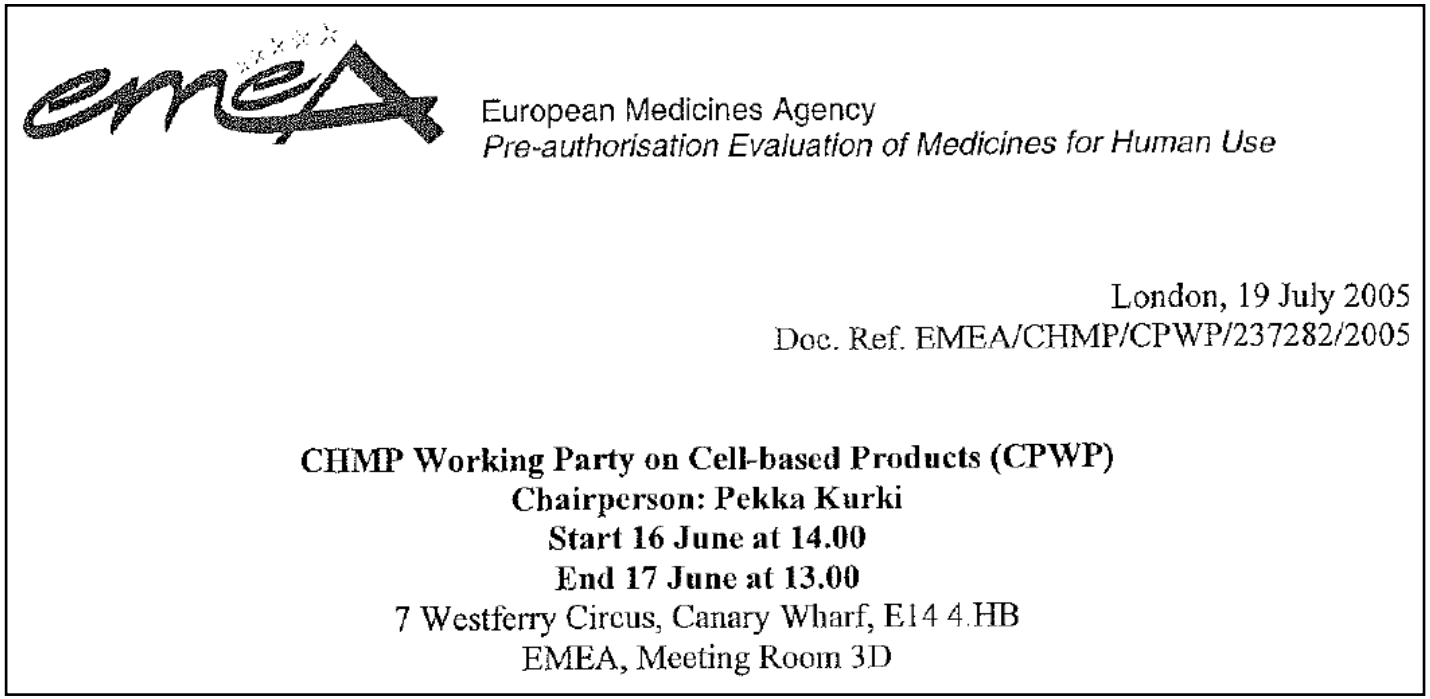
Stem cell-based medicinal products as ATMPs in the EU



European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

London, 19 July 2005
Doc. Ref. EMEA/CHMP/CPWP/237282/2005

CHMP Working Party on Cell-based Products (CPWP)
Chairperson: Pekka Kurki
Start 16 June at 14.00
End 17 June at 13.00
7 Westferry Circus, Canary Wharf, E14 4.HB
EMEA, Meeting Room 3D

- Cell and Gene Therapy Products classified as Medicinal Products (Dir. 2003/63/EC); TEPs not regulated at EU level
- **Directive 2004/23/EC** (+ technical directives 2006/17/EC, 2006/86/EC)
- Points to consider on the manufacture and quality control of human somatic cell therapy products (Quality, 2001)
- Points to consider on Xenogeneic cell therapy medicinal products (Quality, 2003)

Regulation 1394/2007/EC

- **all somatic cell therapy products and tissue engineered products classified as medicinal products (ATMPs)**

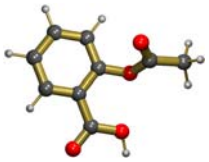
  → **cells either manipulated or intended for heterologous use**

- **a centralised marketing authorisation route for all ATMPs**

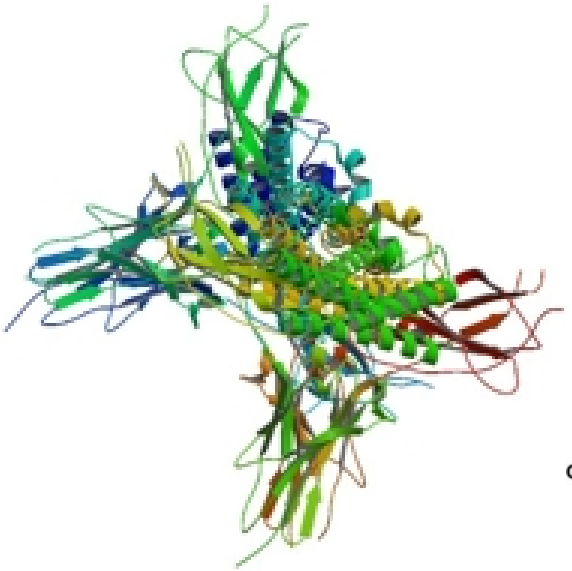
- **revision of dir. 2001/83/EC (2009/120/EC)**
  → **new definitions for cell and gene therapy products**
  → **updated technical requirements (Q, NC, C) for all ATMPs**

- **Certification of quality and non-clinical data (reg. 668/2009)**

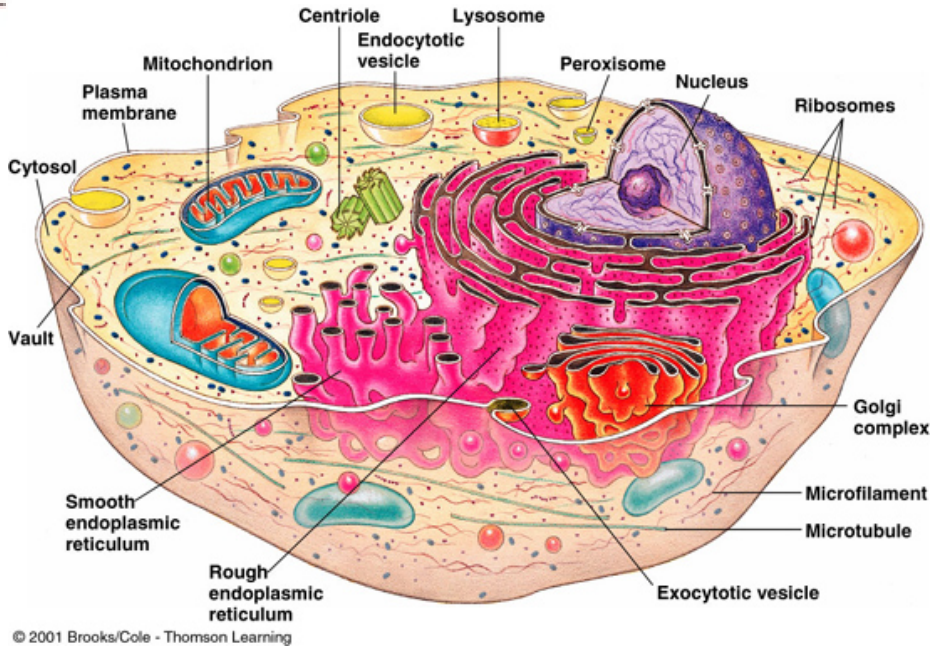
Cell-based products (CBMPs) vs. other MPs



Aspirin

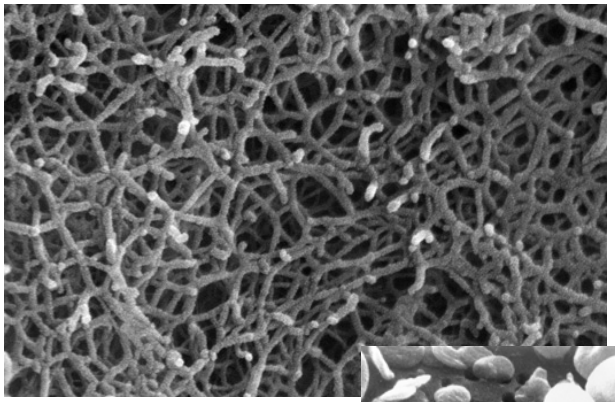


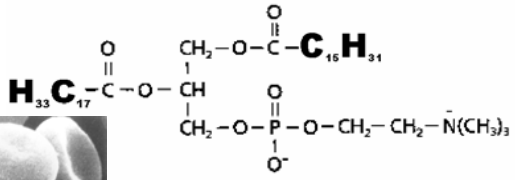
Filgrastim, G-CSF

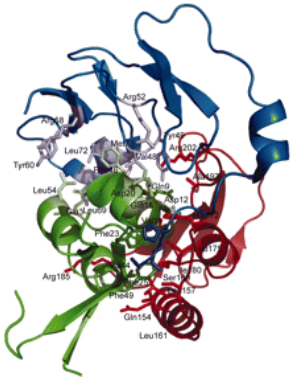


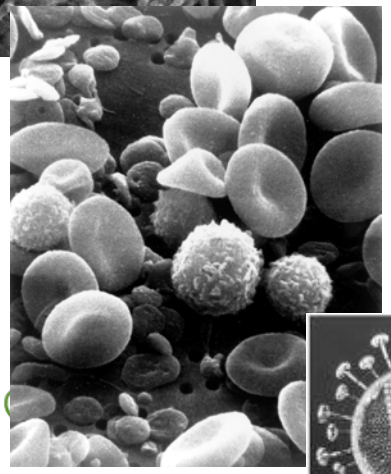
Eucaryotic cell

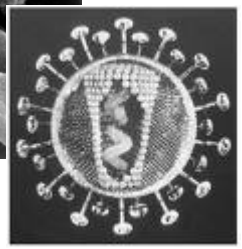
Cells in combination with other molecules / materials

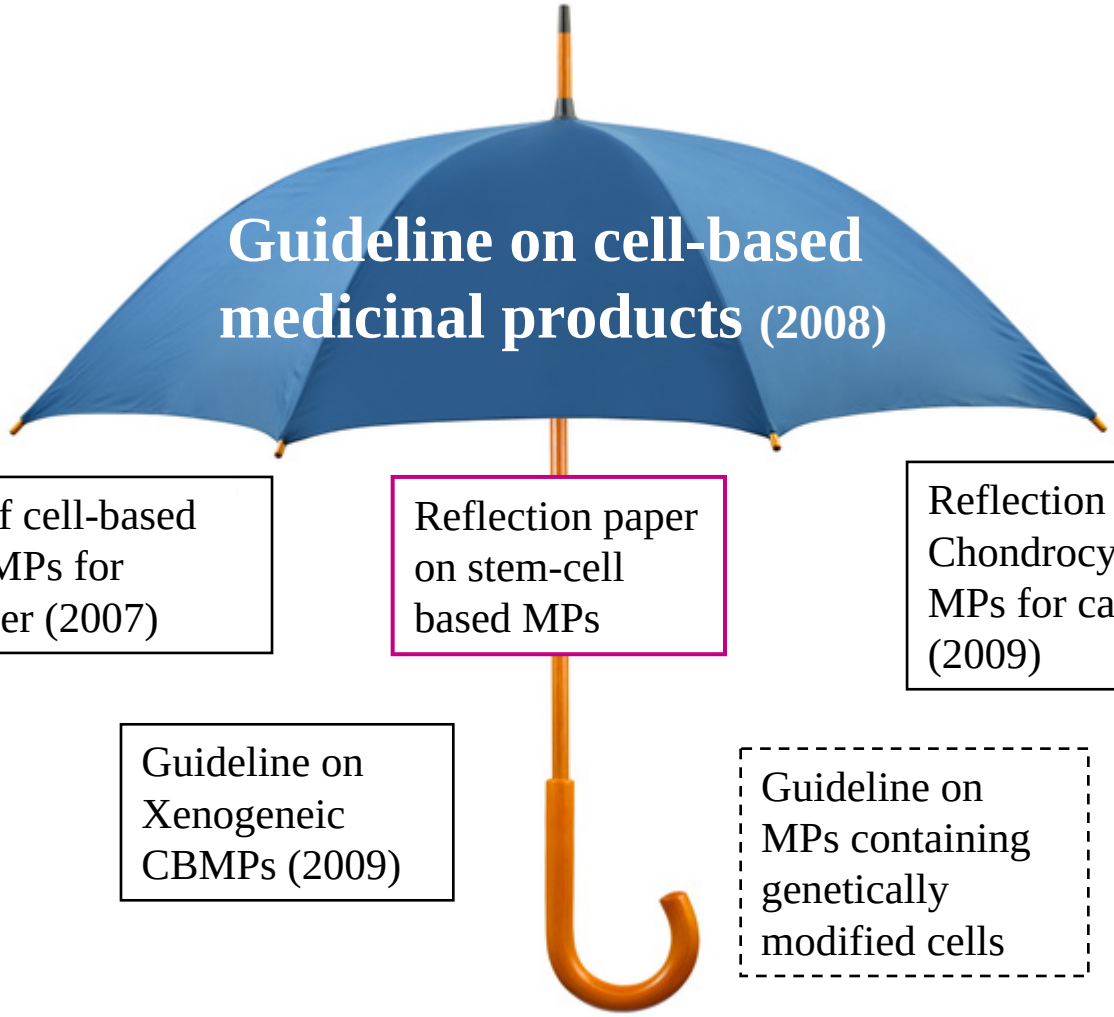


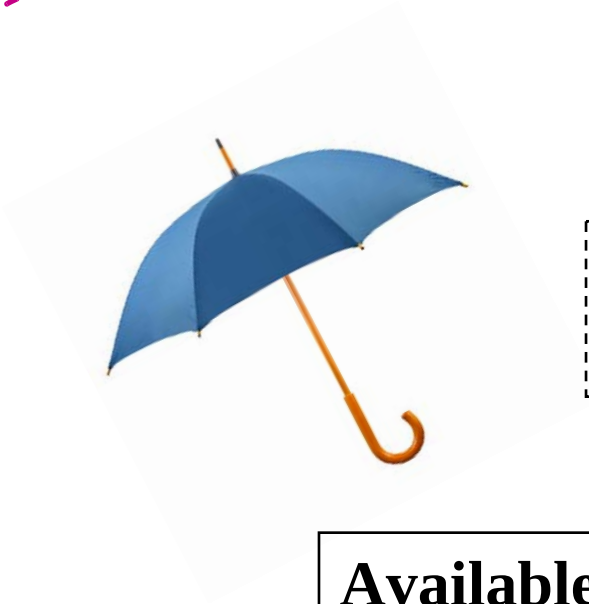









Guideline on cell-based medicinal products (2008)
Potency testing of cell-based immunotherapy MPs for treatment of cancer (2007)
Reflection paper on stem-cell based MPs
Reflection paper on Chondrocyte containing MPs for cartilage repair (2009)
Guideline on Xenogeneic CBMPs (2009)
Guideline on MPs containing genetically modified cells



GMP Guideline Annex 2

Guideline on Safety and Efficacy Follow-up – Risk Management of ATMPs

Available disease specific guidance

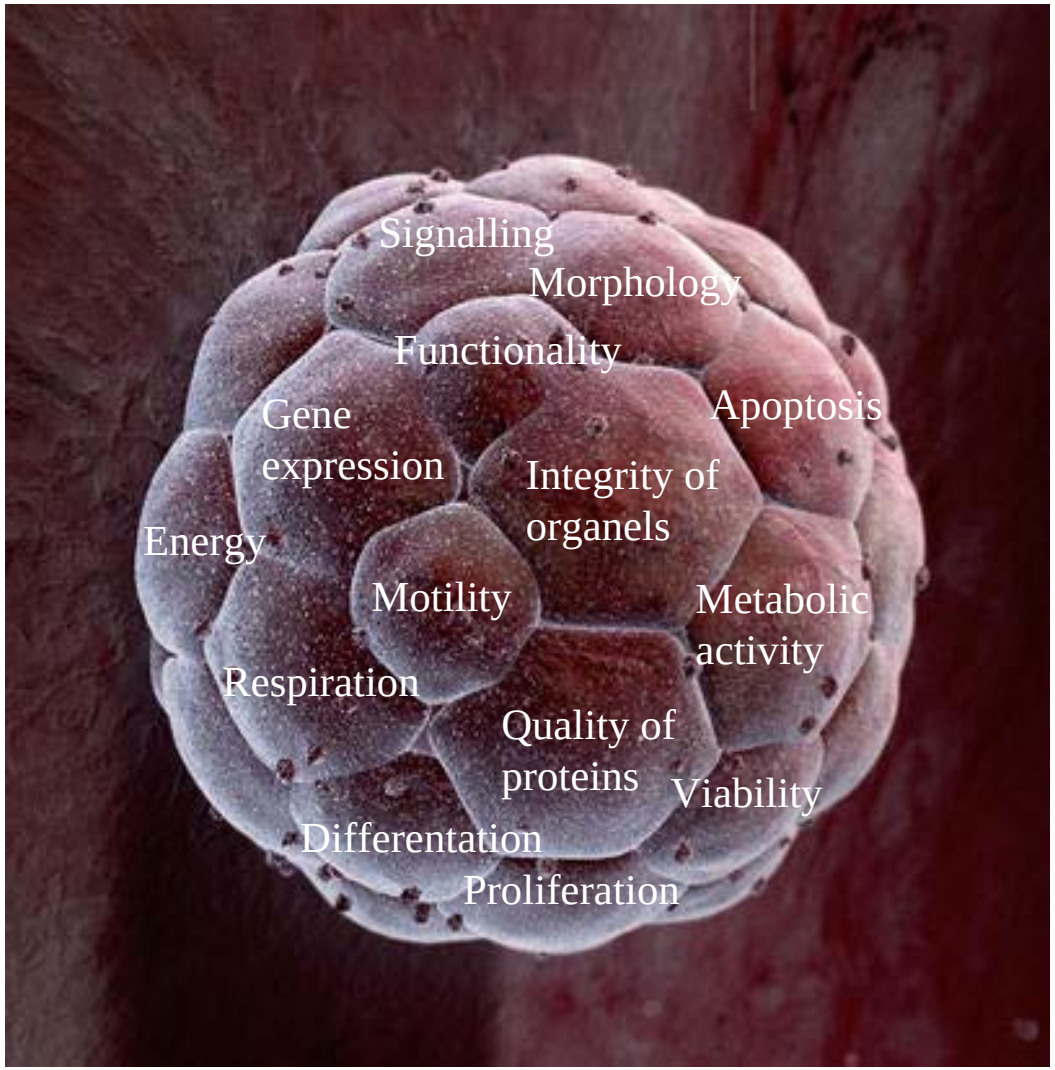
Ph.Eur. monographs

EMA / ICH guidelines Q, S, E

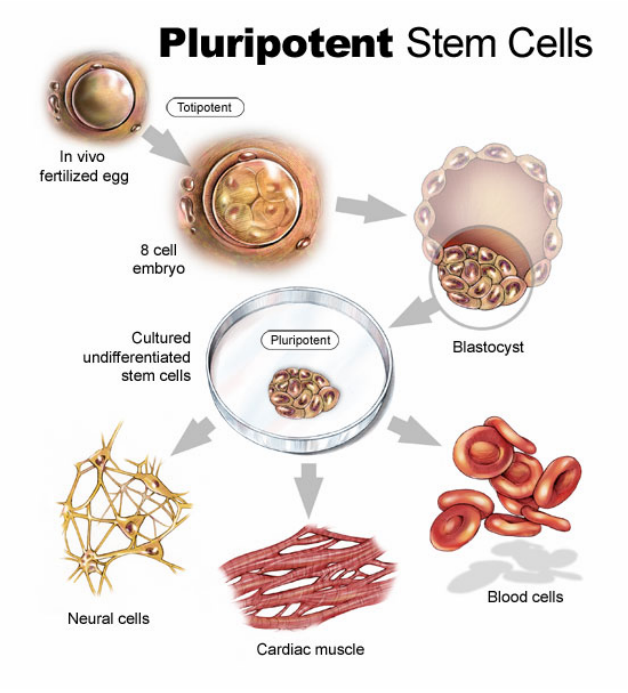
traceability guidance

GCP guidance

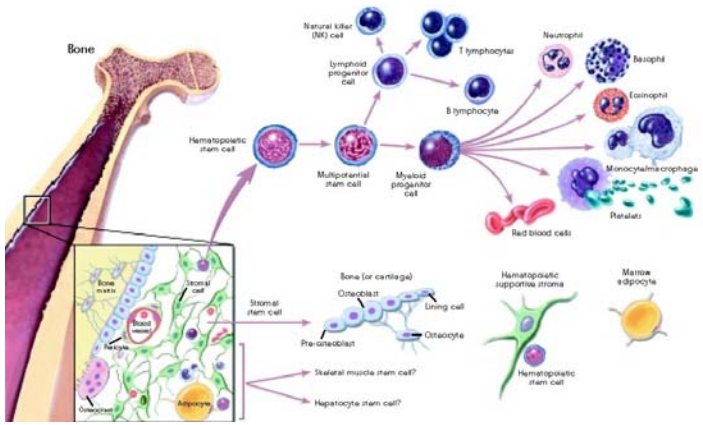
Critical parameters of cells?



- Manufacturing aspects & quality control
- Species specificities on molecular and tissue level
- Biodistribution/engraftment
- Mode of action
- Dosing

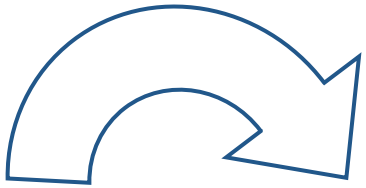


Multipotent Stem Cells



Challenges?

- Signals / factors needed for proliferation and / or persistent differentiation?
- homogeneous or heterogeneous cell population needed for a given indication?
- validated markers for stem cells?
- teratoma formation?
- potency of stem cells?
- integration and functionality of the newly formed tissue? Biodistribution and niche?
- external factors confusing the efficacy and safety signals?



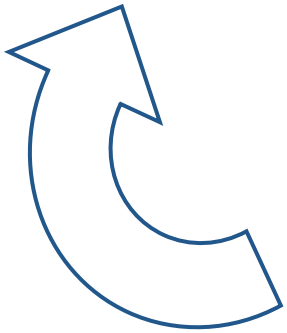
CERTIFICATE OF ANALYSIS

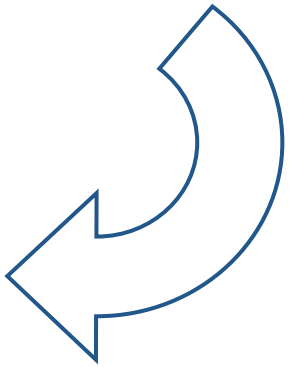
Product Name:	Piracetam
Formula:	C6H10N2O2
Molecular:	142.15
Structure:	
CAS N°:	7491-74-9
Batch N°:	20080306
Description:	White crystalline powder
Identification:	Passes all criteria tests
Batch Quantity:	1000k
Manufacture Date:	Mar 2008
Expiry Date:	Feb 29, 2011

CONTENT	**SPECIFICATION**	**RESULTS OF**
Assay	98% - 102%	99.5%
Identification	Positive reaction	Complies
Acidity (pH)	5 – 7	5.6
Clarity of Solution	Clarity	Complies
Melting Point	151 – 154 °C	151 – 152.5 °C
Heavy Metals	≤ 20 ppm	< 20 ppm
Residue on Ignition	≤ 0.10%	0.05%
Loss on Drying	≤ 0.50%	0.30%
Related Substances	Total area < Standard area	Compli

Storage	Cool & dry place, Do not freeze. Keep away from strong, light and heat.
Shelf	3 years when properly stored.

EXPIRED





Risk-based approach for all cell-based products

- A risk-based approach can be applied for all cell-based products (GL on cell-based products, CHMP/CPWP/410869/06)
- the risk-based approach for all ATMPs included into the legislation (revised Annex I, Part IV, Dir. 2001/83/EC)
- The risk analysis should cover the whole development and should be used to determine the amount of data needed in the MAA
- initial risk evaluation to be included in module 2 of the MAA
- further guidance under development (CHMP/CPWP/708420/09)

Thank you for your attention!