OPTN ORGAN PROCUREMENT AND TRANSPLANTATION NETWORK

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August 19, 2022

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
U.S. Department of Health and Human Services
P.O. Box 8016
Baltimore, MD 21244

RE: Proposed Rule; Clinical Laboratory Improvement Amendments of 1988 (CLIA) Fees; Histocompatibility, Personnel, and Alternative Sanctions for Certificate of Waiver Laboratories [CMS-3326-P]

Dear Ms. Brooks-LaSure,

The Organ Procurement and Transplantation Network (OPTN) would like to thank CMS for the opportunity to respond to the Proposed Rule [CMS-3326-P] related to Histocompatibility. We strongly support the effort to update, streamline, and modernize these federal regulations, which will in turn help facilitate organ transplantation.

The OPTN **strongly supports** the removal of the requirement for prospective physical crossmatching in renal transplantation. Allowing additional flexibility for virtual crossmatching and newer forms of immunologic assessment will greatly increase efficiency of transplantation and reduce cold ischemic time, as physical crossmatches often occur after transplant programs receive the procured organ due to logistical constraints. In some cases a prospective physical crossmatch may still be warranted, but the use of virtual crossmatching will allow laboratories and transplant programs to develop appropriate evidence-based protocols on determining which form of immunologic assessment is required.

We also strongly support the written criteria identified for performing a crossmatch, as these are essential components to an immunologic assessment. We believe that allowing laboratories to develop these written criteria will allow flexibility to maintain current practices, while still specifying required considerations to protect recipient safety.

We would appreciate additional clarity around the intended use of the proposed recipient specimen for crossmatch to be obtained on the day of transplant, and what the required use of that sample would be. We believe that the laboratory and clinical team should be able to define how current a sample must be for candidate testing, as already required in the proposed 42 CFR

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§ 493.1278 (d)(2)(viii). We believe the laboratory and clinical team should be able to assess need for an updated sample after considering timing, potential sensitizing events, and previous candidate alloantibody levels, and that it may not be necessary to draw an additional recipient specimen in all cases.

We also believe there needs to be additional flexibility on pre-transplant samples drawn for young pediatric candidates. The small size of some pediatric candidates can make additional blood volume drawn immediately pre-transplant harmful. We recommend that this regulation balance the risk of undetected candidate antibodies with the risk for overdrawing blood in small pediatric candidates, and thus create an exception for this requirement for candidates under 12 years of age. The OPTN and US Public Health Service (PHS) have created a similar exception for pediatric candidate pre-transplant infectious disease testing due to concerns raised by pediatric transplant programs.

We also believe that there should be some additional language changes for clarity in expectations for laboratory members. The proposed rule refers to typing of the donor at the "serologic" level, which we believe is not the intent of the rule. Serologic typing is insufficient for current clinical histocompatibility testing due to its many limitations, including low specificity at certain loci and a potential for certain false negative results. OPTN policy requires that deceased organ donor typing be performed using molecular methods, and we believe the intent of this proposed rule is to require "typing of the donor by molecular methods at the serologic split antigen equivalent". We believe that specifying the requirement in this way would allow for additional clarity and reduce the likelihood for misinterpretation.

We also believe that the proposed rule should use the terminology "immunologic assessment" instead of "testing" throughout the rule to reduce ambiguity when referring to crossmatching. As specified in the background of the proposal, virtual crossmatching is not a test. A "test" requires a specific procedure be performed, and virtual crossmatches are often assessments of existing candidate and donor test results to determine potential immunologic compatibility and/or the need for additional testing to occur. Therefore, we recommend changing the proposed language in 42 CFR § 493.1278(d)(3) and 42 CFR § 493.1278(e) so that it is also inclusive of immunologic assessments. We believe this would be clearer to the community and better aligned with the intent of the changes.

Overall, the OPTN **strongly supports** the proposed changes, and we believe that allowing virtual crossmatching as a method of immunologic assessment prior to renal transplantation will greatly benefit transplant candidates and recipients by reducing unnecessary cold ischemic time for deceased donor kidney transplantation.

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Sincerely,

Jerry McCauley, MD, MPH
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