Bringing Stem Cell Therapies To The Patient

A European Roadshow

IMCAS Annual Meeting 2016

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Paris, 28th January 2016

Overview

- Background
  - Autologous stem cell therapy
  - Same surgical procedure
  - No banking and treating of cells
- Assumption in the ideal world
  - Physicians all over Europe can simply apply the medical device
  - Physicians can treat patients with the specific autologous stem cell therapy without any additional requirements

Is this assumption correct?

Current EU Regulation for Autologous Cells

Art. 2 (2) Tissue and Cells Directive 2004/23/EC (EUTCD) exempts

- cells used for autologous graft,
- extracted, processed and
- used as part of the same surgical procedure

from the requirement of tissue handling license

Current EU Regulation for Autologous Cells

Risks associated with use of autologous same surgical procedure cells are significantly lower:

- donor and recipient are identical
- cells are extracted and reinserted in one surgical procedure
- cells never leave the operating room

Current EU Regulation for Autologous Cells

- Rationale for exemption in Art. 2 (2) also recognized by Recital 8 EUTCD:

  "Tissues and cells used as an autologous graft (tissues removed and transplanted back to the same individual), within the same surgical procedure and without being subject to any banking process, are also excluded from the Directive. The quality and safety considerations associated with this process are completely different."

- Quality and safety considerations associated with these cells are completely different to those which apply to other tissues, e.g. banked tissues!

Current EU Regulation for Autologous Cells

- Regulation 1394/2007 sets out (amongst others) a regime for the evaluation and grant of marketing authorization in respect of ATMP (ATMP Regulation)

- Critical question: Does the ATMP Regulation apply to autologous cells used same surgical procedure?

Current EU Regulation for Autologous Cells

- ATMP Regulation applies, if cells
  - are human and viable
  - fall within one the applicable category of ATMP, i.e. Tissue Engineered Products (TEPs)
  - are industrially manufactured or manufactured by a method involving and industrial process
  - are placed on the market [Art. 2 (1) 2001/83/EC]
- Critical question in our case: Are autologous same surgical procedure cells TEPs?

Current EU Regulation for Autologous Cells

- Cell may be a TEP, if
  - it is presented having properties for, or is used in or administrated to human beings with a view to regenerating, repairing or replacing a human tissue, and
  - it contains or consists of *engineered cells* or tissue
- Cells or tissue are engineered, if they
  - have been subject to *substantial manipulation*, i.e. biological characteristics, physiological functions are structural properties relevant for the intended regeneration, repair or replacement are achieved, or
  - are not intended to be used for the *same essential function* in the recipient as in the donor

Current EU Regulation for Autologous Cells

- Annex I to ATMP Regulation lists manipulations not considered substantial manipulations:

  "cutting; grinding; shaping; *centrifuging*; soaking in antibiotic or antimicrobial solutions; sterilizing; irradiation; *cell separation, concentration or purification*; filtering, lyophilization, freezing, cryopreservation"

- Cells manipulated in ways listed in Annex I are by definition not considered to be engineered

- Autologous cells used in the same surgical procedure are not placed on the market!

Summary of Status on EU Level

- Autologous cells used in same surgical procedure
  - not subject to the EUTCD due to exemption in Art. 2 (2) EUTCD
  - not subject to ATMP Regulation since they are not a TEP
  - not considered medicine since not placed on the market
- EU legislation has taken a reasonable and risk-related approach in case of autologous same surgical procedure cells!
- Current EU legislation complies with principle of proportionality!

Implementation in the Member States

- Coherent legislative concept on EU level but adverse side effect in implementation and application in the Member States
- Fragmented legislation in the Member States
- Different interpretation of crucial terms in the Member States

Implementation in the Member States

Example UK:

- physicians do not need additional licenses to treat patients with autologous same surgical procedure cells (involving the Cytori Celution 800 Device)
- reimbursement agreed by NICE

Example The Netherlands:

- autologous same surgical procedure cells (involving the Cytori Celution 800 Device) are classified as ATMP

Implementation in the Member States

Example Germany:

- Physicians require at least a manufacturing license to treat patients with autologous same surgical procedure cells
- No DRG code for treatment

Example Czech Republic:

- Czech regulator considers this procedure to require a tissue handling license, despite of Art. 2 (2) EUTCD

Implementation in the Member States

Example France:

- France refuses to acknowledge the UK's HTA decision regarding adipose tissue processed in the same conditions as the patient do not require an additional GMP license.

- France refuses to acknowledge the decision from the Meeting of Competent Authorities for Cells and Tissues (June 2011) regarding autologous adipose tissue processed in the same surgical procedure do are not ATMPs

Implementation in the Member States

Example Poland:

- Physicians do not need additional licenses to treat patients with autologous same surgical procedure cells

Example Italy:

- Physicians do not need additional licenses to treat patients with autologous same surgical procedure cells

Summary of Status on Member States' Level

- Fragmented national legislation
- However, a therapy can only have the same risk for all European patients and not different levels of danger in the Member States
- No level playing field
- Barrier to trade
- Creates medical tourism
- Principle of free movement of goods and provision of services is not respected (devices and physicians)

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