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Committee for Medicinal Products for Human Use (CHMP)
Committee for Advanced Therapies (CAT)

CHMP/CAT position statement on Creutzfeldt-Jakob disease and advanced therapy medicinal products

Draft[1]

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7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
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In the European regulation advanced therapy medicinal products (ATMP) include those based on gene therapy, cell therapy and tissue engineering. Although they are considered biological medicinal products as described in the directive 2001/83/EC, specific legislation has also been developed (*Regulation (EC) no 1394/2007 of the European Parliament and of the Council of 13 November 2007 on advanced therapy medicinal products*).[1a,1b] The composition of ATMPs may include components of human origin (either as active ingredient, excipients, or raw materials used in their manufacture) and, therefore, the risk of transmitting CJD or vCJD agents has to be considered.

Gene therapy and somatic cell therapy medicinal products have been recently redefined in Commission Directive 2009/120/EC amending Directive 2001/83/EC.[1a,1c] For gene therapy products no specific considerations are given regarding the minimization of transmission of CJD or vCJD as the same requirements as for other biological products, biotechnological medicinal products obtained using recombinant DNA technology or vaccines could apply. For genetically modified cells the same considerations as for somatic cell therapy products (sCTP) will be appropriate. Directives 2004/23/EC, 2006/17 and 2006/86 set standards of quality and safety for human tissues and cells intended for human applications and, therefore, their donation (in particular the donor history and screening), procurement and testing are to follow the described requirements.[1d,1e,1f] The exclusion criteria for donors related to risk of transmission of diseases caused by prions in Directive 2006/17 apply.[1e] Similarly where blood cells are used, the standards of quality and safety for collection and testing in Directives 2002/98/EC, 2004/33/EC, 2005/61/EC and 2005/62/EC should be followed.[1g,1h,1i,1j] The exclusion criteria for transmissible spongiform encephalopathies in Directive 2004/33/EC apply.[1h] Other official guidance on donor selection criteria for tissue and blood donation, respectively, should also be taken into account.

Most of the cell based medicinal products currently under clinical investigation or already in use in some members states are from autologous donors, therefore, no specific considerations regarding CJD or vCJD risk are required. For cell based products from allogeneic donors, the WHO classification and guidelines on tissue infectivity (*WHO Guidelines on Tissue Infectivity Distribution in Transmissible Spongiform Encephalopathies 2010)*[2a] should also be considered as a part of the benefit-risk assessment of the medicinal product. Tissue infectivity in CJD seems mainly confined to the central nervous system and tissues anatomically associated with it. Regarding vCJD, infectivity has also been shown associated with blood and lymphoreticular tissues so precautionary measures should be considered if any of those tissues are used as the starting material for a cell based product. Where relevant, the recommendations of the CHMP Position statement on Creutzfeldt-Jakob disease and plasma-derived and urine-derived medicinal products should be taken into account.[3a] For human cells contained in ATMPs, there is no manufacturing process to add a further barrier to transmission of a TSE agent. In any case, the final risk-benefit for the therapeutic use of these medicinal products derived from human cells and tissues will have to be decided on a case-by-case basis.

The collection and storage of cells from umbilical cords is becoming increasingly common in both allogeneic and autologous transplantation in children and adults. These cells are of foetal origin but the possibility of low levels of contamination with maternal blood can not be definitively excluded. However, the likelihood of infection is considered as extremely low, since vertical transmission in humans has not been observed in any prion disease.

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3. **European Medicines Agency**

3a CHMP Position Statement on Creutzfeldt-Jacob and plasma-derived and urine-derived medicinal products. (EMEA/CPMP/BWP/2879/02/rev 1) (Currently under revision)
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