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
  - Requirements
- Transplant Products
  - Licenses
  - GMP
  - Marketing authorisation
  - Examples
  - Requirements
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.

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

1 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 Comittee

2 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.
3 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

Front. Surg., 28 January 2015
Examples of 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)

<table>
<thead>
<tr>
<th>Activity</th>
<th>Who</th>
<th>License</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tissue procurement / liposuction</td>
<td>Physician</td>
<td>No license required</td>
</tr>
<tr>
<td>Transportation of tissue</td>
<td>Physician or Tissue establishment</td>
<td>No license required</td>
</tr>
<tr>
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Legal aspects of Transplant Products
Legal Aspects of Transplant Products

- Law on Transplants
  - Art. 49 makes for transplant products reference to Therapeutic Products Act
  - Transplant Products regulated analogously to Medical Products

- Therapeutic Products Act (TPA)
  - Ordinance on establishment licences
  - Ordinance on medical products
  - Ordinance on clinical trials
  - Ordinance on medical devices
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

- Ex vivo gene therapy products
- Transplant products
- Cell therapy products
- Tissue engineering products
- Non homologous use 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

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<td>Physician</td>
<td>No license required</td>
</tr>
<tr>
<td>Import or Export of tissue Not ready to use</td>
<td>Manufacturer or Distributor</td>
<td>Wholesale license</td>
</tr>
<tr>
<td>Processing of SVF</td>
<td>Manufacturer</td>
<td>Manufacturing license</td>
</tr>
<tr>
<td>Import or Export of final SVF Product</td>
<td>Manufacturer or Distributor</td>
<td>Import or Export license</td>
</tr>
<tr>
<td>Transplantation of tissue</td>
<td>Physician</td>
<td>No license required</td>
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Storage of SVF for future Transplant Products

Intermediate Transplant Products cannot be applied to patients

- Stromal vascular Fraction
- Umbilical Cord Tissue
- Dental Bulp
- Placental Tissue

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**

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Thank you for your attention