From: **Richards, Paul** Paul.Richards@fda.hhs.gov
Subject: Regulatory Issue - Access to Islet Transplantation for Patients with Diabetes
Date: September 23, 2020 at 9:21 AM
To: pwitkowski@surgery.bsd.uchicago.edu

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Dear Dr. Witkowski,

Thank you for your recent inquiry to the Secretary of the U.S. Department of Health and Human Services, Alex Azar, regarding the regulatory status of allogeneic human islet cells for transplantation. Your email, dated September 12, 2020, was referred to the Food and Drug Administration's (FDA) Center for Biologics Evaluation and Research (CBER) for response. One of seven centers within the FDA, CBER is responsible for the regulation of many biologically-derived products, including blood intended for transfusion, blood components and derivatives, vaccines, allergenic products, tissues, and cell and gene therapy products.

As explained in the November 11, 2018, and December 14, 2019, communications from CBER, the FDA does not agree that allogeneic pancreatic islets meet the criteria for regulation solely under section 361 of the Public Health Service (PHS) Act and the regulations in Title 21 of the Code of Federal Regulations (CFR) Part 1271 - nor is transfer of these cells analogous to organ transplantation with regard to safety and efficacy considerations.

Under the FDA's risk-based approach for human cell, tissue or cell or tissue-based products (HCT/Ps), in order to be eligible for regulation solely under section 361 of the PHS Act and the regulations in 21 CFR Part 1271, products must meet all of the criteria listed in 21 CFR 1271(a), or be subject to one of the exceptions listed in 21 CFR 1271.15. Products that do not meet all four criteria present safety and/or efficacy questions, including potential concerns related to product consistency, that should be addressed through the premarket review and licensure process. As you note in your October 10, 2019 letter, allogeneic islet cells fail two of the four criteria in 21 CFR 1271.10(a) that must be met for an HCT/P to be regulated solely under section 361 of the PHS Act and the regulations in 21 CFR Part 1271. Accordingly, allogeneic islet cells are regulated as biological products subject to premarket requirements under Section 351 of the Public Health Service Act.

CBER is committed to working with sponsors to address the unique clinical and manufacturing challenges associated with development of cellular therapies. FDA guidance entitled *Expedited Programs for Regenerative Medicine Therapies for Serious Conditions*, emphasizes our commitment to facilitating the development of regenerative medicine therapies that are being developed to address unmet medical needs in patients with serious conditions, including rare diseases. We will work with sponsors of these products and encourage consideration of flexible approaches to clinical trial design. CBER is amenable to considering innovative trial designs whereby multiple clinical sites participate in a trial investigating a regenerative medicine therapy with the intent of sharing the combined clinical trial data to support BLAs from each of the individual centers/institutions. This paradigm is

support BLAs from each of the individual centers/institutions. This paradigm is described in more detail in our guidance and in the March 2018 article by Drs. Peter Marks and Scott Gottlieb (NEJM 2018; 378: 954-959; https://www.nejm.org/doi/full/10.1056/NEJMsr1715626).

The FDA would be happy to meet further with you or your colleagues to discuss how to support a biologics license application (BLA) based on such a development program, as well as other innovative approaches to clinical development that you may be considering.

Information about formal meetings between the FDA and sponsors applicants related to the development and review of biological drug products can be found in FDA guidance entitled *Guidance for Industry – Formal Meetings Between the FDA and Sponsors or Applicants*.

Additional background related to meetings between the FDA and industry (including sponsors/applicants) is available in Standard Operating Policy and Procedure (SOPP) 8101.1 (Regulatory Meetings with Sponsors and Applicants for Drugs and Biological Products).

I hope that this information is helpful.

Best regards,

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