SAHPRA
South African
Health Products
Regulatory Authority

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# VALIDATION TEMPLATE FOR ELECTRONIC APPLICATIONS FOR REGISTRATION OF COMPLEMENTARY MEDICINES

The Validation Template is to be used with submission of an application for registration of a complementary medicinal product for human use to the South African Regulatory Authority to verify that all required information has been supplied in electronic format, for SAHPRA to evaluate the application. 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.

**Usually a separate dossier for each pharmaceutical form is required.**

**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 according to the information in the dossier Module 1.0*

| **Product information** | | |
|---|---|---|
| 1 | Applicant | *<LICENSED NAME>* |
| 2 | Master product application number/s | |
| 3 | Duplicate product application number/s | |
| 4 | eCTD sequence number (*if applicable*) | |
| 5 | Master product proprietary name/s | *<Name, strength; pharmaceutical form>* |
| 6 | Duplicate product proprietary name/s | *<Name, strength; pharmaceutical form>* |
| 7 | Dosage form | *<pharmaceutical form>* |
| 8 | Sub-category:<br>Discipline-Specific (DS) / Health Supplement (HS) | |

| **Product information** | | | |
|---|---|---|---|
| 8a | If DS, state *Complementary discipline(s) | | |
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| | | | |
| 9 | Indication | *<state below>* | |
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| 9a | Is the indication submitted as LOW or HIGH risk? | Low ☐ | High ☐ |
| 9b | Has a justification been included in Modules 1.5.1 and 2.5 for the origin of all substances within the discipline specified and has the traditional use of the substance been aligned with its intended use/ indication? | Y ☐ | N ☐ |
| 9c | If HIGH, has pre-clinical and clinical evidence been submitted in modules 2.5, 4 and 5 as may be required to justify the indication? | Y ☐ N ☐ N/A ☐ | |
| 10 | †API/s *(include extra rows as appropriate)* | *<APIs>* | |
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| 11 | Date of letter of application (Module 1.0) | *<date of letter>* | |
| 12 | Date of receipt *(SAHPRA use only)* | *<date submitted>* | |

* Refer to guideline(s) on Safety and Efficacy of Complementary Medicines

† Refer to guideline on Quality of Complementary Medicines

*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 | Where applicable, is each CD / DVD 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) | | |
| | • Is the letter of application on the official company letterhead? | | |
| | • Is the letter copied single sided? | | |
| | • 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 the current version of Module 1.2.1 reflected in the name in the footer *(i.e. footer not to be changed)* | | |
| | • Is Module 1.2.1(c) signed by the authorised pharmacist (original signature) and dated? *(pp not accepted; scanned signature not accepted; consultant may not sign)* | | |
| | • Has the designation of the pharmacist been indicated? | | |
| | • 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):***<br>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:***<br>Validation fee (and, if relevant, amendment 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) | | |
| | • Is the current version of the validation template reflected in the name in the footer *(i.e. footer not to be changed)* | | |
| 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) | | |

| Dossier Information | | Yes | N/A |
|---|---|---|---|
| | • Validation tool used and version stated? | | |
| 3 | Are the paper documents suitably bound and divided with tabbed dividers? | | |
| 4 | First submission (sequence 0000) | | |
| | • Is a sample included in an envelope (include motivation for sample not being included when relevant)? | | |
| | • Is a sample provided for the smallest pack size? | | |

## 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 and/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? | | |
| 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 (API name) | | |
| | • eCTD sequence number | | |
| | • Related eCTD sequence number | | |
| | • Submission type | | |
| | • Submission data type – proof of efficacy | | |
| 3 | PI and PIL | | |
| 3a | Have the PI and PIL been typed with double line spacing? | | |
| 3b | Are the PI and PIL line numbered in the left margin? | | |
| 3c | Is the PI hyperlinked to the references? | | |
| 3d | If sequence 0000, has the PI been included in Module 1.3.1.1? | | |
| 3e | If sequence 0000, has the PIL been included in Module 1.3.2? | | |
| 3f | Is the PIL hyperlinked to the PI? | | |

| **Dossier Information** | | **Yes** | **N/A** |
|---|---|---|---|
| 3g | 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? | | |
| 9 | Are the documents, including copies of chromatograms and chromatogram text in Modules 5.3.1 & 3.2.S legible? | | |

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

*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) | | |
| **Manufacturing** | | **Yes** | **No** |
| 2a | Are the GMP certificates or a copy of the appropriate licences of the manufacturers, packers and FPRCs included in 1.7.3? | | |
| 2b | 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)*? | | |
| 2c | 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)*? | | |
| 2d | 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)*? | | |
| 2e | If GMP certificates are not included or are not valid from last 3 years, is the site a South African site (1.2.1)? | | |
| 3 | Has the inspection flow diagram been attached (1.7.12)? | | |
| **Laboratory** | | **Yes** | **No** |
| 4a | Is a certificate of analysis for the API present? | | |
| 4b | Has a Confirmation of sample been included (1.7.10)? | | |
| 4c | Is there a declaration that the batch manufacturing record of the sample is available for inspection at the request of the regulator? | | |
| 4d | Is there a declaration that the executed batch manufacturing record is available for inspection at the request of the regulator? | | |

| **Motivation for any question answered as "No"** *(use the numbering in the checklist to link comments to specific questions):* |
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| |

## C.1 TECHNICAL VERIFICATION - PHARMACEUTICAL QUALITY ASSESSOR

***Applicant to indicate location in dossier in the "Yes" Column where relevant***

*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 the relevant question.*

*Applicant to complete Section 1 for each API in the product being applied for.*
*Please replace <<API name>> with the name of the API. Additional rows for Section 1 can be duplicated if necessary by copying and pasting.*

| **Critical Pharmaceutical Quality Information** | | **Yes** | **No** | **N/A** |
|---|---|---|---|---|
| 1 | Module 3.2.S **<<API name>>** | | | |
| 1a | Is Module 3.2.S for each API included? | | | |
| 1b | Is a GACP certificate or equivalent included for relevant ingredients? | | | |
| | Clearly indicate where these may be located | | | |
| 1d | Have valid CoAs for each API been included in each Module 3.2.S.4.4? | | | |
| 2 | Stability data on the pharmaceutical product (FPP): | | | |
| 2a | At least 6 months long-term and 3 months accelerated data? | | | |
| | If not, is a motivation/explanation included in Module 3.2.P.8.1? | | | |
| 2b | Is a tabulated summary of the batches, i.e. sizes, numbers, type, packaging material, and conditions and period of testing included for each manufacturer? | | | |
| 2c | Are details of the API manufacturer, container, batch number, batch size, date of manufacture of the batch, and storage conditions reflected in Module 3.2.P.8.1 or Module 3.2.P.8.3? | | | |
| 2d | Do the APIs in 1.2.1; 1.3; 3.2.S and 3.2.P.1 concur? | | | |
| 2e | Is the API manufacturer identified in Module 3.2.S.2.1 (refer Module 1.2.2.3) the same as that of developmental batches and/or other submitted batches? | | | |
| 2f | Have stability data been derived from the product packed in packaging material(s) detailed in Module 3.2.P.7? | | | |
| 2g | Are validation data for the stability testing assay method (if not pharmacopoeial and/or different to that in Module 3.2.P.5.2) included? | | | |

| **Motivation for questions answered "No"** *(use the numbering in the checklist to link comments to specific questions):* |
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## C.2 TECHNICAL VERIFICATION - BIOEQUIVALENCE DATA

***Not applicable. However if applicable, use the relevant section of the validation template for orthodox medicines.***

## D TECHNICAL VERIFICATION - PRE-CLINICAL AND CLINICAL INFORMATION

*Applicant to indicate location in dossier in the "Yes" Column* ***where relevant.***

*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.*

| **Critical Information** | | **Yes** | **No** | **N/A** |
|---|---|---|---|---|
| 1 | Formulation | | | |
| 1a | Does the formulation appear to conform to the definition of a CM in its entirety? | | | |
| 1b | Does the formulation conform to use within the relevant sub-category? | | | |
| | Discipline-Specific (DS) | | | |
| | Health Supplement (HS) | | | |
| 2 | LOW-risk Indication<br>*("Yes" if the indication been submitted as LOW-risk. If not, then N/A and move to item 3)* | | | |
| 2a | Is the indication stated the same throughout the application (Modules 1.3.1, 1.3.2, 1.3.3)? | | | |
| 2b | Is the indication verified as being LOW-risk? | | | |
| 2c | If yes for 2b, has a justification been listed in Modules 1.5.1 and 2.5 for the origin of all substances within the discipline specified? | | | |
| 2d | If yes for 2b, has the traditional use / accepted use (in the case of monographs) of all substances been substantiated and aligned with its intended use / indication? | | | |
| 2e | If yes for 2b and if HS included in the formulation, is it suitably demonstrated in module 1.5.1 that the substance is listed in the HS Annexures and that the indication accords with and is confirmed by the Guideline? | | | |
| 3 | HIGH-risk Indication<br>*("Yes" if the indication been submitted as HIGH-risk. If not, then N/A and move to item 4)* | | | |
| 3a | Is the indication stated the same through the application (Modules 1.3.1, 1.3.2, 1.3.3)? | | | |
| 3b | Is the indication verified as being HIGH-risk? | | | |

| Critical Information | | Yes | No | N/A |
|---|---|---|---|---|
| 3c | If yes for 3b, has a justification been listed in Modules 1.5.1 and 2.5 for the origin of all substances within the discipline specified? | | | |
| 3d | If yes for 3b, has the traditional use / accepted use (in the case of monographs) of all substances been substantiated and aligned with its intended use / indication? | | | |
| 3e | If yes for 3b, has information been submitted in modules 4 and 5 as may be required to justify the indication? | | | |
| 3f | If HS included in the formulation, is it suitably demonstrated in module 1.5.1 that the substance is listed in the HS Annexures and that the indication accords with and is confirmed by the Guideline? | | | |
| 4 | Are the proposed Professional Information (PI) and the proposed Patient Information Leaflet (PIL) included in Modules 1.3.1 and 1.3.2? | | | |
| 5 | Is the information in the proposed PI cross-referenced to accepted references? | | | |
| 6 | Has the information in the proposed PIL been cross-referenced to the proposed PI? | | | |
| 7 | Has the information in Modules 2.4, 2.5, 2.6 and 2.7 been included?<br>*(as merited by items 2 or 3, Module 2.5 required for DS)* | | | |
| 8 | If HIGH-risk, has the information of Modules 4 and 5 been included and is the proposed PI cross-referenced to this information? | | | |
| 9 | Are the references referred to in the proposed PIL included? | | | |
| 10 | Are the cross-references complete, accurate and properly indexed? | | | |
| 11 | Is the information in the proposed PIL cross-referenced to acceptable references? *Note: SPI, Unregistered Old Medicines, MIMS and Micromedex are not acceptable references.* | | | |
| 12 | Is the information in the proposed PIL based on the latest editions of the standard acceptable references? | | | |
| 13 | Are all references legible and of good quality? | | | |
| 14 | Have all the raw data (individual patient data and line listings) been removed? | | | |

**Motivation for questions answered "No"** *(use the numbering in the checklist to link comments to specific questions):*

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**NOTES:**

1. *In case of any one or more answers being "No", refer to SAHPRA section coordinator.*
2. *Unless otherwise decided, the assessment should not continue if these matters have not been (adequately) addressed. Communications to the applicants regarding these matters must be initiated as a priority. Any final recommendation could be made at the relevant CM sub-committee or CMC meeting.*

## E TECHNICAL VERIFICATION (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 section E should be submitted for master and duplicate submissions.**

| | |
|---|---|
| **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 | | |
| 1a | identical to the proprietary name of an existing registered medicine? | | |
| 1b | identical to the proprietary names of medicines previously marketed, but subsequently withdrawn, discontinued or no longer marketed? | | |
| 1c | If YES, is adequate motivation supplied for use of the withdrawn / discontinued name? | | |
| 2 | Is the proposed proprietary name | | |
| 2a | similar in print, handwriting (orthography) or speech to the proprietary name of an existing registered medicine? | | |
| 2a | 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? | | |
| 3a | Is the proposed proprietary name confusing or similar to the WHO International Non-proprietary Name (INN) of the Active Pharmaceutical Ingredient (API)? | | |
| 3b | Does the proposed proprietary name contain 50 % or more of the approved WHO INN of the API? | | |

| **Proposed proprietary name** | | **Yes** | **No** |
|---|---|---|---|
| 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 or similar 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? | | |

| **Proposed proprietary name** | | **Yes** | **No** |
|---|---|---|---|
| 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*? | | |

| **Motivation for questions answered "Yes"** *(use the numbering in the checklist to link comments to specific questions):* |
|---|
| |

## UPDATE HISTORY

| **Date** | **Reason for update** | **Version & publication** |
|---|---|---|
| April 2019 | First version to apply specifically to complementary medicines | v1, May 2019 |
| With immediate effect | Implementation | |
| June 2020 | Changed from screening template for paper submission to validation template for electronic submission | v2, June 2020 |
| With immediate effect | Implementation | |