

# Regulatory aspects of the storage and transplantation of stem cells



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# Outline

- Law on Transplants
- Definition Transplants and Transplant Products
- Transplants
  - Licenses
  - Examples
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- Transplant Products
  - Licenses
  - GMP
  - Marketing authorisation
  - Examples
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# Law on Transplants

# Law on Transplants

## Art. 1 Objective

This law defines, under which prerequisites organs, tissues and cell can be used for transplantation purposes.

## Art. 2 Scope

This law is applicable for the handling of organs, tissues and cells of human or animal origin as well as products made out of them, destined to be transplanted to humans.

**Transplants**

A red bracket is positioned above the text "Transplants", spanning the width of the text below it.

**Transplant Products**

A red bracket is positioned below the text "Transplant Products", spanning the width of the text above it.

Law is only partially applicable for **autologous transplantation**.

# What are Transplants and what are Transplant Products ?

Why is this differentiation so important?

Different regulations apply regarding:

- › Licensing
- › Manufacturing
- › Distribution
- › Clinical trials
- › Putting on market

# Definitions

# What are Transplants ?

- Defined in Law on Transplants (Art. 2 Scope)
- **Organs, tissue and cells of human and animal source to be transplanted to a human being**
- The scope excludes
  - Devitalized organs, tissue and cells
  - Blood, except blood stem cells
  - Blood products
  - Gametes and embryos in the context of assisted reproduction
- Only **partially applicable to autologous tissues and cells**
  - No license required
- Scope does not exclude cells and tissues for non-medical purposes (e.g. cosmetics)

# What are Transplant Products ?

Products manufactured from organs, tissues or cells (human or animal origin) of which the process of manufacturing can be standardized (Law on Transplants, Art. 3 Definitions)

Working definition by Federal Office of Public Health / Swissmedic based on ATMP 1394/2007 (EC) regulation:

- Cells and tissues subjected to **substantial manipulation** (biological characteristics, physiological functions and structural properties modified)

OR

- Cells and tissues **are not intended to fulfil the same function** in the recipient as in the donor (non-homologous use)



# What are not substantial manipulations?

According to ATMP 1394/2007 regulation

- cutting,
- grinding,
- shaping,
- centrifugation,
- soaking in antibiotic or antimicrobial solutions,
- sterilization,
- irradiation,
- cell separation, concentration or purification,
- filtering,
- lyophilization,
- freezing,
- cryopreservation,
- vitrification.

# Legal aspects of Transplants

# Clinical trials with transplants

- Federal Office of Public Health authorizes Clinical Trials

<sup>1</sup> Ein klinischer Versuch der Transplantation menschlicher Organe, Gewebe und Zellen entspricht der **Kategorie A**, wenn die zu untersuchende Transplantation in einer nach **international anerkannten** Qualitätskriterien verfassten **Leitlinie** als **Standard** ausgewiesen ist.

- ➡ No authorisation by Federal Office of Public Health
- ➡ Authorized by Ethical Comitee

<sup>2</sup> Ein klinischer Versuch der Transplantation menschlicher Organe, Gewebe und Zellen entspricht der **Kategorie C**, wenn die zu untersuchende Transplantation nicht als Standard nach Absatz 1 ausgewiesen ist.

<sup>3</sup> Klinische Versuche der Transplantation embryonaler und fötaler Gewebe und Zellen entsprechen der Kategorie C.

- ➡ Authorisation by Federal Office of Public Health required
- ➡ Authorized by Ethical Comitee

# Allogenic Transplants: Licensed activities

- **Transplantation**
    - Organs
    - embryonic and foetal tissues and cells
    - genetically modified tissues and cells
  - **Storage** of tissues and cells
  - **Import and Export** of tissues and cells
- ➔ Licenses are issued by the **Federal Office of Public Health**

## Activities that do not require license

- **Procurement** of organs, tissues and cells
- **Processing** of organs, tissues and cells
- **Distribution** of organs, tissues and cells within Switzerland

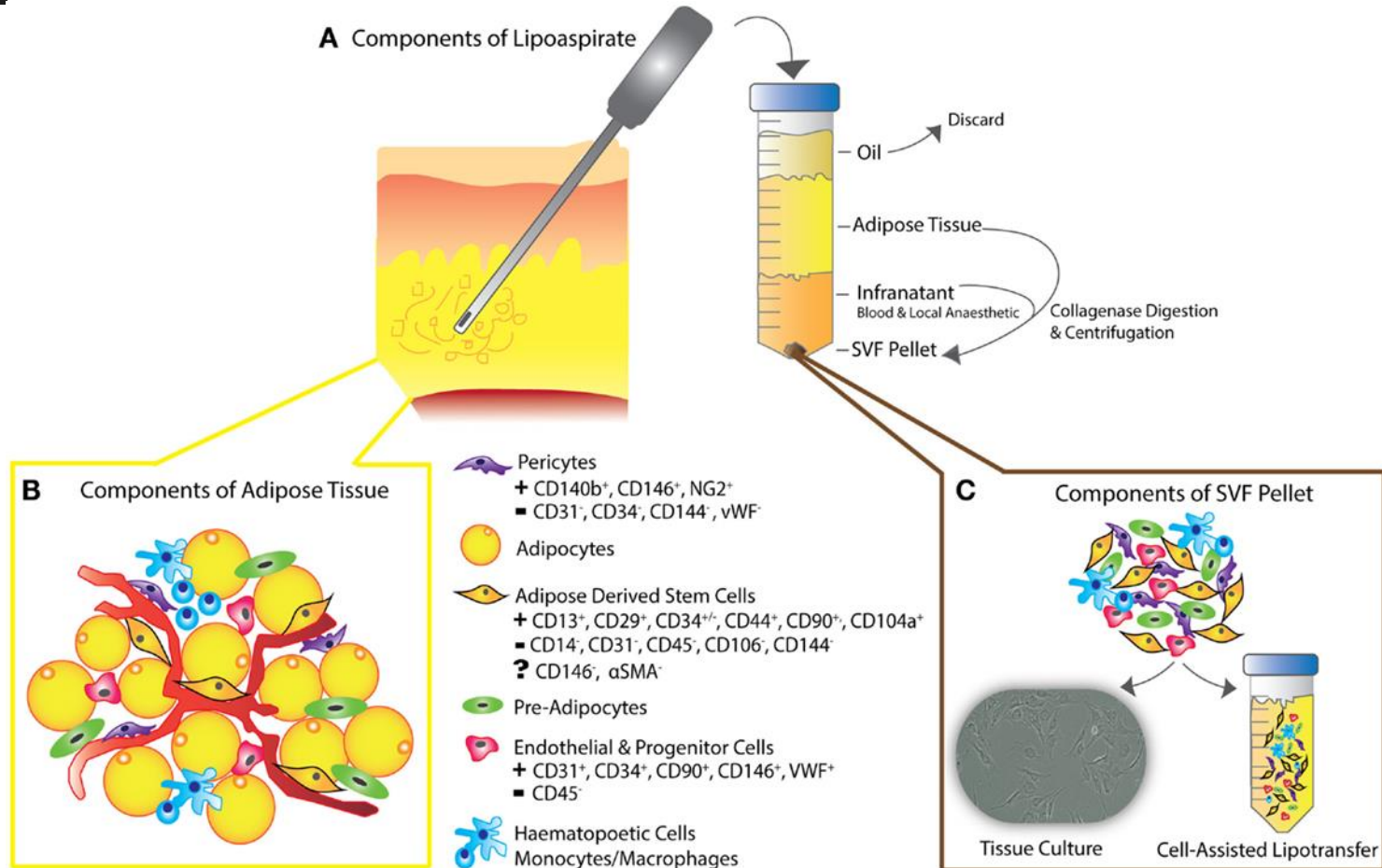
**→ Any activity with autologous cells ←**

# Examples of Transplants

## Examples of transplants

- Organ transplantation (allogenic)
- Islet Cell transplantation (allogenic)
- Cornea Transplantation (allogenic)
- Bone transplantation (allogenic)
- Amniotic membrane Transplantation (allogenic)
- Blood stem cell transplantation (autologous & allogenic)
- **Lipofilling** (autologous)

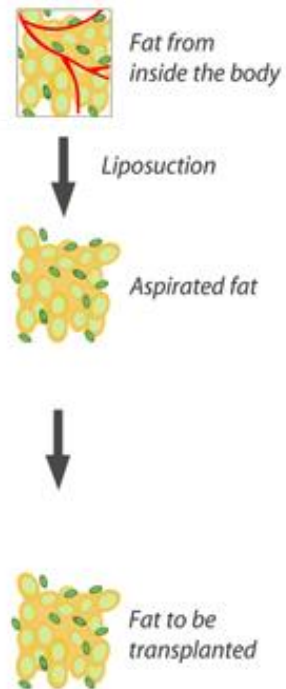
# Adipose tissue and Stromal Vascular Fraction





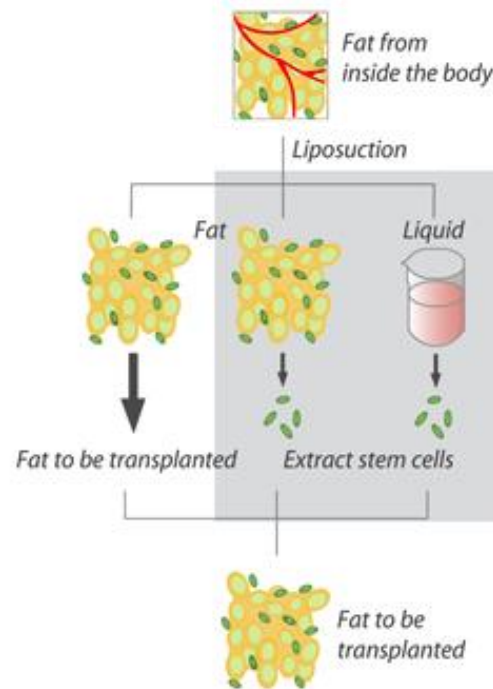
# Examples of lipofilling

Normal Lipo-Transplantation



*The density of stem cells is low because cells are not processed*

CAL: Cell-Assisted Lipotransfer



*The density of stem cells is high*

# Lipofilling

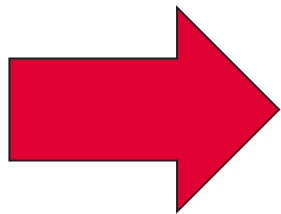
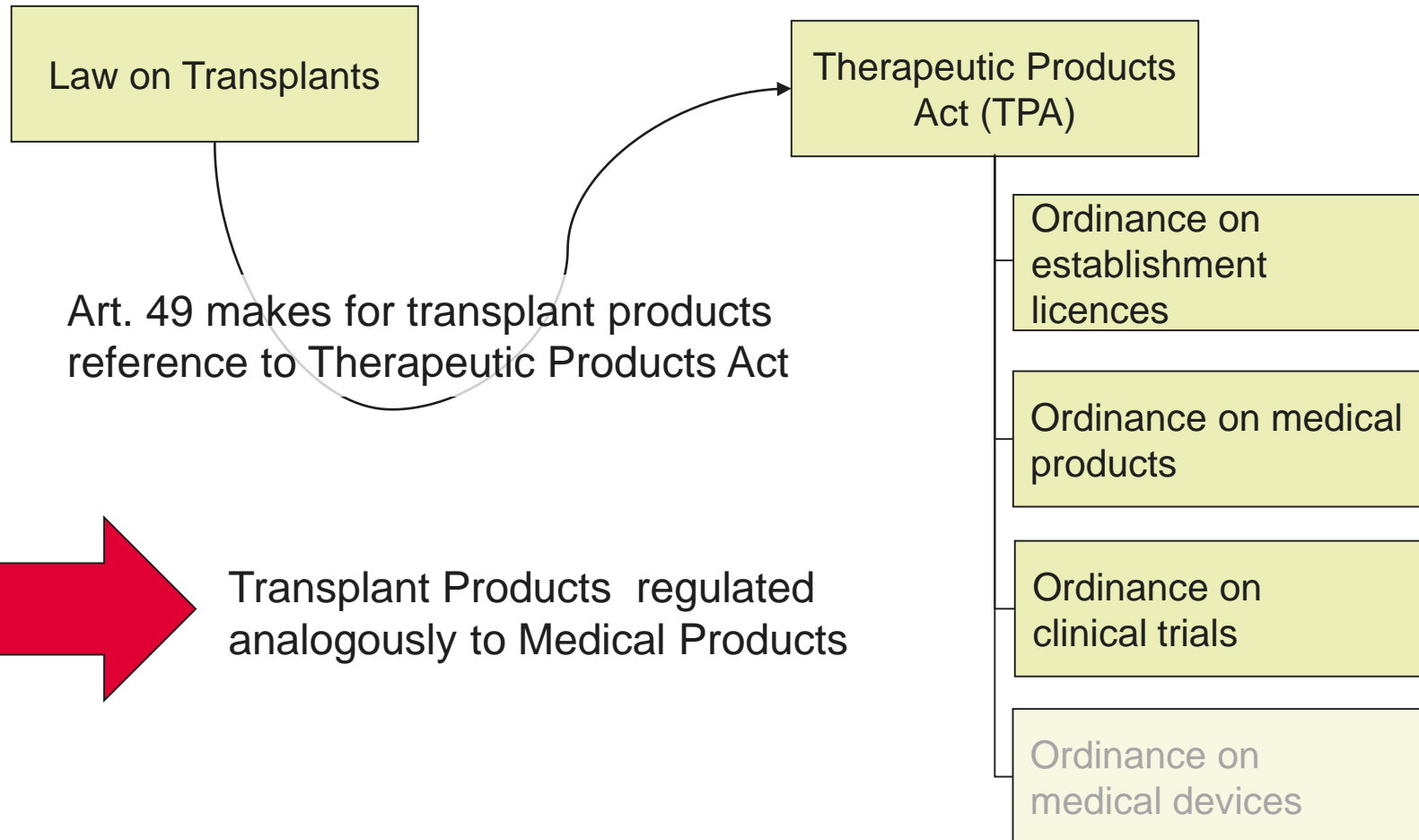
- Prerequisite for Lipofilling:
  - Purpose of treatment is to build up fat
  - Autologous use
  - Homologous use = cell exert in source tissue and target tissue the same function
  - Cell are reinjected into fat tissue
  - Cells are not substantially manipulated
- Locus of cell source is not relevant
- Destiny of cells is not relevant
- Device used to isolate and process cells does not have an impact on classification

## Required licenses for Lipofilling (autologous)

Activity	Who	License
Tissue procurement / liposuction	Physician	No license required
Transportation of tissue	Physician or Tissue establishment	No license required
Import or Export of tissue	Physician or Tissue establishment	No license required
Processing of tissue	Physician or Tissue establishment	No license required
Transplantation of tissue	Physician	No license required

# Legal aspects of Transplant Products

# Legal Aspects of Transplant Products



Transplant Products regulated analogously to Medical Products

# Licensed activities

- Manufacturing
  - Procurements of starting materials, processing, packaging, storage, quality control and delivery
  - Investigational transplant products (clinical trial)
  - Not ready to use transplant products
  - PIC/S GMP guidelines apply
- Wholesale
  - Storage, marketing release and distribution
  - Import and export of non-ready to use transplant products
  - GDP Principles apply
- Import and Export
  - GDP Principles apply
- Business abroad
  - GDP Principles apply

# What does GMP stand for

- Good Manufacturing Practice (GMP)
  - Guideline that provides principles for the correct manufacturing (processing, packaging, testing) of a medicinal product or active pharmaceutical ingredient
  - Covers: quality management, facility and equipment, personnel, documentation, production, quality control etc.
  - Different countries and international organizations are issuing such guidelines
    - **Pharmaceutical Inspection Co-operation Scheme (PIC/S)**
    - US Food and Drug Administration (Food, Drug and Cosmetic Act)
    - World Health Organization
    - European Union Eudralex Volume 4
- Wording

GMP conform facility 

GMP conform Quality Management System 

~~GMP-Cells~~  
~~GMP-Protocols~~

# Marketing authorisation

Marketing authorization mandatory for Transplant products (TPA)

- **No** Application of transplants Products to patients **without** marketing authorisation

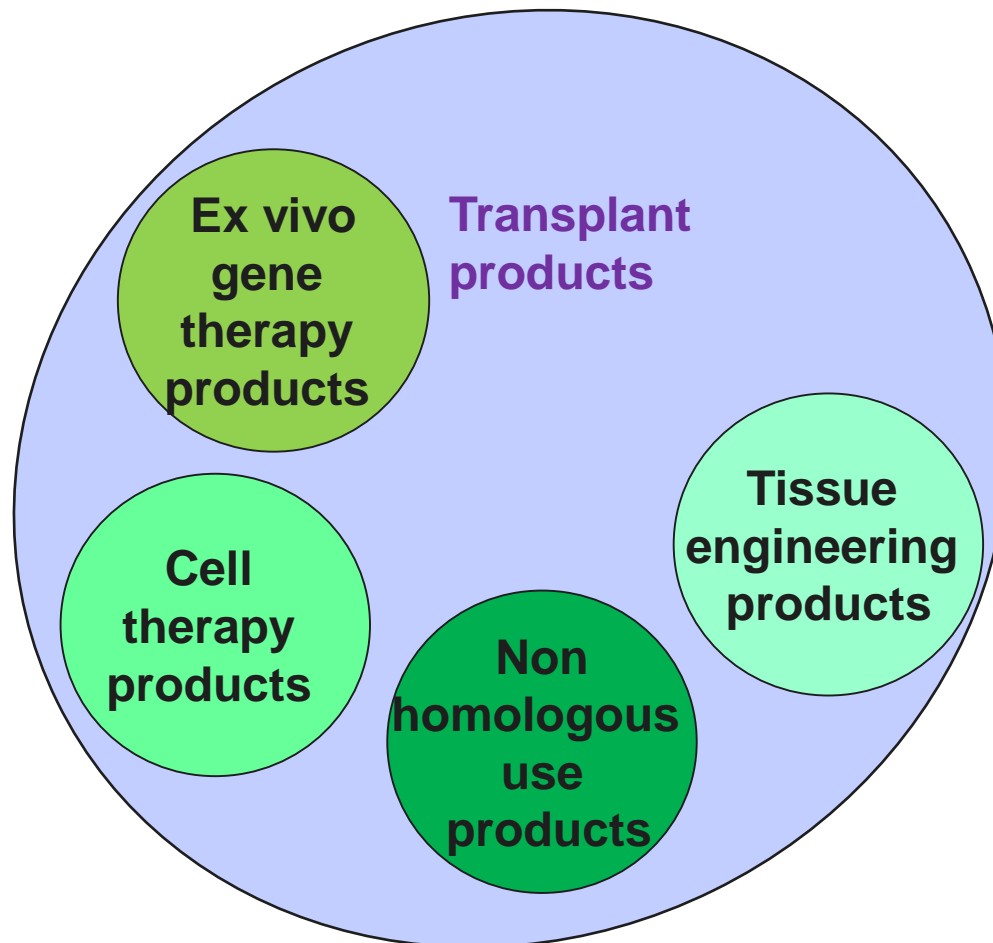
Requirements to obtain marketing authorisation:

- License to manufacture, import or conduct wholesale
- Submitted documentation demonstrating:
  - Safety (preclinical and clinical studies)
  - Efficacy (clinical studies)
  - Quality
- In Switzerland registered Company staffed with a responsible person



# Examples of Transplant Products

# Transplant products



## Non-homologous use (transplant product)

SVF in scar treatment



SVF in anti-aging



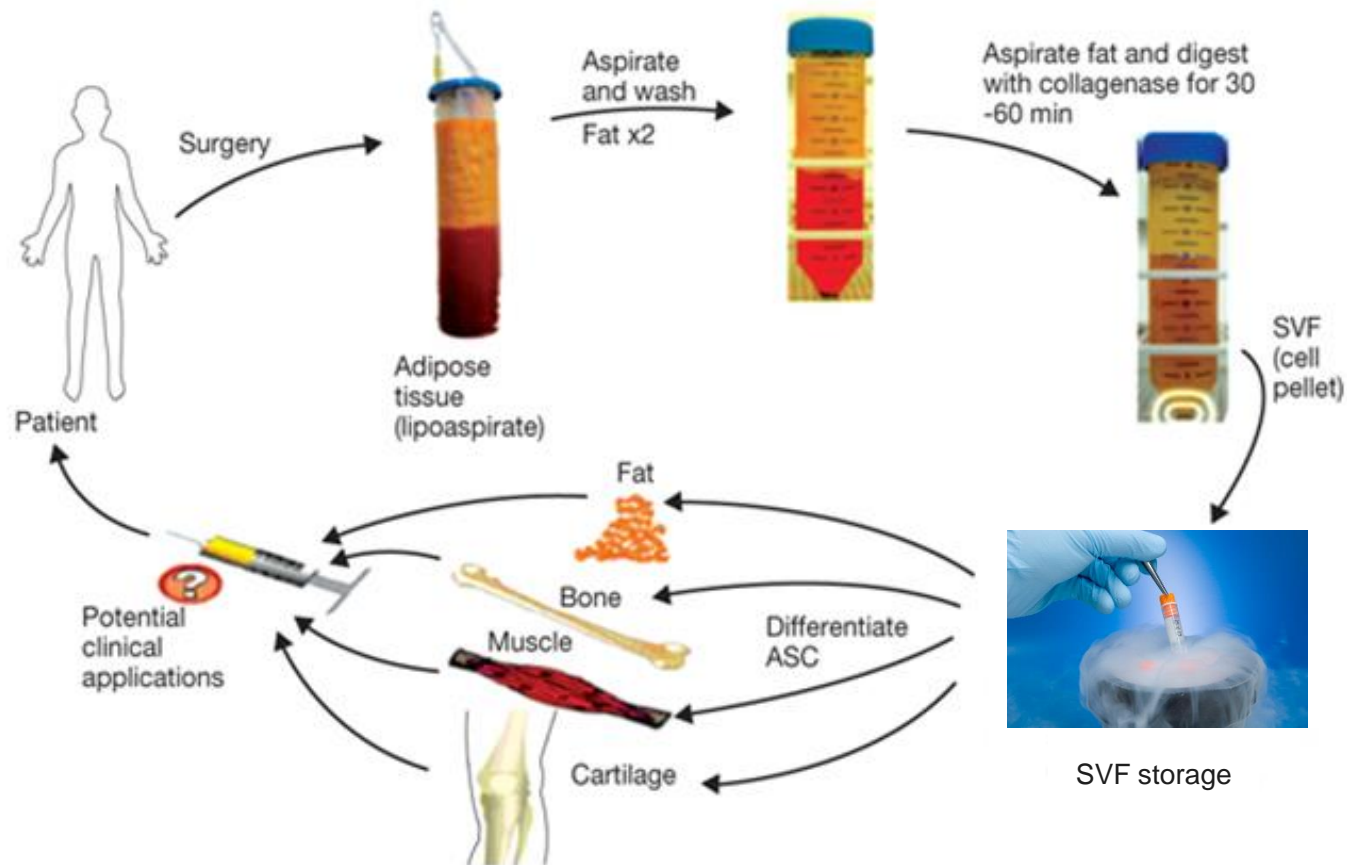
# Required licenses for non-homologous use SVF

## Prerequisite:

- Clinical trials
- Marketing authorization

Activity	Who	License
Tissue procurement / liposuction	Physician	No license required
Import or Export of tissue Not ready to use	Manufacturer or Distributor	Wholesale license
Processing of SVF	Manufacturer	Manufacturing license
Import or Export of final SVF Product	Manufacturer or Distributor	Import or Export license
Transplantation of tissue	Physician	No license required

# Storage of SVF for future Transplant Products



- J Korean Med Assoc. 2012 Aug;55(8):757-769.

## Intermediate Transplant Products

**→ cannot be applied to patients ←**

- Stromal vascular Fraction
  - Umbilical Cord Tissue
  - Dental Bulp
  - Placental Tissue
- } Intermediate Transplant Products
- Requirements for banking
    - Manufacturing license
    - GMP conform quality assurance system
    - Aseptic processing (cleanrom grade A in Background grade B)
    - Trained and qualified staff
    - Qualified equipment and facility
    - Validated processes and analytical methods
    - Authorized qualified person

# Required licenses for banking of intermediate transplant products (TpP)

**Important: Products cannot be applied to patients**

Activity	Who	License
Tissue procurement / liposuction	Physician	No license required
Import or Export of intermediate TpP	Manufacturer or Distributor	Wholesale license
Processing of intermediate TpP	Manufacturer	Manufacturing license
Storage of intermediate TpP	Manufacturer	Manufacturing license

Thank you for your attention