Islets for US Collaborative

THE CURE ALLIANCE

Dear Secretary Xavier Becerra

Congratulation on your historic nomination!

On behalf of the Islets for US Collaborative ("Islets for US Collaborative", www.isletsforus.org), I am writing you to express our deep and urgent concern that patients with type 1 diabetes are being denied access to potentially life-saving therapy because of FDA's incorrect regulatory approach.

Islets for US Collaborative comprises a group of more than 40 experts who are leaders in the field of transplantation and diabetes. There is a subset of type 1 diabetes patients for whom islet transplantation has been proven to be a life saving therapy. Despite modern insulin therapy, these patients suffer from the debilitating, life-threatening severe hypoglycemic episodes (extremely low blood sugars). These patients and their families live in constant fear of sudden death, develop anxiety and, in many cases, depression.

Islet transplantation is the only minimal invasive procedure that can save these patients and allow them to resume normal life and normal blood glucose control. Islets, which are a subpart of the pancreas, have a distinct structure, vasculature and highly specialized functions regulating secretion of insulin, glucagon and other hormones. Islets, like the pancreas, are harvested from organ donors. Once transplanted, islets are the only source of insulin secretion in the diabetic recipient as they were in the donor and help restoring recipients optimal blood glucose control. The safety and effectiveness of islet transplantation has been demonstrated in thousands of patients through NIH-supported research ($100M).

However, because of FDA's jurisdictional overreach, islets are not regulated like all other organs in the United States, to the detriment of the public. Pursuant to the 1984 National Organ Transplant Act (NOTA), the United Organ Network Sharing/Organ Procurement Transplant Network (UNOS/OPTN), under the aegis of the Health Resources and Services Administration (HRSA), is responsible for the allocation, procurement and transplantation of human organs. In deference to HRSA's oversight function, FDA regulations expressly exclude vascularized human organs for transplantation from the agency's oversight. 21 C.F.R. 1271.3(d)(1).

**Yet, for the past 20 years, FDA has taken the position that islets are a biological drug**. As a consequence, islet transplantation has been permitted only in the very limited capacity of sponsored clinical studies, pursuant to FDA's investigational new drug (IND) regulations. In order for transplant surgeons to offer islet transplantation therapeutically (which would expand availability and permit insurance coverage), it would first be necessary to submit a biologics license application (BLA) as for any other manufactured drug product. **Essentially, FDA is treating transplant surgeons as manufacturers and human organs as commodities.**

In contrast, islet transplantation is a standard of care therapy in Canada, Australia, Japan, and the EU, all of which regulate it as a type of organ transplantation.

The problem may soon get much worse; a BLA for islets was submitted by a for-profit company, is currently pending with FDA and may be approved as soon as March 2021. By approving this BLA, FDA would be giving a commercial entity **the exclusive right to obtain human pancreas**, retrieve human islets from it and **sell human islets for a profit as a biological product for use in transplantation**. Such distribution of human organs for transplantation is in clear conflict with NOTA's prohibition of the sale of human organs and its subparts (42 U.S.C. § 274e).

In addition, regulating islets as a biological product would effectively remove the safeguards that apply to all other organ transplantation in the United States, because the commercial entity would not subject to oversight by UNOS/OPTN, which ensures the safe and ethical allocation and use of organs in the US.

FDA's misguided regulatory approach foreseeably will allow unethical and unsafe commercialization of human organs, inflate costs and limit access to this life-saving therapy especially for patients with a low socio-economic status in the US due to inflated cost of the procedure.

Our comprehensive report has been just published in the American Journal of Transplantation (Attachment 1). It describes the unintended negative consequences of FDA's current regulatory approach and strongly recommends regulatory updates that reflect the current state of scientific knowledge and clinical practice.

Our discussions with FDA leadership over last 18 months (Attachment 2) has not resulted in any progress toward a solution.

**We believe that your immediate, decisive action is critical to ensure that Americans have access to safe, effective, ethical, and affordable islet transplantation as a standard of care therapy**. We are requesting to exercise your authority and to include human islets for transplantation into the statutory definition human organs for transplantation under the already developed regulatory structure of OPTN/UNOS, which would not only be fully consistent with the definition of human organs under NOTA and with existing FDA regulations, it would be in keeping with NOTA's prohibition of the sale of human organs (42 U.S.C. § 274e).

Indeed, there is precedent for moving oversight of donated tissue from FDA to HRSA; in 2013 in the Secretary of HHS determined that vascularized composite tissue for transplantation (e.g., hand and face transplants) should be regulated by HRSA/OPTN and not FDA. (Attachment 3). Although that change required rulemaking, in this case islets are already plainly within the definition of human organ under NOTA and clearly constitute vascularized human organs under FDA regulations. Thus, an Executive Order would simply be effectuating the intent of Congress in the face of FDA's continued failure to do so.

We would be grateful for your assistance in resolving this urgent public health issue.

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Attachments

1. Demise of islet allotransplantation in the US: A cell for an urgent regulatory update. The Islets for US Collaborative. 2021 Report.
2. Letter to the FDA and response from the FDA.
3. Final rule about inclusion of vascularized composite tissue into the definition of organ. https://www.govinfo.gov/content/pkg/FR-2013-07-03/html/2013-15731.htm