

Cara Pembuatan Stem Cell Yang Baik dan Benar Sesuai Dengan Standard Internasional

Dr Sandy Qlintang

Head of Stem Cell and Cancer Institute

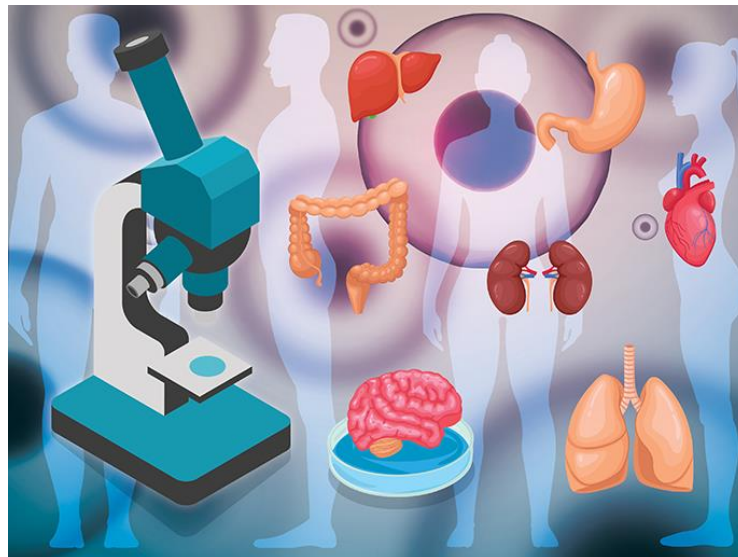
19 Juni 2022

Tiga Faktor Utama yang Mempengaruhi Keberhasilan Dalam Terapi Stem Cell

Pembuatan Stem Cell



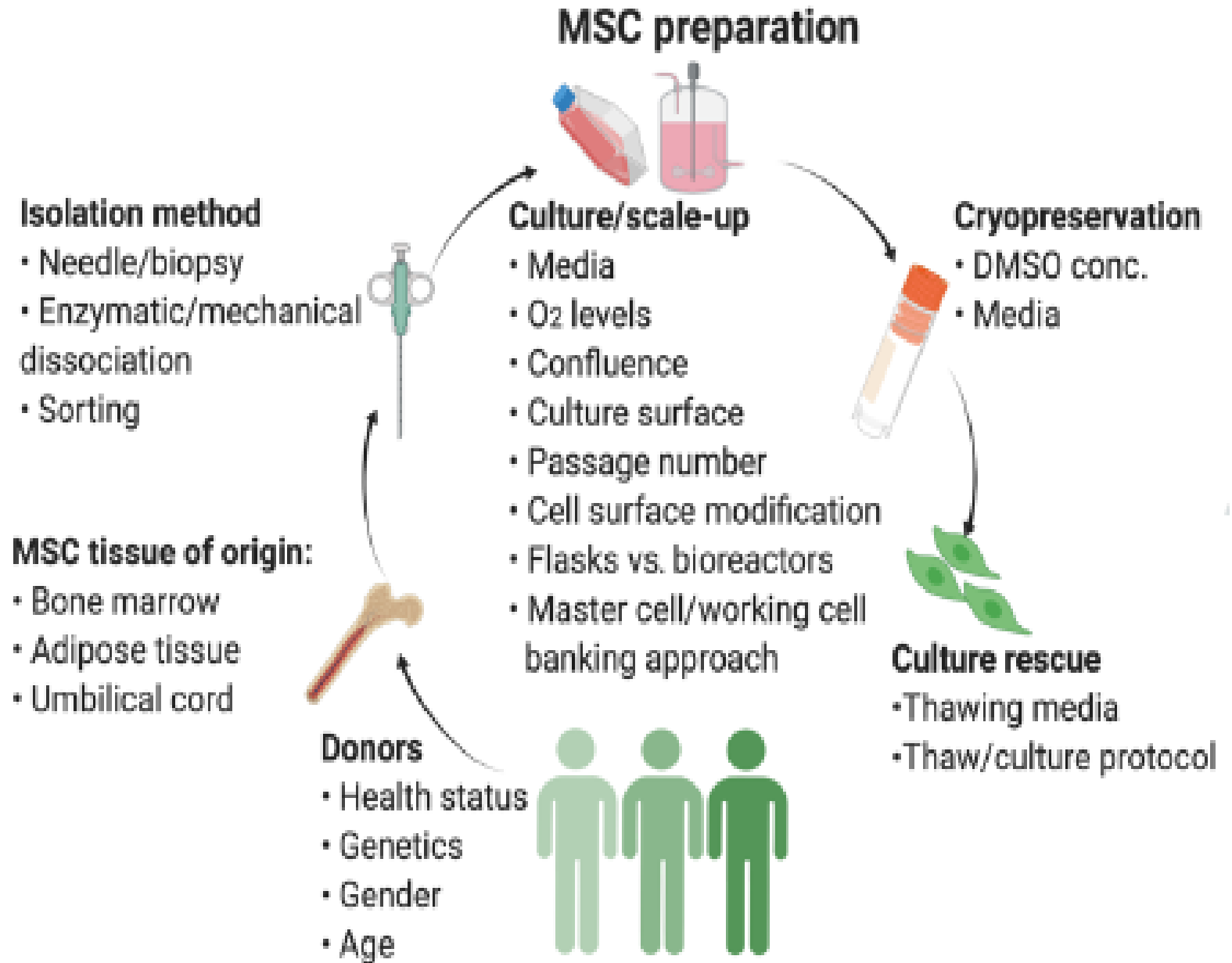
Cara Pemberian



Kondisi Pasien



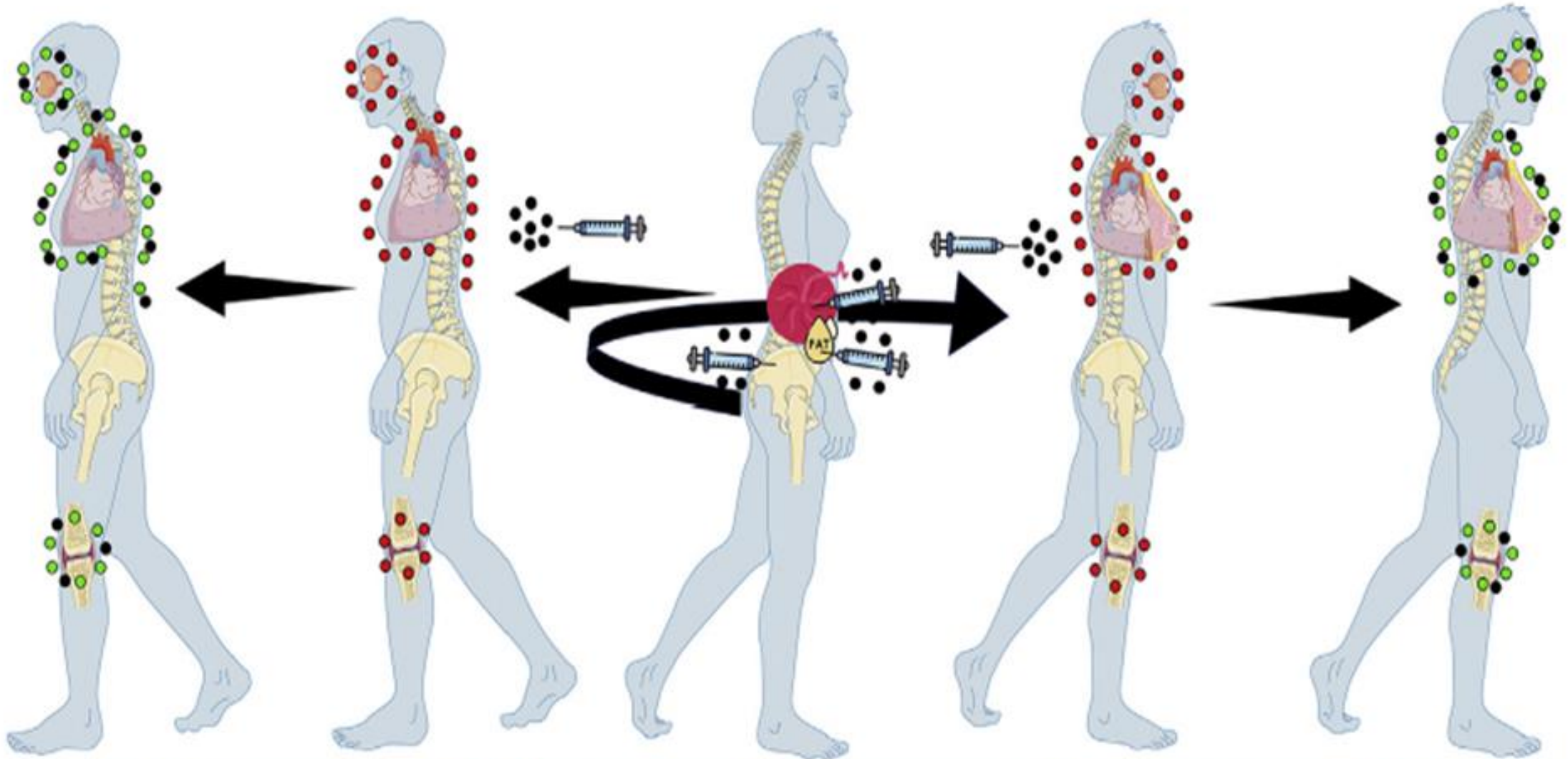
Pembuatan Stem Cells



Allogeneic

DONOR

Autologous



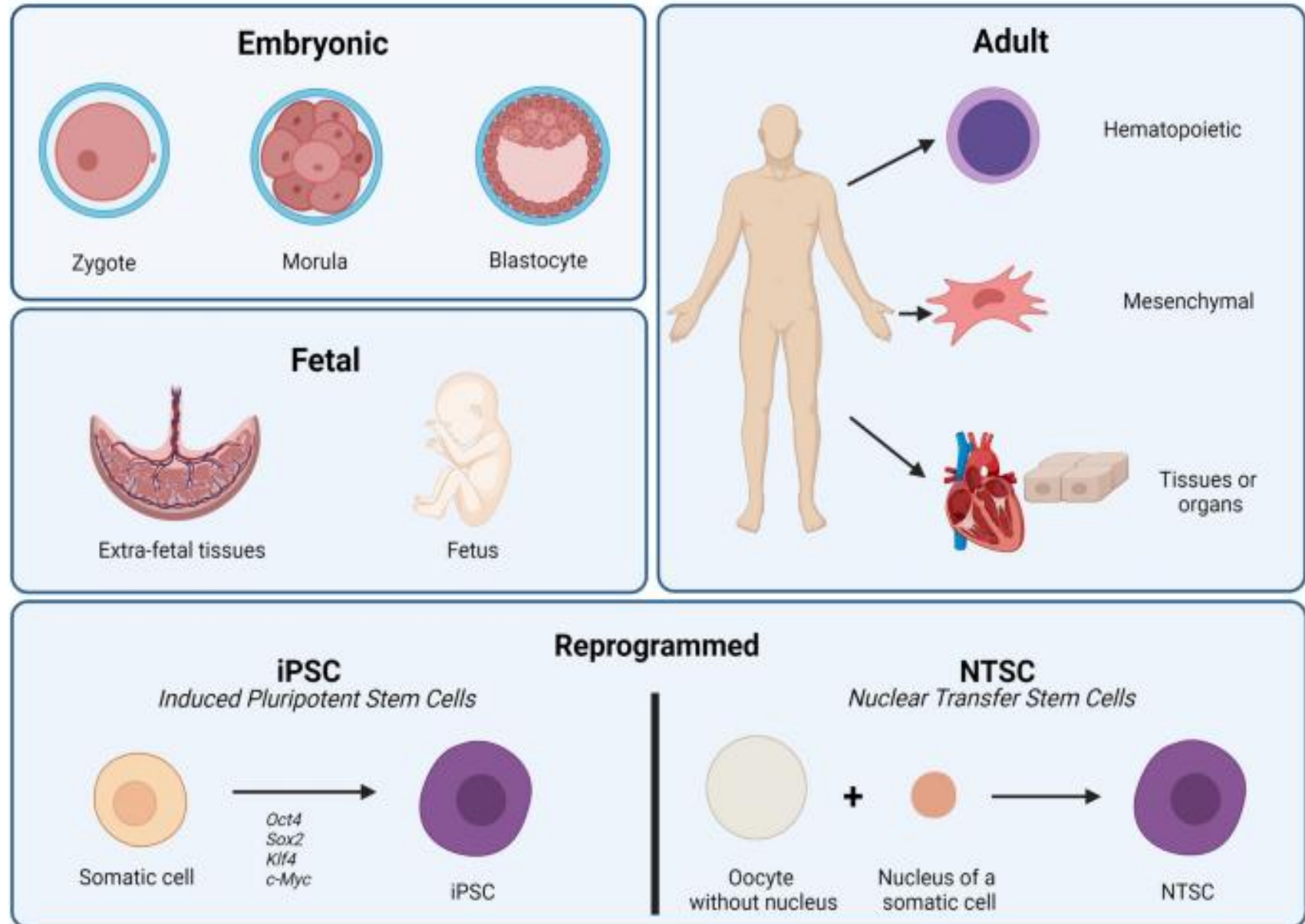
C

Main sources

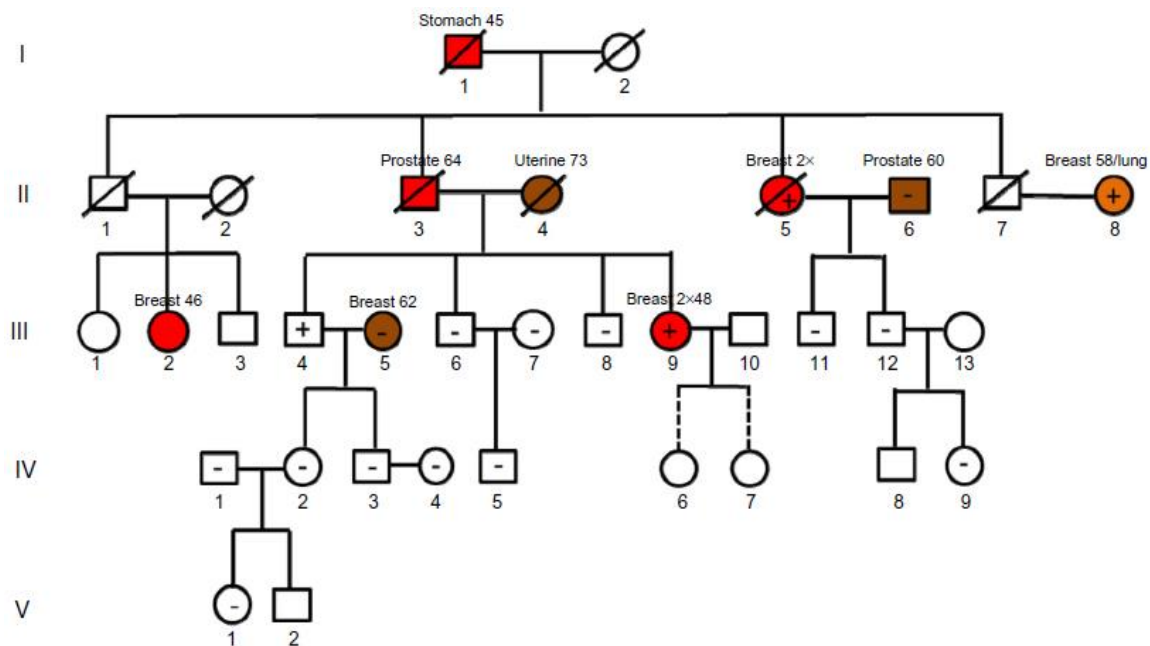
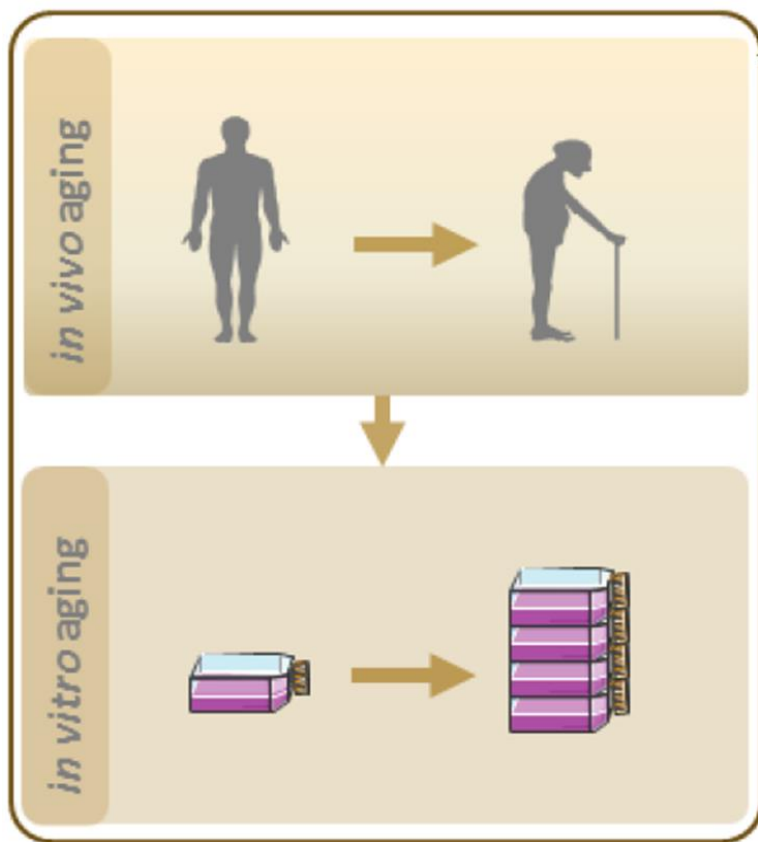


DONOR

Stem Cells

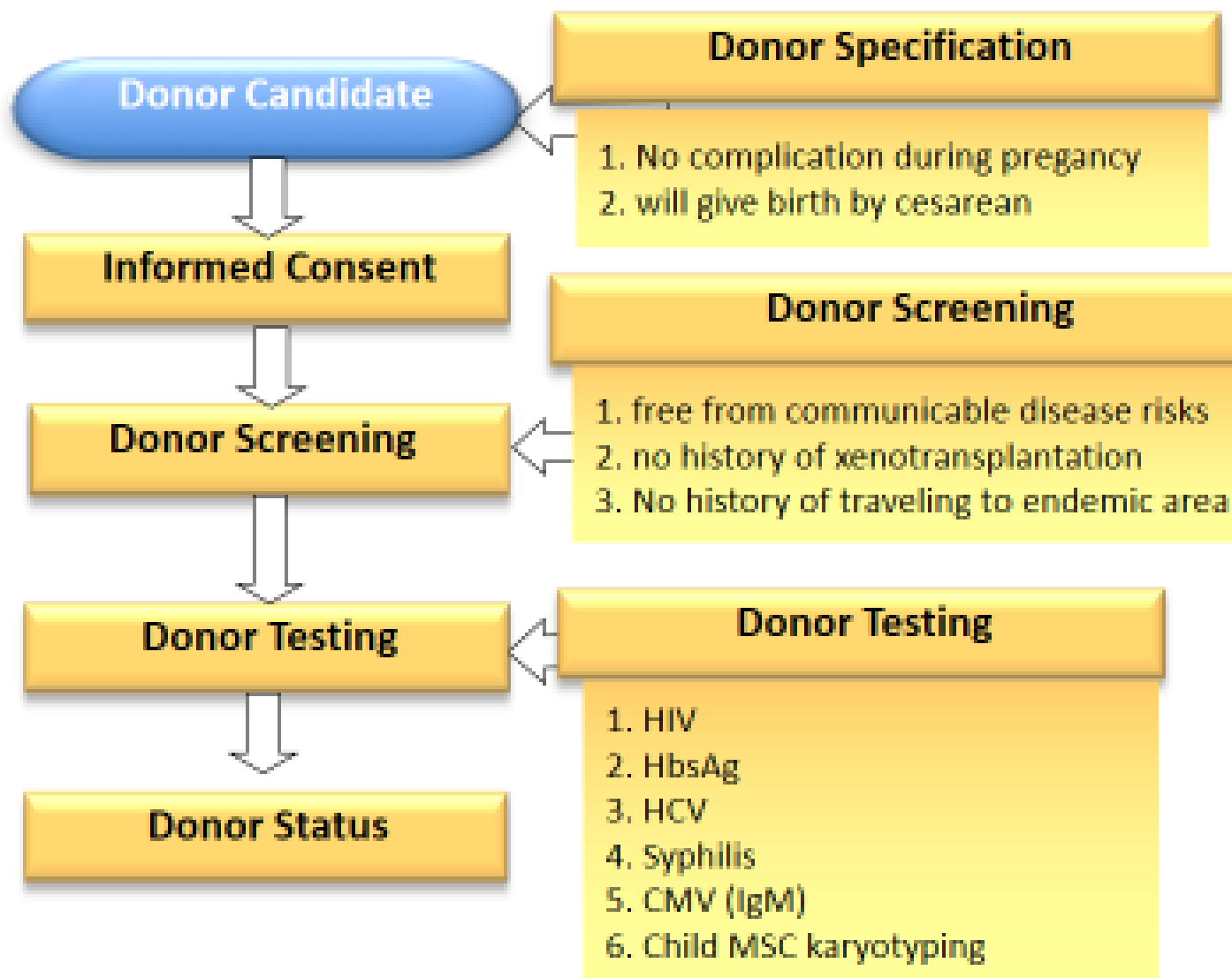


DONOR



Riwayat Kanker & Kelainan Genetik di Keluarga ?

Donor Qualification



Singapore
General Hospital
SingHealth

Division of Pathology Tel: 6321-4950/6321-4952/6321-4104 Fax: (65) 6732-8934

REF: 08/20/08/19

SINGAPORE GENERAL HOSPITAL
CYTOGENETICS REPORT

UCRSC: P7

AGE/SEX: 0/0

CLASS: P75

REGIONAL REFERENCE CLINIC

DEPT: P85

RM/REG:

REQUESTED BY: CS - OTHER DOCTORS

1508:0300626R REQUEST FORM# PO NO#00X190023

RECEIVED DATE/TIME:

COMMENTS: CULTURE #: 190626 (UCRSC P7)

SOURCE : CELL LINE

CLINICAL DIAGNOSIS: FOR KARYOTYPING

REQUESTER : PT. FALSE PARRA TRK.

JL. LETJEND SOEPHARPO SW.4

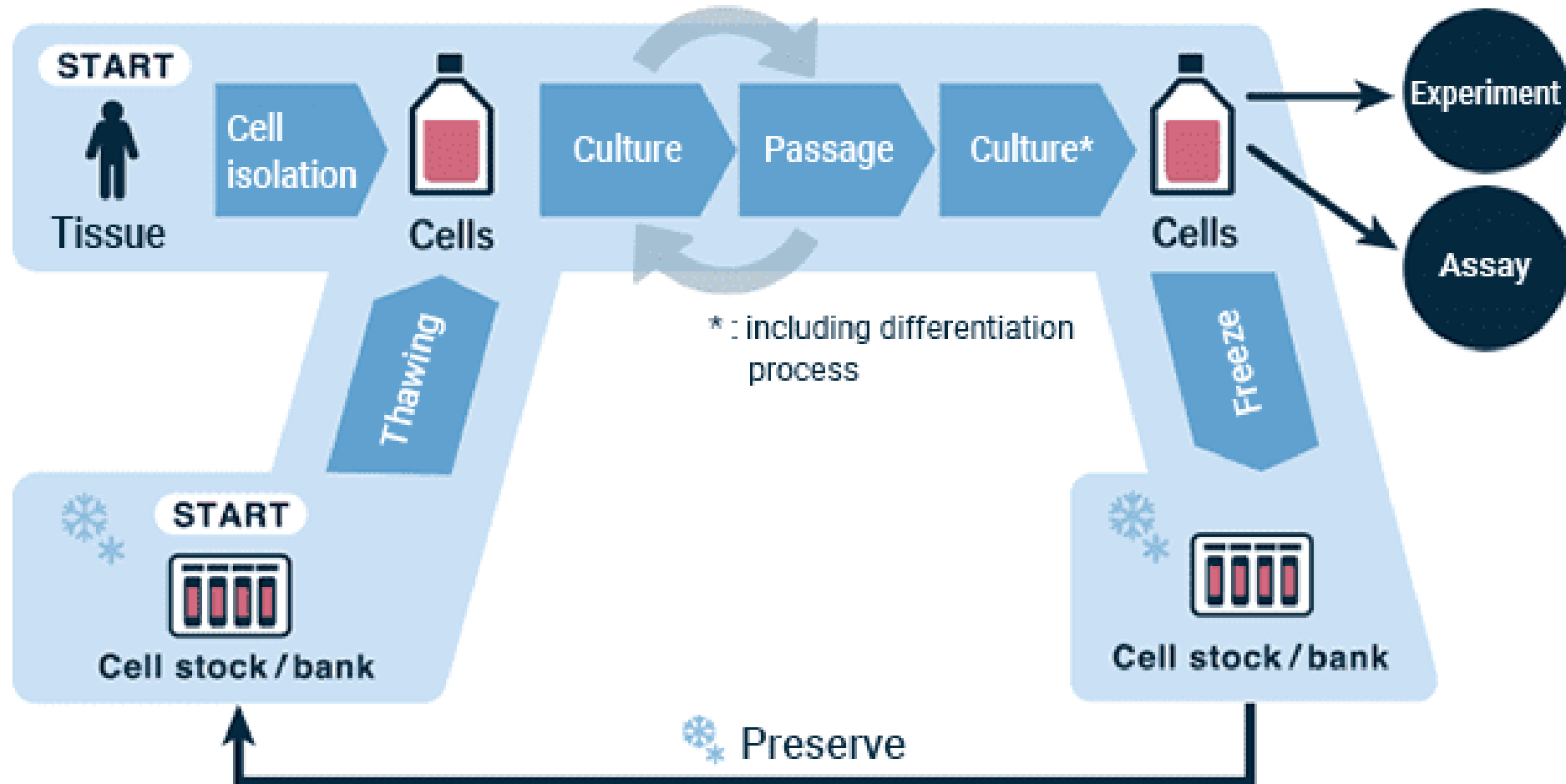
NO.1 CEMPAK PUTIH TOWER

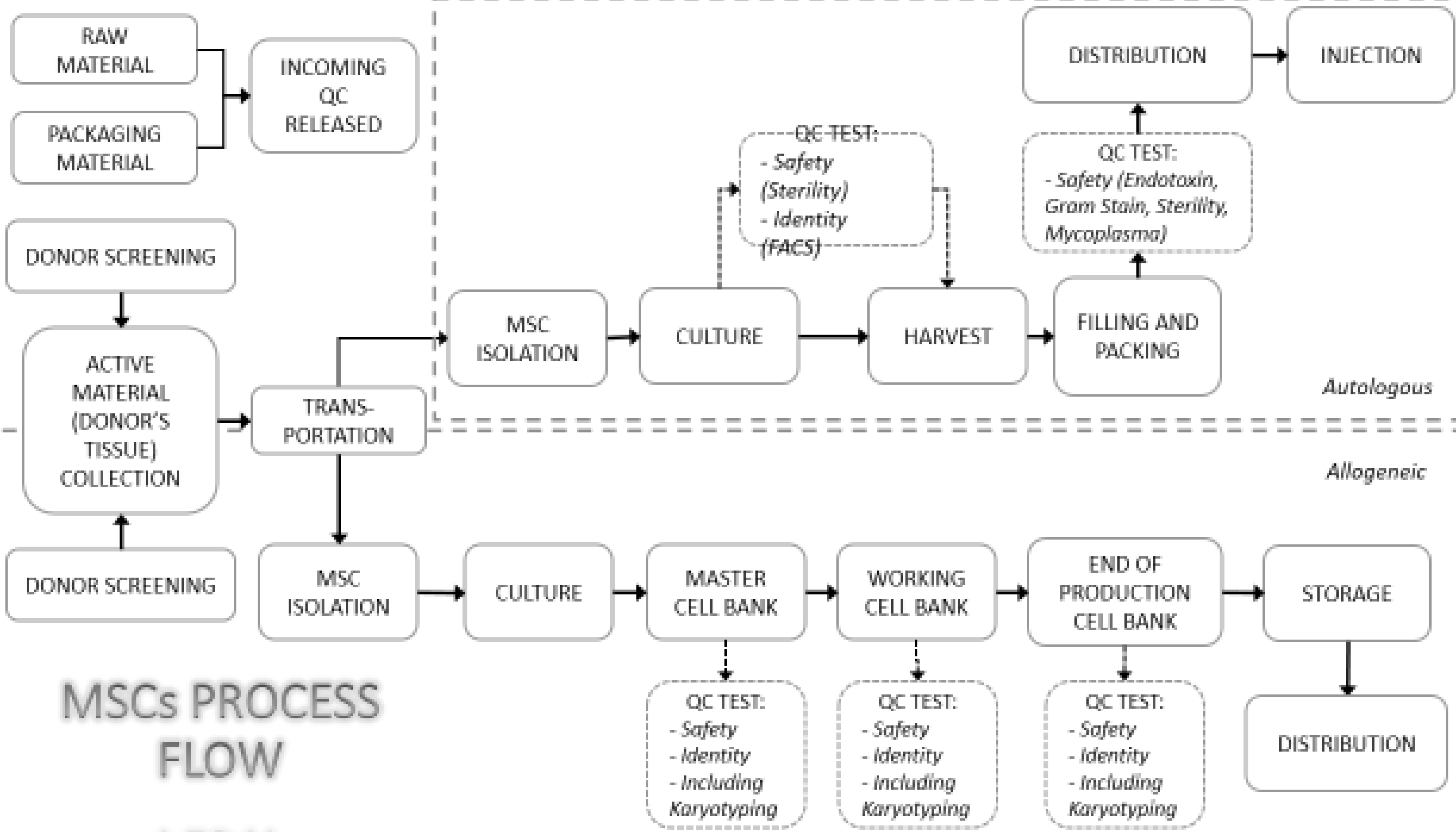
JAKARTA PUSAT 10530, PO BOX 3105 JAK

JAKARTA, INDONESIA

ORDERED: FARIS C L PRO

Proses Pembuatan Stem Cell





MSCs PROCESS FLOW

Autologous

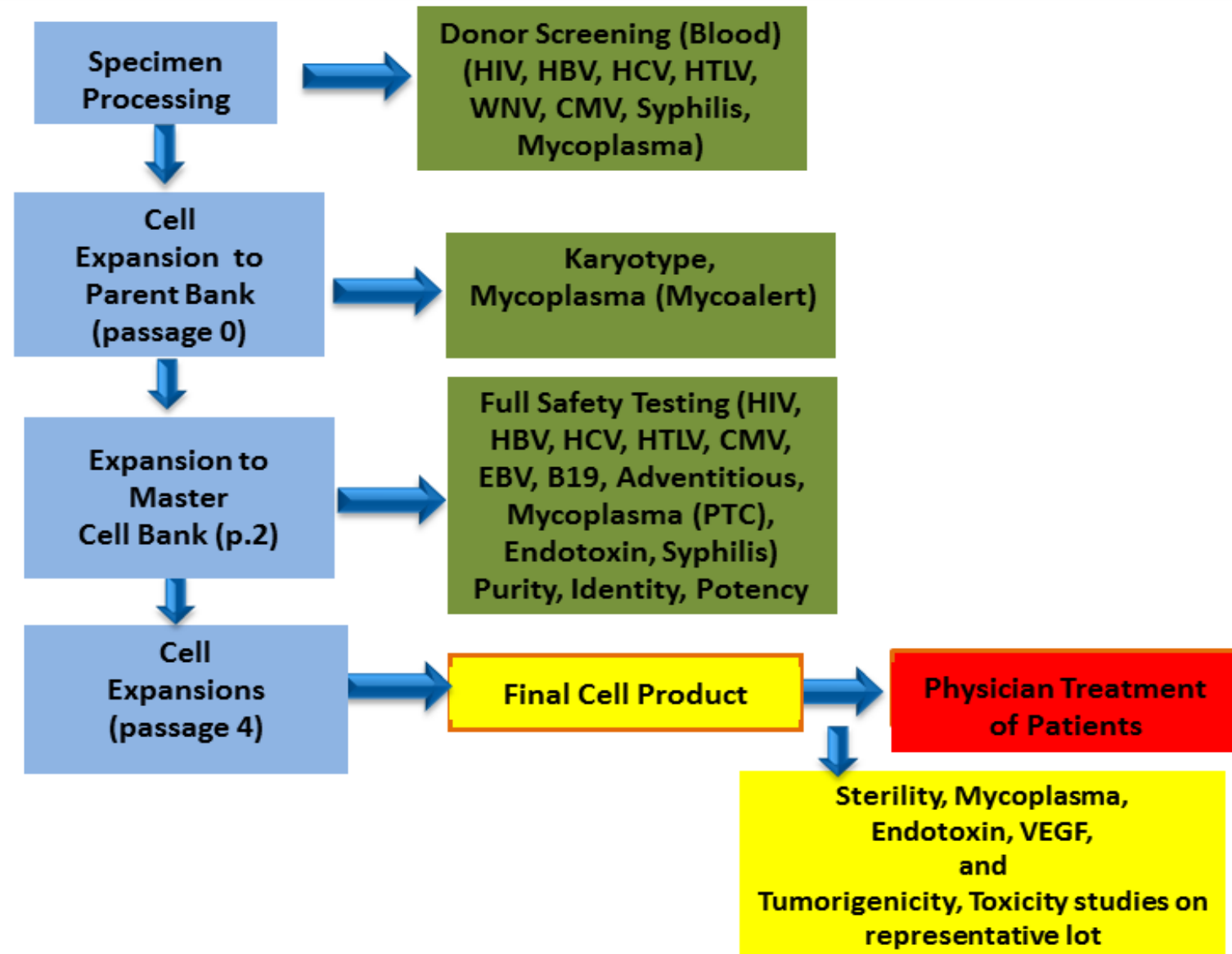
Allogeneic

QC TEST:
- Safety
- Identity
- Including Karyotyping

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- Identity
- Including Karyotyping

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- Identity
- Including Karyotyping

GMP stem cells manufacturing flow chart



Bebas dari....



- Phenol RED

Change today / check
for contamination

Change within
24-48h

Leave

Change or re-gas with
CO₂ / check incubator /
CO₂ supply



pH

6.5

7.0

7.4

7.8



- ANTIBIOTIC



- Growth Factor (Foetal Bovine Serum)



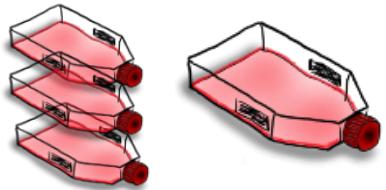
- DMSO
(Cryoprotectant)

PROSES PRODUKSI SECRETOME DI FASILITAS TERSERTIFIKASI BPOM



Isolasi *Umbilical Cord Mesenchymal Stem Cell* (UCMSC)

- Dari tali pusat donor.
- Kualifikasi donor sesuai dengan standar FDA.



Pembuatan *Master Cell Bank* (MCB)

- Proses perbanyak sel dengan medium pertumbuhan khusus.



Penggantian medium pertumbuhan

- Medium pertumbuhan diganti dengan medium khusus pengkoleksian secretome.
- AMAN, karena tidak mengandung serum, antibiotik dan phenol red.



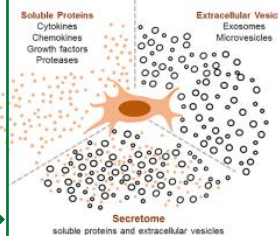
Pengemasan & Penyimpanan

- Secretome dikemas dengan vial steril
- Penyimpanan suhu -20°C



Filtrasi

- Filtrasi dengan filter $0.22 \mu\text{m}$
- Agar produk tidak mengandung sel, pengotor & kontaminan



Inkubasi sel (proses starving)

- Dilakukan dengan medium khusus
- Tanpa serum dan growth factor

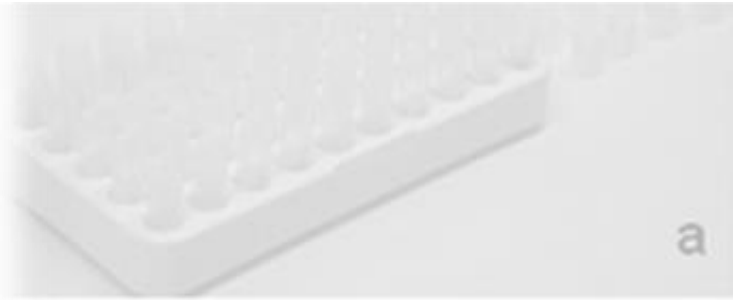


Kontrol kualitas

- Standarisasi zat aktif
- Uji sterilitas
- Gram stain
- Uji endotoksin

Jaminan keamanan & keseragaman produk





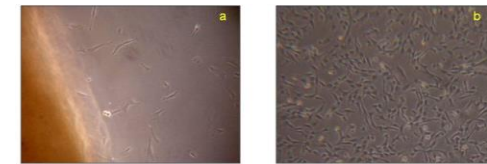
Penyimpanan Stem Cell



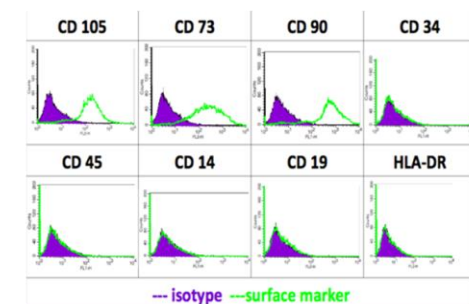
Pemeriksaan Berkala (Stability)

Parameter	Specification
Visual Inspection	Small fibroblast-like spindle-shaped cells, plastic adherent cells
Sterility	Sterile
Endotoxin	<0.25 EU/ml
Mycoplasma	Negative
Identity	Expression ($\geq 95\%$ CD105, CD73, CD90, $\leq 2\%$ SD34, CD19, CD14, HLA-DR)
Differentiation	Differentiate to osteocyte, adipocyte, chondrocyte
Viral Test	Negative HIV-1, HBV, HCV, CMV
Viability	$\geq 70\%$
Karyotyping	Chromosomal normalities
Penicillin Residue	Negative

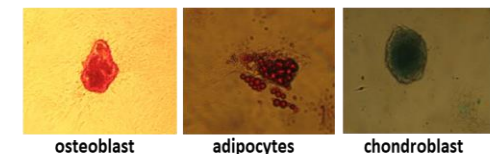
Adherence to plastic in standard culture conditions



Expression of the surface markers CD105, CD73 and CD90, as well as lack of expression of CD45, CD34, CD14 or CD11b, CD79a or CD19, and HLA-DR



Ability to differentiate into osteoblasts, adipocytes, and chondroblasts in vitro when given appropriate cues



Uji Keamanan Produk pada Hewan





Badan Pengawas Obat dan Makanan Republik Indonesia
Indonesian Food and Drug Authority

Seuai dengan Peraturan Badan Pengawas Obat dan Makanan RI (Badan POM RI) No. 34 tanggal 7 Desember tahun 2018 tentang Pedoman Cara Pembuatan Obat yang Baik, Kepala Badan POM RI dengan ini memberikan:

By virtue of the Regulation of the Indonesian Food and Drug Authority (Indonesian FDA) No. 34 dated December 7, 2018 on the implementation of Good Manufacturing Practice, hereby the Head of Indonesian FDA confers:

SERTIFIKAT

A Certificate

On

Cara Pembuatan Obat Yang Baik

Good Manufacturing Practice

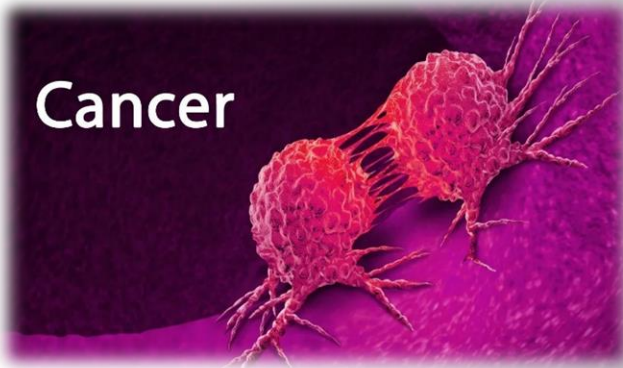
Nomor Sertifikat
Certificate Number
Kepada
To
Alamat
Address

| PW-5.01.04.1.3.333.09.21-0082

| PT. Bifema Adibintang

| Gedung Kalbe Business Innovation Center, Lantai 1 B,
PuloGadung No. 23, Kel. Jatinegara, Kec. Cakung, Kota
Administrasi Jakarta Timur, DKI Jakarta, Kelurahan Jati
Kecamatan Cakung, Kota Jakarta Timur, Prov. Jakarta

**Good Manufacturing
Practice**



Risiko Pembuatan Stem Cell yang Tidak Standard



**Clump of Cells
Embolism**



Impurities



Contamination

Rangkuman



PP6: CD90; CD73; CD105; CD44
PP7: CD34; CD45; CD14; CD19

Surface markers are indicated as positive or negative in the box.

CD	CD	CD	CD	HLA	CD	CD	CD	CD	CD	CD	HLA
19a	34	45	79a	DR	29	44	75	90	105	166	ABC
-	-	-	-	-	+	+	+	+	+	+	+
-	-	-	-	-	+	+	+	+	+	+	+
-	-	-	-	-	+	+	+	+	+	+	+

+ more than 20%; - less than 2%



Stem Cell Transplantation



- Sterility Test**
- Mycoplasma
 - Gram + / -
 - Endotoksin
 - Culture -

Bebas DMSO & PhenolRed



GMP Processed "Clinical Grade Cells"

Cell Priming Subpopulations Selection

Chondrocyte, Osteoblast, Adipocyte

Terima Kasih

