

TARGETED



GENETICS

December 28, 2006

Division of Dockets Management
Food and Drug Administration
5630 Fishers Lane Room 1061 (HFA-305)
Rockville, MD 20852

RE: [Docket Number 2006D-0383] *Draft Guidance for Industry: Characterization and Qualification of Cell Substrates and Other Biological Starting Materials Used in the Production of Viral Vaccines for the Prevention and Treatment of Infectious Diseases*

Targeted Genetics Corporation (TGC) develops viral-vectored gene-based therapies and vaccines to prevent or treat acquired, inherited and infectious diseases. We appreciate the FDA's efforts in developing this draft guidance document and the opportunity to provide comments.

General Comments

We believe that this guidance will assist both the industry and the agency in setting reasonable science-based expectations for characterization and qualification of cell substrates to be used for the production of viral vaccines. This rapidly evolving area holds great promise and must be fostered.

Specific Comments

Section II.B.1 Vaccine Purity

Because live attenuated viruses, whole inactivated virions, or virus-like particles often cannot be purified as rigorouslyIn addition such vaccines are often minimally purified and are not subjected to inactivation steps.

The purification processes for highly-purified viral-based products may be much more analogous to the purification processes typical for protein-based products than to the traditional vaccine production processes and may actually be more rigorously purified than viral subunit vaccines.

You should validate any methods used to inactivate or clear potential viral contaminants...

Given that the introduction to the guidance states that these recommendations may be used to support a BLA or an IND application, please clarify the level of validation for inactivation or clearance processes expected at early stages of development.

Certificates of Analysis (COA) for all reagents and biological raw materials used for vaccine production should be included in your submission.

It is unclear whether the agency is requesting an example COA for each reagent or the COA for every lot used to produce vaccine throughout the IND period. Please clarify the agency's intent. Provision of every COA for every lot of every reagent could prove to be onerous for both the industry and the agency. Provision of example COAs in the initial IND and the BLA, as well as if any new reagents are added or significant changes are made to an existing reagent, should be sufficient.

Section II.B.4 Use of Control-Cell Cultures

Please clarify whether control-cell cultures are expected to be processed at the same scale as production cultures or if smaller scale, such as 1/10 scale, handled in the same manner as production cultures is acceptable.

Section II.B.5 Assay Validation

Please provide guidance regarding the extent of assay validation expected at early stages of development.

Section III.A.7 Generation of Cell Substrate

In addition, a cell substrate that has been derived by cell cloning might have different characteristics from the parental cell line...

Some properties of the production cell substrate, such as PrP gene sequence, may be unlikely to be affected by manipulations required for cell line generation. If the parental cell line has been thoroughly characterized for properties such as tumorigenicity, oncogenicity, etc., at what stage of development and to what extent would it be required to characterize all aspects of the new cell substrate? Please comment particularly on those properties unlikely to be affected by the manipulations, such as sequence of the PrP gene?

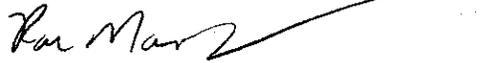
Section IV.C.1 Testing for the Presence of Residual Cells

The requirement for validation of residual cell removal may be excessive for a highly purified product. The purification process for many viral-based products incorporates multiple 0.22 μm filtration steps and may also include a nanofilter for removal of viral particles much smaller than any intact mammalian cell.

If the purification process includes one or more steps which incorporate filters validated for removal of bacteria or viruses, would the filter vendor's validation be sufficient, particularly for early phase clinical trials? We urge the agency to consider including language regarding the applicability of validation of bacteria and/or virus removal as evidence that much larger intact mammalian cells would also be removed.

We welcome the opportunity to provide feedback on this draft guidance and look forward to the agency's progress in this area. Please contact me if you require clarification or further information regarding our comments.

Sincerely,

A handwritten signature in black ink, appearing to read "Rae Saltzstein", with a long, sweeping horizontal line extending to the right.

Rae Saltzstein
Sr. Director, Quality and Regulatory Affairs
Targeted Genetics Corporation