

Chicago, May 4, 2021

The Honorable Xavier Becerra  
Secretary,  
U.S. Department of Health and Human Services  
200 Independence Avenue, S.W.  
Washington, DC 20201  
Secretary@HHS.gov

Dear Secretary Becerra:

We are writing to you on behalf of the *Islets for US Collaborative* ([www.isletsforus.org](http://www.isletsforus.org)), a group of more than 40 leaders in the field of transplantation and diabetes to request your urgent intervention to adjust the regulatory framework that currently governs human islets for transplantation in the US.

On April 15<sup>th</sup>, 2021, during the Advisory Committee Meeting, FDA officials reviewed the first biological license application for human islets submitted by a private-for-profit company and made public statements, which unequivocally confirm the rationale and urgency for our request for regulatory updates.

In our previous letter, we provided a long list of evidence that the FDA's position to regulate human islets as a drug has been detrimental to the field of islet transplantation and particularly devastating for patients with type 1 diabetes. At the same time, **we provided evidence that inclusion of the human islet to the list of human organs regulated under the OPTN Final Rule would ensure that our patients have access to safe and effective islet transplantation therapy. We respectfully request your executive decision for this adjustment.**

The FDA has been holding a steadfast position that human islets should remain regulated as any biological drug; consequently, the FDA argues that approval of a biological license application is essential to ensure quality and potency of human islet cells.

However, during the Cellular, Tissue, and Gene Therapies FDA Advisory Committee meeting Dr. Sukhanya Jayachandra, representing the Center for Biologics and Research (CBER), summarized her team's review of the Chemistry, Manufacture and Control (CMC) data accompanying the aforementioned submitted BLA with the following statement: **"critical quality attributes for islet product, purity and potency did not correlate with the clinical effectiveness and that the critical quality attributes may not adequately evaluate lot-to-lot manufacturing consistency"**.

In practical terms, this means that even though the islet product may meet the release criteria, **the quality and potency of the human islet final product cannot be confirmed or verified**, prior to clinical use. *Simply put, transplant physicians as well as patients cannot be reassured about the quality and potency of the drug (islets), which they purchase from a commercial BLA*

*holder, and if the drug (islets) will provide a desired clinical effect.* Moreover, classifying human islets as a drug does not have any scientific basis and is in fact potentially harmful not only to patients but also to further developments in the field.

In the light of these new revelations, it is apparent the main goal of the BLA- to reassure islet product quality and potency, will not be achieved. Consequently, the BLA requirement is obsolete and application of drug manufacturing regulations to reassure islet product quality and potency has been recognized as ineffective by the FDA itself.

These recent FDA findings have been well known to the transplant community as we have previously described (1,2) and are consistent with the facts regarding all human organs for clinical transplantation including human islets (which are in fact small organs). The quality and potency of any human organ cannot be reassured by any testing prior to the actual transplantation procedure, **which is the rationale behind the FDA not regulating human organs for transplantation and the reason that regulations developed for drug manufacturing are ineffective when applied to organs (including islets) for transplantation.**

The quality and potency of the human organs (including human islets) can only be reassured by the transplant team's continuous assessment of complex clinical parameters and constant supervision during the process of donor selection, pancreas recovery, islet isolation and processing, preservation, transplantation and, finally, post-transplant patient care and monitoring, which is the only way to ensure a safe, effective and appropriate clinical outcome.

**Based on this rationale, human organs including human islets should be regulated under the HRSA and submitted to the OPTN/UNOS regulatory framework, which is specifically designed and developed to reassure human organ quality and potency as well as safety and effectiveness of the transplantation therapy.**

Altogether, the application of the BLA and FDA drug manufacturing regulations to human organs including human islets is flawed and obsolete. This regulatory pathway fails to achieve the main goal, which is to assure the quality and potency of islets. The BLA should not be approved; instead, regulation of islet transplantation should occur under the supervision of the OPTN and UNOS.

**We would be grateful for your assistance in resolving this urgent public health issue by exercising your authority to ensure that human islets are included in the definition of human organs under the OPTN Final Rule.** We enclose additional pertinent articles that support this rationale.

Thank you very much for considering this urgent request.

Camillo Ricordi M.D.

Professor of Surgery, Medicine, Biomedical Bioengineering, Immunology at University of Miami  
Director of the Diabetes Research Institute (DRI) and the Cell Transplant Center

Piotr Witkowski M.D. Ph.D.

Associate Professor of Surgery

Director, Pancreatic Islet Transplant Program, Director, Transplant Fellowship Program

UNOS, Pancreas and Islet Transplantation Committee

The University of Chicago Medicine

The Transplantation Institute

5841 S. Maryland Ave. MC5027, Room J-517

Chicago, IL 60637

mobile 773-251-6167

[pwitkowski@surgery.bsd.uchicago.edu](mailto:pwitkowski@surgery.bsd.uchicago.edu)

[www.pwitkowski.org](http://www.pwitkowski.org)

Enclosed:

1. Witkowski P, Philipson L, Kaufman DB, Ratner L, Abouljoud, Bellin M, Buse J, Kandeel F, Stock P, Mulligan D, Markmann F, Kozlowski T, Andreoni K, Alejandro R, Baidal D, Hardy MA, Wickrema A, Mirmira RG, John Fung J, Becker YT, Josephson MA, Bachul PJ, Pyda JS, Charlton M, Millis JM, Gaglia J, Stratta RJ, Fridell JA, Niederhaus S, Forbes RC, Jayant K, Robertson RP, Odorico J, Levy M, Harland R, Abrams PL, Olaitan OK, Kandaswamy R, Wellen J, Japour AJ, Desai CS, Naziruddin B, Balamurugan AN, Barth RN, Ricordi C. The “Islets for US” Collaborative. The Demise of Islet Allograft Transplantation in the US: A Call for an Urgent Regulatory Update. *Am J Transplant*, 2020, Nov 29, doi:10.1111/ajt.16397.
2. Witkowski P, Barth RN, Japour AJ, Bachul PJ, Pyda JS, Nowicki E, Ricordi C. on behalf of the “Islet for US Collaborative”. Regulatory updates are needed to prevent the commercialization of islet transplantation in the US. *Am J Transplant*, 2021, March 8, <https://doi.org/10.1111/ajt.16555>.
3. Abdulreda MH, Berggren PO. The pancreatic islet: a micro-organ in control. *CellR4* 2021; 9: e3093.
4. Weir GC, S. Bonner-Weir S. Why pancreatic islets should be regarded and regulated like organs. *CellR4* 2021; 9: e3083.
5. Letter to the Secretary of HHS from Islet for US Collaborative on March 25<sup>th</sup>, 2021.
6. Respond to the letter from FDA on behalf of the Secretary of HHS