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, E and F where applicable.**

# 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 the correct FTP file naming convention followed and unit all applicable units 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? |  |  |
| * 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 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:***  Variation fee, where applicable, (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 | Variation validation template (Module 1.8) |  |  |
| 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? |  |  |

# 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 | Variation validation template (Module 1.8) |  |  |
| * Have the relevant sections B, C, D, E & F been hyperlinked to the modules where relevant? (hyperlinking to the word “hyperlink”) |  |  |
| 1f | QOS/QIS 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 in Module 1.5.5 hyperlinked to the references? |  |  |
| 3b | Has the SAHPRA approved dated PI and clean proposed PI been included in Module 1.3.1.1? |  |  |
| 3c | Has the SAHPRA approved dated PIL and clean proposed 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? |  |  |
| 3f | Are MS word versions of the annotated proposed and Clean proposed PI and PIL included in the Working Documents folder? |  |  |
| 4 | Is Module 2 hyperlinked to Modules 3 / 4 / 5, where 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: are the operation attributes 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

**A.4 ADMINISTRATIVE SCREENING (CERTIFICATION)**

*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.***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Variation: A.1 Transfer of Applicancy (HCR/FPRR) and/or A.2.b Change in the proprietary name of the authorised medicine | | YES | NO | N/A |
| 1 | Module 1.2.1 Application form |  |  |  |
| 1.1 | Does all the manufacturing, packaging, testing and FPRR sites align to the proposed column in Module 1.5.2.2.1 |  |  |  |
| 2 | Module 1.2.2.1 Proof of payment |  |  |  |
| 2.1 | Has the applicable variation fee been paid? |  |  |  |
| 2.2 | For bulk payments or payments without adequate referencing, has the payment breakdown been provided, on the SAHPRA payments cover page? If applicable |  |  |  |
| 3 | Module 1.5.2.2.1 Medicine Register Details |  |  |  |
| 3.1 | 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.* |  |  |  |
| 3.2 | 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? |  |  |  |
| 3.3 | 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? |  |  |  |
| 4 | Module 1.5.2.2.2 Medicine Registration Certificate/Old Medicines Letter |  |  |  |
| 4.1 | Is the current registration certificate included in Module 1.5.2.2.2 |  |  |  |
| 4.2 | Is the variation summary appended to Module 1.5.2.2.2? If applicable |  |  |  |
| 5 | No technical variations (additional/new manufacturers or primary packers) are included with this TOA/proprietary name change variation |  |  |  |

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

Applicant:

# 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 (proof of registration status from SAPC website (App) or POP for current year’s registration) 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). (The latest copy of the medicine registration certificate should be submitted as well to indicate the current HCR of the product) |  |  |
| 7 | Letters of Cessation and Acceptance. (1.7.9) |  |  |
| 8 | Is the proof (valid reliance GMP certificate or SA resolution letter) that all sites listed in the application form and Medicines Register Details appropriately authorised for the pharmaceutical form or product concerned. (1.7.2; 1.7.3) been included(Certificate of GMP compliance must be issued within the last 3 years by SAHPRA or an authority in which a GMP MRA with SAHPRA exists (i.e., a PIC/S member state, Zazibona work-sharing agreement or WHO PQ)) |  |  |
| B.1 Change of address and/or name of the Applicant (HCR/FPRR) | | YES | NO |
| 9 | Is the letter of authorisation to communicate with SAHPRA included? (1.2.2.2) |  |  |
| 10 | Is the proof of registration with the registrar of companies included? (1.7.8) |  |  |
| 11 | Has the licence of the Proposed Holder of Certificate of Registration been included in the submission? (1.7.3) |  |  |
| 12 | 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 |
| 13 | Is the letter of authorisation to communicate with SAHPRA included? (1.2.2.2) |  |  |
| 14 | 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 |
| 15 | Is the letter of authorisation to communicate with SAHPRA included? (1.2.2.2) |  |  |
| 16 | The Medicines Register Details should clearly outline the “current” and “proposed” HCR (1.5.2.2) |  |  |
| 17 | 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.a and/or b Replacement or addition of a manufacturing site for part or all of the manufacturing process of the finished product (Primary Packer and Secondary packer) | | YES | NO |
| 18 | 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. (1.7.1; 1.7.2; 1.7.3) (Certificate of GMP compliance must be issued within the last 3 years by SAHPRA or an authority in which a GMP MRA with SAHPRA exists (i.e., a PIC/S member state, Zazibona work-sharing agreement or WHO PQ)) |  |  |
| 19 | The Medicines Register Details should clearly outline the “current” and “proposed” HCR (1.5.2.2) |  |  |
| 20 | Is the letter of authorisation to communicate with SAHPRA included? (1.2.2.2) |  |  |
| B.II.b.1. e and f; B.II.b.1.c and d /Replacement or addition of a manufacturing site for part or all of the manufacturing process of the finished product | | YES | NO |
| 21 | Is the letter of authorisation to communicate with SAHPRA included? (1.2.2.2) |  |  |
| 22 | 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. (1.7.1; 1.7.2; 1.7.3) (Certificate of GMP compliance must be issued within the last 3 years by SAHPRA or an authority in which a GMP MRA with SAHPRA exists (i.e., a PIC/S member state, Zazibona work-sharing agreement or WHO PQ)) |  |  |
| 23 | The Medicines Register Details should clearly outline the “current” and “proposed” HCR (1.5.2.2) |  |  |
| Proprietary Name Change (PNC) | | YES | NO |
| 24 | 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) |  |  |
| 25 | Is the letter of authorisation to communicate with SAHPRA included? (1.2.2.2) |  |  |
| 26 | Has proof of the responsible pharmacist’s SAPC registration certificate and proof of current registration (proof of registration status from SAPC website (App) or POP for current year’s registration) been included and is it valid at the time of submission? (1.7.7.1) |  |  |
| 27 | The Medicines Register Details should clearly outline the “current” and “proposed” HCR (1.5.2.2). (The latest copy of the medicine registration certificates should be submitted as well to indicate the current proprietary name of the product) |  |  |
| 28 | Have the proposed proprietary name applications and changes been listed? (1.5.3) |  |  |
| 29 | Is the proof (valid reliance GMP certificate or SA resolution letter) that all sites listed in the application form and Appendix A1 appropriately authorised for the pharmaceutical form or product concerned. (1.7.1; 1.7.2; 1.7.3) been included(Certificate of GMP compliance must be issued within the last 3 years by SAHPRA or an authority in which a GMP MRA with SAHPRA exists (i.e., a PIC/S member state, Zazibona work-sharing agreement or WHO PQ)) |  |  |

**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 (PHARMACEUTICAL EVALUATION MANAGEMENT - PEM)

***Please complete table C.1 and tick the relevant check boxes using a tick (✓). If an abridged, verified or recognition evaluation pathway is requested, please provide the approval certificate from the recognized RRA and unredacted assessment reports as supportive data and complete section C.3, otherwise a full review evaluation would be conducted.***

***Table C.1:***

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| 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 5.08 Reliance 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. | | | | | | | | | | | | | | | | | |

**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.***

***Table C.2:***

|  |  |  |  |
| --- | --- | --- | --- |
| Critical Information | | **Yes (Y)** | **No (N)** |
| 1 | Has the working code on the cover page been verified with the variation applied for? |  |  |
| 2a | Have all the variations with working codes included in the amendments schedule been mentioned in the covering letter? |  |  |
| 2b | Have the reasons for each variation been included on the amendment schedule? |  |  |
| 2c | Have all the supporting documents reflected on the amendment schedule been hyperlinked with the dossier? |  |  |
| 3 | Is the amendment history included on the application form? |  |  |
| 4a | Does this variation fall within the EMA classification? |  |  |
| 4b | If no, has a motivation been included in the covering letter? e.g z-code allocation email from SAHPRA |  |  |
| 5a | Have all the supporting documents as per variation guideline, been included? The inclusion of relevant documents should be stipulated in the tables below |  |  |
| 5b | Have the relevant sections of the QOS/QIS document been completed? |  |  |

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

Applicant:

***For Type I codes, kindly populate the below table (do not change the format) with a comment for each condition and document applicable to the variation, extracted from the EU variation guideline.***

***Generate a new table for each Type I variation in the submission.***

***Should any additional supportive documents be submitted, please indicate in the amendment schedule with the reasons.***

Type I

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Variations/changes included in this application (Codes as per the EMA variations guideline) | | | | |
| Code | Code description | Details | Conditions | Documents |
| 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 (Hyper link the submitted documents) |

***Conditions:***

|  |  |
| --- | --- |
| Populate the applicant’s comments for each applicable condition/document | SAHPRA’s comments |
| 1. **The change is not a consequence of any commitment from previous assessments to review specification limits (e.g. made during the procedure for the marketing authorisation application or a type II variation procedure).** |  |
| Applicant’s comments: | |
| 1. **The change does not result from unexpected events arising during manufacture, e.g. new unqualified impurity; change in total impurity limits.** |  |
| Applicant’s comments: | |
| 1. **Any change should be within the range of currently approved limits.** |  |
| Applicant’s comments: | |
| 1. **The test procedure remains the same, or changes in the test procedure are minor.** |  |
| Applicant’s comments: | |
| 1. Any new test method does not concern a novel non-standard technique or a standard technique used in a novel way. |  |
| Applicant’s comments: | |
| 1. The new test method is not a biological/immunological/immunochemical method or a method using a biological reagent for a biological active substance (does not include standard pharmacopoeial microbiological methods). |  |
| Applicant’s comments: | |
| 1. The specification parameter does not concern a critical parameter for example any of the following: assay, impurities (unless a particular solvent is definitely not used in the manufacture of the active substance), any critical physical characteristics, e.g. particle size, bulk or tapped density, identity test, water, any request for changing the frequency of testing |  |
| Applicant’s comments: | |

***Documentation:***

|  |  |
| --- | --- |
| Populate the applicant’s comments for each applicable document | SAHPRA’s comments |
| 1. **Amendment of the relevant section(s) of the dossier (presented in the EU-CTD format or NTA volume 6B format for veterinary products, as appropriate).** |  |
| Applicant’s comments: | |
| 1. **Comparative table of current and proposed in-process tests.** |  |
| Applicant’s comments: | |
| 1. Details of any new non-pharmacopoeial analytical method and validation data, where relevant. |  |
| Applicant’s comments: | |
| 1. Batch analysis data on two production batches (3 production batches for biologicals, unless otherwise justified) of the active substance for all specification parameters. |  |
| Applicant’s Comments: | |
| 1. Justification/risk assessment from the marketing authorisation holder or the ASMF Holder, as appropriate, that the in-process tests are non-significant, or that the in-process tests are obsolete***.*** |  |
| Applicant’s Comments: |  |
| 1. Justification from the MAH or ASMF Holder as appropriate for the new in-process test and limits. |  |
| Applicant’s comments: | |

Type II

***Please indicate, in a list, the documents affected by the change under the documents column.***

***Generate a new table for each individual Type II variation in the submission***

|  |  |  |  |
| --- | --- | --- | --- |
| 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.2** | **Changes in the manufacturing process of the active substance** | **b) Substantial change to the manufacturing process of the active substance which may have a significant impact on the quality, safety or efficacy of the medicinal product** | List all supporting information and documents as per EMA Quality guidelines and SAHPRA Quality and Bioequivalence Guideline |

## C.3 FOREIGN REGULATORY STATUS

Please see SAHPRA’s *5.08 Reliance 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[[2]](#footnote-2)** | | **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[[3]](#footnote-3) for SAHPRA to obtain full, unredacted assessment reports from the RRA? (Appended to letter of application) |  |  |  |
| 2d | Sameness declaration[[4]](#footnote-4) (Module 1.10.4) |  |  |  |
| 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[[5]](#footnote-5)** |  | **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 (NON-CLINICAL AND CLINICAL)

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | | | | | Type of Variation application (tick all applicable options) | | | | | | | | | | | | | | |
| Type IAIN | |  | | Type IA | | | | |  | | Type IB | | |  | Type II | |  | USRN |  | |
|  |  | | | | | Proposed evaluation pathway (as required by the type of Variation) | | | | | | | | | | | | | | |
| Full review | | |  | |  | | |  | | | | Abridged review  \*Submission of unredacted assessment reports (or access letter) is a prequalifying criterion | | | |  | 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 annotated proposed and Clean 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 underlining with 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 all supporting cross-references in the proposed PI hyperlinked to exact page/s and location on the target documents? [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 current SAHPRA approved PI (including, date of revision of text tr/approval date) included in Module 1.3? Include a hyperlink to its location. | |  |  |  |
| 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. | |  |  |  |
| 1.17 | If the applicant has added a shelf-life in the proposed PI has a copy of approval from SAHPRA been included as annex to the Application letter)? |  |  |  |

# 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)? |  |  |  |
| 2.2 | If not marketed any longer, is the most recently SAHPRA-approved generic PI submitted (if the proposed amendment is based on the said generic)? |  |  |  |
| 2.3 | 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]. |  |  |  |
| 2.4 | Was 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] |  |  |  |
| 2.4 | Has all added safety information emanating from foreign innovator PI (SmPC) been clearly highlighted? This does not preclude normal hyperlinking. |  |  |  |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **~~3.~~** | **Type II variations** | **Yes** | **No** | **N/A** |
| 3.1 | 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. |  |  |  |
| 3.2 | Has the information of Modules 5 (Clinical study reports) been included and is the proposed PI cross-referenced to this information? Include hyperlink |  |  |  |
| 3.3 | Do the formulations and dosage strengths make provision for the proposed new THERAPEUTIC INDICATIONS, POSOLOGY AND METHOD OF  ADMINISTRATION in the target population(s)? |  |  |  |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **~~4.~~** | **USRN (provide hyperlinks)** | **Yes** | **No** | **N/A** |
| 4.1 | Has a justification for application for being an USRN been included in the cover letter (M1.0)? |  |  |  |
| 4.2 | Has any decision taken or any change made by other regulatory authorities that SAHPRA aligns itself been included? |  |  |  |
| 4.3 | Has a Dear Healthcare Professional (DHCP) letter been submitted as per DHCP letter guideline/process? |  |  |  |
| 4.4 | Has a comment on how the variation 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
* The WHO international Stembook

**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.*

|  |  |  |  |
| --- | --- | --- | --- |
|  | **QUESTIONS** | **Primary review** | **Secondary review** |
| **1.** | Is the proposed proprietary name(s) identical to the proprietary name of an existing South African registered medicine? | Yes  No | Yes  No |
| Is the proposed proprietary name(s) identical to the proprietary name(s) of medicines previously marketed, but subsequently withdrawn, discontinued or no longer marketed? | Yes  No | Yes  No |
| If YES, is adequate motivation supplied for use of the withdrawn/discontinued name? | Yes  No | Yes  No |
| **2.** | Is the proposed proprietary name(s) similar in print, handwriting (orthography) or speech to the proprietary name of an existing registered medicine? | Yes  No | Yes  No |
| Is the proposed proprietary name(s) similar in print, handwriting (orthography) or speech to the proprietary name of medicines previously marketed, but subsequently withdrawn, discontinued, or no longer marketed? | Yes  No | Yes  No |
| If YES, is adequate motivation supplied for the use of the similar/withdrawn/discontinued name? | Yes  No | Yes  No |
| **3.** | Is the proposed proprietary name(s) identical or similar to the proprietary name of an internationally registered medicine(s)? | Yes  No | Yes  No |
| If YES would the use of the same proposed name(s) lead to confusion which could ultimately compromise the safety of the patient? | Yes  No | Yes  No |
| **4.** | Is the proposed proprietary name(s) confusing or similar to the WHO International Non-Proprietary Name (INN) of the Active Pharmaceutical Ingredient (API)? | Yes  No | Yes  No |
| Does the proposed proprietary name(s) contain **more** than 50% of the approved WHO INN of the API in the order that they appear? | Yes  No | Yes  No |
| **5.** | Does the proposed proprietary name(s) include either a prohibited INN stem (as defined by WHO) or elements from the biochemical nomenclature which may in future be included in INN stems i.e., feron from interferon; leukin from interleukin, as specified in SAHPGL-CEM-NS-03 Proprietary Names for Medicines Guideline? | Yes  No | Yes  No |
| **6.** | Does the proposed proprietary name(s) contain any of the following symbols:  **+, &, #, @, =, [ ], hyphens -.** | Yes  No | Yes  No |
| **7.** | Does the proposed proprietary name(s) contain an unacceptable abbreviation, not in line with SAHPGL-CEM-NS-03 Proprietary Names for Medicines Guideline? | Yes  No | Yes  No |
| **8.** | Does the proposed proprietary name(s) include a qualifier comprising of letters or numerals, that appropriately differentiates the medicine from other medicines? | Yes  No | Yes  No |
| If YES, is there adequate justification for the use of the qualifier or abbreviation? | Yes  No | Yes  No |
| **9.** | Does the proposed proprietary name(s) include promotional qualifications, or manufacturers own codes? | Yes  No | Yes  No |
| **10.** | Does the proposed proprietary name(s) contain non-English names derived from local or international languages? | Yes  No | Yes  No |
| If YES does the application include an English interpretation, translation, transliteration, explanation, and motivation for the use of the word/phrase? | Yes  No | Yes  No |
| If YES, are these names misleading or create inappropriate impressions or implicit claims of superiority or greater potency, efficacy or speed of action in any way? | Yes  No | Yes  No |
| **11.** | Does the proposed proprietary name(s) contain ordinary English words or phrases that are read/interpreted separately from the name?  i.e. Whisper, Hello | Yes  No | Yes  No |
| **12.** | Does the proposed proprietary name(s) contain personal names of people, whether fictional or non-fictional?  i.e. Hippocrates, Diana etc. | Yes  No | Yes  No |
| Does the proposed proprietary name(s) contain the names of places, things, items or any other reference that will imply that the name is not unique or distinctive? | Yes  No | Yes  No |
| **13.** | Does the proposed proprietary name(s) comprise one or two letters, ciphers and/or acronyms? | Yes  No | Yes  No |
| **14.** | Does the proposed proprietary name(s) make reference to non-medicine products or the use of terms which imply that the product is not a medicine and trivializes its medicinal properties? | Yes  No | Yes  No |
| **15.** | Does the proposed proprietary name(s) create inappropriate impressions or implicit claims of superiority or greater potency, efficacy or speed of action? | Yes  No | Yes  No |
| If YES, is there adequate scientific evidence to support these claims? | Yes  No | Yes  No |
| **16** | Does the proposed proprietary name(s) contain an inappropriate promotional element or make/imply a medicinal claim that is not in line with the approved professional information? | Yes  No | Yes  No |
| **17.** | 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? | Yes  No | Yes  No |
| If YES, did the applicant provide proof that they can use the company identifier in the proposed proprietary name(s)? | Yes  No | Yes  No |
| **18.** | Does the proposed proprietary name(s) include the entire INN together with the company identifier/house brand in the unacceptable format- “Company Identifier INN”? | Yes  No | Yes  No |
| **19.** | Does the proposed proprietary name(s) include the company identifier with an invented name? | Yes  No | Yes  No |
| If YES, is the proposed proprietary name(s) unique and distinctive and not likely to be confused with another existing proprietary name? | Yes  No | Yes  No |
| **20.** | Does the proposed proprietary name(s) include a company identifier with a description of the indication, pharmacological action or therapeutic class? | Yes  No | Yes  No |
| **21.** | Does the proposed proprietary name(s) include an umbrella name? | Yes  No | Yes  No |
| If YES, is adequate motivation supplied for the use of the umbrella name as per SAHPGL-CEM-NS-03 Proprietary Names for Medicines Guideline? | Yes  No | Yes  No |
| If YES, is the name misleading in terms of composition, indications, pharmacological action or therapeutic class? |  |  |

**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?*

**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 |
| WHO | World Health Organization |

1. This pathway is not currently available [↑](#footnote-ref-1)
2. Additional information can be provided (please see section 5.5 of 2.02 Quality and Bioequivalence Guideline) [↑](#footnote-ref-2)
3. Appendix of the General Information Guideline [↑](#footnote-ref-3)
4. Appendix 2 of 2.02 Quality and Bioequivalence Guideline [↑](#footnote-ref-4)
5. These pathways are not currently available [↑](#footnote-ref-5)