KEMENTERIAN KESIHATAN MALAYSIA
(*Ministry of Health Malaysia*)
Bahagian Regulatori Farmasi Negara (NPRA)
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Ruj. Kami : NPRA.600-1/9/12 (30)
Tarikh : 19 September 2025

SEMUA PEMEGANG PENDAFTARAN PRODUK

SEMUA PERSATUAN BERKENAAN
(SEPERTI DI SENARAI EDARAN)

Tuan/Puan,

PEKELILING BERKENAAN PENGEMASKINIAN *GUIDANCE DOCUMENT AND GUIDELINES FOR REGISTRATION OF CELL AND GENE THERAPY PRODUCTS (CGTPs) IN MALAYSIA (SECOND EDITION)*

Saya dengan hormatnya merujuk kepada perkara di atas.

2. Seperti yang tuan/puan sedia maklum, Bahagian Regulatori Farmasi Negara (NPRA) telah menerbitkan *Guidance Document and Guidelines for Registration of Cell and Gene Therapy Products (CGTPs) in Malaysia* pada Januari 2016. Seterusnya, Direktif Bilangan 6 Tahun 2017 dengan rujukan (11) dlm. BPFK/PPP/07/25 Jld.1 bertarikh 29 Mei 2017 telah dikeluarkan untuk memaklumkan bahawa permohonan pendaftaran mandatori dan penguatkuasaan kawalan ke atas CGTPs kelas II bermula pada **1 Januari 2021.**

3. Walaubagaimanapun, Direktif Bilangan 19 Tahun 2020 dengan rujukan NPRA.600-1/9/13(10) bertarikh 14 Disember 2020 telah memberi kelonggaran bagi sesetengah CGTPs yang tidak berdaftar tetapi memenuhi kriteria yang telah ditetapkan, untuk terus dipasarkan di Malaysia jika telah lulus penyaringan peringkat pertama dan kedua dalam tempoh peralihan yang telah tamat pada **31 Disember 2024**.

4. Garis panduan ini telah dikemaskini selaras dengan perkembangan semasa bagi menjelaskan maklumat sedia ada dan juga mengambil kira penerbitan garis panduan terkini dari negara rujukan.

5. Pihak Berkuasa Kawalan Dadah (PBKD) dalam mesyuaratnya kali ke-**412** pada **8 September 2025** telah bersetuju dan mengambil maklum berkenaan pengemaskinian *Guidance Document and Guidelines for Registration of Cell and Gene Therapy Products (CGTPs) in Malaysia (Second Edition).* Rumusan pengemaskinian adalah seperti di **Lampiran A**.

6. Tarikh pelaksanaan *Guidance Document and Guidelines for Registration of Cell and Gene Therapy Products (CGTPs) in Malaysia (Second Edition)* seperti di **Lampiran B** adalah **SERTA-MERTA** dari tarikh pekeliling ini.

7. Selaras dengan pengemaskinian garis panduan ini, *Good Tissue Practice Guideline, 2nd Edition, December 2015* yang telah dikeluarkan oleh NPRA sebelum ini adalah terbatal memandangkan pengilangan produk CGTP perlu mematuhi keperluan garis panduan PIC/S yang terkini.

8. Sekiranya tuan/puan ingin mendapatkan maklumat lanjut, sila hubungi Seksyen Biologik, Pusat Penilaian Produk dan Kosmetik, NPRA. Pihak tuan/puan dikehendaki untuk mengambil maklum dan mematuhi perkara tersebut di atas.

Sekian, terima kasih

"MALAYSIA MADANI"

"BERKHIDMAT UNTUK NEGARA"

Saya yang menjalankan amanah,

(WAN NORAIMI BINTI WAN IBRAHIM) RPh. 1627
Pengarah
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s.k. 1. Pengarah Bahagian Penguatkuasaan Farmasi, KKM

2. Pengarah Bahagian Amalan dan Perkembangan Farmasi, KKM

3. Pengarah Bahagian Dasar dan Perancangan Strategik Farmasi, KKM

4. Timbalan Pengarah Pusat Komplians & Kawalan Kualiti, NPRA, KKM

5. Timbalan Pengarah Pusat Penilaian Produk & Kosmetik, NPRA, KKM

6. Timbalan Pengarah Pusat Koordinasi & Perancangan Strategik Regulatori, NPRA, KKM

LAMPIRAN A

PEKELILING BERKENAAN PENGEMASKINIAN *GUIDANCE DOCUMENT AND GUIDELINES FOR REGISTRATION OF CELL AND GENE THERAPY PRODUCTS (CGTPs) IN MALAYSIA (SECOND EDITION)*

Bil.	Edisi Pertama (2016)	Edisi Kedua (2025)
1.	***SCOPE***	
	*The following are **not included** in the framework:* • *Fresh viable human organs, or parts of human organs, for direct donor-to host transplantation.* • *Fresh viable human haematopoietic stem/ progenitor cells for direct donor to-host transplantation for the purpose of haematopoietic reconstitution.* • *Labile (fresh) blood and blood components (e.g. fresh frozen plasma, platelet rich plasma)* • *Unprocessed tissues including reproductive tissues (e.g. sperm, eggs, embryos for in vitro fertilization (IVF) and other assisted reproductive technology procedures)* • *Secreted or extracted human products (e.g. milk, collagen)* • *Samples of human cells or tissues that are solely for diagnostic purposes in the same individual* • *In vitro diagnostic devices* *The inclusion and exclusion lists are not self-contained. The lists may be amended as required.* ***4.2 GENE THERAPY PRODUCTS*** *Gene therapy products shall **not include**:* • *vaccines against infectious diseases* • **chemically synthesised nucleic acids (e.g. RNA, DNA, oligonucleotides)*	*The following are **not included** in the framework:* *a) Fresh viable human organs, or parts of human organs, for direct donor-to host transplantation.* *b) Fresh viable human haematopoietic stem/ progenitor cells for direct donor to-host transplantation for the purpose of haematopoietic reconstitution.* *c) Labile (fresh) blood and blood components (e.g. fresh frozen plasma, **platelet rich plasma**)* *d) Unprocessed **tissues including** reproductive tissues (e.g. sperm, eggs, embryos for in vitro fertilization (IVF) and other assisted reproductive technology procedures)* *e) Secreted or extracted human products (e.g. milk, collagen)* *f) Samples of human cells or tissues that are solely for diagnostic purposes in the same individual* *g) In vitro diagnostic devices* ***h) Established therapy standard of care (S) listed in the National Guidelines for Haemopoietic Stem Cell Therapy (Directive Bil 19 year 2020)*** ***i) Prophylactic vaccines for infectious diseases (e.g. mRNA, plasmid DNA, or viral-vectored vaccines)*** ***j) Cell or tissue lysates, extracellular vesicles and secretomes*** *The inclusion and exclusion lists are not self-contained. The lists may be amended as required.* ***Products indicated for general well-being, cosmetic/aesthetic purposes (anti-aging) and rejuvenation are not allowed unless they are intended for a medicinal purpose and substantiated by clinical studies with appropriate and clearly defined endpoints to demonstrate efficacy and safety.***

Bil.	Edisi Pertama (2016)	Edisi Kedua (2025)
2.	***ABOUT THIS FRAMEWORK***	
	The cross-boundary nature CGTPs involves a multidisciplinary approach; therefore its full control will also be subject to various other regulations (authorities), hence an integrated oversight is imperative, as follows: • *The clinical use/medical procedure of the product will be under the ambit of Medical Development Division and Medical Practice Division of the Ministry of Health, Malaysia* • *The device element of such products must comply with the Medical Device Act and regulations under the ambit of Medical Device Authority (MDA) of Malaysia, and* • *NPCB will ensure the medicinal product's quality, efficacy and safety.*	*The cross-boundary nature of CGTPs involves a multidisciplinary approach; therefore, its full control will also be subject to various other regulations (authorities), hence an integrated oversight is imperative, as follows:* a. *The clinical use/ medical procedure of the product will be under the ambit of Medical Development Division of the Ministry of Health, Malaysia* b. ***The private healthcare facilities and services (PHFS) will be under the Medical Practice Division of the Ministry of Health, Malaysia*** c. ***The medical practitioners are regulated by the Malaysian Medical Council (MMC) while dental practitioners are regulated by the Malaysian Dental Council (MDC)*** d. *The device element of such products must comply with the Medical Device Act and regulations under the ambit of Medical Device Authority (MDA) of Malaysia, and* e. *NPRA will ensure the product's quality, efficacy and safety.*
3.	***RISK CLASSIFICATION OF CELL AND GENE THERAPY PRODUCTS (CGTPS)***	
	7.1 CLASS I: LOWER RISK CELL THERAPY PRODUCTS *For lower risk products, the regulatory framework focuses on minimising the risk of transmission of infectious diseases. A product eligible for regulation as Class I is not subjected to premarket review requirements or approval. However, the product must be listed at the practitioner's premises. The product is further regulated by: (i) site/facility licensure and listing by the Medical Practice Division under the purview of the Private Healthcare Facilities and Services Act 1998 (Act 586) (ii) donor screening and testing (iii) Good Tissue*	***6.1 CLASS I CGTPs: LOWER RISK CELL THERAPY PRODUCTS (CTPs)*** *For lower risk products, the regulatory framework focuses on minimising the risk of transmission of infectious diseases.* ***A Class I CGTP is not regulated under the Control of Drugs and Cosmetics Regulations 1984. However, the private healthcare facilities and services (PHFS) are regulated through site or facility licensure by the Medical Practice Division under the Private Healthcare Facilities and Services Act 1998 (Act 586). The use of such products in clinical setting will be regulated under the Medical Development Divisions, Ministry of Health Malaysia.***

Bil.	Edisi Pertama (2016)	Edisi Kedua (2025)
	Practices (please refer to National Pharmaceutical Control Bureau, Ministry of Health: Good Tissue Practice Guideline, 2 nd Ed., December 2015) (iv) labelling (v) adverse event reporting and; (vi) inspection and enforcement.	***The medical practitioners are regulated by the Malaysian Medical Council (MMC) according to the Medical Act 1971 [Act 50] while dental practitioners are regulated by the Malaysian Dental Council (MDC) according to the Dental Act 2018 [Act 804], respectively.*** ***The manufacturer and practitioner are responsible for ensuring that the handling of cells/ tissue complies with Good Tissue Practice principles.***
4.	***CHEMISTRY, MANUFACTURING AND CONTROL (CMC)***	

Table 2: Illustrative guide to manufacturing activities for CGTPs

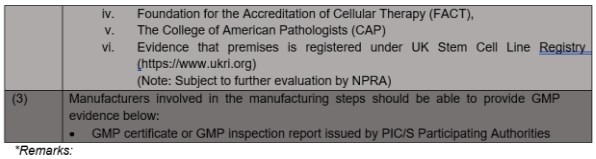
Type and source of material	Example product	Application of cGMP to manufacturing steps shown in grey			
Human and/or animal sources	Gene therapy: genetically modified cells	Donation, procurement and testing of starting tissue / cells	Manufacture vector and cell purification and processing	*Ex vivo* genetic modification of cells, Establish MCB, WCB or primary cell lot	Formulation, filling
	Somatic cell therapy		Establish MCB, WCB or primary cell lot	Cell isolation, culture purification, combination with non-cellular components	Formulation, combination, fil
	Tissue engineered products		Initial processing, isolation and purification Establish MCB, WCB or primary cell lot	Cell isolation, culture purification, combination with non-cellular components	Formulation, combination, fil
Animal source: non-transgenic	CGTPs immunosera	Collection of plant, organ, tissue or fluid	Cutting, mixing, and /or initial processing	Isolation and purification	Formulation, filling
Virus or bacteria/ fermentation/ cell culture	Viral or bacterial vaccines	Establishment and maintenance of MCB, WCB, MVS, WVS	Cell culture and/or fermentation	Inactivation when applicable, isolation and purification	Formulation, filling
Biotechnology fermentation/ cell culture	Gene therapy vaccines (viral and non-viral vectors, plasmids)	Establishment and maintenance of MCB, WCB, MSL, WSL	Cell culture and/or fermentation	Isolation, purification, modification	Formulation, filling
Increasing GMP requirements					

Example products	
Gene Therapy: mRNA	Linear DNA template preparation (1)
Gene Therapy: in vivo viral vector	Plasmid manufacturing (1)
Gene therapy: in vivo nonviral vectors (naked DNA, lipoplexes, polyplexes, etc.)	Plasmid manufacturing (1)
Gene therapy: ex-vivo genetically modified cells	Donation, procurement and testing of starting tissue / cells (0)
Somatic cell therapy	Donation, procurement and testing of starting tissue / cells (0)
Tissue engineered products	Donation, procurement and testing of starting tissue / cells (0)

Step of Processes involved		
In vitro cell free transcription (3)	mRNA purification (3)	Formulation, filling (3)
Establishment of MCB, WCB (3)	Vector manufacturing and purification (3)	Formulation, filling (3)
Establishment of bacterial bank (3)	Fermentation and purification (3)	Formulation, filling (3)
Plasmid manufacturing (1)	Ex-vivo genetic modification of cells (3)	Formulation, filling (3)
Vector manufacturing (2)		
Establishment of MCB, WCB or primary cell lot or cell pool (3)	Cell isolation, culture purification, combination with non-cellular components (3)	Formulation, combination, filling (3)
Initial processing, isolation and purification, establish MCB, WCB, primary cell lot or cell pool (3)	Cell isolation, culture, purification, combination with non-cellular components (3)	Formulation, combination, filling (3)

Note:

(0)	No GMP evidence required for the related manufacturer
(1)	Manufacturers involved in the manufacturing steps should be able to provide GMP evidence below: a. GMP certificate or GMP inspection report issued by: i. PIC/S Participating Authorities or; ii. World Health Organization (WHO) or; iii. Drug Regulatory Authority or b. Declaration from Qualified Person (QP) (for EU countries) or c. Self-declaration from competent person of related manufacturer or finished product manufacturer
(2)	Manufacturers involved in the manufacturing steps should be able to provide GMP evidence below: a. GMP certificate or GMP inspection report issued by: i. PIC/S Participating Authorities or; ii. World Health Organization (WHO) or; iii. Drug Regulatory Authority or b. Declaration from Qualified Person (QP) (for EU countries) or c. Accreditation evidence issued by (but not limited to): i. American Association of Blood Bank (AABB), ii. American Association of Tissue Bank (AATB), iii. Joint Accreditation Committee – International Society for Cellular Therapy & European Blood and Bone Marrow Transplantation (JACIE),

Bil.	Edisi Pertama (2016)	Edisi Kedua (2025)
		

	iv. Foundation for the Accreditation of Cellular Therapy (FACT), v. The College of American Pathologists (CAP) vi. Evidence that premises is registered under UK Stem Cell Line Registry (https://www.ukri.org) (Note: Subject to further evaluation by NPRA)
(3)	Manufacturers involved in the manufacturing steps should be able to provide GMP evidence below: • GMP certificate or GMP inspection report issued by PIC/S Participating Authorities

**Remarks:*
Qualified person is the Authorized Person of the manufacturer or importer as described in the country's Marketing Authorization under the national law. The content of a declaration or batch certificate is recommended in PIC/S Annex 16 or as required under national law, or as required to facilitate arrangements between National Competent Authorities.

5.	***COMPARABILITY CONSIDERATIONS***	
	NONE	***8.1.10 COMPARABILITY CONSIDERATIONS*** *Changes in the process such as equipment changes, raw materials, starting materials, processes, manufacturing sites are common and frequent especially in the early stages of development.* *The criticality of the changes and estimation of impact on the product should determine the amount of comparability data needed. Comparability study becomes a tool to demonstrate that the quality, safety and efficacy are not affected after the changes were introduced.* *The following are references from EMA/US FDA that can be referred:* *a. Questions and answers on comparability considerations for advanced therapy medicinal products (ATMP) (EMA)* *b. Guideline on quality, non-clinical and clinical aspects of medicinal products containing genetically modified cells (EMA)* *c. Reflection paper on design modifications of gene therapy medicinal products during development (EMA)* *d. Draft Guidance for Industry: Manufacturing Changes and Comparability for Human Cellular and Gene Therapy Products (US FDA)*

Bil.	Edisi Pertama (2016)	Edisi Kedua (2025)
6.	***PRE-CLINICAL STUDIES***	
	NONE	***Good Laboratory Practice (GLP)*** *It is generally expected that pivotal pre-clinical safety studies are carried out in conformity with the principles of OECD GLP. However, it is recognised that, due to the specific characteristics of CGTPs, it would not always be possible to conduct these studies in full conformity with GLP. For example, when certain technical expertise, unique animal care issues or endpoints may not be available at a GLP testing facility. If a pivotal pre-clinical safety study has not been conducted in conformity with the GLP principles, a proper justification should be submitted. This justification should also address the potential impact of the non-compliance on the reliability of the safety data.*
7.	***ANNEX I. ADDITIONAL REQUIREMENTS ON XENOTRANSPLANTATION***	
	*Xenotransplantation refers to procedure that uses living, **non-human** animal cells, tissues **or organs** for human therapeutic purposes. Non-viable animal tissue such as porcine heart valves and bone has been used for many years, offsetting limited supply of human equivalents. One example is pancreatic islets intended to treat diabetes.* *Xenotransplantation involves the transplantation, implantation, or infusion into a human recipient of either:* *a. live cells, tissues, or **organs** from a non-human animal source; or* *b. human body fluids, cells, tissues, or **organs** that have had ex vivo contact with live **non-human** animal cells, tissues, or **organs** (e.g. extracorporeal perfusion)*	*Xenotransplantation refers to procedure that uses living animal cells or tissues for human therapeutic purposes. Non-viable animal tissue such as porcine heart valves and bone has been used for many years, offsetting limited supply of human equivalents. One example is pancreatic islets intended to treat diabetes.* *Xenotransplantation involves the transplantation, implantation, or infusion into a human recipient of either:* a. *live cells or tissues from animal source; or* b. *human body fluids, cells or tissues that have had ex vivo contact with live animal cells or tissues (e.g. extracorporeal perfusion)*

Bil.	Edisi Pertama (2016)	Edisi Kedua (2025)
	NONE	*The evaluation requires special disciplines, expertise and skills and as such an application for registration for xenotransplantation products will only be accepted if the product had already been approved by any of our reference regulatory agencies.*
8.	***1.0 INTRODUCTION*** ***7.1 CLASS I: LOWER RISK CELL THERAPY PRODUCTS*** ***8.0 QUALITY ASSURANCE FOR CGTPs***	
	Good Tissue Practice Guideline, 2nd Ed., December 2015	***Removed***