**NDA CHECKLIST FOR CLASS 2 CELL, TISSUE AND GENE THERAPY PRODUCTS (ICH CTD FORMAT)**

* This application checklist should be used to ensure the submission of a complete dataset in the ICH Common Technical Dossier (ICH CTD) format for NDA.
* Colour scanned copies of the original documents should be submitted and hard copies of original 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/documents during the evaluation.
* This checklist should be completed by checking each item against the dossier according to the application type relevant for your submission.

**Note:**

* Cells with ☐ indicate that the documents shown are mandatory for the selected application type and evaluation route.
* Cells with ☐\* indicate that the documents shown may be optional depending on the application type/product/change.
* Cells without ☐ indicate that the documents shown 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 Cell, Tissue and Gene Therapy Products 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 | **NDA** | New Drug Application |
| Evaluation route | **F** | Full Dossier |
| **A** | Abridged Dossier |

**Module 1 - Administrative Documentation**

| **Section** | **Documents** | | **Evaluation Route** | | **HSA Screening** | |
| --- | --- | --- | --- | --- | --- | --- |
| **F** | **A** | **Submitted?** | **Remarks** |
| 1.1 | **Cover letter** | |  |  |  |  |
| * Include a cover letter stating the product name, the proposed evaluation route, the referenced drug regulatory authority (for Abridged route), the proposed indication. * A concise summary of the application and justification for the need for the application should be provided. * The absence/omission of certain documents and deviation(s) from guidelines should be justified. | |
| 1.2 | **Comprehensive Table of Contents** | |  |  |  |  |
| * A complete list of all 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 proposed in Singapore** | |  |  |  |  |
| * All proposed labels have to be submitted for registration in Singapore. * Handwritten information is not acceptable. * Movable text boxes/pictures placed over other hidden information/text are not acceptable. * If the proposed labels contain QR code, the website and information that will be provided by the QR code should be submitted. * 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 Label** |  |  |  |  |
| * 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 different pack size of the product. |
| 1.4.2 | **Inner Label** |  |  |  |  |
| * The draft artwork of the inner 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. |
| 1.4.3 | **Package Insert (PI)** |  |  |  |  |
| * A PI is required for all CTGT product registration. * The submission of one common PI for all strengths or dosage forms is encouraged. |
|  | 1.4.4 | **Patient Information Leaflet (PIL)** | \* | \* |  |  |
| * The PIL is optional for Class 2 CTGTP. * The PIL should be written in a language easily understood by consumers/patients and be consistent with the CTGTP labels and/or PI. |
| 1.5 | **Registration status in other countries** | |  |  |  |  |
| 1.5.1 | **Tabulation of worldwide registration status** |
| 1.5.2 | **Approved SmPC/PI** |  |  |  |  |
| * The approved SmPC/PI currently approved by each of HSA’s reference agencies should be submitted, where applicable. |
| * The submitted SmPC / PI should state the country that the document originated from. |
| * SmPC/PI approved by Country of Origin/Country of Manufacture. Please provide justification if the document is not available. |  | \* |  |  |
| * The approved SmPC / PI from the drug regulatory agency that issued the proof of approval, should be submitted if it is not from the Country of Origin. Please provide justification if the document is not available. |  | \* |  |  |
| * The submitted SmPC / PI should state the country that the document originated from. |
|  | 1.5.3 | **Assessment report issued by HSA’s reference regulatory agency, where applicable** |  | \* |  |  |
| * The submitted assessment reports and supporting documents must be unredacted and unedited. |
| 1.6 | **Description of Batch Numbering System** | |  |  |  |  |
| * Examples of batch numbering system should be included to illustrate how the batch number enables identification, where applicable. | |
| 1.7 | **Proof of Approval** | |  |  |  |  |
| * 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. * 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 of the original document (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 websites. * 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. * Proof of approval must be accompanied by the SmPC/PI and/or PIL as approved in the country that issued the proof of approval. | |
| 1.8 | **Authorisation Letters** | |  |  |  |  |
| * All scanned copies of the authorisation letters shall be on the authorising company’s (i.e. Product Owner’s) letterhead, dated and signed by the designated authorised person in the company. * The company names and addresses, and product name stated in the letters should be consistent with the information provided in the application form and dossier. * Authorisation letters stated below may be combined into one document provided that all names, addresses and responsibilities are clearly stated. | |
| 1.8.1 | **Authorisation Letter from Product Owner to the Applicant company** |  |  |  |  |
| * This letter authorises the local applicant company to apply for and be the Product Registrant for a specific product and be responsible for all matters pertaining to the registration of this product in Singapore. |
| 1.8.2 | **Authorisation Letter from Product Owner to the Manufacturer(s)** |  |  |  |  |
| * This letter authorises the specified manufacturer to produce, pack and/or label the product intended for Singapore, including active substance and critical starting materials manufacturers. * If there are multiple CTGT product manufacturers, the applicant may opt to submit one authorisation letter which clearly states all of the manufacturers (names and addresses) and their responsibilities related to the product. |
| 1.8.3 | **Authorisation Letter from Product Owner to the Batch Releaser** |  |  |  |  |
| * This letter authorises the specified company to batch release the product. * If there are multiple sites responsible for the batch release of the product, then the applicant may opt to submit one authorisation letter which clearly states all of the batch releasers (names and addresses) and their responsibilities. |
| 1.8.4 | **Authorisation Letter from Product Registrant to Secondary Packager located in Singapore** | \* | \* |  |  |
| * This letter authorises the specified company to pack and/or label the product. |
| 1.9 | **GMP certification/proof of GMP compliance for each manufacturer, which is inclusive of active substance, critical starting materials and finished product manufacturer (including solvent/diluent and CTGT product intermediate), primary and secondary packer(s) and batch releaser.** | |  |  |  |  |
| * A colour scanned copy of the original or certified true copy of GMP certification or an equivalent document issued by the relevant drug regulatory agency should be submitted, certifying that the manufacturer concerned complies with current applicable GMP standards. | |
| * If applicable, either the GMP Documentary Evidence Verification Application or Overseas GMP Audit application should be submitted for manufacturing sites which are **new** to Singapore. | |
| * Examples of Acceptable Proof of GMP Compliance (other than GMP Certificate): * EU:   + Screenshots of EUDRA GMP Database website   + Certificate printed from EUDRA GMP website which includes the EUDRA GMP watermark. * US/FDA:   + Establishment Inspection Report **(Complete set)**   + Covering letter (stating the status of the audit) * Health Canada:   + Drug Establishment Licences (DEL) **AND**   + Inspection Exit Notice * SwissMedic: * For manufacturers located in Switzerland, a Manufacturer’s Licence issued by SwissMedic is an acceptable documentary GMP evidence. * Certain accreditation documents/certificates issued by other drug regulatory agencies (for example, Japan/PMDA Accreditation Certificate of Foreign Drug Manufacturer), US/FDA Establishment Licence and the Canada/Health Canada Establishment Licence are not acceptable proof of GMP compliance. | |
| * Validity period of Proof of GMP Compliance:   + The submitted Proof of GMP compliance must be valid at the time of submission to HSA.   + If the validity period/expiry date is not stated on the GMP Certificate, HSA will consider the certificate valid for a period of 3 years from date of last inspection or date of issuance of the certificate. | |
| * The names and addresses of manufacturer(s) and batch releaser(s) should be consistent with information provided in the Proof of GMP Compliance submitted and CTD sections S.2.1 and P.3.1. | |
| * Diluents used for reconstituting the product which are packaged together with the product will be considered as part of the final product. Manufacturer(s) of the supplied diluent(s) will follow the same requirements applicable to the product, e.g. proof of GMP compliance. | |
| 1.10 | **Relevant accreditation certificates or licences for sites responsible for human cell/tissue procurement site (e.g. apheresis site, tissue bank), quality control testing (e.g. sterility testing laboratory) and storage** | |  |  |  |  |
| * Valid and relevant accreditation certificates or licences (e.g. AABB, AATB, JACIE, FACT, CAP, ISO 13485, ISO/IEC 17025, GMP, GTP). | |
| 1.11 | **Declaration on rejection, withdrawal and deferral** | |  |  |  |  |
| * The product name that is stated on the declaration letter must be same as that in the 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. | |
| 1.12 | **Declaration of Reference Agency’s approval of Chemistry & Manufacturing Control (CMC) Aspects** | |  |  |  |  |
| * Please indicate the Specified Reference Agency: | |
| * Please confirm the following CMC information for the critical starting materials (where applicable), active substance, and/or CTGT product proposed for registration in Singapore are the same as that **approved** by the Specified Reference Agency by ticking the respective checkbox   + The manufacturing processes   + The specification | |  |  |  |  |
| * Please tabulate the differences between the critical starting materials (where applicable), active substance, and/or CTGTP product proposed for registration in Singapore and that approved by the Specified Reference Agency in a separate document. | |  |  |  |  |

**Module 2 - Common Technical Document Summaries**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Section** | **Documents** | | **Evaluation Route** | | **HSA Screening** | |
| **F** | **A** | **Submitted?** | **Remarks** |
| 2.1 | Overall CTD Table of Contents of Modules 2, 3, 4 and 5 | |  |  |  |  |
| 2.2 | Introduction | |  |  |  |  |
| 2.3 | Quality Overall Summary | |  |  |  |  |
| 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 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 | Synopses of Individual Studies |  |  |  |  |

**Module 3 - Quality**

| **Section** | **Documents** | | | | **Evaluation Route** | | **HSA Screening** | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **F** | **A** | **Submitted?** | **Remarks** |
| 3.1 | Table of Contents of Module 3 | | | |  |  |  |  |
| 3.2 | Body of Data | | | |  |  |  |  |
| 3.2.S | **Active Substance** | | | | | | | |
| * If a CTGT product contains more than one active substance, the information within Module 3.2.S must be provided in its entirety for each active substance. The S section checklist should be duplicated accordingly for each additional active substance. * For critical starting materials (e.g. viral vector used for ex vivo transduction of a cellular product), the information required within 3.2.S must be provided in its entirety for the critical starting material. The S section checklist should be duplicated accordingly for each critical starting material. | | | | | | | |
| 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 | Manufacture | | |  |  |  |  |
| 3.2.S.2.1 | Manufacturer(s) | |  |  |  |  |
| * Name(s), address(es) and responsibilities of all site(s) | |
| 3.2.S.2.2 | Description of Manufacturing Process and Process Controls | |  |  |  |  |
| 3.2.S.2.3 | Controls of Materials | |  |  |  |  |
| * Certificate of Analysis (CoAs) or specifications of all reagents used in the manufacturing process | |
| 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 | |  |  |  |  |
| * Discussion on the presence of potential mutagenic impurities | |
| 3.2.S.4 | Control of Active Substance | | |  |  |  |  |
| 3.2.S.4.1 | Active Substance Specifications | |  |  |  |  |
| * Release and stability indicating parameters should be clearly defined or differentiated. | |
| 3.2.S.4.2 | Analytical Procedures | |  |  |  |  |
| 3.2.S.4.3 | Validation of Analytical Procedures | |  |  |  |  |
| 3.2.S.4.4 | Batch Analyses | |  |  |  |  |
| 3.2.S.4.5 | Justification of Specification(s) | |  |  |  |  |
| 3.2.S.5 | Reference standards or materials | | |  |  |  |  |
| * The source of reference standard (in house or official with reference to compendial standard) used for testing of the active substance should be stated. * Evidence of characterisation for in-house / working standards is required. | | |
| 3.2.S.6 | Container Closure System (CCS) | | |  |  |  |  |
| * Complete technical information should be provided on the type of container closure used. * A declaration of compliance to the appropriate international standards or pharmacopoeia is to be provided, e.g. food contact EC/10/2011, Ph. Eur. Chapter 3. * For active substance(s) in solution(s), the suitability of the CCS should be demonstrated (e.g. extractable and leachable studies, CCS integrity study). | | |
| 3.2.S.7 | Stability | | |  |  |  |  |
| 3.2.S.7.1 | Stability Summary and Conclusions | |  |  |  |  |
| * The conclusion of the stability studies, stress studies, storage condition and proposed re-test/shelf-life period should be stated in the summary. * Information such as the batch size, date of manufacture, site of manufacture and container closure system should be stated. * The stability batches should be manufactured by the same process and packaged in the same container closure system as that proposed for Singapore. | |
| 3.2.S.7.2 | Post-Approval Stability Protocol and Stability Commitment | |  |  |  |  |
| * This should be based on proposed storage condition. If any results fall outside of the re-test / shelf-life specifications, these should be reported together with proposed action. | |
| 3.2.S.7.3 | Stability Data | |  |  |  |  |
| * If the active substance is sourced from multiple sites, stability data from each site should be provided, unless otherwise justified. * Results from Stress Testing (including Photostability testing) should be submitted, unless otherwise justified. | |
| 3.2.P | **Final Product** | | | | | | | |
| 3.2.P.1 | Description and Composition of CTGTP | | |  |  |  |  |
| 3.2.P.2 | Pharmaceutical and Manufacturing Process Development | | |  |  |  |  |
| 3.2.P.2.1 | Components of the Final Product | |  |  |  |  |
| 3.2.P.2.1.1 | Active Substance |  |  |  |  |
| 3.2.P.2.1.2 | Excipients |  |  |  |  |
| 3.2.P.2.2 | Final Product | |  |  |  |  |
| 3.2.P.2.2.1 | Formulation Development |  |  |  |  |
| 3.2.P.2.2.2 | Overages |  |  |  |  |
| 3.2.P.2.2.3 | Physiochemical and Biological Properties |  |  |  |  |
| 3.2.P.2.3 | Manufacturing Process Development | |  |  |  |  |
| 3.2.P.2.4 | Container Closure System (CCS) | |  |  |  |  |
| * For sterile products, container closure integrity data should be submitted. * For liquid preparations, the suitability of Container Closure System should be demonstrated (e.g. extractable and leachable studies). * For Container Closure Systems which are also a delivery device e.g. nasal sprays, inhalers, prefilled syringes, the technical properties of the container closure system with respect to patient use should be considered and submitted. | |
| 3.2.P.2.5 | Microbiological Attributes | |  |  |  |  |
| 3.2.P.2.6 | Compatibility | | \* | \* |  |  |
| * This is applicable for CTGT products which have reconstitution diluents or dosage device (e.g. infusion bags, tubings). | |
| 3.2.P.3 | Manufacture | | |  |  |  |  |
| 3.2.P.3.1 | Manufacturer(s) | |  |  |  |  |
| * Name(s), address(es) and responsibilities of all site(s) | |
| 3.2.P.3.2 | Batch formula | |  |  |  |  |
| 3.2.P.3.3 | Description of manufacturing process and process controls | |  |  |  |  |
| * The flow chart and IPC should be submitted. * Any proposed holding time(s) should be stated for each process and accompanied by relevant supportive data. | |
| 3.2.P.3.4 | Control of Critical Steps and Intermediates | |  |  |  |  |
| 3.2.P.3.5 | Process Validation | |  |  |  |  |
| 3.2.P.4 | Control of Excipients   * State if excipient used is compendial or non-compendial. * Information on proprietary ingredients, should be as detailed as possible. In cases where the formula of the proprietary ingredient is confidential, the formula should then be provided by the ingredient manufacturer directly to HSA. | | | | | | |
| 3.2.P.4.1 | Specifications or Certificate of Analyses | |  |  |  |  |
| 3.2.P.4.2 | Analytical Procedures | | \* | \* |  |  |
| * This is optional for compendial test method and specifications set according to BP/JP/Ph. Eur./USP. | |
| 3.2.P.4.3 | Validation of Analytical Procedures | | \* | \* |  |  |
| * This is optional for compendial test method and specifications set according to BP/JP/Ph. Eur./USP. | |
| 3.2.P.4.4 | Justification of Specifications | | \* | \* |  |  |
| * This is optional for compendial test method and specifications set according to BP/JP/Ph. Eur./USP. | |
| 3.2.P.4.5 | Excipients of Human or Animal Origin | | \* | \* |  |  |
| * For animal derived excipient, please refer to Annex 2 for registration requirements. | |
| 3.2.P.4.6 | Novel Excipients | |  |  |  |  |
| * The information provided should be as per full active substance section and submitted in section 3.2.A.3. | |
| 3.2.P.5 | Control of CTGTP | | |  |  |  |  |
| 3.2.P.5.1 | CTGTP Specification(s) | |  |  |  |  |
| * Release and stability indicating parameters should be clearly defined or differentiated. | |
| 3.2.P.5.2 | Analytical Procedures | |  |  |  |  |
| 3.2.P.5.3 | Validation of Analytical Procedures | |  |  |  |  |
| 3.2.P.5.4 | Batch Analyses | |  |  |  |  |
| 3.2.P.5.5 | Characteristics of Impurities | |  |  |  |  |
| 3.2.P.5.6 | Justification of Specification(s) | |  |  |  |  |
| 3.2.P.6 | Reference Standards or Materials | | |  |  |  |  |
| * The source of the reference standard (in-house or official with reference to compendia standard), used for the testing of the CTGT product, should be stated. * For in-house reference standards, the specifications of the reference standard are to be submitted. * Evidence of characterisation for in-house / working standards should be submitted. | | |
| 3.2.P.7 | Container Closure System (CCS) | | |  |  |  |  |
| * Complete technical information on the type of container closure used should be submitted. * A declaration of compliance to the appropriate international standards or pharmacopoeia, e.g. food contact EC/10/2011, Ph. Eur. Chapter 3, should be submitted. | | |
| 3.2.P.8 | Stability data | | |  |  |  |  |
| 3.2.P.8.1 | Stability Summary and Conclusions | |  |  |  |  |
| * The conclusion of the stability studies, stress studies, storage condition and proposed shelf-life period should be stated in the summary. * Information such as the batch size, date of manufacture, site of manufacture, container closure system, and source and batch number of active substance used for each CTGT product stability batch should be stated. * The stability batches should be manufactured by the same process and packaged in the same container closure system as that proposed for Singapore. | |
| 3.2.P.8.2 | Post-Approval Stability Protocol and Stability Commitment | |  |  |  |  |
| * This should be based on the proposed storage condition. If any results fall outside of the retest / shelf-life specifications, these should be reported together with the proposed action. | |
| 3.2.P.8.3 | Stability Data | |  |  |  |  |
| * For in-use stability studies, information such as the batch number, in-use storage condition(s), length of storage prior to start of in-use stability testing and completed in-use test intervals should be stated. | |
| 3.2.A | Appendices | | | |  |  |  |  |
| 3.2.A.1 | Facilities and Equipment | | |  |  |  |  |
| 3.2.A.2 | Adventitious Agents Safety Evaluation | | |  |  |  |  |
| 3.2.A.3 | Excipients | | |  |  |  |  |
| 3.2.A.4 | Environmental Risk Assessment† [Genetic Modification Advisory Committee (GMAC) recommendations]  †Applicable to CTGTP containing genetically modified organisms (e.g. viral vectors) | | | \* | \* |  |  |
| 3.2.R | Regional Information | | | | \* | \* |  |  |
| 3.2.R.1 | ANNEX 2 Checklist for the registration of Cell, Tissue and Gene Therapy Products containing materials of animal origin | | |
| 3.3 | Literature References | | | |  |  |  |  |

**Module 4 - Non-Clinical Study Reports**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Section** | **Documents** | | **Evaluation Route** | | **HSA Screening** | |
| **F** | **A** | **Submitted?** | **Remarks** |
| 4.1 | Table of Contents of Module 4 | |  | \* |  |  |
| 4.2 | Study Reports | |  |  |  |  |
| 4.2.1 | Pharmacology (Primary Pharmacodynamics, Secondary Pharmacodynamics, Safety Pharmacology) |  | \* |  |  |
| 4.2.2 | Pharmacokinetics (Analytical Methods and Validation Reports, Biodistribution) |  | \* |  |  |
| 4.2.3 | Toxicology (Single-Dose Toxicity, Repeated-Dose Toxicity, Genotoxicity, Carcinogenicity, Reproductive and Developmental Toxicity, Local Tolerance) |  | \* |  |  |
| 4.2.4 | Additional Supporting Studies | \* | \* |  |  |
| 4.3 | Literature References | |  |  |  |  |

**Module 5 - Clinical Study Reports**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Section** | **Documents** | | **Evaluation Route** | | **HSA Screening** | |
| **F** | **A** | **Submitted?** | **Remarks** |
| 5.1 | Table of Contents of Module 5 | |  |  |  |  |
| 5.2 | Tabular Listing 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 provided in the Clinical Overview/Summary. * A declaration letter is to be provided to HSA to indicate whether the clinical trial formulation or the manufacturing process used in the pivotal studies is the same as the commercial formulation proposed for registration in Singapore. * 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 comparability 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 Human Pharmacokinetic Studies | \* | \* |  |  |
| 5.3.4 | Reports of Human Pharmacodynamic Studies | \* | \* |  |  |
| 5.3.5 | Reports of Efficacy and Safety Studies |  |  |  |  |
| * Study reports of ALL clinical trials (including the appendices and tables) should be submitted. * The clinical trials should be conducted using the CTGT 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 information on the comparability between the clinical trial formulation and the proposed 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 proposed for registration in Singapore. * Pivotal trials conducted in compliance with Good Clinical Practice (GCP) are required to support each requested indication and dosing regimen, 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 | Literature References | |  |  |  |  |
| 5.5 | Risk management plan (RMP) documents ***(Mandatory for all NDA-1)*** | | \* | \* |  |  |
| 5.6 | Other Supporting Documents | | \* | \* |  |  |