APPENDIX 2B *APPLICATION CHECKLIST (ICH CTD – MAV)*

This Application Checklist should be used to ensure submission of a complete dataset in the ICH Common Technical Dossier (ICH CTD) format for MAV applications only.

All documents required under Module 1 must be submitted in softcopy in PRISM.

Colour scanned copies of the original documents should be submitted and original hard copies of documents are not required.

However, HSA reserves the rights to request for the original or certified true copy of submitted documents if there is any doubt that a submitted scanned document is not an accurate reflection of the original document.

The acceptance of the application after screening does not preclude requests by HSA for additional documents or changes to the information/document during evaluation.

This Checklist should be completed by checking each item against the dossier according to the application type relevant for your submission.

The Application Checklist should be submitted in MS WORD format.

**Note**:

* Cells with  indicate that the documents are mandatory for the selected application type and evaluation route.
* Cells with \* indicate that the documents may be optional depending on the application type/product/change concerned.
* Cells without  indicate that the documents are not required for the selected application type and evaluation route.
* If a mandatory document is not included in the submission (i.e. applicant is unable to select any of the cells with  for a particular document), justifications for the omission must be provided in the cover letter.

Please refer to the *Guidance on Therapeutic Product Registration in Singapore* and the ICH technical guidance for explanatory notes on the preparation ofdocuments for a submission in ICH CTD format.

Legend:

|  |  |  |
| --- | --- | --- |
| Application type | MAV-1 | Major Variation Type-1 |
| MAV-2 | Major Variation Type-2 |
| Evaluation route | F | Full Dossier |
| A | Abridged Dossier |
| V | Verification Dossier |

**REVISION HISTORY**

Form Version (Publish Date)

TPB-SUB-004-005 (Version 5; Updated 30 June 2023)

Module 1 – Administrative Documentation

| Section | Documents | | | Application Type & Evaluation Route | | | | HSA Screening | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **MAV-1** | | | **MAV-2** |
| F | A | V | A | Submitted? | Remarks |
| 1.0 | PRISM Application Form | | |  |  |  |  |  |  |
|  | 1.0.1 | Section 1: Company Particulars | |  |  |  |  |  | . |
|  |  | * The Company is based and registered in Singapore. | |
|  | 1.0.2 | Section 2: Applicant Particulars | |  |  |  |  |  |  |
|  |  | * The applicant of a product registration refers to the local company that is applying for the product registration. The applicant company may authorise officers, permanent employees, or designated external parties, all of whom are referred to as the “applicant representative”, to submit the application for product registration in Singapore. * The NRIC/FIN of the applicant representative entered must be the same as that used to access the PRISM application. * Note: Section 2.4.5 of the PRISM application form does not support entry of multiple email addresses. | |
|  |  |
|  | 1.0.3 | Section 3: Application Details | |  |  |  |  |  |  |
|  |  | 3.1 | Type of Application |  |  |  |  |  |  |
|  |  | 3.2 | Type of Product |  |  |  |  |  |  |
|  |  | 3.3 | Reference Product |  |  |  |  |  |  |
|  | 3.4 | Product intended for export |  |  |  |  |  |  |
|  |  | 3.5 | Type of Dossier |  |  |  |  |  |  |
|  |  | 3.6 | Type of Format |  |  |  |  |  |  |
|  | 1.0.4 | Section 4: Product Information | |  |  |  |  |  |  |
|  |  | 4.1 | Product Name |  |  |  |  |  |  |
|  |  | 4.2 | Product Formula |  |  |  |  |  |  |
|  |  | 4.3 | Ingredients derived from human blood or animal sources |  |  |  |  |  |  |
|  | 4.4 | Pharmacotherapeutic Group (ATC Code) | **\*** | **\*** | **\*** |  |  |  |
|  |  | \*: Applicable if the MAV is in relation to a change in ATC code |  |  |
| * If the WHO ATC code is not available at the time of the application submission, **“Pending”** should be stated in this field. |  |  |
|  |  | * There should be no spacing in-between the characters entered |  |  |  |  |  |  |
|  |  | 4.5 | Dosage Form |  |  |  |  |  |  |
|  |  | 4.6 | Route of Administration | **\*** | **\*** | **\*** |  |  |  |
|  |  |  | \*: Applicable if the MAV is in relation to a change in route of administration |
|  |  | 4.7 | Packaging, Shelf Life & Storage Condition |  |  |  |  |  |  |
|  |  | 4.8 | Forensic Classification |  |  |  |  |  |  |
|  | * Refer to Guidance document, Section 1.2 for details. |
|  | 4.9 | Registration Status in Other Countries |  |  |  |  |  |  |
|  |  | * As the PRISM fields are not amendable in a variation application, the full details should be attached in softcopy (PDF) in PRISM section 7 (Supporting Attachments). |  |  |
|  |  | * For each country, state the application status, status date and forensic classification (if applicable). |  |  |
|  |  | * For all of HSA’s reference agencies, state the application status, status date, application details and forensic classification. |  |  |
|  |  |  | * If an application is pending or not submitted in any of HSA’s reference agencies, state that the application is pending (with submission date), or not submitted (date not required). |  |  |
|  |  | * For products approved via an appeal process, following either a negative opinion/rejection/non-approvable decision or an approvable/conditional approvable decision, the reasons for the initial regulatory decision should be provided, along with the reasons for the subsequent approval. |  |  |
|  |  |  | * For applications submitted to the European Union agencies, the type of authorisation procedure, i.e. centralised, decentralised, mutual recognition or national, should be identified; for decentralised and mutual recognition procedures, the reference member state should be indicated. |  |  |
|  | * For applications approved by the UK MHRA, indicate whether approval was granted through a national procedure or whether MHRA acted as the RMS or CMS for decentralised and mutual recognition procedures on or prior to 31 January 2020 when the UK has formally left the European Union. |  |  |
|  |  |  | * For approved indication(s) and dosing regimen(s) for an approved application, applicants can make reference to the approved PI of the reference agency instead of typing out the information under Application Details (e.g. “Refer to approved PI attached in PRISM 1.5.1 for indication and dosing regimen”). |  |  |  |  |  |  |
|  |  | 4.10 | Product Owner |  |  |  |  |  |  |
| 1.0.5 | Section 5: Manufacturer’s Particulars | |  |  |  |  |  |  |
| 1.0.6 | Section 6: Batch Release Details | |  |  |  |  |  |  |
| 1.0.7 | Supporting Documents | |  |  |  |  |  |  |
|  |  | * All documents relating to Module 1 of the CTD must be attached. | |  |  |
|  |  | * Other Modules should either be attached in full in this PRISM section or submitted as soft copies in a CD/DVD. | |  |  |

| Section | Documents | | | Application Type & Evaluation Route | | | | HSA Screening | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **MAV-1** | | | **MAV-2** |
| F | A | V | A | Submitted? | Remarks |
|  | **Important Note:** All documents submitted in support of an application to HSA must be in English. For documents in their original language which is not English, a certified translation or a verified translation may be acceptable. Please refer to Guidance document, Section 23.2.2.2 (Language and Translation) for more information. | | | | | | | | |
| 1.1 | Cover Letter | | | **\*** | **\*** | **\*** | **\*** |  |  |
|  | * The cover letter should state the product name, and the number of CD/DVDs submitted in the application dossier. * A concise and precise summary of the application should be provided. * Applicants should ensure that the application dossier is complete. * The omission of certain documents within the dossier or any deviation from the guidelines must be appropriately justified. | | |
| 1.2 | Comprehensive Table of Contents | | |  |  |  |  |  |  |
|  | * A complete list of all the documents, organised by Module, should be provided in the application dossier. | | |
|  | * The location of each document should be identified by the Module number. | | |
| 1.3 | Introduction *(Refer to 1.1 Cover Letter)* | | |  |  |  |  |  |  |
| 1.4 | Labelling and PI/PIL **proposed and currently approved** in Singapore. | | | **\*** | **\*** | **\*** | **\*** |  |  |
|  | * All proposed labels have to be submitted for registration in Singapore. | | |  |  |
|  | * For the proposed labelling/PI/PIL, a pristine and an annotated version (which highlights the changes made to the currently approved labelling) are required.   + Annotations should be made on the current approved labelling materials based on the actual text to be added.   + Current approved text proposed for deletion should be struck through, whereas newly added and proposed text should be underlined or highlighted.   + Current approved text that is not intended to be deleted should not be annotated.   + Proposed changes to all labels must be clearly annotated, and the **final approved changes would be as annotated** in the final label submitted in PRISM. | | |  |  |
|  | * The product name to be stated on the labels should be the same as that in PRISM | | |  |  |
|  | * Labelling must be in English. Any non-English country-specific labelling requirements on the artwork/drafts should be highlighted if the labelling is shared with other countries. | | |  |  |
|  | * \*: If non-English text is included in the labelling, applicants must provide an official statement to declare that the non-English text is complete, accurate and unbiased information and is consistent with the English text. | | |  |  |
|  | 1.4.1 | Outer Carton Labels   * The draft artwork of the outer carton labels should be in the actual format, design and colour that are to be printed. * Separate labels must be submitted for each pack size of the product. | | **\*** | **\*** | **\*** | **\*** |  |  |
|  | 1.4.2 | Inner/Blister Labels   * The draft artwork of the inner/blister labels should be in the actual format, design and colour that are to be printed. * Separate labels must be submitted for each different pack size of the product. | | **\*** | **\*** | **\*** | **\*** |  |  |
|  | 1.4.3 | Package Insert (PI)   * A PI is required for TPs registered with Prescription Only Medicines (POM) forensic classification. | |  |  |  |  |  |  |
| 1.4.4 | Patient Information Leaflet (PIL)   * A PIL is required for TPs registered with Pharmacy Only (P) or General Sale List (GSL) forensic classification. * The PIL should be written in a language easily understood by the consumers/patients. | |  |  |  |  |  |  |
| 1.5 | Approved SmPC/PI/PIL | | |  |  |  |  |  |  |
|  | 1.5.1 | SmPC/PI/PIL approved by HSA’s reference regulatory agencies | |  |  |  |  |  |  |
|  | * The approved SmPC / PI / PIL currently approved by each of HSA’s reference agencies should be submitted, where applicable. | |
| * The submitted SmPC, PI and/or PIL should state the country that the document originated from. | |  |  |
| 1.5.2 | SmPC/PI/PIL approved by Country of Origin/Country of Manufacture | |  | **\*** | **\*** | **\*** |  |  |
| 1.5.3 | PI / SmPC / PIL approved by other regulatory agency | |  |  |  |  |  |  |
|  |  | * The approved SmPC / PI / PIL from the drug regulatory agency that issued the proof of approval should be submitted, if it is not from the Country of Origin. | |
|  | * The submitted SmPC, PI and/or PIL should state the country that the document originated from. | |  |  |
|  | 1.5.4 | If applicable, a declaration that the translation of the SmPC/PI/PIL conforms to the SmPC/PI/PIL currently approved should be submitted. | |  |  |  |  |  |  |
| 1.6 | Assessment report issued by HSA’s reference regulatory agency: | | (Please specify) |  |  |  |  |  |  |
| * Assessment reports and supporting documents submitted must be unredacted and unedited. | | |  |  |
| * Refer to Guidance document, section 24.2.5.3 for details. | | |  |  |
| 1.7 | Description of Batch Numbering System | | |  |  |  |  |  |  |
| 1.8 | Proof of Approval from:  Competent Drug Regulatory Agency:  \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ | | |  |  |  | **\*** |  |  |
| * The proof of approval must come in the form of a Certificate of Pharmaceutical Product (CPP) that is valid at the time of submission, or an official approval letter that certifies the product’s registration status in the country at the point of submission to HSA; and * the SPC, PI and/or PIL approved by the drug regulatory agency that issued the proof of approval. | | |  |  |
| * CPPs that indicate that the product is not licensed in the exporting country (including the scenario where the product is licensed “solely for export only”) are not acceptable proof of approval. | | |  |  |
| * The approval letter should be a colour scanned copy of either the original copy or a certified true copy (certified by the drug agency that issued the approval letter) and in English. | | |  |  |
| * Reference to drug regulatory authority websites in the form of website screenshots and URLs (for the website) as proof of the approval status of the products by that regulatory authority are acceptable, provided that the product’s identity and product’s ownership can be confirmed from the website. | | |  |  |
| * All aspects of the product’s quality and intended direction(s) for use in Singapore should be the same as those approved by the drug regulatory agency that issued the approval letter. | | |  |  |
| * If the brand name (trade name) of the product registered in the country which issued the proof of approval is different from that proposed in Singapore, a declaration letter from the product owner should be submitted declaring that both products marketed under the different brand names are identical in all aspects of quality, safety and efficacy except for the brand name. | | |  |  |
| * The following Proof of Approval that are **not** acceptable as Proof of Approval:   + WHO Prequalified Products Listing   + Free Sale Certificates   + Statements of Licensing Status of Pharmaceutical Product   + EU Decentralised/MRP procedure outcome letters/documents | | |  |  |
|  | \*: Proof of approval for MAV-2 should be in the form of documentation which proves that that the product had been reclassified (for specific indication(s) or dosing regimen(s)) in the UK, US, Canada and/or Australia. This is not required for me-too reclassification. | | |  |  |
| 1.9 | Proof of Approval from at least 2 of HSA’s reference regulatory agencies  Please specify issuing agencies: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ | | |  |  |  |  |  |  |
| * For a verification evaluation of an MAV-1, proof of approval from at least two of HSA’s reference drug regulatory agencies, including the chosen primary reference agency, is required. Proof of approval must come in the form of:   + an official approval letter, or equivalent document (e.g. Certificate of Pharmaceutical Product; CPP), which certifies the registration status of the drug product; and   + the SPC, PI and/or PIL approved by the drug regulatory agency that issued the approval letter. | | |  |  |
| * The validity period of the approval from the chosen primary reference agency for the verification route is not more than 3 years for MAV. | | |  |  |
| 1.10 | Authorisation Letters | | |  |  |  |  |  |  |
| 1.11 | GMP certification/proof of GMP compliance for each finished product manufacturer inclusive secondary packer(s) | | |  |  |  |  |  |  |
| 1.12 | Patent Declaration Form | | |  |  |  |  |  |  |
| 1.13 | Declaration on rejection, withdrawal and deferral | | |  |  |  |  |  |  |
| * The product name that is stated on the letter must be same as that in the PRISM application form. | | |  |  |
| * The declaration letter should be issued by the product owner or local registrant, and state that the application as submitted to HSA and directions of use including indication(s), dosing regimen(s) and patient population(s) have not been rejected or withdrawn, have not been approved via an appeal process, and are not pending deferral, by any drug regulatory agency.   + If any of the above applies, details and reasons must be provided. | | |  |  |
| 1.14 | Declaration for MAV Verification | | |  |  |  |  |  |  |
| * Declaration that all aspects of the Singapore product’s quality are identical to that currently approved by the chosen primary reference agency. | | |  |  |  |  |  |  |
| 1.15 | Registration Status in Other Countries | | |  |  |  |  |  |  |
|  | * The full details should then be attached in softcopy (PDF) in this PRISM under [7] “Supporting Attachments” | | |  |  |
|  | * For MAV-2 applications, the registration status should also include the forensic classification of the product in the approved countries. | | |  |  |

|  |  |  |
| --- | --- | --- |
| **Consent to Disclosure of Information** | **Yes** | **No** |
| The applicant hereby consents to the disclosure of information submitted in this application, including information provided in response to an Input Request, by the HSA to partner regulatory authorities within the Access Consortium. Such disclosure, if made, will be in accordance with the [Terms of Reference](https://www.hsa.gov.sg/therapeutic-products/international-collaboration/access) of the Access; in particular, for the purpose of information exchange and enabling work-sharing. The HSA will notify the applicant in writing if such disclosure of information submitted in this application is made. |  |  |

Module 2 – Common Technical Document Summaries

| Section | Documents | | Application Type & Evaluation Route | | | | HSA Screening | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **MAV-1** | | | **MAV-2** |
| F | A | V | A | Submitted? | Remarks |
| 2.1 | Overall CTD Table of Contents of Modules 2, 3, 4 and 5 | |  |  |  |  |  |  |
| 2.2 | Introduction | |  |  |  |  |  |  |
| 2.3 | Singapore Quality Overall Summary (QOS) & QOS in other format, if available | |  |  |  |  |  |  |
| 2.4 | Non-clinical Overview | | **\*** | **\*** | **\*** |  |  |  |
| 2.5 | Clinical Overview | |  |  |  |  |  |  |
| 2.6 | Non-clinical Summary | |  |  |  |  |  |  |
|  | 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 | **\*** |  |  |  |  |  |
|  | 2.6.6 | Toxicology Written Summary | **\*** |  |  |  |  |  |
|  | 2.6.7 | Toxicology Tabulated Summary | **\*** |  |  |  |  |  |
| 2.7 | Clinical Summary | |  |  |  |  |  |  |
|  | 2.7.1 | Summary of Biopharmaceutics 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 |  |  |  | **\*** |  |  |
| * \*: Not required for me-too reclassification |  |  |
| 2.7.5 | Synopses of Individual Studies |  |  |  |  |  |  |

Module 4 – Non-clinical Study Reports

| Section | Documents | | | Application Type & Evaluation Route | | | | HSA Screening | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **MAV-1** | | | **MAV-2** |
| F | A | V | A | Submitted? | Remarks |
| 4.1 | Module 4 Table of Contents | | | **\*** |  |  |  |  |  |
| 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 (non-clinical) | **\*** |  |  |  |  |  |
|  | 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 | **\*** |  |  |  |  |  |
| 4.2.3.4 | Carcinogenicity | **\*** |  |  |  |  |  |
| 4.2.3.5 | Reproductive and Developmental Toxicity | **\*** |  |  |  |  |  |
|  | 4.2.3.6 | Local Tolerance | **\*** |  |  |  |  |  |
|  | 4.2.3.7 | Other Toxicity Studies | **\*** |  |  |  |  |  |
|  | 4.3 | List of Literature References | | **\*** |  |  |  |  |  |

Module 5 – Clinical Study Reports

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Section | Documents | | Application Type & Evaluation Route | | | | HSA Screening | |
| **MAV-1** | | | **MAV-2** |
| F | A | V | A | Submitted? | Remarks |
| 5.1 | Module 5 Table of Contents | |  |  |  |  |  |  |
| 5.2 | Tabular Listings of All Clinical Studies | |  |  |  |  |  |  |
| 5.3 | Clinical Study Reports | |  |  |  |  |  |  |
| 5.3.1 | Reports of Biopharmaceutic Studies | **\*** | **\*** | **\*** |  |  |  |
| * Information on the comparability between clinical trial (pivotal studies) and commercial formulations should be available in the Clinical Overview/Summary. If the commercial formulation for the Singapore market differs from the clinical trial formulation used in the pivotal studies, the final study report(s) of biopharmaceutic studies to establish bioequivalence between the commercial product formulation and the clinical trial formulation used in pivotal studies should be submitted. |
| 5.3.2 | Reports of Studies Pertinent to Pharmacokinetics using Human Biomaterials | **\*** |  |  |  |  |  |
| 5.3.3 | Reports of Pharmacokinetic (PK) Studies | **\*** |  |  |  |  |  |
| 5.3.4 | Reports of Pharmacodynamic (PD) Studies | **\*** |  |  |  |  |  |
| 5.3.5 | Reports of Efficacy and Safety Studies |  |  |  |  |  |  |
| * For Full Dossiers, study reports of ALL clinical trials (including the appendices and tables) should be submitted. |  |  |  |
| * For Abridged and Verification Dossiers, study reports of pivotal or relevant clinical trials should be submitted (appendices and tables are required only upon request by HSA). |  |  |  |
| * The clinical trials should be conducted using the drug product formulation submitted in the application and in the appropriate patient population for the indication(s) and/or dosing regimen(s) as requested in the application. |  |  |  |
| * If the commercial formulation for the Singapore market differs from the clinical trial formulation used in the pivotal studies, biopharmaceutic study reports are required (see section 5.3.1). |  |  |  |
| * If the information on the comparability between the clinical trial formulation and the commercial formulation is not available in the clinical study reports or the Clinical Overview/Summaries, a separate declaration letter should be submitted to confirm that the clinical trial formulation is the same as the commercial formulation marketed in Singapore. |  |  |  |
| * Phase III, confirmatory, randomised, controlled pivotal trials conducted in compliance with Good Clinical Practice (GCP) are required to support each requested indication and dosing regimen, unless adequately justified. Active-controlled studies should use relevant active comparators that are locally registered, unless adequately justified. |  |  |  |
|  | 5.3.6 | Reports of Post-marketing Experience | **\*** | **\*** | **\*** |  |  |  |
|  | 5.3.7 | Case Report Forms and Individual Patient Listings (required upon request by HSA) |  |  |  |  |  |  |
| 5.4 | List of Key Literature References | |  |  |  |  |  |  |
| 5.5 | Risk management plan (RMP) documents as separate attachment in PRISM under [7] “Supporting Attachments” | | **\*** | **\*** | **\*** |  |  |  |
| 5.6 | Other Supporting Documents | | **\*** | **\*** | **\*** |  |  |  |