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Ministry of Health Malaysia
Lot 36, Jalan Universiti, 46200 Petaling Jaya, Selangor.
Tel. No. : 03-78835400
Fax No. : 03-79571200
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GUIDANCE NOTE FOR BIOLOGICAL PRODUCTS FACILITY ESTABLISHMENT IN MALAYSIA

2nd Edition
1st October 2017

Section GMP 3

Centre for Compliance and Licensing

National Pharmaceutical Regulatory Division (NPRA)

TABLE OF CONTENTS

1.0 INTRODUCTION

The guide is established to facilitate and provide guidance to organisations in setting up a manufacturing facility for medicine-based biological products in Malaysia, including cell and tissue products, blood/plasma derived products and biotechnology products. It is also a guide for a laboratory / manufacturing facility to obtain Good Manufacturing Practice (GMP) status from National Pharmaceutical Regulatory Division (NPRA).

2.0 GUIDELINES IN USE

Applicants must be fully aware and understand the legal requirements and guidelines used in initiating the set up of manufacturing facility in Malaysia. For this purpose, the guide enlisted the related regulations and guidelines for applicants' reference;

a) *Regulations*

1. Control of Drugs and Cosmetics Regulations 1984
2. Sales of Drugs Act 1952
3. *Arahan Pengarah Kanan Perkhidmatan Farmasi Bilangan 6 Tahun 2017: Direktif Kuatkuasa Pelaksanaan* Guidance Document and Guidelines for Registration of Cell and Gene Therapy Products (CGTPS), December 2015 *dan* Good Tissue Practice Guideline, 2nd Edition, December 2015; 29 May 2017

b) *Guidelines*

1. PIC/S Guide to Good Manufacturing Practice for Medicinal Product and its related Annexes (http://www.picscheme.org)
2. Drug Registration Guidance Document
3. Guideline on Good Distribution Practice
4. Guidance Document and Guidelines for Registration of Biosimilar in Malaysia
5. Guidance Document and Guidelines for Registration of Cell and Gene Therapy Products (CGTPs) in Malaysia
6. Good Tissue Practice Guideline

Please refer npra.moh.gov.my for current guidelines 2 – 6.

The list is non-exhaustive. Applicants are encouraged to acquire additional information and to share other guidelines used with NPRA.

3.0 REGULATORY PROCESS DESCRIPTION

3.1.1 Product Classification

The purpose of this step is to classify the product of intent, which by the regulations Sale of Drugs Act 1952 and Control of Drugs and Cosmetics 1984, requires to be registered. Please apply through form **NPRA-300.1 Product Classification Application**. Beginning 1st January 2016, each product classification will be charged at RM300/product.

3.1.2 Facility Layout Submission

Please submit an application through **BPFK-503** ***Application for the Evaluation of Manufacturing Plant Layout*** along with the required supporting documents as stated in the application form. Currently this service is charged at RM1,000 for new application and RM500 for any further amendment on an approved layout.

During this stage, the applicant required to present a concise presentation of **company's background, product/s information, a clear, defined facility layout plan, project progress (i.e. Gantt Chart)** along with the **manufacturing process flow** and other related information at CCL, NPRA. The presentation will be arranged between the company and the officer in charge.

Applicants are **strongly advised** to consult other related authorities such as Medical Practise Division or CKAPS, Ministry of Health, local municipal council, fire department or others, for any issue pertaining to the facility set up.

3.1.3 Preparation of Quality Management System (QMS)

Upon the facility layout plan and other authorities' approval, applicant may begin the set up of the Quality Management System for the facility according to guidelines mentioned in Chapter 2.0 in this document. This includes the construction of the facility, qualifications of equipments and Standard Operating Procedures (SOPs) preparation, process validation, etc.

In case of delay of any sort, applicant is responsible to inform CCL through official letters or e-mails prior to the agreed completion date. In failure to do so, may result in new application submission.

Once the preparation finalised, an inspection will be conducted. Prior which, applicant is required to apply through **online system QUEST 3+ for Good Manufacturing Practice (GMP) Inspection**. the inspection is charged at RM1,000/day/inspector (maximum RM10,000).

Note: All mentioned document in this chapter are obtainable from npra.moh.gov.my

3.1.4 Inspections

There will be two types of inspection conducted depending on the product category as aforementioned.

1. Pre-Certification is an inspection conducted on premises that are not regulated by Drug Control Authority.
2. Pre-Licensing inspection is meant for new manufacturing facilities that have never been licensed.
3. Pre-Approval inspection is for the additional manufacturing line in an existing licensed manufacturing facility.
4. Routine inspection is a surveillance inspection conducted according to a planned schedule.

3.1.5 Application for Additional Source/s for CGTPs

It is advisable for company to apply for additional source/s through the same procedure, or otherwise stipulated by NPRA.

4.0 DEPARTMENT/ PERSON IN-CHARGE

For any queries pertaining to this guidance note, applicants may contact;

GMP 3 Section
Centre for Compliance and Licensing
National Pharmaceutical Regulatory Division
Ministry of Health Malaysia
Lot 36 Jalan Universiti
46200 Petaling Jaya, SELANGOR

Telephone no.: 03 7801 8557 (Desk Officer)
Fax no.: 03 7957 1200
Website: npra.moh.gov.my

5.0 RELATED AUTHORITIES

For matters related to licensing of the private healthcare related facility, applicants are advised to contact;

Cawangan Kawalan Amalan Perubatan Swasta (CKAPS)
Bahagian Amalan Perubatan
Kementerian Kesihatan Malaysia
Aras 3, Blok E1, Kompleks Kerajaan Parcel E,
Pusat Pentadbiran Kerajaan Persekutuan,

62590 PUTRAJAYA

Telephone no. : 03-88831307 / 03-88831277 / 03-88831278
Fax no. : 03-88810901 / 03-88810902

E-mail address: ckaps@moh.gov.my

Website: http://medpcs.moh.gov.my

6.0 GLOSSARY

CCL	: Centre for Compliance and Licensing
CGTP	: Cell and Gene Therapy Products
CKAPS	: *Cawangan Kawalan Amalan Perubatan Swasta*
GMP	: Good Manufacturing Practice
GTP	: Good Tissue Practice

7.0 FREQUENTLY ASKED QUESTIONS (FAQs)

1. Does NPRA issue a manufacturing license after inspection?

   At the moment, the manufacturing license will be issued to biotechnology products manufacturers only.

2. Who should apply for the GMP Certificate?

   The manufacturer of registered product with Drug Control Authority (DCA) who intend to export products to overseas should apply the GMP Certificate. This certificate is charged at RM50/certificate.

3. Does cell and tissue establishment require an annual inspection?

   No. At the moment, the compliance status is valid for three (3) years.

   However, for biotechnology products manufacturers, after an acceptable compliance, they will be subjected to routine GMP inspection.

4. Is there any charge for the applications mentioned?

   Besides the aforementioned charges, there is no additional charge, otherwise mentioned.

5. What is a repacker?

   The definition can be referred from the Explanatory Notes for Repackers in the Drug Registration Guidance Document (DRGD) which obtainable from npra.moh.gov.my.

6. Who should I contact if I still have questions about the biological products?

   In relation to;
   a) Manufacturing facility set up / GMP related issue: GMP 3 Section, Centre for Compliance and Licensing, NPRA
   b) Product registration enquiry: Biotechnology Section, Centre for Product Registration, NPRA
   c) Clinical Trial enquiry: Investigational Product Trial Section, Centre for Investigational New Product, NPRA

Figure 1: General Inspection Process Flow for Biological Products (except for CGTPs)

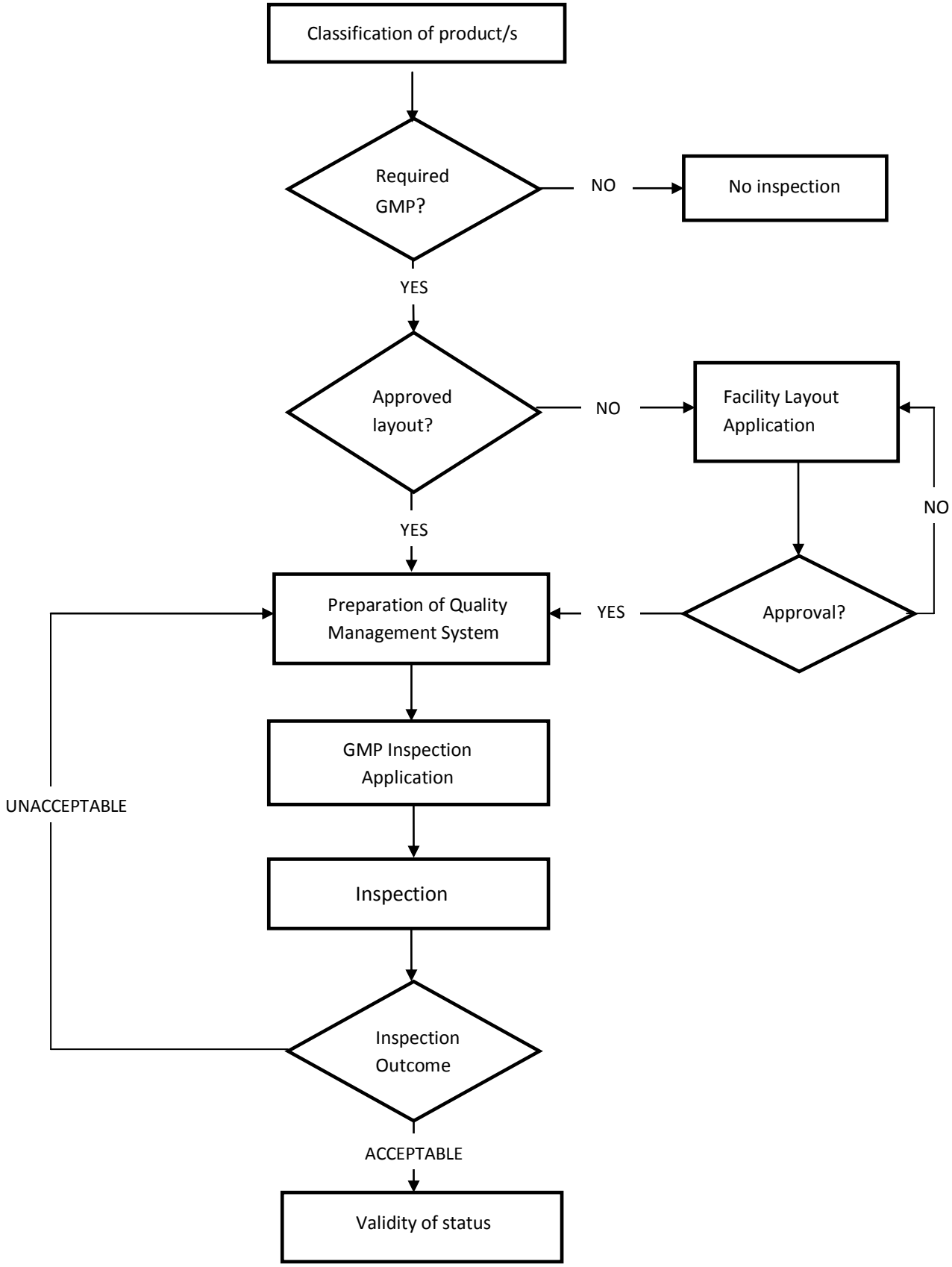
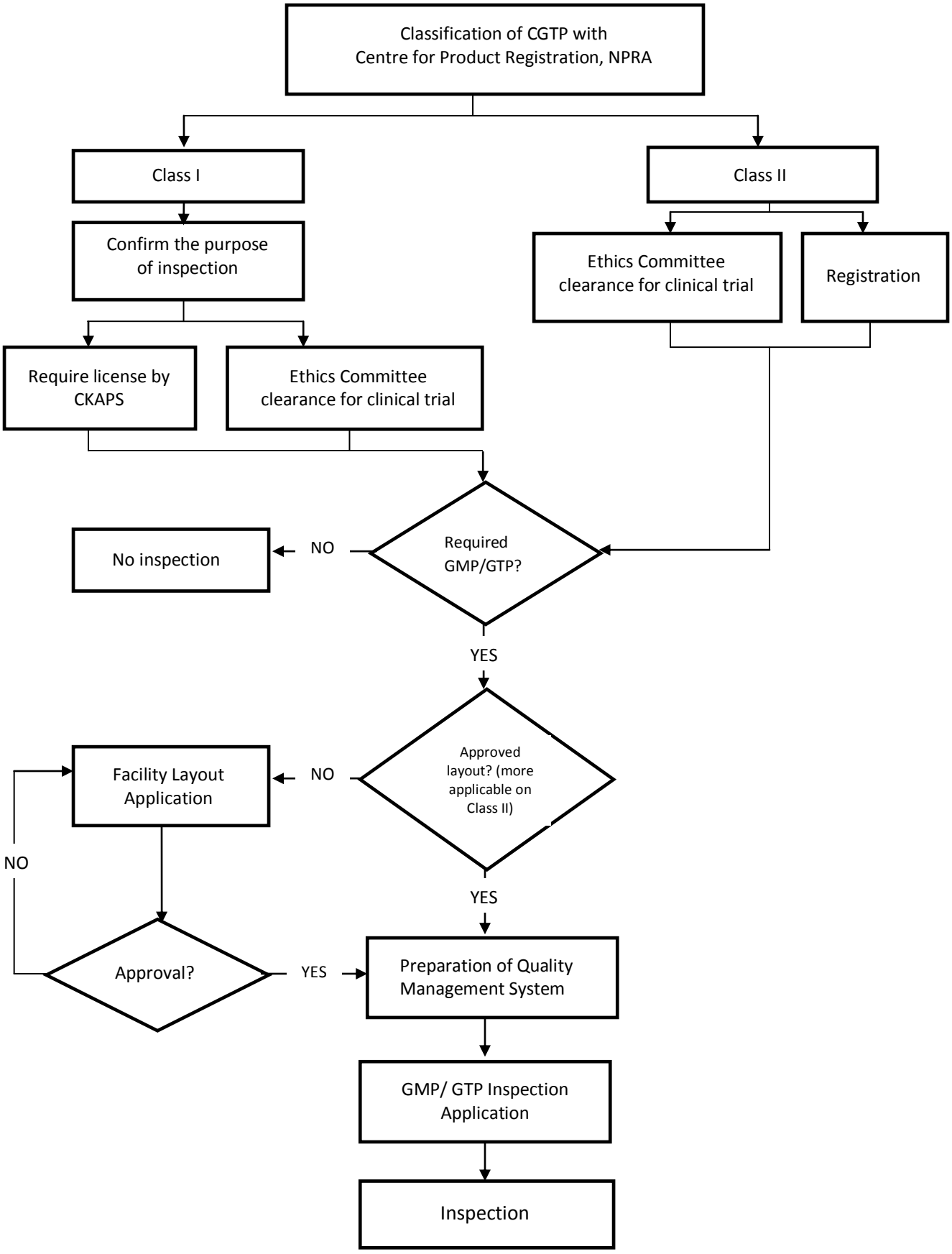


Figure 2: General Inspection Process Flow for Cell and Gene Therapy Facility (CGTPs)



Appendix – to be attached along with Facility Layout Application *or* GMP Inspection Application

<table>
<tr><th colspan="6">ACTIVITY DESCRIPTION</th></tr>
<tr><td colspan="2">Company Name & Address:

Type of Company:</td><td colspan="4">Government: ☐ MOH ☐ Non-MOH
☐ Non-Government</td></tr>
<tr><td colspan="6">Part I (Application):</td></tr>
<tr><td rowspan="3"></td><td colspan="2">Application type:</td><td colspan="2">Required to be licensed by CKAPS
(please provide supporting document)</td><td>Layout approved by NPRA :</td></tr>
<tr><td>☐</td><td>New Source</td><td colspan="2">☐ Yes;</td><td>☐ Yes; Ref no.:
Date of approval:</td></tr>
<tr><td>☐</td><td>Additional source/s</td><td colspan="2">☐ No</td><td>☐ No</td></tr>
<tr><td colspan="6">Part II (Type of source/s):</td></tr>
<tr><td rowspan="8">*please separate different product/s name and active ingredients by semi colon (;) respectively</td><td colspan="2">Product type and source</td><td colspan="2">Product/s name*:</td><td>Product/s active ingredients*;</td></tr>
<tr><td>☐</td><td>a. Animal or plant source; non-transgenic</td><td colspan="2"></td><td></td></tr>
<tr><td>☐</td><td>b. Biotechnology fermentation / cell culture</td><td colspan="2"></td><td></td></tr>
<tr><td>☐</td><td>c. Virus or bacteria / fermentation / cell culture</td><td colspan="2"></td><td></td></tr>
<tr><td>☐</td><td>d. Animal sources; transgenic</td><td colspan="2"></td><td></td></tr>
<tr><td>☐</td><td>e. Human sources (go to Part IV)</td><td colspan="2"></td><td></td></tr>
<tr><td>☐</td><td>f. Human and/or animal sources (go to Part IV)</td><td colspan="2"></td><td></td></tr>
<tr><td>☐</td><td>g. Others: (please specify)

.....</td><td colspan="2"></td><td></td></tr>
<tr><td colspan="6">Part III (Activities conducted for a - d & g (if applicable)):</td></tr>
<tr><td rowspan="2"></td><td>☐</td><td>Collection</td><td>☐</td><td>Processing; such as manipulation, fermentation, centrifuge</td><td rowspan="2">☐ Others; (Please specify)

.....</td></tr>
<tr><td>☐</td><td>Fill and Finish</td><td>☐</td><td>Quality Control testing</td></tr>
</table>

Part IV: Types of Cell & Tissue Based Products and Functions (***for Cell & Tissue Based manufacturers only***)

Types of Cell & Tissue			Establishment functions								CGTPs Classification
			Recover	Screen	Test	Package	Process	Store	Label	Distribute	Class I **OR** Class II
a.	Bone		☐	☐	☐	☐	☐	☐	☐	☐	
b.	Cartilage		☐	☐	☐	☐	☐	☐	☐	☐	
c.	Cornea		☐	☐	☐	☐	☐	☐	☐	☐	
d.	Dura Mater		☐	☐	☐	☐	☐	☐	☐	☐	
e.	Embryo	☐ SIP ☐ Directed ☐ Autonomous	☐	☐	☐	☐	☐	☐	☐	☐	
f.	Fascia		☐	☐	☐	☐	☐	☐	☐	☐	
g.	Heart Valve		☐	☐	☐	☐	☐	☐	☐	☐	
h.	Ligament		☐	☐	☐	☐	☐	☐	☐	☐	
i.	Oocyte	☐ SIP ☐ Directed ☐ Autonomous	☐	☐	☐	☐	☐	☐	☐	☐	
j.	Pericardium		☐	☐	☐	☐	☐	☐	☐	☐	
k.	Peripheral blood stem cells	☐ Autologous ☐ Family related ☐ Allogeneic	☐	☐	☐	☐	☐	☐	☐	☐	
l.	Sclera		☐	☐	☐	☐	☐	☐	☐	☐	
m	Semen	☐ SIP ☐ Directed ☐ Autonomous	☐	☐	☐	☐	☐	☐	☐	☐	
n.	Skin		☐	☐	☐	☐	☐	☐	☐	☐	
o.	Somatic cell therapy products	☐ Autologous ☐ Family related ☐ Allogeneic	☐	☐	☐	☐	☐	☐	☐	☐	
p.	Tendon		☐	☐	☐	☐	☐	☐	☐	☐	
q.	Umbilical cord blood stem cells	☐ Autologous ☐ Family related ☐ Allogeneic	☐	☐	☐	☐	☐	☐	☐	☐	
r.	Vascular graft		☐	☐	☐	☐	☐	☐	☐	☐	
s.	Others:		☐	☐	☐	☐	☐	☐	☐	☐	

**SIP: Sexually Intimate Partner*

Part V

Supporting documents (to attach if available)
☐Classification letter from NPRA (mandatory)
☐*CKAPS license*
☐*Clinical Trial Import License / Clinical Trial Exemption*

-Document end-