July 13, 2026

Kyle A. Diamantas, J.D.
Acting Commissioner
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, Maryland 20993

Submitted electronically via regulations.gov

Re: Docket No. FDA-2026-N-4492 "Drug Repurposing for Unmet Medical Needs; Request for Information."

Dear Acting Administrator Diamantas:

The American Society of Transplant Surgeons (ASTS) is pleased to have the opportunity to submit these comments in response to the RFI. We appreciate the FDA's interest in repurposing of FDA-approved drugs and believe that a repurposing initiative has the potential to significantly expand transplant recipients' access to a broad range of immunosuppressive drugs that are currently used off-label but that are already clinically accepted as the standard of care.

The use of immunosuppressive drugs in solid organ transplantation is exceptionally high, with some studies estimating that **up to 100% of maintenance immunosuppression for certain organs (like lungs) is prescribed off-label**. Across all organ transplants, the vast majority of these life-saving drugs lack sponsor-conducted, organ-specific FDA approvals, making off-label use the clinical standard. [1, 2]

The rate of off-label and off-compendia (medication use neither FDA-approved nor endorsed by major clinical compendia) prescriptions varies widely depending on the type of organ transplanted: [1, 2, 3, 4]

- **Lung Transplants:** Up to **66.5%** are off-label and off-compendia (with certain critical drugs reaching **100%** off-label use). No maintenance immunosuppressants are specifically FDA-approved for lung transplants. [1, 2, 3]
- **Heart Transplants:** Approximately **21.8%** are off-label and off-compendia, with some studies showing induction-phase off-label use as high as **91.3%**. [1, 2]
- **Intestine & Pancreas Transplants: 34.2%** (intestine) and **33.4%** (pancreas) are off-label and off-compendia. No maintenance immunosuppressive agents are FDA-approved for either of these organs. [1, 2]
- **Liver Transplants: 16.5%** are off-label and off-compendia. [1]
- **Kidney Transplants:** Kidney transplant maintenance has the highest rate of on-label usage. While specific induction agents (like Alemtuzumab) are used off-label, standard maintenance is primarily FDA-approved. [1, 2, 3, 4]

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Off-label use is the standard of care in transplantation because conducting phase 3, sponsor-driven trials for specific organ types is cost-prohibitive due to the smaller patient populations [1, 2, 3]. Moreover, there is a clinical consensus that individualized "triple-drug" regimens (e.g., tacrolimus, mycophenolate, and corticosteroids), work for various organs even without specific organ-labeling from the FDA. [1, 2, 3, 4]

Because of the extensive off-label use of immunosuppressive drugs for transplant recipients, transplant recipients—especially non-renal transplant recipients—face extensive reimbursement barriers. Commercial insurance plans often deny coverage if a drug is prescribed for an off-label indication, and transplant recipients who utilize Medicare Part D face coverage denials for off-label medications unless the prescription is specifically supported by two outdated Centers for Medicare & Medicaid Services (CMS)–approved compendia [1, 2] (Merative Micromedex and AHFS-Drug Information [1, 2, 3]). Medicare Advantage plans likewise are required to cover off-label uses of immunosuppressive drugs only if the specific indication is supported by standard CMS-approved drug compendia, such as AHFS-Drug Information or Merative Micromedex. Otherwise, plans may deny coverage for off-label indications not explicitly recognized by these resources. Lung, heart, and liver patients face frequent denials because their standard therapies are often missing from these official logs. [1, 2]. The majority of these coverage denials are upheld, forcing patients to pay entirely out-of-pocket or apply for pharmaceutical discount programs. Without insurance, life-saving immunosuppressive drugs can cost $10,000 to $14,000 or more per year. The reimbursement barriers resulting from restrictive insurance coverage of off-label indications could be eliminated if there were a viable pathway to repurpose immunosuppressive drugs already approved for kidney transplants for recipients of extra-renal transplants.

We also believe that a number of drugs not initially approved for the use in solid organ transplant recipients could be repurposed to meet the critical needs of these patients. For example, drugs that are approved for graft-versus-host disease (GVHD) and/or autoimmune indications may be helpful for solid organ transplant recipients, and certain anti-virals (e.g. Cidofovir/brincidofovir) have significant potential to address BK Virus, a common human polyomavirus that remains dormant in most people but can cause serious kidney complications or graft failure in transplant and other immunocompromised patients.

We would appreciate the opportunity to meet with the FDA to explore potential pathways for repurposing approved drugs to reduce the barriers caused by off-label use. If you have any questions, please do not hesitate to contact ASTS' Director, Advocacy and Professional Practices, Emily.Besser@asts.org.

Sincerely,

Henry B Randall MD, MBA

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President