use only*

*Can the application proceed to evaluation?*

# UPDATE HISTORY

|  |  |  |
| --- | --- | --- |
| **Date** | **Reason for update** | **Version & publication** |
| Feb 2014 | First publication as part of screening template 6.15 | v1, March 2013 |
| April 2014 | Separation from screening form for paper dossiers – new number and name | v1 draft April 2014 |
| June 2014 | Finalised version | v1 Aug 2014 |
| Immediate | Implementation |
| Sept 2016 | Updated to cover administrative issues identified in the pilot phase | v2 November 2016 |
| 15 December 2016 | Implementation |
| July 2019 | Updated to cover new processes and to include technical screening | v3 July 2019 |

1. Note that the evaluation pathway for ME&R is independent to that of Clinical (e.g. ME&R can follow a verified review, while Clinical can follow a full review based on the documentation submitted) [↑](#footnote-ref-1)
2. Latest implemented versions of 2.05 Stability Guideline and/or SADC Stability Guideline [↑](#footnote-ref-2)
3. Latest implemented version of 2.24 Guidance General Module 1 [↑](#footnote-ref-3)
4. Latest implemented versions of 2.05 Stability Guideline and/or SADC Stability Guideline [↑](#footnote-ref-4)
5. Certificate of Suitability to the monographs of the European Pharmacopoeia [↑](#footnote-ref-5)
6. Confirmation of API Prequalification Document [↑](#footnote-ref-6)
7. Blank / master production documents for a pilot scale batch or bracketing for commercial batch sizes are permitted, provided the requirements in 2.02 Quality and Bioequivalence Guideline are satisfied [↑](#footnote-ref-7)
8. International Pharmaceutical Regulators Program [↑](#footnote-ref-8)
9. A representative number of chromatograms or other raw data should be provided covering the whole concentration range for all standard and quality control samples as well as the specimens analysed. [↑](#footnote-ref-9)
10. Latest implemented version of 2.07 Dissolution Guideline [↑](#footnote-ref-10)
11. Additional information can be provided (please see section 5.5 of 2.02 Quality and Bioequivalence Guideline) [↑](#footnote-ref-11)
12. Appendix of the General Information Guideline [↑](#footnote-ref-12)
13. Appendix 2 of 2.02 Quality and Bioequivalence Guideline [↑](#footnote-ref-13)
14. Applicants may reference the latest SAHPRA-approved generic where the local innovator is no longer marketed, or has been deregistered [↑](#footnote-ref-14)
15. Note that the evaluation pathway for Clinical is independent to that of ME&R (e.g. Clinical follows a verified review, while ME&R follows a full review based on the documentation submitted) [↑](#footnote-ref-15)
16. All reference PIs should be sourced from the database of latest-approved PIs provided on the SAHPRA website, if available (separate guidance on this process will be issued by SAHPRA) [↑](#footnote-ref-16)
17. Subset of extension applications applicable to the Clinical unit [↑](#footnote-ref-17)
18. Where the strength is defined as “the content of the active substances expressed quantitatively per dosage unit, per unit of volume or weight according to the dosage form” (as per EC Directive 2001/83) [↑](#footnote-ref-18)