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WHITE PAPER

April 2018

The Shifting Landscape of Organ Allocation for Transplantation

Recent policy changes and the prospect of new organ sources have markedly altered the landscape for organ transplantation. In particular, new allocation policies for lung and liver transplants, and advances in gene-editing technology that could potentially facilitate the animal-to-human transplant process, are affecting the organ transplant community. This Jones Day White Paper reviews these developments, with particular attention to recent legal challenges and the resulting policy changes, the potential for extended use of animal organs, and the bylaws revisions under consideration by the United Network for Organ Sharing.

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EXECUTIVE SUMMARY

The Organ Procurement and Transplantation Network ("OPTN")/ United Network for Organ Sharing ("UNOS") has recently modified the national lung allocation policy as a result of a court-ordered emergency review of a lawsuit by a lung transplant candidate in New York against the Department of Health and Human Services ("HHS"). The national liver allocation policy was similarly revised by OPTN/UNOS following a lengthy review period. In parallel, the use of CRISPR, the new gene-editing technology, has removed a key barrier to animal-to-human transplants, which could begin to ease organ allocation concerns within the next few years.

For an interim period, there is additional transplant priority for liver and lung candidates meeting certain severity of illness requirements and who are within 150-250 nautical miles of the donor hospital but in a different donor service area ("DSA"). This shift in allocation policy reflects a greater emphasis on utility and equity, but it could raise other inequities in distributing a valuable resource. As scientists move closer to achieving successful animal-to-human transplants, organ allocation concerns may diminish while burdens on the resources and administrative infrastructure of transplant programs intensify.

A report from an Ad Hoc Committee on Geography is expected in the coming months to outline protocols and establish guidelines for the use of geography within the OPTN/UNOS policies more broadly. In addition, a variety of operational and regulatory changes may be on the horizon with recent advancements in animal-to-human organ transplants. These changes could extend not only to the daily operational needs of transplant centers but to shifts in billing policies, related services such as dialysis, and attendant research and animal ethics concerns.

Nevertheless, transplant programs will continue to be subject to rigorous and complex regulatory oversight. Transplant programs and their institutions should be aware that UNOS has recently proposed modifications to "Appendix L," the section of its bylaws outlining compliance monitoring and disciplinary oversight of transplant programs.

BACKGROUND

In the field of solid organ transplantation, one of the most oft-debated topics is how best to manage organ allocation. The gap between supply and demand continues to grow, placing pressure on UNOS, which operates the national OPTN under contract with HHS, to review its organ allocation policies. According to UNOS, 20 people die waiting for an organ transplant each day, and a new transplant candidate joins the waitlist every 10 minutes.

UNOS divides the country into 11 distinct regions, each known as a donor service area ("DSA"). These regions are designed to balance an interest in keeping organs local to reduce time from retrieval to transplantation, with an interest in distributing organs over as broad a geographic area as feasible based on medical urgency. Until recently, many OPTN/UNOS organ allocation policies generally required that procured organs be offered to all transplant candidates within the DSA, including those with a relatively low severity of illness, before they are offered to patients with high severity of illness within a certain radius outside of the DSA. For example, with respect to adult lung allocation, only after all lung candidates in the donor's DSA had been offered the donor lung could it be available to patients within 500 nautical miles of the donor hospital.

However, recent shifts in policy represent a movement away from strict adherence to the DSA model. And a breakthrough scientific development could permanently alter the organ allocation landscape and create new issues for the transplant community.

LEGAL INTERVENTION AND RECENT POLICY AMENDMENTS

In November 2017, a 21-year-old New York City patient suffering from a fatal lung disease sued HHS and challenged the DSA system for lung allocation. The patient claimed that the DSAs were skewed such that she would be secondary to a less medically needy individual located farther away in New Jersey when being considered for a lung from a donor in New Jersey, just outside of the New York City area. As a result, the patient would be denied the lung solely because of her DSA listing. The suit was originally brought against HHS in federal District Court for the Southern District of New York, with the patient seeking a temporary restraining order. The court denied the request, and the decision was appealed to the U.S. Court of Appeals for the Second Circuit. HHS directed OPTN/UNOS to conduct an emergent review of its lung allocation policy, which was revised within a few days. HHS notified the court of the

policy change in advance of the appeal ruling, and the patient dropped the injunction suit as a result.

Under the new lung allocation policy, a 250-nautical mile concentric circle around the donor hospital serves as the first level of distribution, rather than the DSA. The policy was revised by the OPTN/UNOS Executive Committee as a temporary measure, and will remain in effect for one year as OPTN/UNOS and HHS assess the changes it may have on the transplant allocation system.

While the lung allocation policy was amended in response to a legal challenge, OPTN/UNOS has been evaluating the effect of geography on transplant access in the liver program for the past five years. The liver allocation policy was amended in December 2017 following this lengthy review period and multiple opportunities for public comment. Among the key provisions is additional transplant priority for liver candidates meeting certain severity of illness requirements and who are either within the same DSA as the liver donor or are within 150 nautical miles of the donor hospital but in a different DSA. Coincidentally, this policy amendment was issued within days of HHS's receipt of a letter from the attorneys who represented the New York City lung patient seeking intervention on behalf of a liver patient.

While these amendments affect only the lung and liver transplant programs, this shift in policy may expand to other thoracic and abdominal organs, such as the heart, pancreas, and kidney. An Ad Hoc Committee on Geography was recently formed to establish guidelines for the use of geography within OPTN/UNOS policies generally. The Committee's report is expected in the coming months.

In focusing on medical need, rather than a patient's geographic residence and listing, the new lung and liver allocation policies reflect a greater emphasis on utility and equity. However, there are concerns that the policies' geographic shift will simply replace current disparities with new ones. In highly concentrated population centers, a shift away from DSA priority may move organs to centralized locations, thereby reducing access for smaller or rural transplant centers. Additionally, some members of the transplant community are skeptical of the use of legal challenges by individual patients to change transplant policy rather than a more thoughtful, systematic review process focused on the needs of all patients. The report of the Ad Hoc Committee on Geography is highly anticipated in the transplant community.

NOVEL ORGAN SOURCES

Organ allocation policy amendments were not the only transplant-related developments in 2017. Researchers recently overcame a major obstacle in the road toward alleviating the shortage of organs, which could lead to a significant increase in the number of transplant surgeries. Pigs have long been attractive to scientists looking for a solution to the organ shortage problem because pig organs, particularly the heart and kidneys, are similar in size and function to human organs. However, pig cells have retroviruses that are able to infect human cells and risk causing dangerous infections in organ recipients. While scientists debate the extent of the danger of such retroviruses in humans, researchers might have solved the problem using CRISPR technology. As published in *Science* in August 2017, researchers were able to remove the viral DNA from the pig cell genome and successfully clone piglets that did not carry the retroviruses.

Removal of the retroviruses is a critical step toward the possibility of increasing the volume of transplant surgeries and shortening waiting lists through pig organ transplants. Dr. George Church, a professor at Harvard Medical School and the lead researcher, said the first pig-to-human transplants could occur within two years. If successful, pig organ transplants have the potential to dramatically increase the number of organs available for transplant. This will have a ripple effect throughout the transplant community—increasing demands on transplant centers and affecting the legal landscape for organ transplants.

As the research continues to develop, transplant centers and other health care providers should consider the following issues when preparing for a future involving pig organ transplants:

Increased Demand Requires Increased Resources

According to UNOS, there were 34,800 organ transplants last year, with more than 115,000 patients currently on waiting lists for new organs. Of those, about 95,000 patients await kidney transplants and nearly 4,000 are waiting for hearts. If these organs become available through genetically modified pigs, a large percentage of those waiting for human organs may elect instead to have prompt surgery using pig organs, potentially doubling

or even tripling the number of organ transplant surgeries performed each year. This significant increase in surgeries would create a massive operational burden on transplant centers, especially in the early years of pig organ availability.

In addition to increasing demands for operating room time, transplant surgeons, and skilled clinical personnel, the increase in organs would require significantly greater amounts of induction immunosuppressants and other anti-rejection drugs. Researchers are working to genetically engineer pigs with organs that would not require anti-rejection drugs, but achieving that goal is unlikely to happen before pig organs are otherwise ready for transplant.

As pig organ transplants become more of a reality, transplant centers should start evaluating their operating room efficiencies and supply chain options for increasing the supply of specialized drugs. In the future, hiring additional clinical and administrative personnel will be necessary to keep up with the demand for surgeries. Demand may exceed supply initially, and additional efforts may be needed to recruit qualified personnel to transplant medicine training programs.

Changes to Standard Acquisition Charges and Revenue

Medicare currently reimburses hospitals for organ procurement based on standard acquisition charges for either a living donor or cadaveric donor. These rates are an average charge per type of organ that estimate the hospital's reasonable and necessary expected costs to procure the organ, including the cost of transporting the organ, surgeon fees for excising the organ, costs of tissue typing, and operating room costs. Indirect costs, including preservation technicians and transplant coordinators, are also included.

If organs were no longer procured from human donors, the standard acquisition charges may change dramatically. Medicare may end up developing a third category of standard acquisition charges for organs procured from pigs, which presumably would have lower surgery, transportation, and operating costs, but may come with a high price tag from the commercial company that developed and sold the pig organ.

Initially, hospital revenue may increase with the additional volume of surgeries, but if the reimbursement rates decline because of the simpler procurement model, overall revenue for transplant surgeries may be reduced over time until reimbursement rates stabilize.

Regulatory and Administrative Changes

Much of the regulatory and administrative infrastructure surrounding organ transplantation, including the policies of OPTN/UNOS and Organ Procurement Organizations ("OPOs"), are centered on responsible organ stewardship and preservation of these precious resources—i.e., producing the greatest good. Because human organs sufficient for transplant are so rare, as described above, an extensive policy framework has developed around the allocation of organs, determining waitlist priority, and seeking donations from patients and families. If organs were more readily available, there would be less of a need to scrutinize waitlists and facilitate human donations. Efforts directed toward these activities could be redirected toward maximizing each patient's opportunity for survival, much like any other clinical service line.

With pig organs, there will also be less of an administrative burden on the transplant center in terms of the need to manage emergency surgeries. Transplant surgeries could be scheduled in advance. Additionally, transplant surgeons and centers may realize efficiencies by scheduling back-to-back procedures, akin to joint replacement surgeries, knowing that the necessary organs will be available when needed.

Fewer Patients Requiring Dialysis

According to the United States Renal Data System, in 2014, Medicare spent $32.8 billion on end-stage renal disease, which accounted for 7.2 percent of overall Medicare fee-for-service claims. Medicare is currently covering more than 450,000 patients on dialysis for kidney failure and nearly 200,000 patients who have a functioning kidney transplant. According to the UCSF Kidney Project, dialysis costs an average of $89,000 per patient annually, while post-surgery care for a transplant recipient costs about $25,000 a year. If more patients could receive a transplant, Medicare has the potential to save billions of dollars a year in reduced dialysis costs. If pig kidneys were available for transplant, more patients might opt for transplants, significantly reducing the demand for dialysis centers.

Animal Rights and Ethical Considerations

Animal rights groups frequently target high-profile research. If major academic medical centers start leading the charge in pursuing pig organ transplants clinically, animal rights groups are likely to challenge the treatment of the donor pigs and the ethical merits of creating a pig solely for its organs and not allowing the pig to live a full life. People for the Ethical Treatment of Animals ("PETA") has previously stated in a

letter to the Food & Drug Administration that it is against the use of animals for organ transplants.

Transplant centers thinking about pursuing pig organ transplants should make sure that their animal research and transplant policies are up-to-date and that researchers and transplant teams know how to report suspicious activity or safety concerns.

UNOS REEVALUATING BYLAWS AND DISCIPLINARY SYSTEM

During this period of significant change, UNOS will continue to monitor and investigate members for potential policy violations. Notably, this process is also scheduled for an amendment. UNOS has embarked on an intensive project of rewriting "Appendix L," the section of its bylaws regarding compliance monitoring and disciplinary oversight of transplant programs. This reevaluation comes after nearly 30 years of the existing disciplinary system that has over time become disfavored in the transplant community and within UNOS itself.

This process has now entered a final stage—public comment on the proposed Appendix L and the revised disciplinary approach. Jones Day has played a significant role in addressing these changes by participating side-by-side with UNOS and by providing suggestions and recommendations throughout the bylaw revision process.

KEY TAKEAWAYS

1. An Ad Hoc Committee on Geography's report is expected to establish guidelines for the use of geography within OPTN/UNOS policies. In the interim, amendments to the lung and liver transplant programs are in effect for one year and may expand to other thoracic and abdominal organs, such as the heart, pancreas, and kidney. Specifically, the new lung and liver allocation policies shift the focus from defined DSAs to geographic proximity to the donor hospital.
2. There is a renewed debate on how, and to what extent, legal challenges by individual patients should affect transplant policy. The lung allocation policy was amended by OPTN/UNOS following a legal challenge from a lung transplant candidate, while the liver policy was amended following a multiyear review process. Some members of the transplant community are concerned that significant shifts in transplant policy will come at the foot of legal challenges rather than a more holistic and systematic review process focused on the needs of all patients.
3. Transplant centers and other health care providers should be considering a host of regulatory and operational issues as novel animal-to-human transplant models may increase organ supply in the near future. Providers and institutions must anticipate increased demand for facilities, personnel, and immunosuppressants, as well as shifting needs for patients receiving related services, such as dialysis. There will also be significant discussion and debate regarding animal ethics, additional research, and long-term organ viability in humans.

LAWYER CONTACTS

For assistance in interpreting UNOS's policies and navigating the new disciplinary process, as well as advice on compliance with transplantation allocation requirements generally, please contact your principal Firm representative or the lawyers listed below. General email messages may be sent using our "Contact Us" form, which can be found at www.jonesday.com/contactus/.

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