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30 April 2021

Mr. Peter Fox
Office of Regulatory Affairs
Food and Drug Administration
12420 Parklawn Dr. Rm. 4146
Rockville MD 20857

Re: Manufacturing Considerations for Licensed and Investigational Cellular and Gene Therapy Products during COVID-19 Public Health Emergency (Docket No. FDA-2020-D-1137)

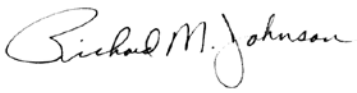
Dear Mr. Fox:

The PDA's COVID-19 Task Force appreciates the opportunity to comment on FDA's Guidance for Industry and Staff regarding Manufacturing Considerations for Licensed and Investigational Cellular and Gene Therapy Products during COVID-19 Public Health Emergency. In general, the draft guidance provides useful information. In our attached comments, the PDA COVID-19 Task Force proposes a clarification to the interpretation of referenced literature. The clarification will ensure a common understanding for agency staff and regulated industry.

PDA is a non-profit international professional association of more than 10,000 individual member scientists having an interest in the fields of pharmaceutical, biological, and device manufacturing and quality. Our comments have been prepared by a committee of volunteers with expertise in pharmaceutical and biopharmaceutical manufacturing on behalf of PDA's Advanced Therapy Medicinal Products Advisory Board and Board of Directors.

If you have any questions, please do not hesitate to contact me via email at johnson@pda.org.

Sincerely,



Richard Johnson
President and CEO

cc: Glenn Wright, PDA; Josh Eaton, PDA

U.S. Food and Drug Administration
Guidance for Industry:
Manufacturing Considerations for Licensed and Investigational Cellular and Gene Therapy Products during COVID-19 Public Health Emergency (Docket Number: FDA-2020-D-1137)
January 26, 2021

General Comments

General Comments	Rationale

Specific Comments to the Text

Page	Current Text	Proposed Change	Rationale
4, Section C	"SARS-CoV-2 has been shown to be capable of infecting and replicating in cells commonly used for vector production (e.g., HEK293 and Vero cells) (Refs 2 and 3)."	We proposed that the Guidance document does not contain the statement cited.	When we reviewed the content of the referenced scientific articles, we found that the HEK293 cells discussed in the articles were genetically modified to express proteins required for / supportive of infection by SARS-CoV-2. As such, the referenced HEK293 cells would not represent the HEK293 cell lines used in biologics manufacturing. For the likelihood of the SARS-CoV-2 infecting or replicating in non-modified HEK293 cell lines, we would like to direct your attention to the Modrof, Kerschbaum, Farcet, Niemeyer, Corman, and Kreil publication 2020 SARS-CoV-2 and the safety margins of cell-based biological medicinal products, published online in Biologicals on August 29, 2020 (for the full text, please see: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7456270/pdf/main.pdf). As the article states, with the pandemic emergence of SARS-CoV-2, the exposure of cell substrates used for manufacturing of medicines had become a possibility. Cell lines used in biomanufacturing, including HEK293 and Vero, were evaluated for their SARS-CoV-2 susceptibility and the detection of SARS-CoV-2 in culture supernatants by routine adventitious virus testing of fermenter harvest tested. Data presented in the article confirms that Vero cells are susceptible to SARS-CoV-2 infection while the HEK293 cells are not susceptible to SARS-CoV-2 infection. Therefore, the inclusion of the HEK293 cell line as an example of cell lines that support the SARS-CoV-2 infection is not appropriate in the guidance, unless listed as the genetically modified HEK293 cell line referenced in the article.