

October 27, 2023

Robert Califf, M.D.
Commissioner
U.S. Food and Drug Administration
White Oak Campus
10903 New Hampshire Avenue
Silver Spring, MD 20993

Via e-mail: commissioner@fda.hhs.gov

Dear Commissioner Califf:

On behalf of the American Society of Transplant Surgeons (ASTS)¹ and the American Society of Transplantation (AST)², we writing to express our support for the Biomarker Qualification Plan submitted in July 2023 to the FDA by the Transplant Therapeutics Consortium (TCC). As the two largest transplantation societies in the United States representing experts in the field, we believe strongly that without the qualification of surrogate endpoints such as the iBox, innovation in the field of immunosuppressants in transplantation will continue to stagnate, significantly and adversely impacting our patients and their families. We are concerned, however, about certain informal communications received from the FDA expressing doubts about the need for surrogate endpoints for use in evaluating the safety and efficacy of immunosuppressants indicated for kidney transplant recipients.

The unmet need for new immunosuppressive drugs in kidney transplantation is clear. While early graft survival has improved, long-term renal allograft survival has improved minimally over the past two decades. Patients want their kidneys to last many years, but there are no clinical trial endpoints or surrogate endpoints to develop new drugs to accomplish this goal. The last novel agent approved for de novo immunosuppression following kidney transplantation was approved more than a decade ago (belatacept in 2011). This stagnation is due in large measure to the difficulty of obtaining approval of new agents utilizing the FDA's current clinical trial endpoint--a composite endpoint of death, graft loss, and rejection assessed at one-year post-transplant.

Under the Accelerated Approval Program, the ASTS and AST have worked through a public-private partnership between the FDA and the TTC to gather data in support of a qualification plan for a composite biomarker panel for use as a reasonably likely surrogate endpoint for clinical trials in de novo kidney

¹ ASTS is a medical specialty society representing approximately 2,000 professionals dedicated to advancing the art and science of transplant surgery through patient care, research, education, and advocacy.

² The American Society of Transplantation (AST) is a multidisciplinary medical professional society representing over 4,900 members engaged in advancing the field of organ transplantation through a lens of equity and inclusion.

transplantation. The qualification plan is a consensus document developed with great care and hard work over seven years by a team of experts in the field. As the two major transplant societies, we have fully vetted this plan and support it. The qualification plan was submitted in July 2023, and a determination regarding whether the qualification plan meets FDA requirements is anticipated by the end of the year. However, after more than five years of apparent alignment between FDA and the TTC, FDA staff recently suggested that the current composite endpoint best meets the needs of patients, and that the agency intends to continue to utilize the current composite endpoint.

Over the past eight years, the FDA sponsored four public meetings on the future of transplant drug innovation and unmet patient needs, during which patients consistently emphasized the pressing need for the agency to accelerate approval of new immunosuppressants and to focus on long term graft and patient survival (beyond one year). The same concerns were expressed in a survey recent fielded by the American Association of Kidney Patients (AAKP).

Given the gravity of our concern, we ask your office to take an active role with the review of the qualification plan submitted by the TTC. We are of the strong opinion that there can be no disputing the unmet need for new drug development tools/endpoints for clinical trials in transplantation and for innovation in this area. The qualification plan recognizes these needs and warrants expeditious consideration and approval.

We appreciate the opportunity to comment on this important topic. If you have any questions regarding these comments or need any further information, please contact Emily Besser, MA, CAE, at emily.besser@asts.org or Bill Applegate at bapplegate@polsinelli.com.

Respectfully,



Elizabeth Pomfret, MD, PhD
President, American Society of Transplant Surgeons



Josh Levitsky, MD, MS, FAST
President, American Society of Transplantation