

**Issues Regarding Draft Policy Proposals for the Use of
Neoplastic Cells as Substrates for Vaccine Manufacture for
Committee Discussion
May 12, 2000**

To fulfill its obligation to regulate vaccine safety and efficacy, one of CBER's missions is to promote the development of new and better viral vaccines. Several current public health challenges, including AIDS, the emergence of new strains of influenza in chickens and the threat posed by bioweapons require new approaches to vaccine development. New technologies are making the development of new vaccines possible, and the successful application of these technologies can be greatly facilitated by the use of neoplastic cell substrates for virus propagation. Tumor cells have been proscribed for use as vaccine substrates since 1954. However, over the past four decades, advances in the understanding of neoplasia and neoplastic development and in vaccine regulation have permitted a re-assessment of the proscription against the use of all types of neoplastic cells as vaccine substrates. This re-assessment has been underway in OVRP since 1998 and will continue until policy proposals regarding the use of neoplastic cells as vaccine substrates that are more comprehensive are developed. To meet its obligation to sustain the continued application of new technologies to vaccine development, CBER has developed initial draft policy proposals on the use of neoplastic cells as substrates for vaccine development and manufacture. We have presented these proposal to the Committee today, and we ask the Committee to please comment on:

- 1- CBER's Draft Policy Proposals regarding the use of neoplastic cells as substrates for vaccine manufacture;
- 2- Any of the concepts or perspectives used in the development of the Draft Policy Proposals;
- 3- Any issues CBER is considering (or may need to consider) regarding the use of neoplastic cells as substrates for viral vaccine manufacture that the Committee finds appropriate.

Draft Policy Proposal 1

(Inactivated-Viral Vaccines, Purified Viral-Vectored Vaccines or Purified, Viral Subunit Vaccines)

When produced by manufacturing processes that meet the criteria for viral clearance/inactivation required for purified biotech products, these types of viral vaccines can be developed in neoplastic cell substrates provided the passage history of the substrate is appropriately documented and the cell substrate does not contain adventitious agents.

If these vaccines are manufactured in Vero cells (see below) then conditions required for Vero cells should apply.

Residual cell substrate DNA in these products should not exceed 100 pg per dose.

Draft Policy Proposal 2
(Minimally-Purified: 1- Live-Attenuated Viral Vaccines
and 2- Virus-Vectored Vaccines)

These types of vaccines can be developed/manufactured in non-tumorigenic Vero cells based on current recommendations for cell substrate evaluation.

Residual Vero cell DNA in the final product should not exceed 10 ng per dose limit set by the WHO.

Draft Policy Proposal 3

(Minimally-Purified: 1- Live-Attenuated Viral Vaccines and 2- Virus-Vectored Vaccines)

These types of vaccines can be developed/manufactured in neoplastic human and mammalian cells that have been transformed by defined viral or cellular oncogenes and that do not contain adventitious agents provided that:

- 1- Current recommendations for cell substrates are met;
- 2- Any additional recommendations that are deemed appropriate for cells originating from a specific source and tissue are followed.

Residual cell substrate DNA in these products should not exceed the 10 ng per dose limit.

Draft Policy Proposal 4

(Minimally-Purified: 1- Live-Attenuated Viral Vaccines and 2- Virus-Vectored Vaccines)

These types of vaccines can be developed/manufactured in neoplastic human and mammalian cells (cells of defined origin that do not contain adventitious agents) that have been transformed in tissue culture by oncogenic viruses provided that:

- 1- It can be documented that the vaccine does not contain the transforming virus at the limit of detection of this virus; this limit will need to be defined.
- 2- Current recommendations for cell substrates are met;
- 3- Any additional recommendations that are deemed appropriate for cells originating from a specific source and tissue are followed.

Residual cell substrate DNA in these products should not exceed 10 ng per dose.

Draft Policy Proposal 5
(Minimally-Purified: 1- Live-Attenuated Viral Vaccines
and 2- Virus-Vectored Vaccines)

The development of these types of vaccines in neoplastic cells derived from naturally occurring tumors from humans and other mammals or from human cells and mammalian cells that have been transformed by unknown mechanisms is discouraged at this time.