APPLICATION FOR GMP CONFORMITY ASSESSMENT VIA GMP DOCUMENTARY EVIDENCE VERIFICATION APPLICATION (DEVA) FOR CELL, TISSUE AND GENE THERAPY PRODUCTS (CTGTP)

NOTES:

1. Your company must have a CRIS account with HSA and obtain a client code in order to submit this application.

2. This form is intended for a local sponsor to request for Good Manufacturing Practice (GMP) compliance of overseas manufacturer(s), also known as documentary evidence verification application (DEVA), to be submitted as part of product registration of a CTGTP.

3. Each form is intended for one applicable overseas manufacturing site. Separate forms are to be submitted if there are multiple overseas manufacturing sites even if it is the same manufacturer.

4. The form should be completed by the local sponsor (applicant) who is authorised by the company to submit the application. The applicant will be the point of contact for all clarification or issues related to this application.

5. This form may take you 30 minutes to fill in. You will need the following information to fill in the form:
   a. Details of local sponsor and applicant
   b. Details of overseas manufacturer
   c. Supporting documents

6. All entries shall be made in English. All the information required in the form should be supplied as far as they are applicable.

7. If the space provided in any section of this form is insufficient, the information pertaining to the affected section(s) may be submitted as an attachment together with this completed form as a PDF document. Please indicate the section numbers clearly in the attachment for ease of reference.

8. File names of the submitted documents per Section 8 should be assigned according to the recommended format such as “8.1_Product Name_GMP Cert”, “8.2_Product Name_Inspection Report”, “8.3_Product Name_List of Regulatory Inspections”.

9. This completed form with its relevant supporting documents should be submitted to the Advanced Therapeutic Product Branch (ATPB) as part of the submission for CTGTP product registration.

APPLICATION FOR GMP CONFORMITY ASSESSMENT VIA GMP DOCUMENTARY EVIDENCE VERIFICATION APPLICATION (DEVA) FOR CELL, TISSUE AND GENE THERAPY PRODUCTS (CTGTP)

Name of CTGTP Product:	

Information of Overseas Manufacturer Site	
Name of Manufacturer Site:	
Address of Manufacturer Site:	_____ _____ _____ _____

Type of Manufacturer

(You may select more than one option)

- ☐ CTGTP Finished Product Manufacturer
- ☐ Active Substance Manufacturer used in manufacture of CTGTP
- ☐ CTGTP Starting Materials Manufacturer such as Viral Vector Manufacture used in the manufacture of CTGTP
- ☐ Others, please specify: _____

Responsible Activities / Manufacturing Processes

(You may select more than one option)

- ☐ Manufacture of Fully Packaged Finished Product
- ☐ Bulk Production (Prior to Secondary Packaging)
- ☐ Bulk Production (Prior to Sterile Filling)
- ☐ Sterilisation and/or Sterile Filling Only
- ☐ Partial Bulk Production (i.e. only one or more specific manufacturing steps were performed) (*Please provide details of the manufacturing steps*):

  _____
- ☐ Manufacture of Starting Materials such as Viral Vector
- ☐ Manufacture of Active Substance only
- ☐ Secondary Packager Only
- ☐ Others, please specify: _____

Section 1 - Company Information (Local Sponsor)	
1.1 Name of Company:	
1.2 UEN and Client Code:	
1.3 Company Address	
1.3.1 Postal Code:	
1.3.2 Block/House No. :	
1.3.3 Level – Unit:	
1.3.4 Street Name:	
1.4.5 Building Name:	
1.4 Billing Address (if different from Company Address)	
1.4.1 Postal Code:	
1.4.2 Block/House No.:	
1.4.3 Level – Unit:	
1.4.4 Street Name:	
1.4.5 Building Name:	
Section 2 - Applicant Information (Local Sponsor)	
2.1 Name (Mr/Ms/Mrs/Mdm/Dr):	
2.2 Designation:	
2.3 Contact Number:	
2.4 Contact Email address:	
Section 3 - Overseas Manufacturer Information	
3.1 Name of Overseas Manufacturer:	
3.2 Overseas Manufacturing Site Address	
3.2.1 Postal Code:	
3.2.2 Block/House No.:	
3.2.3 Level – Unit:	

3.2.4 Street Name:	
3.2.5 Building Name:	
3.2.6 Country:	
3.2.7 Contact Email address:	
3.2.8 Contact number:	

3.3 Additional Manufacturing Site Address (*if different from above*)

(Please include additional field for each address if there are more than one)

☐ QC Only

☐ Warehouse Storage and Handling Only

☐ Not applicable

3.3.1 Postal Code:	
3.3.2 Block/House No.:	
3.3.3 Level – Unit:	
3.3.4 Street Name:	
3.3.5 Building Name:	
3.3.6 Country:	

3.4 Storage Condition (For Storage and Handling site only)

3.4.1 Temperature:

☐ Non-cold chain (> 8°C)

☐ Cold chain (≤ 8°C)

☐ Cryogenic storage temperature _____°C

3.4.2 Relative Humidity: Min% - Max%: _____

3.4.3 Other Storage Conditions: _____

Section 4 - Scope of GMP Evidence

Manufacturing:

☐ CTGTP (finished product)

☐ Active substances used in the manufacture of CTGTP

☐ Starting materials used in the manufacture of CTGTP

☐ Secondary Packaging Only

Section 5 - Manufacturing Operations

5.1 Manufacturing process:

Type of dosage form	Aseptically prepared
Large volume liquids (>100 ml/unit)	☐
Semi-solids	☐
Small volume liquids (≤100 ml/unit)	☐
Solids and implants	☐
Others, please specify: _____	☐

5.2 Type of CTGTP:

☐ Cell or tissue therapy product

☐ Gene therapy product

☐ CTGTP combined with a therapeutic product or a medical device

☐ Active substances, please specify: _____

☐ Starting materials, please specify: _____

☐ Others, please specify: _____

5.3 Packaging:

☐ Secondary packaging

5.4 Quality Control Testing:

- ☐ Chemical / Physical
- ☐ Microbiological
- ☐ Biological
- ☐ Not applicable

5.5 Other manufacturing activities

- ☐ Manufacture of starting materials
- ☐ Manufacture of active substances
- ☐ Manufacture of products other than CTGTP
- ☐ Manufacture involving viral vectors or viruses
- ☐ Manufacture of pathogenic organisms (biosafety level 3 and 4)
- ☐ Sterilisation of active substances/starting materials/finished product
- ☐ Others, please specify: _____
- ☐ Not applicable

5.6 Batch Release

Is the manufacturer responsible for performing the final batch release (including release testing of products or approving or certifying the batch for release)?

☐ Yes ☐ No, Clarifying remarks (if any) _____

5.7 Sterilisation of starting materials, active substances and finished products:

☐ Filtration	☐ Gamma irradiation
☐ Dry heat	☐ Others (please specify):
☐ Moist heat	_____
☐ Chemical	☐ Not applicable
☐ Electron beam	

Section 6 - Outsourced activities

☐ Manufacturing *(fill in section 6.1)*

☐ Warehouse *(fill in section 6.2)*

☐ QC testing *(fill in section 6.3)*

☐ None

Are written contracts or quality agreements with all outsourced sites in place?

☐ Yes (Attach in Section 8) ☐ No

If No, please explain why:

_____

_____

_____

6.1 Contract Manufacturer Particulars	
6.1.1 Name of contract manufacturer:	
6.1.2 Name of contract manufacturer:	
6.1.3 Name of contract manufacturer:	
6.1.4 Name of contract manufacturer:	

6.2 Contract Warehouse Particulars (attach additional sheets if necessary)	
6.2.1 Name of contract warehouse:	
6.2.2 Address of contract warehouse	
6.2.2.1 Postal Code:	
6.2.2.2 Block/House No:	
6.2.2.3 Level – Unit:	
6.2.2.4 Street Name:	
6.2.2.5 Building Name:	
6.2.2.6 Country:	
6.2.2.7 Contact Email Address:	
6.2.2.8 Contact Number:	

6.2.3 Storage Condition:

6.2.3.1 Temperature:

☐ Non-cold chain (> 8°C)

☐ Cold chain (≤ 8°C)

☐ Cryogenic storage temperature _____ °C

6.2.3.2 Relative Humidity: Min% - Max% _____

6.2.3.3 Other Storage Conditions: _____

6.3 Contract Testing Laboratory Particulars *(attach additional sheets if necessary)*	
6.3.1 Name of contract testing laboratory:	
6.3.2 Address of contract testing laboratory	
6.3.2.1 Postal Code:	
6.3.2.2 Block/House No:	
6.3.2.3 Level – Unit:	
6.3.2.4 Street Name:	
6.3.2.5 Building Name:	
6.3.2.6 Country:	
6.3.2.7 Contact Email Address:	
6.3.2.8 Contact Number:	

6.3.3 Testing activities outsourced to contract testing laboratory

Testing activity	**Type of Test performed**
☐ Finished product testing including in-process testing for batch release	☐ Chemical / Physical ☐ Microbiological ☐ Biological
☐ Starting materials testing	☐ Chemical / Physical ☐ Microbiological ☐ Biological
☐ Stability testing on finished products or active substances or starting materials	☐ Chemical / Physical ☐ Microbiological ☐ Biological
☐ Others, e.g. environmental monitoring for sterile manufacturing, identification of microorganisms (please state below): _____ _____ _____	☐ Chemical / Physical ☐ Microbiological ☐ Biological

Section 7 - Particulars of Key Personnel	
7.1 Person in-charge of Production	
7.1.1 Name:	
7.1.2 Designation:	
7.1.3 Directly reporting to:	
7.1.4 Contact Email or Number:	
7.1.5 Experience:	
7.1.6 Qualifications (relevant to this application):	
7.2 Person in-charge of Quality Operations	
7.2.1 Name:	
7.2.2 Designation:	
7.2.3 Directly reporting to:	
7.2.4 Contact Email or Number:	
7.2.5 Experience:	
7.2.6 Qualifications (relevant to this application):	

Section 8 - Supporting Documents		
The following documents (where applicable) should be submitted with this completed form. Tick the checkboxes to confirm that the supporting documents have been included with this form. Otherwise, check "N/A" box. Refer to Notes Section (Page 1) for the recommended file names assignation for the submitted documents.		
Evidence of GMP Compliance		
8.1	☐ Submitted **GMP Evidence Issued By:** _____ _____ _____ **Expiry Date:** _____	**<u>Valid documentary GMP evidence</u>** such as latest GMP Certificate issued by PIC/S member authority or equivalent such as US FDA Cover Letter with EIR Inspection Report. <u>Note1:</u> Scope of documentary GMP evidence should cover the manufacturing activities stated in this form and includes the names of the products or active substances to be registered for Singapore. <u>Note 2:</u> Redacted certificate or report will not be accepted. For expiring or expired GMP evidence , HSA reserves the right to request for an updated document as part of evaluation.
8.2	☐ Submitted	**<u>Corresponding inspection report</u>** <u>Note 1:</u> Scope of inspection report should cover the manufacturing activities stated in this form and include the name(s) of the product(s) or active substance(s) to be registered for Singapore. <u>Note 2:</u> Redacted report will not be accepted. <u>Note 3:</u> The corresponding GMP inspection report which is performed by the same PIC/S member regulatory authority should indicate: a. Name of manufacturer b. Manufacturing address c. Date of the inspection (not more than 3 years ago) d. Standard of GMP guidelines used for assessment e. List of manufacturing activities inspected – list of products (product intended to be listed in the application should be included in the scope of the GMP inspection), processes, QC testing, batch release including facilities

8.3	☐ Submitted ☐ N/A	**<u>Additional Supporting Documents:</u>** **a)** List of all on-site regulatory inspections for the last 3 years. This list should include the name(s) of the inspecting authorities, audit dates, scope, deficiencies and the outcome of the inspection
	☐ Submitted ☐ N/A	**b)** List of regulatory action(s) (including product alerts, warning letters, import alerts or recalls) (if applicable) Where applicable, provide further details about or event that occurred. This should include information about the subsequent investigations and root cause analysis conducted, and any resulting corrective or preventative actions that were implemented
	☐ Submitted ☐ N/A	**c)** Latest Site Master File of the drug product and/or drug substance manufacturing site including all appendices per the PIC/S explanatory notes for pharmaceutical manufacturer(accessible at https://www.picscheme.org/). This document should also include the list of products manufactured or assembled at the same site.
	☐ Submitted ☐ N/A	**d)** List of products intended for supply to SG specific to this application (please provide information on the product name, international non-proprietary name (INN), dosage form and other relevant information)
	☐ Submitted ☐ N/A	**e)** Written contract or quality agreement with contract acceptor(s) (if applicable). A latest copy (valid within 3 years assessment) of the certificate or report that indicates the contract acceptor complies with relevant quality system standard (i.e. GMP, GDP, ISO 17025) for the specific outsourced activities. Note: The **signed** quality agreement should meet the full requirements of chapter 7 of the PIC/S guide to Good Manufacturing Practice for medicinal products – Part I.

	☐ Submitted ☐ N/A	**f)** Written contract or quality agreement with the Singapore product registrant (marketing authorisation holder). The agreement should: ○ clearly identifies the products, steps of manufacture (activities) and manufacturing site (where there are multiple sites contained in the one agreement) relevant to the scope of your GMP Compliance Assessment application ○ clearly describes the role of each party subject to the agreement, particularly the communication processes agreed upon has been signed by all parties to the agreement
	☐ Submitted ☐ N/A	**g)** Other supporting documents. Please specify: _____

Section 9 - Declaration	
☐ I, on behalf of my company, confirm that the information submitted in this application is true and accurate. ☐ I, on behalf of my company, confirm that there are no additional amendments made to this application or to the attachments thereof.	
Name of Applicant:	Signature and Date:

Application Fee

Verification of compilance with GMP Standard (for overseas CTGTP manufacturer)	$ 650

An invoice for the applicable fee will be sent to the billing address. For companies on the GIRO scheme, the fee will be deducted from the GIRO-linked bank account. For companies not on the GIRO scheme, the fee can be made by bank transfer. More information will be provided on the invoice.