|  |
| --- |
| eCTD VALIDATION and TECHNICAL SCREENING FOR VARIATIONS |

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| --- |
| **VALIDATION TEMPLATE FOR eCTD VARIATION 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 a variation application for a medicinal product for human use submitted in eCTD format. It is also used for follow-up sequences that may be required for the variation. The applicant must ensure that all relevant fields are completed.

**Please complete sections A.1, A.3, and the relevant sub-sections of B, C, D and E where applicable to your variation application.**

# A ADMINISTRATIVE VALIDATION

# A.1 COMPLIANCE CHECK

*Holder of certificate of registration to fill in the table below as per the application M1.0*

|  |  |
| --- | --- |
| **Product information** | |
| Holder of certificate of registration name | {Licensed Name} |
| Master product registration number/s |  |
| Duplicate product registration 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 | ***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) |  |  |
| 2d | Electronic copy declaration (Module 1.2.2.4) |  |  |
| 2e | Validation template (Module 1.8) with declaration letter attached |  |  |
| 2f | MD5 checksum – identifiable, signed and dated |  |  |
| 2g | 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) |  |  |

# 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

*If Yes, holder of certificate of registration to hyperlink to the relevant document in the “Yes” column.*

*If Not applicable based on the variation application, tick in the “N/A” column.*

| **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 duplicate) 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) |  |  |
| * Have the relevant sections B, C, D & E been hyperlinked to the modules where relevant? (hyperlinking to the word “hyperlink”) |  |  |
|  | * Are all relevant declarations attached to the validation template? |  |  |
| 1f | SCoRE document in 3.2.R.8 |  |  |
| 1g | Module 1.10 reliance documentation |  |  |
| 2 | Check eCTD envelope for correctness of information: |  |  |
| * Registration number/s (stated separately) |  |  |
| * Holder of certificate of registration |  |  |
| * Proprietary name/s (stated separately) |  |  |
| * Multiple / duplicate applications – name and registration 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 | Has the SAHPRA approved PI been included in Module 1.3.1.1? |  |  |
| 3c | Has the SAHPRA approved PIL been included in Module 1.3.2? |  |  |
| 3d | Is the annotated PIL hyperlinked to the annotated PI in Module 1.5.5? |  |  |
| 3e | Have the annotated PI and PIL been included in Module 1.5.5? |  |  |
| 4 | Is Module 2 hyperlinked to Modules 3 / 4 / 5, when relevant? |  |  |
| 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)

*If Yes, applicant to hyperlink to the relevant document in the “Yes” column.*

*If No, applicant to tick in the “No” column and provide a motivation in the comments section, referencing the question number.*

*If Not applicable based on the variation application, tick in the “N/A” column.*

Note: The table below covers documentation/data requirements for a given submission. This represents the key requirements for variations applications – applicants may submit other relevant documentation not listed in the table below as deemed necessary.

1. **ADMINISTRATIVE CHECK**

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

|  |  |  |  |
| --- | --- | --- | --- |
| A.1 Change of Applicancy (HCR/FPRR) | | YES | NO |
| 1 | Has the licence and the latest SAHPRA resolution letter (indicating whether HCR is compliant to GMP requirements) of the Proposed Holder of Certificate of Registration been included in the submission? (1.7.3) |  |  |
| 2 | Is the letter of authorisation to communicate with SAHPRA included? (1.2.2.2) |  |  |
| 3 | 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) |  |  |
| 4 | Is the proof of registration with the registrar of companies included? (1.7.8) |  |  |
| 5 | Is the curriculum vitae of the qualified person for pharmacovigilance included? (1.2.2.5) |  |  |
| 6 | The Medicines Register Details should clearly outline the “current” and “proposed” HCR (1.5.2.2) |  |  |
| 7 | Letters of Cessation and Acceptance. (1.7.9) |  |  |
| A.1 Change of address and/or name of the Applicant (HCR/FPRR) | | YES | NO |
| 8 | Is the letter of authorisation to communicate with SAHPRA included? (1.2.2.2) |  |  |
| 9 | Is the proof of registration with the registrar of companies included? (1.7.8) |  |  |
| 10 | Has the licence of the Proposed Holder of Certificate of Registration been included in the submission? (1.7.3) |  |  |
| 11 | The Medicines Register Details should clearly outline the “current” and “proposed” HCR (1.5.2.2) |  |  |
| A.7 Deletion of manufacturing sites (including for an active substance, intermediate or finished product, packaging site, manufacturer responsible for batch release, site where batch control takes place, or supplier of a starting material, reagent or excipient (when mentioned in the dossier). | | YES | NO |
| 12 | Is the letter of authorisation to communicate with SAHPRA included? (1.2.2.2) |  |  |
| 13 | The Medicines Register Details should clearly outline the “current” and “proposed” HCR (1.5.2.2) |  |  |
| A.5.a Change in the name and/or address of a manufacturer of the finished product, including quality control sites | | YES | NO |
| 14 | Is the letter of authorisation to communicate with SAHPRA included? (1.2.2.2) |  |  |
| 15 | The Medicines Register Details should clearly outline the “current” and “proposed” HCR (1.5.2.2) |  |  |
| 16 | Amendment of the relevant section(s) of the dossier, including revised product information as appropriate. (e.g. 1.2.1, 1.7.1, 1.7.2; 1.7.3) |  |  |
| B.II.b.1.b Replacement or addition of a manufacturing site for part or all of the manufacturing process of the finished product (Primary Packer) | | YES | NO |
| 17 | Proof (valid reliance GMP certificate or SA resolution letter) that the proposed site is appropriately authorised for the pharmaceutical form or product concerned. Last inspection date / inspection report / GMP certificate of the additional manufacturing site. (1.7.2; 1.7.3; 1.7.7.3) |  |  |
| 18 | The Medicines Register Details should clearly outline the “current” and “proposed” HCR (1.5.2.2) |  |  |
| 19 | Is the letter of authorisation to communicate with SAHPRA included? (1.2.2.2) |  |  |
| B.II.b.1.a Replacement or addition of a manufacturing site for part or all of the manufacturing process of the finished product (Secondary Packer) | | YES | NO |
| 20 | Is the letter of authorisation to communicate with SAHPRA included? (1.2.2.2) |  |  |
| 21 | Proof (valid reliance GMP certificate or SA resolution letter) that the proposed site is appropriately authorised for the pharmaceutical form or product concerned. Last inspection date / inspection report / GMP certificate of the additional manufacturing site. (1.7.2; 1.7.3; 1.7.7.3) |  |  |
| 22 | The Medicines Register Details should clearly outline the “current” and “proposed” HCR (1.5.2.2) |  |  |

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

Applicant:

*SAHPRA use only*

*Approved – Import into the system and notify applicant of Inspectorate Approval*

*Rejected Notify the applicant of rejection with the reason*

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

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Associated finished product name | | | | | | | | | | |  | | | | | | |
| Associated finished product application number | | | | | | | | | | |  | | | | | | |
| Other products affected by variation | | | | | | | | | | |  | | | | | | |
| Single variation (tick) | | | | |  | | | | | | Grouped variation (tick) | | | |  | | |
| Number of variation applications (tick all applicable options) | | | | | | | | | | | | | | | | | |
| Type IA |  | | | Type IAIN | | |  | | Type IB | | |  | | Type II | |  | |
| **Proposed evaluation pathway** (as required by the type of Variation) (refer to 2.02 Quality and Bioequivalence Guideline for more information) | | | | | | | | | | | | | | | | | |
| Full review | |  | Abridged review | | | | |  | | Verified review | |  | Recognition[[1]](#footnote-1) | | | |  |
| 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. | | | | | | | | | | | | | | | | | |

Type I

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Variations/changes included in this application (Codes as per the EMA variations guideline) Include as many lines as required | | | | | |
| Code | Code description | Details | Conditions | Documents | Yes/No |
| E.g.  **B.I.a.4** | **Change to in-process tests or limits applied during the manufacture of the active substance** | a) Tightening of in-process limits | 1, 2, 3, 4 | 1, 2 |  |

Type II

|  |  |  |  |
| --- | --- | --- | --- |
| Variations/changes included in this application (Codes as per the EMA variations guideline) Include as many lines as required | | | |
| Code | Code description | Details | Documents |
| E.g.  **B.I.a.4** | **Change to in-process tests or limits applied during the manufacture of the active substance** | d) Widening of the approved in-process test limits, which may have a significant effect on the overall quality of the active substance | All supporting information and documents as per EMA Quality guidelines |

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

**TECHNICAL VERIFICATION – VARIATIONS QUALITY**

***Applicant to indicate using a tick (✓) in the yes column if the required documents have been included.***

***If No, provide a motivation in the comments section.***

|  |  |  |  |
| --- | --- | --- | --- |
| Critical Information | | **Yes (Y)** | **No (N)** |
| 1 | Has the working code on the cover page been verified with the variation applied for? |  |  |
| 2a | Is the amendment schedule included in Module 1.5.2.1? |  |  |
| 2b | Is the signed covering letter included in Module 1.0? |  |  |
| 3 | Have all the variations included in the amendments schedule been mentioned in the covering letter? |  |  |
| 4 | Is the signed application form included in Module 1.2.1? (application form format should not be changed) |  |  |
| 5 | Is the amendment history included on the application form? |  |  |
| 6a | Does this variation fall within the EMA classification? |  |  |
| 6b | If no, has a motivation been included in the covering letter? |  |  |
| 7a | Have all the supporting documents as per variation guideline, been included? The inclusion of relevant documents should be stipulated in the tables below (B.1, B.2, B.3) |  |  |
| 7b | Have the relevant sections of the SCoRE document been completed? |  |  |
|  |  |  |  |

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

Applicant:

## B.1 QUALITY

*Where relevant to the variation application, applicant to indicate using a tick (✔) in the YES column if the required documents have been included. If ticking NO for a document that is relevant, 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.*

*If Yes, holder of certificate of registration to hyperlink to the relevant document in the “Yes” column.*

*If No, applicant to tick in the “No” column and provide a motivation in the comments section, referencing the question number.*

*If Not applicable based on the variation application, tick in the “N/A” column.*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **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)[[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? |  |  |  |
| 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[[4]](#footnote-4) 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[[5]](#footnote-5) [[6]](#footnote-6) |  |  |  |
| 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[[7]](#footnote-7) is submitted, is the declaration of access completed? **OR** If a CPQ[[8]](#footnote-8) 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? (where relevant) (Module 3.2.R.7.1) |  |  |  |
| 3e | Have blank / master batch manufacturing records been included for each proposed batch size[[9]](#footnote-9) 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:

## B.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.

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

| **Requirements[[10]](#footnote-10)** | | **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 | Registration / marketing authorisation certificate? (Module 1.10) |  |  |  |
| 2b | Full, unredacted assessment reports from the RRA? (Module 1.10)  Note*: Public assessment reports will not be accepted* |  |  |  |
| 2c | If **NO** to 2b, letter of access[[11]](#footnote-11) for SAHPRA to obtain full, unredacted assessment reports from the RRA? (Appended to letter of application) |  |  |  |
| 2d | Sameness declaration[[12]](#footnote-12) (Appended to validation template) |  |  |  |
| 2e | 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:

*SAHPRA use only*

# The application can proceed to the evaluation phase: Yes/No

Recommended review type:

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Full review** |  | **Abridged review** |  | **Verification** |  | **Recognition[[13]](#footnote-13)** |  | **Notification13** |  |

The application will be treated as:

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Type IAIN** |  | **Type IA** |  | **Type IB** |  | **Type II** |  |

Screened by:

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Initial screening / query** | **Name** | **Date** |
| 1 | Initial screening |  |  |
| 2 | Query |  |  |

# D TECHNICAL SCREENING (PRE CLINICAL AND CLINICAL)

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | | | | | Type of Variation application (tick all applicable options) | | | | | | | | | | | | | | |
| Type IAIN | |  | | Type IA | | | | |  | | Type 1B | | |  | Type II | |  | USRN |  | |
|  |  | | | | | Proposed evaluation pathway (as required by the type of Variation) | | | | | | | | | | | | | | |
| Full review | | |  | |  | | |  | | | | Abridged review | | | |  | Verified review | | |  |
| Motivation for proposed pathway | | | | | | |  | | |  | | |  | | | | | | | |
|  |  | | | | | Note: The final evaluation pathway decision for a variation application is at the discretion of SAHPRA, and will depend on the quality of reliance documentation submitted. | | | | | | | | | | | | | | |

|  |  |  |
| --- | --- | --- |
| Variations/changes included in this application (Codes as per the EMA variations guideline) | | |
| Code | Code description | Details |
| E.g. C.I.2a | Change(s) in the SmPC/PI or PL of a generic/hybrid/biosimilar medicinal products following assessment of the same change for the reference product | Special warnings and precautions updated to reflect content of published local innovator PI [product name X, published 2018/05/21] |

**APPLICATION DETAILS**

***Applicant to fill the below table as per the application letter.***

|  |  |
| --- | --- |
| Standard Reference product A: ***Local innovator***  [for Generics only] | |
| HCR |  |
| Product name |  |
| Dosage strength and range |  |
| Method(s) of administration |  |
| Registration number(s) |  |
| Registration / revision date |  |
| Standard Reference product B: ***Foreign innovator***  [Applicant to supply details of innovator SmPC registered with a regulatory authority with which SAHPRA aligns itself where applicable, as per documentation required for the variation type. Generic applications may only submit a foreign innovator PI as a reference where the local innovator is outdated or no longer marketed.] | |
| MAH |  |
| Product name |  |
| Dosage strength and range |  |
| Method(s) of administration |  |
| Authorisation number(s) |  |
| Authorisation / revision date |  |
| Foreign RA with which SAHPRA aligns itself |  |

| **1. General Information** | | **Yes** | **No** | **N/A** |
| --- | --- | --- | --- | --- |
| 1.1 | Has the amendment history been included on the application form in Module 1.2.1 (if applicable)? |  |  |  |
| 1.2 | Are the proposed professional information (PI) and the proposed patient information leaflet (PIL) included in Modules 1.5.5.1 and 1.5.5.2 respectively? Include hyperlink. |  |  |  |
| 1.3 | Are MS word versions of the proposed PI and PIL included in the ‘working documents’ folder? |  |  |  |
| 1.4 | Are all additions in the proposed PI and PIL indicated by underlining with a solid line? |  |  |  |
| 1.5 | Are all deletions in the proposed PI and PIL indicated by strike through? |  |  |  |
| 1.6 | Are all rephrasing in the proposed PI and PIL denoted by a broken line? |  |  |  |
| 1.7 | Is each page of the proposed PI and PIL dated and paginated as page X of Y? |  |  |  |
| 1.8 | Are the proposed PI and PIL documents line numbered? |  |  |  |
| 1.9 | Do the cross-references in the PI contain the exact page/s and location on the page/s (e.g. column, 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.* |  |  |  |
| 1.10 | Are the references legible and complete? |  |  |  |
| 1.11 | Are the cross-references hyperlinked to exact page/s and location on the page/s? [Ensure no hyperlinks are broken] |  |  |  |
| 1.12 | Are all *scanned* references OCR-scanned (optical character recognition), such that one can search and copy text? |  |  |  |
| 1.13 | 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 to the bottom of the re-typed PI? |  |  |  |
| 1.14 | Is the previously approved PI by SAHPRA included in Module 1.3? Include hyperlink. |  |  |  |
| 1.15 | Are the standard references referred to in the proposed PI included in Module 1.3.1.2? |  |  |  |
| 1.16 | 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 allergy reaction should be referenced to immune system disorders in the PI. |  |  |  |

# E. TECHNICAL VERIFICATION – VARIATIONS CLINICAL

***Applicant to tick (********) in the Yes column if the required documents have been included.***

***If No, provide a motivation in the comments section, referencing the number on the checklist.***

***\*Each question that the applicant answers as “yes” below in the screening checklist should be hyperlinked to where it can be verified (this will speed up verification/screening time)***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **2.** | **Type IB variations** | **Yes** | **No** | **N/A** |
| 2.1 | Is the most recently SAHPRA-approved innovator PI submitted (if the proposed amendment is based on the South African innovator)? |  |  |  |
| 2.1.1 | If not marketed any longer, is the most recently SAHPRA-approved generic PI submitted (if the proposed amendment is based on the said generic)? |  |  |  |
| 2.2 | If changes are based on a foreign reference from a regulatory authority with which SAHPRA aligns itself, has the associated innovator PI been submitted? [Note: Foreign innovator PIs may be referenced for safety-related variations only]. |  |  |  |
| 2.2.1 | Has the foreign reference PI (SmPC) used to update safety only? [Any information, safety or other, not related to South African approved therapeutic indications and posology and method of administration may not be added in the proposed PI] |  |  |  |
| 2.2.2 | Has all added safety information emanating from foreign innovator PI (SmPC) been clearly highlighted This does not preclude normal hyperlinking. |  |  |  |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **5** | **Type II variations** | **Yes** | **No** | **N/A** |
| 5.1 | For change(s) to therapeutic indications (C.I.6a/b), and/or changes to other sections of the PI due to new quality, preclinical, clinical or pharmacovigilance data (C.I.4):  Has the information in Modules 2.5 and 2.7 (Clinical Overviews and Summaries) been included? [where applicable] include hyperlink. |  |  |  |
| 5.1.1 | Has the information of Modules 5 (Clinical study reports) been included and is the proposed PI cross-referenced to this information? Include hyperlink |  |  |  |
| 5.1.3 | Do the formulations and dosage strengths make provision for the proposed new THERAPEUTIC INDICATIONS, POSOLOGY AND METHOD OF  ADMINISTRATION in the target population(s)? |  |  |  |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **6** | **USRN (provide hyperlinks)** | **Yes** | **No** | **N/A** |
| 6.1 | Has a justification for application for being an USRN been included in the cover letter (M1.0)? |  |  |  |
| 6.2 | Has any decision taken or any change made by other regulatory authorities that SAHPRA aligns itself been included? |  |  |  |
| 6.3 | Has a Dear Healthcare Professional (DHCP) letter been submitted as per DHCP letter guideline/process? |  |  |  |
| 6.4 | Has a comment on how the amendment will affect the benefit risk ratio of the use of the medicine been included? |  |  |  |

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

Applicant:

SAHPRA:

***SAHPRA use only:***

# The application can proceed to the evaluation phase: Yes/No

Recommended review type:

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Full review** |  | **Abridged review** |  | **Verification** | | | | **Notification** |  |
| **Scenario A** |  | **Scenario B** |  |

# The application will be treated as:

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Type IAIN** |  | **Type IA** |  | **Type 1B** |  | **Type II** |  | **USRN** |  |

Screened by:

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Initial screening / query** | **Name** | **Date** |
| 1 | Initial screening |  |  |
| 2 | Query |  |  |

# F TECHNICAL SCREENING (NAMES)

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.**

|  |  |
| --- | --- |
| **Current proprietary name** |  |
| **Proposed proprietary name** | {Proposed proprietary name} |

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:***

**Summary of queries to applicant**

| **Query #** | **Description** |
| --- | --- |
| 1 |  |
| 2 |  |
| 3 |  |
| 4 |  |
| 5 |  |

# The application can proceed to the evaluation phase: Yes/No

*SAHPRA use only*

*Can the application proceed to evaluation?*

# UPDATE HISTORY

|  |  |  |
| --- | --- | --- |
| **Date** | **Reason for update** | **Version & publication** |
| Feb 2020 | First publication | v1, Feb 2020 |

# GLOSSARY of TERMS

|  |  |
| --- | --- |
| Generic | Multisource medicine |
| HCR | Holder of Certificate of Registration |
| MAH | Marketing Authorisation Holder |
| PI / SmPC | Professional information / Summary of Product Characteristics |
| PIL/PL | Patient information leaflet / Package Leaflet |

1. This pathway is not currently available [↑](#footnote-ref-1)
2. Latest implemented versions of 2.05 Stability Guideline and/or SADC Stability Guideline [↑](#footnote-ref-2)
3. For variations stability data as per EMA variation guideline is required [↑](#footnote-ref-3)
4. Latest implemented version of 2.24 Guidance General Module 1 [↑](#footnote-ref-4)
5. Latest implemented versions of 2.05 Stability Guideline and/or SADC Stability Guideline [↑](#footnote-ref-5)
6. For variations stability data as per EMA variation guideline is required [↑](#footnote-ref-6)
7. Certificate of Suitability to the monographs of the European Pharmacopoeia [↑](#footnote-ref-7)
8. Confirmation of API Prequalification Document [↑](#footnote-ref-8)
9. [↑](#footnote-ref-9)
10. 9 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 Additional information can be provided (please see section 5.5 of 2.02 Quality and Bioequivalence Guideline) [↑](#footnote-ref-10)
11. Appendix of the General Information Guideline [↑](#footnote-ref-11)
12. Appendix 2 of 2.02 Quality and Bioequivalence Guideline [↑](#footnote-ref-12)
13. These pathways are not currently available [↑](#footnote-ref-13)