Considerations for the Development of Chimeric Antigen Receptor (CAR) T Cell Products; Guidance for Industry Docket No. FDA-2021-D-0404

## I. REFERENCES

- 1. Formal Meetings Between the FDA and Sponsors or Applicants; Draft Guidance for Industry, December 2017, <u>https://www.fda.gov/media/109951/download</u>.\*
- 2. Guidance for Industry: Q8, Q9, & Q10 Questions and Answers -- Appendix: Q&As from Training Sessions (Q8, Q9, & Q10 Points to Consider), July 2012, https://www.fda.gov/media/83904/download.
- 3. Chemistry, Manufacturing, and Control (CMC) Information for Human Gene Therapy Investigational New Drug Applications (INDs): Guidance for Industry, January 2020, <u>https://www.fda.gov/media/113760/download</u>.
- 4. Jensen, M.C. and S.R. Riddell, Designing chimeric antigen receptors to effectively and safely target tumors. Curr Opin Immunol, 2015. 33: p. 9-15.
- 5. June, C.H. and M. Sadelain, Chimeric Antigen Receptor Therapy. N Engl J Med, 2018. 379(1): p. 64-73.
- 6. Weinkove, R., et al., Selecting costimulatory domains for chimeric antigen receptors: functional and clinical considerations. Clin Transl Immunology, 2019. 8(5): p. e1049.
- 7. Alabanza, L., et al., Function of Novel Anti-CD19 Chimeric Antigen Receptors with Human Variable Regions Is Affected by Hinge and Transmembrane Domains. Mol Ther, 2017. 25(11): p. 2452-2465.
- 8. Hudecek, M., et al., The nonsignaling extracellular spacer domain of chimeric antigen receptors is decisive for in vivo antitumor activity. Cancer Immunol Res, 2015. 3(2): p. 125-135.
- 9. Jonnalagadda, M., et al., Chimeric antigen receptors with mutated IgG4 Fc spacer avoid fc receptor binding and improve T cell persistence and antitumor efficacy. Mol Ther, 2015. 23(4): p. 757-768.
- 10. Long Term Follow-up After Administration of Human Gene Therapy Products: Guidance for Industry, January 2020, <u>https://www.fda.gov/media/113768/download</u>.
- 11. Tasian, S.K., et al., Optimized depletion of chimeric antigen receptor T cells in murine xenograft models of human acute myeloid leukemia. Blood, 2017. 129(17): p. 2395-2407.
- 12. Budde, L.E., et al., Combining a CD20 chimeric antigen receptor and an inducible caspase 9 suicide switch to improve the efficacy and safety of T cell adoptive immunotherapy for lymphoma. PLoS One, 2013. 8(12): p. e82742.
- 13. Di Stasi, A., et al., Inducible apoptosis as a safety switch for adoptive cell therapy. N Engl J Med, 2011. 365(18): p. 1673-1683.
- 14. Kamiya, T., et al., A novel method to generate T-cell receptor-deficient chimeric antigen receptor T cells. Blood Adv, 2018. 2(5): p. 517-528.
- 15. Human Gene Therapy Products Incorporating Human Genome Editing: Guidance for Industry, January 2024, <u>https://www.fda.gov/media/156894/download</u>.
- 16. Guidance for Industry: M4Q: The CTD Quality, August 2001, https://www.fda.gov/media/71581/download.
- 17. Guidance for Industry: CGMP for Phase I Investigational Drugs, July 2008, https://www.fda.gov/media/70975/download.

- 18. Guidance for Industry: Q2B Validation of Analytical Procedures: Methodology, May 1997, <u>https://www.fda.gov/media/71725/download</u>.
- 19. Testing of Retroviral Vector-Based Human Gene Therapy Products for Replication Competent Retrovirus During Product Manufacture and Patient Follow-up: Guidance for Industry, January 2020, <u>https://www.fda.gov/media/113790/download</u>.
- 20. Guidance for Industry: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products, August 2007, https://www.fda.gov/media/73072/download.^
- 21. Elavia, N., et al., Effects of starting cellular material composition on chimeric antigen receptor T-cell expansion and characteristics. Transfusion, 2019. 59(5): p. 1755-1764.
- 22. Stroncek, D.F., et al., Elutriated lymphocytes for manufacturing chimeric antigen receptor T cells. J Transl Med, 2017. 15(1): p. 59.
- 23. Stroncek, D.F., et al., Myeloid cells in peripheral blood mononuclear cell concentrates inhibit the expansion of chimeric antigen receptor T cells. Cytotherapy, 2016. 18(7): p. 893-901.
- 24. Levine, B.L., et al., Global Manufacturing of CAR T Cell Therapy. Mol Ther Methods Clin Dev, 2017. 4: p. 92-101.
- 25. Vormittag, P., et al., A guide to manufacturing CAR T cell therapies. Curr Opin Biotechnol, 2018. 53: p. 164-181.
- 26. Guidance for Industry: Q8(R2) Pharmaceutical Development, November 2009, <u>https://www.fda.gov/media/71535/download</u>.
- 27. Federal Register: Amendments to Sterility Test Requirements for Biological Products; Final Rule (77 FR 26162, May 3, 2012), <u>https://www.govinfo.gov/content/pkg/FR-2012-05-03/pdf/2012-10649.pdf</u>.
- 28. Guidance for Industry: Sterile Drug Products Produced by Aseptic Processing Current Good Manufacturing Practice, September 2004, https://www.fda.gov/media/71026/download.^
- 29. Guidance for Industry: Analytical Procedures and Methods Validation for Drugs and Biologics, July 2015, <u>https://www.fda.gov/media/87801/download</u>.^
- 30. ICH Harmonised Tripartite Guideline: Validation of Analytical Procedures: Text and Methodology Q2(R1), November 2005, <u>https://www.fda.gov/media/152208/download</u>.
- 31. Hacein-Bey-Abina, S., et al., LMO2-associated clonal T cell proliferation in two patients after gene therapy for SCID-X1. Science, 2003. 302(5644): p. 415-419.
- 32. Heinrich, T., et al., Mature T-cell lymphomagenesis induced by retroviral insertional activation of Janus kinase 1. Mol Ther, 2013. 21(6): p. 1160-1168.
- 33. Guidance for Industry: Potency Tests for Cellular and Gene Therapy Products, January 2011, <u>https://www.fda.gov/media/79856/download</u>.
- 34. Guidance for Industry: Studying Multiple Versions of a Cellular or Gene Therapy Product in an Early-Phase Clinical Trial, November 2022, <u>https://www.fda.gov/media/152536/download</u>.^
- 35. ICH Harmonized Tripartite Guideline: Comparability of Biotechnological/Biological Products Subject to Changes in their Manufacturing Process: Q5E, November 2004, <u>https://www.fda.gov/media/71489/download</u>.
- 36. Guidance for Industry: Q5E Comparability of Biotechnological/Biological Products Subject to Changes in Their Manufacturing Process, June 2005, <u>https://www.fda.gov/media/71489/download</u>.

- 37. Comparability Protocols for Human Drugs and Biologics: Chemistry, Manufacturing, and Controls Information: Draft Guidance for Industry,\* April 2016, <u>https://www.fda.gov/media/97148/download</u>.
- 38. Contract Manufacturing Arrangements for Drugs: Quality Agreements; Guidance for Industry, November 2016, <u>https://www.fda.gov/media/86193/download</u>.
- 39. Guidance for Industry: Preclinical Assessment of Investigational Cellular and Gene Therapy Products, November 2013, <u>https://www.fda.gov/media/87564/download</u>.
- 40. Fujiwara, K, et al., Hinge and transmembrane domains of chimeric antigen receptor regulate receptor expression and signaling threshold. Cells, 2020. 9(5): p. 1182.^
- 41. In Vitro Companion Diagnostic Devices: Guidance for Industry and Food and Drug Administration Staff, August 2014, <u>https://www.fda.gov/media/81309/download</u>.
- 42. Investigational In Vitro Diagnostics in Oncology Trials: Streamlined Submission Process for Study Risk Determination: Guidance for Industry, October 2019, https://www.fda.gov/media/112605/download.
- 43. Principles for Codevelopment of an In Vitro Companion Diagnostic Device with a Therapeutic Product: Draft Guidance for Industry and Food and Drug Administration Staff, July 2016, <u>https://www.fda.gov/media/99030/download</u>.\*^
- 44. Considerations for the Design of Early-Phase Clinical Trials of Cellular and Gene Therapy Products: Guidance for Industry, June 2017, https://www.fda.gov/media/106369/download.
- 45. Ethical Considerations for Clinical Investigations of Medical Products Involving Children; Draft Guidance for Industry, Sponsors, and IRBs, September 2022, https://www.fda.gov/media/161740/download.\*^
- 46. Bioanalytical Method Validation: Guidance for Industry, May 2018, <u>https://www.fda.gov/media/70858/download</u>.
- 47. Lee, D.W., et al., ASTCT Consensus Grading for Cytokine Release Syndrome and Neurologic Toxicity Associated with Immune Effector Cells. Biol Blood Marrow Transplant, 2019. 25(4): p. 625-638.^
- 48. Harris, A.C., et al., International, Multicenter Standardization of Acute Graft-versus-Host Disease Clinical Data Collection: A Report from the Mount Sinai Acute GVHD International Consortium. Biol Blood Marrow Transplant, 2016. 22(1): p. 4-10.

^ New reference in final guidance.

\* When finalized, this guidance will represent FDA's current thinking on this topic.