

# INFORMATION PACKAGE VRBPAC, Nov 16, 2005

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### **Copies of the CBER presentations to the Committee:**

Presentation (slides) by Philip Krause:  
Presentation by Andrew M. Lewis Jr,  
Presentation by Arifa Khan  
Presentation by Keith Peden

### **References related to CBERs approach to using neoplastic cell substrates for vaccine manufacture: Krause talk**

Lewis, Peden, and Krause, A defined-risks approach to the regulatory assessment of the use of neoplastic cells as substrates for viral vaccine manufacture, *Dev Biol*, 106, 513-535, 2001

### **References related to tumorigenicity testing: Lewis talk**

Lewis et al. Evaluating virus-transformed cell tumorigenicity, *J Virol Meth* 79: 41-50, 1999

Reid et al. Virus carrier state suppresses tumorigenicity of tumor cells in athymic (nude) mice, *J Gen Virol* 42: 609-614, 1979

Hahn and Weinberg, Modeling the molecular circuitry of cancer, *Nature Rev* 2: 331, 2002

Dragan, et al. Biochemical events during initiation of rat hepatocarcinogenesis, *Carcinogenesis*, 15: 1451-1458, 1994

### **References related to adventitious agent testing including cell lysates: Khan talk**

Nicklas et al., Contamination of transplantable tumors, cell lines, and monoclonal antibodies with rodent viruses, *Laboratory Animal Science* 43: 296-299, 1993

Khan and Sears, Pert analysis of endogenous retroviruses induced from K-BALB mouse cells treated with 5-iododeoxyuridine: a potential strategy for detection of inducible retroviruses from vaccine cell substrates, in *Evolving Scientific and Regulatory Perspectives on Cell Substrates for Vaccine Development*, *Dev Bio* 106: 387-393, 2001

Ono, Detection and elimination of endogenous retroviruses and retrovirus-like particles in continuous cell lines, *Dev Biol Stand* 70: 69- 81, 1988

Robertson, Viruses and assuring viral safety, *Dev Biol* 113: 73-77, 2003

Onions, Animal virus contaminants of biotechnology products, *Dev Biol* 118: 155-163, 2004

Partial List of Oncogenic Viruses (Table)

**References related to testing of cell substrate DNA for oncogenicity and infectivity: Peden talk**

Burns et al., Transformation of mouse skin endothelial cells in vivo by direct application of plasmid DNA encoding the human T24 H-ras oncogene, *Oncogene* 6: 1973-1978, 1991

Kurth, Risk potential of the chromosomal insertion of foreign DNA, *Dev Biol Stand* 93: 45-56, 1998

Petricciani and Horaud, DNA, Dragons and Sanity, *Biologicals* 23: 233-238, 1995

Peden et al., Biological activity of residual cell substrate DNA, *Dev Biol Stand* 123: 2004.

**Transcripts of the following VRBPAC meeting involving the use of neoplastic cell substrates for vaccine manufacture can be obtained on line at:**

11/19/98 Advisory Committee Meeting Transcript

<http://www.fda.gov/ohrms/dockets/ac/98/transcpt/3476t1.rtf>

5/12/00 Advisory Committee Meeting Transcript (Session 6)

<http://www.fda.gov/ohrms/dockets/ac/00/transcripts/3616t2a.pdf>

<http://www.fda.gov/ohrms/dockets/ac/00/transcripts/3616t2b.pdf>

5/16/01 Advisory Committee Meeting Transcript

<http://www.fda.gov/ohrms/dockets/ac/01/transcripts/3750t1.rtf>

**The regulatory documents listed below can be obtained on line at the indicated web sites.**

CBER Points to Consider on the Characterization of Cell Lines Used to Produce Biologicals 1993

<http://www.fda.gov/cber/gdlns/ptccell.pdf>

ICH Q5D Quality of Biotechnology and Biological Products Fed Reg 63: 182, 50244, 1998

<http://www.fda.gov/cber/gdlns/qualbiot.pdf>

ICH Guidance on Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human and Animal Origin Fed Reg 63 185: 51074, 1998

<http://www.fda.gov/cber/gdlns/virsafe.pdf>

Ianconescue et al., Comparative susceptibility of a canine cell line and bluetongue virus susceptible cell lines to a bluetongue virus isolate pathogenic for dogs, *In Vitro Cell Dev Biol Anim* 32: 249-54, 1996

Khan, Retrovirus screening of vaccines cell substrates, in *Viral safety and evaluation of viral clearance from biopharmaceutical products*, *Dev Biol Stand* 88: 157-162, 1996

Robertson, Viruses and assuring viral safety, *Dev Biol* 113: 73-77, 2003

Jacobson et al., Determinants of spontaneous recovery and persistence in MDCK cells infected with lymphocytic choriomeningitis virus, *J Gen Virol* 44: 113-121, 1979

WHO Technical Report Series Requirements for the use of animal cells as in vitro substrates for the production of biologicals, 878, 19 - 53, 1998,

WHO Technical Report Series Part C Requirements for human diploid cells used for virus vaccine production 673: 64-77, 1982