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| **SCREENING PROCESS INSTRUCTION**This template shall be used on receipt of a new human medicine application for registration to verify that all the required information for evaluation has been provided to the South African Health Products Regulatory Authority (SAHPRA). It is also used for follow-up sequences that may be required for the new registration. Verify if the applicant has completed all relevant fields on the received application form and ensure that all hyperlinks are included and tested for ease of navigation by the screener. For a new sequence related to a response to screening queries, complete the product information and the relevant changes with hyperlinks.**Note** that the greyed-out fields are not required for screening.**C - Compulsory** |

|  |
| --- |
| **Product information** |
| Application ID |  |
| Applicant name | {Licensed Name} |
| Master product application number/s |  |
| Duplicate product application number/s |  |
| Sequence number |  |
| Master product proprietary name/s |  |
| Duplicate product proprietary name/s  |  |
| Product strength(s) |  |
| Dosage form |  |
| API(s) |  |
| API Manufacturer(s) - Name(s) and Address(s) |  |
| DMF No./CEP No./APIMF No. |  |
| FPP Manufacturer(s) - Name(s) and Address(s) |  |
| Pharmacological classification and ATC area |  |
| BE Report/ Study No. |  |
| Contract Research Organisation (CRO) |  |
| Date of letter of application (1.0.1) |  |

|  |  |
| --- | --- |
| **Proposed PEM evaluation pathway**  |  |
| Full review |  | Abridged review |  | Verified review |  | Collaborative Review |  | Specify Collaborative Review |
| Applicant’s motivation for proposed pathway (provide hyperlinks to applicable RRA reports for reliance) |  |  |

|  |
| --- |
| **Proposed CEM evaluation pathway**  |
| Full review |  | Abridged review |  | Verified Review |  | Collaborative Review |  |
| Applicant’s motivation for proposed pathway (provide hyperlinks to applicable RRA reports for reliance) |  |

|  |  |  |  |
| --- | --- | --- | --- |
| **1** |  |  **Yes**  | **N/A** |
| **1.0** | **Correspondence** |  |  |
| 1.0.1 | Letter of Application | C |  |
| 1.0.2 | Note to Evaluator |  |  |
| 1.0.3 | Correspondence from SAHPRA |  |  |
| 1.0.4 | Response to SAHPRA Request |  |  |
| 1.0.5 | Meeting Information |  |  |
| **1.2**  | **Application** |  |  |
| 1.2.1 | Application Form | C |  |
| **1.2.2** | **Annexes** |  |  |
| 1.2.2.1 | Proof of Payment |  |  |
| 1.2.2.2 | Letter of Authorisation |  |  |
| 1.2.2.3 | Dossier Product Batch Information | C |  |
| a) | The API manufacturer is the same as in Module 3.2.S.2.1 |  |  |
| b) | The API manufacturer is not the same as in Module 3.2.S.2.1, and the pharmaceutical equivalence data of the API manufacturers is provided in Module 3.2.R.4 |  |  |
| 1.2.2.4 | Electronic Copy Declaration |  |  |
| 1.2.2.5 | Curriculum Vitae of the Person Responsible for Pharmacovigilance |  |  |
| 1.2.2.6 | API Change Control |  |  |
| 1.2.2.7 | EMA Certificate for a Vaccine Antigen Master File (VAMF) |  |  |
| 1.2.2.8 | EMA Certificate for a Plasma Master File (PMF) |  |  |
| 1.2.2.9 | Declaration of Sameness for Replicas and Clones |  |  |
| 1.2.2.10 | Letter of Permission from HCR for Replica |  |  |
| 1.2.2.A | Additional Annexes |  |  |
| 1.2.4 | Patent Declaration |  |  |
| 1.2.5 | Checklists, Validation Templates | C |  |
| 1.2.A | Additional Administrative Information |  |  |
| **1.3**  | **South African Product Information** |  |  |
| a) | MS Word versions of the proposed PI and PIL are included in 1.3.1.1.1 and 1.3.2.1, respectively | C |  |
| b) | Cross-references are hyperlinked to exact page/s and location on the page/s. | C |  |
| c) | Each page of the proposed PI and PIL is dated and paginated as page X of Y. | C |  |
| d) | The proposed PI and PIL documents are line-numbered | C |  |
| e) | The application complies with the requirements stipulated in the Multiple Submissions guideline. (E.g., for duplicates, only one PI and PIL is to be submitted with the Proprietary Name indicated as “Product Name”) | C |  |
| **1.3.1** | **South African Professional Information** |  |  |
| **1.3.1.1** | **Professional Information (PI)** |  |  |
| a) | The cross-references in the PI are written with the exact page/s and location on the page/s (i.e., column, paragraph, and/or line numbers) of the document that is referenced |  |  |
| b) | The THERAPEUTIC INDICATION(s) and POSOLOGY and METHOD OF ADMINISTRATION are in line with the SA innovator. **Note:** if the SA innovator is no longer marketed or is deregistered, alignment must be to a generic. |  |  |
| c) | The innovator SmPC/ PI from an RRA has been **used to update safety only.** (Any information, safety, or other, not related to SAHPRA-approved therapeutic indications, posology, and method of administration may not be added in the proposed PI.) |  |  |
| d) | In addition to the local innovator, only **one** foreign innovator PI (registered by an RRA) has been referenced in the proposed PI (and included in Module 1.3.1.2). Note that any other foreign PIs should still be included in Module 1.3.5.0, even if not referenced by the proposed PI. |  |  |
| e) | The API is the same as the reference/innovator product. |  |  |
| f) | The API is not the same as the reference/innovator product, but the product yields the same quantity of the API per dosage form as the reference/innovator product. |  |  |
| g) | The strength or concentration of the API is the same as the Reference Product. |  |  |
| h) | The proposed salt/hydrate/ester/pro-drug is the same as that of the innovator/ reference product. |  |  |
| i) | The proposed salt/hydrate/ester/pro-drug is not the same as that of the innovator/reference product, and there are no safety concerns stemming from the different salt/hydrate/ester/pro-drug (e.g., potassium salt versus sodium salt for IV administration.) |  |  |
| j) | The formulations and dosage strengths make provision for the claimed THERAPEUTIC INDICATIONS, POSOLOGY, AND METHOD OF ADMINISTRATION in the target population(s). Ensure that the lowest/initial dose/ titration dose is possible in the target population. |  |  |
| k) | For NCEs and generics with clinical data, the PI is cross-referenced and hyperlinked to Modules 2.4, 2.5, 2.6, and 2.7 (Non-clinical and Clinical Overviews and Summaries). |  |  |
| l) | For NCEs and generics with clinical data, the summaries in module 2 are cross-referenced to information in Modules 4 (Pre-clinical study reports) and 5 (Clinical study reports). |  |  |
| m) | For FDCs, the contribution of each API to the therapeutic effect at the dosages proposed has been established in reference PI(s). |  |  |
| n) | For FDCs, the FDC scenario is stated as per the FD guideline. |  |  |
| o) | The new strength follows the approved target population, approved route of administration, and the approved dosage schedule. |  |  |
| p) | For Clones, the approved PI and PIL of the registered product have been submitted and is hyperlinked. |  |  |
| q) | For Clones and Replicas, the proposed PI has been referenced and hyperlinked to the PI of the registered product only. |  |  |
|  |  |  |  |
| 1.3.1.1.1 | PI – Approved (proposed annotated) | C |  |
| 1.3.1.1.2 | PI – Clean (for responses) | C |  |
| 1.3.1.1.3 | PI – Annotated (for responses) | C |  |
| **1.3.1.2** | **Standard References** |  |  |
| a) | The references are legible and complete. | C |  |
| b) | All **reference** PIs contain the following summary information either on the front page, cover page, or a header:* the reference HCR/ MAH,
* name of the medicine,
* name of the RRA (if applicable),
* date of registration/authorisation and/or revision
 | C |  |
| 1.3.1.2.1 | Reference Product - Local |  |  |
| a) | The most recently SAHPRA-approved innovator PI is submitted and hyperlinked. |  |  |
| b) | If not marketed/de-registered, the most recently SAHPRA-approved generic PI is submitted and hyperlinked. |  |  |
| 1.3.1.2.2 | Other References |  |  |
| **1.3.2** | **Patient Information Leaflet (PIL)** |  |  |
| a) | The information in the proposed PIL has been cross-referenced to the proposed PI only. (Including exact page/s and location on the page/s) For e.g., information in the PIL on symptoms/action to be taken on severe allergic reaction should be referenced to immune system disorders in the PI. | C |  |
| 1.3.2.1 | PIL – Approved (hyperlinked to the PI) - proposed annotated | C |  |
| 1.3.2.2 | PIL – Clean (for responses) | C |  |
| 1.3.2.3 | PIL – Annotated (for responses) | C |  |
| **1.3.3** | **Labels** |  |  |
| 1.3.3.1 | Labels – Approved |  |  |
| 1.3.3.2 | Labels – Clean (for responses) |  |  |
| 1.3.3.3 | Labels – Annotated (for responses) |  |  |
| 1.3.4 | Braille |  |  |
| 1.3.5 | Foreign Prescribing and Patient Information |  |  |
| **1.3.6** | **Artwork and Samples** |  |  |
| 1.3.6.1 | Statement Confirming Submission of Samples |  |  |
| 1.3.6.2 | Artwork and Pictures of Samples |  |  |
| 1.3.6.3 | Batch Manufacturing Record of the Sample |  |  |
| 1.3.6.4 | CoA of the Sample |  |  |
| **1.4**  | **Information about the Experts** |  |  |
| 1.4.1 | Quality |  |  |
| 1.4.2 | Nonclinical |  |  |
| 1.4.3 | Clinical |  |  |
| **1.5**  | **Specific Requirements for Different Types of Applications** |  |  |
| 1.5.1 | Literature-Based Submissions |  |  |
| **1.5.2** | **Amendments/ Variations** |  |  |
| 1.5.2.1 | Tabulated Schedule of Amendments |  |  |
| 1.5.3 | Proprietary Name Applications and Changes  |  |  |
| a) | Three alternate proprietary names in order of preference have been submitted in Module 1.0.1. |  |  |
| b) | The proposed proprietary name(s) are identical to the proprietary name of an existing South African registered medicine, with a motivation supplied in module 1.5.3 to use the name. |  |  |
| c) | The proposed proprietary name(s) is identical to the proprietary name(s) of medicines previously marketed, but subsequently withdrawn, discontinued, cancelled, or no longer marketed, with a motivation supplied in module 1.5.3 to use the name. |  |  |
| d) | The proposed proprietary name is a line extension as stated in module 1.5.3. |  |  |
| e) | The proposed proprietary name(s) is identical to the proprietary name of an internationally registered medicine(s). |  |  |
| f) | The proposed proprietary name(s) contain **more** than 50% of the approved WHO INN of the API in the order that they appear. |  |  |
| g) | The proposed proprietary name(s) include a prohibited/ protected INN stem (as defined by WHO) |  |  |
| h) | The proposed proprietary name(s) contain any of the following symbols:**+, &, #, @, =, [ ], hyphens -.** |  |  |
| i) | The proposed proprietary name(s) contain an unacceptable abbreviation, not in line with the latest version of the SAHPGL-CEM-NS-03 Proprietary Names for Medicines Guideline. |  |  |
| j) | The company identifier is not the same as the Applicant name, but proof of authorisation to use the company identifier is provided in module 1.5.3. |  |  |
| k) | The proposed proprietary name(s) include the entire INN together with the company identifier/house brand in the acceptable format- “INN\_ Qualifier (Strength/Dosage form) Company Identifier”) |  |  |
|  | **Scheduling** |  |  |
| a) | The API is listed in the schedules under schedule (0,1,2,3,4,5,6,7 or 8) |  |  |
| b) | The API is not listed in the schedules, but there are other products containing the API listed in the registered health products database |  |  |
| c) | The scheduling status is listed in section 1 of the proposed PI and PIL |  |  |
| d) | The pharmacological classification is listed in section 5 of the proposed PI |  |  |
| 1.5.4 | Genetically Modified Organisms |  |  |
| **1.5.6** | **Generic Applications (BTIF)** |  |  |
| 1.5.6.1 | BTIF (also included in MS Word format) |  |  |
| 1.5.6.2 | Biowaiver |  |  |
| a) | A completed biowaiver template in MS Word format has been included |  |  |
|  | 1. BCS based biowaiver: IPRP template
 |  |  |
|  | 1. Additional strength biowaiver: WHO template
 |  |  |
| b) | The additional strengths are proportionally formulated and directly proportional to the strength(s) in the bioequivalence study |  |  |
| c) | A motivation and justification for the specified BCS Class I/III is provided |  |  |
| 1.5.7 | Abridged Applications (Abridged/ Verified Review Document) |  |  |
| 1.5.A | Additional Types of Applications: Specific Requirements |  |  |
| **1.6**  | **Environmental Risk Assessment** |  |  |
| 1.6.1 | Non-GMO (Genetically Modified Organisms) |  |  |
| 1.6.2 | GMO (Genetically Modified Organisms) |  |  |
| **1.7**  | **Good Manufacturing Practice** |  |  |
| 1.7.1 | Date of Last Inspection of each Site (within 3 years of date of submission) | C |  |
| a) | A declaration from the site that further inspections conducted after the date on the GMP certificate did not indicate non-performance/negative review is included |  |  |
| 1.7.2 | Inspection Reports or Equivalent Document |  |  |
| 1.7.3 | Latest GMP Certificate or a Copy of the Appropriate Licence of the Proposed Holder of the Certificate of Registration, manufacturers, packers, and FPRCs are included | C |  |
| a) | The dosage form that is being applied for is within the same dosage form grouping as the GMP certificate for foreign manufacturers, packers, or licence and resolution letter for local manufacturers and packers *(refer to the SA Guide to GMP in terms of SAHPRA reliance model)* |  |  |
| b) | The product type being manufactured in the application is similar to the product on the GMP certificate for foreign manufacturers, packers, or licence and resolution letter for local manufacturers and packers *(refer to the SA Guide to GMP in terms of SAHPRA reliance model)* |  |  |
| c) | The activities that the manufacturer is approved for in the GMP certificate for foreign manufacturers, packers, or licence and resolution letter for local manufacturers and packers, are the same as the activities being applied for *(refer to the SA Guide to GMP in terms of SAHPRA reliance model)* |  |  |
| **1.7.4** | **Release** |  |  |
| 1.7.4.1 | API | C |  |
| a) | A declaration that the API has been received by a site that is approved by the EDQM is included |  |  |
| b) | A certificate of analysis for the API is included |  |  |
| 1.7.4.2 | IPIs | C |  |
| 1.7.4.3 | Finished Product Release Control (FPRC) Tests | C |  |
| 1.7.4.4 | Finished Product Release Responsibility (FPRR) Criteria | C |  |
| a) | A declaration that the batch manufacturing record of the sample is available for inspection at the request of the regulator is included |  |  |
| b) | A declaration that the executed batch manufacturing record is available for inspection at the request of the regulator is included |  |  |
| 1.7.5 | Confirmation of Contract |  |  |
| 1.7.7 | SAPC Registration | C |  |
| a) | The declaration of who is authorised to conduct regulatory action is included |  |  |
| b) | Proof of the responsible pharmacist’s SAPC registration, certificate, and proof of current registration (registration card), has been included, and is it valid at the time of submission |  |  |
| 1.7.8 | Registration with Registrar of Companies |  |  |
| 1.7.9 | Other Documents Relating to the Applicant/PHCR |  |  |
| 1.7.11 | Manufacturing Permits |  |  |
| 1.7.12 | Inspection Flow Diagram | C |  |
| 1.7.13 | Organogram | C |  |
| 1.7.14 | PQR |  |  |
| 1.7.A | Additional GMP Documents |  |  |
| **1.8**  | **Information Relating to Pharmacovigilance** |  |  |
| 1.8.1 | Pharmacovigilance Systems |  |  |
| 1.8.2 | Risk Management Plan (and local risk management plan for global supplier) |  |  |
| **1.9**  | **Individual Patient Data - Statement of Availability** |  |  |
| **1.10**  | **Foreign Regulatory Status** |  |  |
| 1.10.1 | Tabulated List of Foreign Regulatory Status |  |  |
| 1.10.2 | Registration Certificate or Marketing Authorisation |  |  |
| **1.10.4** | **Data Set Similarities** |  |  |
| 1.10.4.1 | Data Set Similarities |  |  |
| 1.10.4.2 | Declaration of Sameness |  |  |
| 1.10.5 | RRA Reports |  |  |
| a) | The relevant reliance pathway is indicated in Annexure A |  |  |
| b) | The RRA relied on is stated in Annexure B |  |  |
| c) | The relevant reliance documents as per Annexure B are provided and hyperlinked in the table. |  |  |
| 1.10.6 | CPP (WHO certification scheme) |  |  |
| **1.12**  | **Paediatric Development Programme** |  |  |
| **1.A** | **Additional Data** |  |  |
| **2** | **Summaries and Overviews (Not for screening, no hyperlinks required)** |  |  |
| 2.2 | Introduction |  |  |
| 2.3 | Quality Overall Summary |  |  |
| 2.4 | Nonclinical Overview |  |  |
| 2.5 | Clinical Overview |  |  |
| **2.6** | **Nonclinical Summaries** |  |  |
| 2.6.1 | Introduction |  |  |
| 2.6.2 | Pharmacology Written Summary |  |  |
| 2.6.3 | Pharmacology Tabulated Summary |  |  |
| 2.6.4 | Pharmacokinetics Written Summary |  |  |
| 2.6.5 | Pharmacokinetics Tabulated Summary |  |  |
| .6.6 | Toxicology Written Summary |  |  |
| 2.6.7 | Toxicology Tabulated Summary |  |  |
| **2.7** | **Clinical Summaries** |  |  |
| 2.7.1 | Summary of Biopharmaceutic Studies and Associated Analytical Methods |  |  |
| 2.7.2 | Summary of Clinical Pharmacology Studies |  |  |
| 2.7.3 | Summary of Clinical Efficacy |  |  |
| 2.7.4 | Summary of Clinical Safety |  |  |
| 2.7.5 | Literature References |  |  |
| 2.7.6 | Synopsis of Individual Studies |  |  |
| **3** | **Quality** |  |  |
| **3.2** | **Body of Data** |  |  |
| **3.2.S** | **Drug Substance** |  |  |
| **3.2.S.1** | **General Information** |  |  |
| 3.2.S.1.1 | Nomenclature |  |  |
| 3.2.S.1.2 | Structure |  |  |
| 3.2.S.1.3 | General Properties |  |  |
| **3.2.S.2** | **Manufacturer**  |  |  |
| Note: | Module 3.2.S for each manufacturer |  |  |
| 3.2.S.2.1 | Manufacturer(s) for each API |  |  |
| 3.2.S.2.2 | Description of Manufacturing Process and Process Controls |  |  |
| 3.2.S.2.3 | Control of Materials |  |  |
| 3.2.S.2.4 | Control of Critical Steps and Intermediates |  |  |
| 3.2.S.2.5 | Process Validation and/ or Evaluation |  |  |
| 3.2.S.2.6 | Manufacturing Process Development |  |  |
| **3.2.S.3** | **Characterisation** |  |  |
| 3.2.S.3.1 | Elucidation of Structure and Other Characteristics |  |  |
| 3.2.S.3.2 | Impurities |  |  |
| **3.2.S.4** | **Control of Drug Substance** |  |  |
| 3.2.S.4.0 | Control Strategy |  |  |
| 3.2.S.4.1 | Specification (signed, dated and version-controlled) from the API and FPP manufacturer(s). |  |  |
| 3.2.S.4.2 | Analytical Procedures |  |  |
| 3.2.S.4.3 | Validation of Analytical Procedures |  |  |
| 3.2.S.4.4 | Batch Analyses |  |  |
| a) | Valid certificates of analysis (CoAs) of the API issued by FPP manufacturer and API manufacturer(s), for at least two batches have been provided |  |  |
| 3.2.S.4.5 | Justification of Specification |  |  |
| 3.2.S.5 | Reference Standards or Materials |  |  |
| 3.2.S.6 | Container Closure System |  |  |
| **3.2.S.7** | **Stability** |  |  |
| 3.2.S.7.1 | Stability Summary and Conclusions |  |  |
| 3.2.S.7.2 | Post-approval Stability Protocol and Stability Commitment |  |  |
| 3.2.S.7.3 | Stability Data |  |  |
| a) | At least 12 months long-term and 6 months accelerated for NCE are provided |  |  |
| b) | At least 6 months long-term and 3 months accelerated for generics are provided |  |  |
| **3.2.P** | **Drug Product** |  |  |
| 3.2.P.1 | Description and Composition of the Drug Product |  |  |
| 3.2.P.2 | Pharmaceutical Development |  |  |
| **3.2.P.3** | **Manufacture** |  |  |
| 3.2.P.3.1 | Manufacture(s) |  |  |
| 3.2.P.3.2 | Batch Formula |  |  |
| 3.2.P.3.3 | Description of Manufacturing Process Controls |  |  |
| 3.2.P.3.4 | Controls of Critical Steps and Intermediates |  |  |
| 3.2.P.3.5 | Process Validation and/ or Evaluation |  |  |
| **3.2.P.4** | **Control of Excipients** |  |  |
| 3.2.P.4.1 | Specifications |  |  |
| 3.2.P.4.2 | Analytical Procedures |  |  |
| 3.2.P.4.3 | Validation of Analytical Procedures |  |  |
| 3.2.P.4.4 | Justification of Specifications |  |  |
| 3.2.P.4.5 | Excipients of Human or Animal Origin |  |  |
| 3.2.P.4.6 | Novel Excipients |  |  |
| **3.2.P.5** | **Control of Drug Product** |  |  |
| 3.2.P.5.0 | Control Strategy |  |  |
| 3.2.P.5.1 | Specification (signed, dated and version-controlled) |  |  |
| 3.2.P.5.2 | Analytical Procedures |  |  |
| 3.2.P.5.3 | Validation of Analytical Procedures (assay and impurities) |  |  |
| 3.2.P.5.4 | Batch Analyses (minimum of two) |  |  |
| 3.2.P.5.5 | Characterisation of Impurities |  |  |
| 3.2.P.5.6 | Justification of Specification |  |  |
| 3.2.P.6 | Reference Standards or Materials |  |  |
| 3.2.P.7 | Container Closure System |  |  |
| **3.2.P.8** | **Stability** |  |  |
| 3.2.P.8.1 | Stability Summary (i.e. sizes, numbers, type, packaging material, conditions and period of testing) and Conclusions are provided for each FPP manufacturer |  |  |
| 3.2.P.8.2 | Post-approval Stability Protocol and Stability |  |  |
| 3.2.P.8.3 | Stability Data |  |  |
| a) | At least 12 months long-term and 6 months accelerated for NCE are provided |  |  |
| b) | At least 6 months long-term and 3 months accelerated for generics are provided |  |  |
| c) | Stability data has been generated from the FPP containing API sourced from the manufacturer identified in Module 3.2.S.2.1. |  |  |
| **3.2.R** | **Regional Information** |  |  |
| **3.2.R.1** | **Pharmaceutical and Biological availability** |  |  |
| 3.2.R.1.1 | **Overview** |  |  |
| a) | The batch size of the test product is a minimum of 100,000 units or at least 10% of the production batch, whichever is greater. |  |  |
| b) | A motivation is included for the batch size of less than 100 000 units |  |  |
| c) | The biostudy test product is manufactured by the same manufacturer, at the same site as the product being applied for |  |  |
| d) | The biostudy test product is NOT manufactured by the same manufacturer, at the same site as the product being applied for, hence a tabulated comparison between the formulations, manufacturing process and of the physico-chemical characteristics to show essential similarity have been provided |  |  |
| 3.2.R.1.2 | Reference product/s (local and foreign) |  |  |
| a) | The country of procurement of the reference product and the name and address of the relevant supplier has been stated |  |  |
| 3.2.R.1.3 | Certificates of Analysis |  |  |
| a) | CoAs of the test, reference product and of the API used in the test product are provided |  |  |
| b) | For additional strength biowaiver: CoAs and a comparative dissolution report have been included for the additional strengths |  |  |
| c) | For BCS class biowaiver: CoAs and a full report in accordance with the latest implemented version of the Quality and Bioequivalence guideline with the appropriate data comparing the test and reference products in three dissolution media: pHs 1,2; 4,5 and 6,8, have been included. |  |  |
| 3.2.R.1.4 | Pharmaceutical availability studies |  |  |
| a) | Dissolution profiles of the test and reference products are provided |  |  |
| b) | A full report on comparative dissolution data to demonstrate equivalence of the foreign reference product to the South African reference product has been submitted, if relevant. |  |  |
| d) | The API(s) used in the biostudy test product is manufactured by the same API manufacturer being applied for |  |  |
| e) | The API(s) used in the biostudy test product is NOT manufactured by the same API manufacturer being applied for, hence a comparative dissolution report with data in three media have been provided  |  |  |
| 3.2.R.2 | Parent API Manufacturer/ APIMF holder with various sites, where identical method of synthesis is used – a statement to this effect has been provided. |  |  |
| 3.2.R.3 | Certificates of suitability with respect to the Ph.Eur. (CEPs) |  |  |
| a) | The declaration of access from the APIMF holder is provided for the submitted CEP. |  |  |
| b) | The authorization box is completed and signed for the submitted CPQ. |  |  |
| 3.2.R.4 | Multiple API manufacturers (not same parent company or APIMF holder) |  |  |
| 3.2.R.5 | Medical device |  |  |
| 3.2.R.6 | Materials of animal and-or human origin |  |  |
| 3.2.R.7 | Batch records of sample (executed batch) |  |  |
| a) | Blank/Master (English translated where relevant) batch manufacturing records is included for each proposed batch size of the final product. |  |  |
| b) | Executed (English translated where relevant) batch manufacturing records is included for the biobatch or developmental batch.  |  |  |
| **3.2.R.8** | **Other** |  |  |
| a) | QOS (MS word and PDF formats) |  |  |
| b) | QIS (MS word and PDF formats) |  |  |
| **3.3** | **Literature References** |  |  |
| --- | [AUTHOR DATE] |  |  |
| **4** | **Nonclinical Study Reports (Not for screening, no hyperlinks required)** |  |  |
| **4.2** | **Study Reports** |  |  |
| **4.2.1** | **Pharmacology** |  |  |
| 4.2.1.1 | Primary Pharmacodynamics |  |  |
| 4.2.1.2 | Secondary Pharmacodynamics |  |  |
| 4.2.1.3 | Safety Pharmacology |  |  |
| 4.2.1.4 | Pharmacodynamic Drug Interactions |  |  |
| **4.2.2** | **Pharmacokinetics** |  |  |
| 4.2.2.1 | Analytical Methods and Validation Reports |  |  |
| 4.2.2.2 | Absorption |  |  |
| 4.2.2.3 | Distribution |  |  |
| 4.2.2.4 | Metabolism |  |  |
| 4.2.2.5 | Excretion |  |  |
| 4.2.2.6 | Pharmacokinetic Drug Interactions |  |  |
| 4.2.2.7 | Other Pharmacokinetic Studies |  |  |
| **4.2.3** | **Toxicology** |  |  |
| 4.2.3.1 | Single Dose Toxicity |  |  |
| 4.2.3.2 | Repeat Dose Toxicity |  |  |
| **4.2.3.3** | **Genotoxicity** |  |  |
| 4.2.3.3.1 | In Vitro |  |  |
| 4.2.3.3.2 | In Vivo |  |  |
| **4.2.3.4** | **Carcinogenicity** |  |  |
| 4.2.3.4.1 | Long-term Studies |  |  |
| 4.2.3.4.2 | Short- or Medium-term Studies |  |  |
| 4.2.3.4.3 | Other Studies |  |  |
| **4.2.3.5** | **Reproductive and Developmental Toxicity** |  |  |
| 4.2.3.5.1 | Fertility and Early Embryonic Development |  |  |
| 4.2.3.5.2 | Embryo-foetal Development |  |  |
| 4.2.3.5.3 | Prenatal and Postnatal Development, including Maternal Function |  |  |
| 4.2.3.5.4 | Studies in which the Offspring are Dosed and/or Further Evaluated |  |  |
| 4.2.3.6 | Local Tolerance |  |  |
| **4.2.3.7** | **Other Toxicity Studies** |  |  |
| 4.2.3.7.1 | Antigenicity |  |  |
| 4.2.3.7.2 | Immunotoxicity |  |  |
| 4.2.3.7.3 | Mechanistic Studies |  |  |
| 4.2.3.7.4 | Dependence |  |  |
| 4.2.3.7.5 | Metabolites |  |  |
| 4.2.3.7.6 | Impurities |  |  |
| 4.2.3.7.7 | Other |  |  |
| **4.3** | **Literature References** |  |  |
| --- | [AUTHOR DATE] |  |  |
| **5** | **Clinical Study Reports** |  |  |
| 5.2 | Tabular Listing of All Clinical Studies |  |  |
| **5.3** | **Clinical Study Reports** |  |  |
| **5.3.1** | **Reports of Biopharmaceutic Studies** |  |  |
| 5.3.1.1 | Bioavailability (BA) Study Reports |  |  |
| 5.3.1.2 | Comparative BA and Bioequivalence (BE) Study Reports |  |  |
| a) | Fasting and/ or fed bioequivalence study(ies) report(s) is/ are included. |  |  |
| b) | The study protocol is provided |  |  |
| c) | Evidence of ethical approval provided |  |  |
| d) | Completed Case Report (CRFs) are provided, including CRFs for deaths and adverse events |  |  |
| e) | Individual subject concentration data and pharmacokinetic parameters are provided in tables and graphs, including the Cmax, Tmax, and AUC for all the subjects, for the test product and the reference product |  |  |
| f) | Documentation on statistical methods has been provided and includes the geometric log-transformed pharmacokinetics and statistical summary of the pharmacokinetic data and degrees of freedom. |  |  |
| g) | Investigator’s curriculum vitae is provided |  |  |
| h) | Quality assurance statement is included |  |  |
| 5.3.1.3 | In Vitro - In Vivo Correlation Study Reports |  |  |
| 5.3.1.4 | Reports of Bioanalytical and Analytical Methods for Human Studies |  |  |
| a) | The bioanalytical report and the method validation report are included |  |  |
| b) | The Bioanalytical report includes tables with all results, like the calibration curves, quality control standards (tables and/ or graphs), and analytical results from all subjects, periods, and runs. |  |  |
| c) | Consecutive chromatograms included from analytical runs for at least 20% of the subjects (a minimum of 4 subjects, whichever is greater) are provided and comply with the requirements for legibility |  |  |
| **5.3.2** | **Reports of Studies Pertinent to Pharmacokinetics using Human Biomaterials (Not for screening, no hyperlinks required)** |  |  |
| 5.3.2.1 | Plasma Protein Binding Study Reports |  |  |
| 5.3.2.2 | Reports of Hepatic Metabolism and Drug Interaction Studies |  |  |
| 5.3.2.3 | Reports of Studies Using Other Human Biomaterials |  |  |
| **5.3.3** | **Reports of Human Pharmacokinetic (PK) Studies (Not for screening, no hyperlinks required)** |  |  |
| 5.3.3.1 | Healthy Subject PK and Initial Tolerability Study Reports |  |  |
| 5.3.3.2 | Patient PK and Initial Tolerability Study Reports |  |  |
| 5.3.3.3 | Intrinsic Factor PK Study Reports |  |  |
| 5.3.3.4 | Extrinsic Factor PK Study Reports |  |  |
| 5.3.3.5 | Population PK Study Reports |  |  |
| **5.3.4** | **Reports of Human Pharmacodynamic (PD) Studies (Not for screening, no hyperlinks required)** |  |  |
| 5.3.4.1 | Healthy Subject PD and PK/ PD Study Reports |  |  |
| 5.3.4.2 | Patient PD and PK/ PD Study Reports |  |  |
| **5.3.5** | **Reports of Efficacy and Safety Studies (Not for screening, no hyperlinks required)** |  |  |
| 5.3.5.1 | Study Reports of Controlled Clinical Studies Pertinent to the Claimed Indication |  |  |
| 5.3.5.2 | Study Reports of Uncontrolled Clinical Studies |  |  |
| 5.3.5.3 | Reports of Analyses of Data from More than One Study |  |  |
| 5.3.5.4 | Other Study Reports |  |  |
| **5.3.6** | **Reports of Post-Marketing Experience (Not for screening, no hyperlinks required)** |  |  |
| --- | PBRER [DESCRIPTION] [DATE/DATA LOCK PERIOD] |  |  |
| --- | PSUR [DESCRIPTION] [DATE/DATA LOCK PERIOD] |  |  |
| --- | RMP Report [DESCRIPTION] [DATE/DATA LOCK PERIOD] |  |  |
| **5.3.7** | **Case Report Forms and Individual Patient Listings (Not for screening, no hyperlinks required)** |  |  |
| --- | [DESCRIPTION] |  |  |
| **5.4** | **Literature References (Not for screening, no hyperlinks required)** |  |  |
| --- | [AUTHOR DATE] |  |  |

**ANNEXURES (Documents required for reliance)**

**Annexure A**

**Reliance pathway**

**Table 1 – List of reliance pathways**

|  |  |
| --- | --- |
| **Reliance pathway** | **Applicable types of applications**  |
| WHO-PQ  |  |
| WHO-CRP |  |
| WHO-SRA |  |
| Swissmedic MAGHP |  |
| EU M4ALL |  |
| AMA |  |
| ZaZiBoNA |  |
| Other (please specify) |  |

**Annexure B**

**Name of the RRA: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

**Table 1**: Documentation required for reliance-based evaluation.

|  |  |  |
| --- | --- | --- |
| **Documents required** | **Yes**  | **No** |
| Completed abridged review template |  |  |
| Completed verified review template |  |  |
| Full, unredacted assessment/evaluation reports from the RRA where the product is registered (1.10.5) |  |  |
| Details of the outcomes of the application in all jurisdictions where it has been submitted, and  |  |  |
| Foreign registration certificate(s) (1.10.2)  |  |  |
| SmPC, a copy of the patient information leaflet (PIL) and label of the product that has been registered by the RRA (1.3.5) |  |  |
| If available: initial scientific unredacted assessments, regulatory correspondence with the sponsor/ applicant, follow-up assessments, and any other documentation from the RRA related to the final registration decision (1.10.5) |  |  |
| If available and where applicable: risk management plans and on-site inspection reports (or equivalent), for example, GCP/ GRP. This does not include the data package filed with the RRA  |  |  |
| Letter of approval from the RRA |  |  |
| Declaration: Sameness (1.10.4.2) |  |  |

**Table 2**: Documents that comprise a complete assessment for each RRA.

|  |  |  |  |
| --- | --- | --- | --- |
| **RRA** | **Required documentation** | **Yes**  | **No** |
| Therapeutic Goods Administration, AustraliaEuropean Medicines Agency (EMA) | Comprehensive details of all studies submitted and assessed |  |  |
| All unredacted assessment report(s) (1.10.5) |  |  |
| Questions from the regulator to the Market Authorisation Holder (and answers) |  |  |
| Summaries of meetings with TGA (including pre-submission advice, where relevant) |  |  |
| Approval letter |  |  |
| Post marketing reviews |  |  |
| **Note:** All relevant Milestone dates are specified in the submission evaluation plan. |  |  |
| Comprehensive details of all studies submitted and assessed |  |  |
| Centralised procedure unredacted assessment reports (where applicable): |  |  |
| Day 80 Quality, Non-Clinical, Clinical, and Overview Assessment Reports |  |  |
| Day 120 List of Questions (and answers) • Day 150 Quality, Non-Clinical, Clinical, and Overview Assessment Reports  |  |  |
| Day 180 Joint Assessment Report • Day 180 List of Outstanding Issues |  |  |
| Final Unredacted Assessment Report |  |  |
| Decentralised procedure unredacted assessment reports (where applicable): |  |  |
| All unredacted assessment reports |  |  |
| Questions from the regulator to the Market Authorisation Holder (and responses) |  |  |
| Summaries of meetings with the EMA and/ or assessors (including pre-submission advice, where relevant) |  |  |
| Committee for Medicinal Products for Human Use (CHMP) Summary of Opinion |  |  |
| Committee for Medicinal Products for Human Use (CHMP) Summary of Opinion |  |  |
| Any other questions from the regulator to the Market Authorisation Holder |  |  |
| Letter of undertaking |  |  |
| European Commission decision |  |  |
| Risk Management Plan review(s) |  |  |
| Post marketing review(s) (e.g., Periodic Safety Update Reports) |  |  |
| Pharmaceutical and Medical Devices Agency (PMDA), Japan | Comprehensive details of all studies submitted and assessed |  |  |
| Discussion documents, questions from PMDA, and answers provided, and Finalised Minutes from Scientific Consultation Meetings (if applicable) |  |  |
| Outcome of Orphan designation, priority or SAKIGAKE determination (if relevant) |  |  |
| Copies of questions and answers exchanged between the Sponsor and PMDA |  |  |
| Unredacted English Translated Review Report consisting of: |  |  |
| Review Report 1 |  |  |
| Review Report 2  |  |  |
| Review Result  |  |  |
| Report on the Deliberation Results  |  |  |
| Approval Letter  |  |  |
| Post-marketing review(s) (e.g., Re-examination Review Report, Periodic Safety Reports) |  |  |
| Health Canada | Comprehensive details of all studies submitted and assessed |  |  |
| Screening: Screening Report |  |  |
| Clinical Review: Pharmaceutical Safety and Efficacy Assessment Report (PSEAR) |  |  |
| Quality: Quality Evaluation Summary (QES) and Manager’s Memo |  |  |
| Bioequivalence: Comprehensive Summary – Bioequivalence (CS-BE) and Manager’s Memo |  |  |
| Biostatistics: Biostatistics Consult Report (if applicable) Risk Management Plan: Risk Management Plan Assessment Report (if applicable) |  |  |
| Questions from the regulator to the Market Authorisation Holder (and responses) |  |  |
| Summaries of meetings with Health Canada (including pre-submission advice, where relevant) |  |  |
| Final Manager’s Memo and Executive Summary |  |  |
| Medicines and Healthcare products RegulatoryAgency (MHRA), United Kingdom | Comprehensive details of all studies submitted and assessed |  |  |
| All unredacted assessment reports as part of the iterative process  |  |  |
| Questions from the regulator to the Market Authorisation Holder (and responses) |  |  |
| Committee for Medicinal Products for Human Use |  |  |
| (CHMP) Summary of Opinion  |  |  |
| Summaries of other meetings with the MHRA (including pre-submission advice, where relevant) |  |  |
| Approval letter |  |  |
| Post marketing review(s) (e.g., Periodic Safety Update Reports) |  |  |
| Swiss Medic, Switzerland | Comprehensive details of all studies submitted and assessed |  |  |
| All unredacted assessment report(s) |  |  |
| Questions from the regulator to the Market Authorisation Holder (and answers) |  |  |
| Summaries of meetings with |  |  |
| SwissMedic (including pre-submission advice, where relevant) |  |  |
| Approval letter |  |  |
| Post marketing reviews |  |  |
| United States Food and Drug Administration (US FDA) | Comprehensive details of all studies submitted and assessed (Unredacted reviews) |  |  |
| Medical review(s) |  |  |
| Chemistry review(s) |  |  |
| Pharmacology review(s) |  |  |
| Statistical review(s) |  |  |
| Statistical review(s) |  |  |
| Clinical pharmacology biopharmaceutics review(s) |  |  |
| Risk assessment and risk mitigation review(s) |  |  |
| Administrative document(s) and correspondence |  |  |
| Cross-discipline team leader review |  |  |
| Summaries of meetings with the US FDA (including pre-submission advice, where relevant) |  |  |
| Office Director memo |  |  |
| Summary review |  |  |
| Complete response letter |  |  |
| Approval letter |  |  |
| Post-marketing reviews |  |  |

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|  |  |  |
| --- | --- | --- |
| **Screening Outcome:** | [ ]  **Passed** | [ ]  **In Query** |
| **Comments (If applicable)** |
|  |
| **Review Pathway**  |
| **PEM** | **CEM** |
|  |  |

|  |
| --- |
| **Name and Surname of Screener**:  |
| Signature: | Date: |