



# NIDDK INTEGRATED ISLET DISTRIBUTION PROGRAM

## REQUEST FOR PROPOSALS (RFP) AFFILIATE ISLET ISOLATION CENTERS

### Key Dates

|                            |   |
|----------------------------|---|
| Posted Date:               | December 12, 2022   |
| Informational Webinar      | January 19, 2023 at 12:00 PM PT<br>Click <a href="#">here</a> to register for the meeting |
| Letter of Intent Due Date: | January 30, 2023  |
| Application Due Date:      | March 15, 2023  |
| Scientific Review:         | By April 30, 2023   |
| Announcement of Awardees:  | May 2023  |
| Start Date:                | June 15, 2023   |
| End Date:                  | January 31, 2024<br>Potential renewals annually through July 31, 2026                     |

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## Section I. Funding Opportunity Purpose

The continuing mission of the [Integrated Islet Distribution Program \(IIDP\)](#) is to provide the scientific community with critical islet resources for diabetes research. The IIDP facilitates the distribution of human islets to biomedical researchers by establishing partnerships with qualified islet isolation facilities that prepare and distribute human islets. The program manages an application process to establish investigator eligibility to receive islet shipments, informs investigators of islet availability, manages a cost recovery system through fees collected from islet recipients, and oversees standardized phenotypic and genotypic analyses of islet preparations distributed throughout the IIDP network. The purpose of this RFP is to identify and evaluate expert human islet Isolation centers that can provide the highest quality human isolated islets and related tissues to the IIDP in a dependable, consistent manner.

## Section II. Request for Proposals - Opportunity Description

### II-1. Background

Dependable access to high quality human islets has become a necessity for research programs focused on human islet biology. The NIDDK Integrated Islet Distribution Program (IIDP) supports islet biology researchers by providing reliable, high quality resources to the investigator community from leading Islet Isolation Centers (IICs). IIDP-affiliated IICs use standardized protocols to provide human islets and non-islet tissue to the diabetes research community (<https://iidp.coh.org/Centers/Policies-Standard-Operating-Procedures>). Each tissue shipment to investigators is accompanied by comprehensive donor and isolation information, pre-shipment assessments for purity, viability, and islet quality ranking. The IIDP maintains an exclusive algorithm as part of a fair and equitable Islet Allocation System, which broadcasts the availability of human islets and non-islet tissue from each isolation center to subscribing investigators world-wide, tracks acceptance of tissue, and maintains feedback from the recipients.

### II-2. Objectives and Scope

IICs invited to join the IIDP consortium under this Request for Proposals will be led by experienced investigators with a solid track record of providing resources and services to the diabetes research community. Applicants should document proficiency in procuring and processing human islets for research use.

Applicants to the IIDP-IIC program should demonstrate the following and agree to [IIDP Policies and Procedures for Islet Isolation Centers](#) .

- **Experience** in overseeing large complex resource-oriented programs;
- **Expertise needed to provide high quality human islets** to support diabetes research, including proficiency in procuring tissues, as well as culturing and shipping high quality human islets to investigators;
- **Access to trained personnel and facilities** to support timely and reliable production of human islets from human pancreata;
- **Existing partnerships with organ procurement organizations (OPO)** that will ensure access to pancreata as well as other common biomaterials that may be of interest to the investigator community;
- **IIDP IIC Policies and Procedures**
  - Use the IIDP Islet Allocation System to distribute human islet resources (view the [Checklist of IIDP Requirements for Isolation and Broadcast at the Isolation Centers](#) for more information on the process), including:
    - Purified islets
    - Non-islet pancreatic tissue (NIPT-acinar)
    - Flash frozen islets for distribution
  - Enter required donor and shipping information into the IIDP Islet Allocation System
  - Prepare purified islets per islet isolation to be shipped to Human Islet Phenotyping Program (HIPP)

- Freeze and store a 2 ml sample of acinar tissue per islet isolation to be shipped to the Human Islet Genotyping Initiative (HIGI) quarterly
- Prepare formalin-fixed samples of each native pancreas section for Histology to be shipped to City of Hope monthly
- Agree to utilizing [IIDP SOPs](#) for the following:
  - IIDP Criteria for Accepting Human Cadaveric Pancreata for Islet Isolation
  - Flash Freezing Unclaimed Islets
  - Standardized International Shipping Documentation
  - Culture and Preparation for Cold Shipping
  - Cold Shipping of Human Islets
  - Packaging and Cold Shipping of Non-Islet Pancreatic (Acinar) Tissue (NIPT)
  - Packaging and Shipping of Flash Frozen Non-Islet Pancreatic (Acinar) Tissue (NIPT)
  - Qualitative & Quantitative Assessment of Human Purified Islets for Distribution Using Dithizone (DTZ)
  - Viability Estimation of Islets for Distribution Using Inclusion and Exclusion Fluorescent Dyes (FDA/PI)
  - Microbiology Testing for Islets for Distribution
  - Sentinel Flask Preparation
  - Potency Test: Glucose Stimulated Insulin Release Assay
  - Uploading of Digital Image Count Sample
  - Preparing Pancreas Section for Histology
- Meet the required assessments stated [IIDP Policies and Procedures for Islet Isolation Centers](#)

## Section III. Award Information

|                                      |  |
|--------------------------------------|--|
| <b>Funding Instrument:</b>           | Subcontract, awarded from the IIDP Coordinating Center (City of Hope)  |
| <b>Application Types Allowed:</b>    | New, Renewals  |
| <b>Anticipated Number of Awards:</b> | Approximately 1-3 Islet Isolation Centers will join the IIDP Consortium  |
| <b>Award Budget:</b>                 | Islet Isolation Centers are reimbursed based on the number of high-quality islets and associated tissues offered and placed within the network of IIDP-investigators |
| <b>Project Period:</b>               | Up to 3.5 years: a 6-month initial contract, with annual renewals contingent on satisfactory performance   |

## Section IV. Eligibility Information

### IV-1. Eligible Organizations

#### Higher Education Institutions

- Public/State Controlled Institutions of Higher Education
- Private Institutions of Higher Education
- The following types of Higher Education Institutions are encouraged to apply for support as Public or Private Institutions of Higher Education:
  - Hispanic-serving Institutions
  - Historically Black Colleges and Universities (HBCUs)
  - Tribally Controlled Colleges and Universities (TCCUs)
  - Alaska Native and Native Hawaiian Serving Institutions
  - Asian American Native American Pacific Islander Serving Institutions (AANAPISIs)

### **Nonprofits Other Than Institutions of Higher Education**

- Nonprofits with 501(c)(3) IRS Status (Other than Institutions of Higher Education)
- Nonprofits without 501(c)(3) IRS Status (Other than Institutions of Higher Education)

### **For-Profit Organizations**

- Small Businesses
- For-Profit Organizations (Other than Small Businesses)

### **Domestic and Foreign Institutions**

- Both domestic (U.S.) and non-domestic (non-U.S.) entities (Foreign Institutions) **from North America are** eligible to apply.
- Both Domestic (U.S.) and non-domestic (non-U.S.) components of U.S. Organizations **are** eligible to apply.
- No entities from outside of North America are eligible to apply.

### **IV-2. Eligible Individuals (Program Director/Principal Investigator)**

Any individuals with the requisite knowledge, skills, and track record of success in leading large multi-component resource-intensive programs and experience providing islet resources to the diabetes research community are invited to apply.

## **Section V. Application and Submission Information**

### **V-1. Instructions for Application Submission**

Applicants may access the application package and link to the application submission website associated with this funding opportunity at the IIDP website: <https://iidp.coh.org/iicrfp2022>.

It is critical that applicants follow the Application instructions. Conformance to the requirements as outlined is required and will be strictly enforced. Applications that are out of compliance with these instructions may be returned without review.

### **V-2. IIDP-IIC Application Guide**

The following instructions for formatting and submission must be followed:

#### **Font (size, color, type density) and Line Spacing:**

Text in your attachments must follow these minimum requirements:

- **Font size:** Must be 11 points or larger. Smaller text in figures, graphs, diagrams, and charts is acceptable, as long as it is legible when the page is viewed at 100%.
  - Some PDF conversion software reduces font size. It is important to confirm that the final PDF document complies with the font requirements.
- **Type density:** Must be no more than 15 characters per linear inch (including characters and spaces).
- **Line spacing:** Must be no more than six lines per vertical inch.
- **Text color:** No restriction. Though not required, black or other high-contrast text colors are recommended since they print well and are legible to the largest audience.
- We recommended the following fonts, although other fonts (both serif and non-serif) are acceptable if they meet the above requirements:
  - **Arial**
  - **Georgia**
  - **Helvetica**

*Legibility is of paramount importance.* Applications that include PDF attachments that do not conform to the minimum requirements listed above may be withdrawn from consideration.

## Images

- Digital images of material such as electron micrographs or gels must only be included within the page limits of the Research Strategy. The maximum size of images to be included should be approximately 1200 x 1500 pixels using 256 colors. Figures must be readable as printed on an 8.5" x 11" page at normal (100%) scale.
- Investigators must use image compression such as JPEG or PNG.

## Paper Size and Margins

- Use paper size no larger than *standard letter paper size (8 1/2" x 11")*.
- Provide at least one-half inch margins (1/2") - top, bottom, left, and right - for all pages. No applicant-supplied information can appear in the margins.

## Application Forms and Page Limitations

Each application form has a specific page limitation that must be followed. See specifications in V-3 below.

### V-3. Content and Form of Application Submission

*Applications should be submitted directly to the IIDP Coordinating Center via the submission website, NOT to the Division of Receipt and Referral at the NIH. The link to the submission website will be posted on <https://iidp.coh.org/iicrfp2022>.*

The following are necessary to submit for application.

**1. Letter of Intent:** (1 page – to be sent directly to the IIDP)

By the due date listed above (January 30, 2023), prospective applicants are asked to submit a letter of intent that includes the following information:

- Descriptive title of proposed activity
- Name, address, telephone number, and email address of the PD/PI
- Names of other key personnel
- Participating institution

*The letter of intent should be sent in electronic form to:*

The Integrated Islet Distribution Program Coordinating Center (City of Hope, Duarte, CA) c/o James Cravens, IIDP Program Manager at: [jcravens@coh.org](mailto:jcravens@coh.org)

### V-4. Instructions for Application Submission

The following sections are required and must follow the formatting requirements as noted in the submission website instructions.

**1. Biographical Sketch:** ([NIH Biographical Sketch](#) form should be completed and uploaded (not more than 5 pages)).

**2. IIDP-ICC Resource Implementation Plan**

**Project Abstract:** (up to 500 words)

The Project Abstract should be a summary of the experience, expertise, and important contributions the applicant plans for this application.

**IIC Resource Strategy:** (up to 10 pages and uploaded)

***Note:** Bibliographic citations are not required but if included must fit within the page limit. Figures and illustrations may be included but must also fit within the page limit.*

*The applicant should provide the following information under the indicated headings as outlined below:*

- **Overall Description:** Explain how the project as designed will meet the needs of the IIDP program and the islet research community; describe how the planned activities will be designed to evolve with future research needs.
- **Prior Experience:** Document experience and success in isolating and providing human islet resources to the research community, including purified islets, formalin-fixed samples of each native pancreas, non-islet pancreatic tissue (NIPT-acinar), and flash frozen islets for distribution.
- **Management Plan:** Describe how the center will provide the administrative assistance needed to support IIC operations, including coordinating interactions within the IIC, with their affiliated OPOs and between the IIC and the IIDP and with their other subcontracted institutions. Provide a detailed plan to monitor quality assurance and quality control of resources provided by the center.
- **Personnel and Infrastructure:** Explain how the IIC team and its associated personnel, as well as infrastructure, will be appropriate to address key objectives of the IIDP program. Provide a list of key personnel involved; describe any programs designed to ensure and monitor appropriate staff training. Identify any novel concepts, strategies, instrumentation, or protocols that will be employed to enhance rigor and reliability of resources provided to the research community.
- **Approach:**
  - **Workflow:** Provide an overview of the IIC workflow, including a well-established timeline for pancreas recovery, islet isolation and purification, culture, and shipping. Include standard practices for ensuring islet quantity, quality, viability, and potency.
  - **Isolation Capacity:** The IIDP program expects IICs to provide 15 to 20 high-quality islet isolations to the network each year. Project and explain the minimum, maximum, and average number of islet isolations the IIC may be able to provide to the IIDP network each month. Describe the IIC's ability to provide the additional resources which IIDP distributes to investigators including flash frozen islets, histological sample of each native pancreas pre-digestion, and non-islet pancreatic tissue (NIPT-acinar).
  - **Data Handling:** The IIDP currently requires essential demographic and medical data gleaned from the donor information supplied by OPO as well as procedural and islet qualitative and quantitative information derived from your center, to be transcribed to the IIDP database. These data have been deemed essential to our islet research recipients for them to make an informed decision about the acceptance of offered islets through the IIDP broadcast system. Describe how data handling will be managed to ensure timely transfer of information between the IIC and the IIDP program.
  - **Shipping and Geographical Reach:** Currently the IIDP uses Federal Express (FedEx) for all tissue shipments from IIC to researchers. Describe your institution's methods and pick-up times for all priority FedEx shipments. Provide any experience your center has had with other shipping agencies; summarize any perceived impediments to providing resources to IIDP's national research base.

- Estimated Cost per IEQ: Include a detailed cost calculation of any prior and projected cost-recovery needs for islets manufactured by the facility.

Please note that as an NIH-sponsored project, and the IIC must work within the budget provided by NIH. However, we are continually evaluating our financial planning to see if future changes to our reimbursement structure are warranted. The IIDP currently reimburses its islet production centers according to the following rate structure. Please note that the IIDP is planning increases to this compensation schedule on or before January 1, 2024.

| IIC Compensation Schedule as of December 12, 2022: |                     |                                       |
|--|---------------------|---------------------------------------|
| Human Islets                                       |                     |                                       |
| Non-Profit Recipients                              | Non-diabetic donors | \$0.12 per IEQ                        |
|  | T2D donors          | \$0.20 per IEQ                        |
| For-Profit Recipients                              | Non-diabetic donors | \$0.19 per IEQ                        |
|  | T2D donors          | \$0.24 per IEQ                        |
| Flash Frozen Islets                                |                     | 1,000-IEQ vial \$120 per vial         |
| Pancreas Sample for Histology                      |                     | \$250 per islet isolation             |
| Non-Islet Pancreatic Tissue (Acinar)               |                     | Researchers and HIGI \$200 per sample |

- Innovation: Innovation: The IIDP continuously evaluates potential initiatives to better serve the needs of the researcher community and to leverage the utility of the donor’s precious gift. Describe any unique assays, techniques, resources, or scientific initiatives that may be added to the currently available IIDP features based on your participation in the program. Examples might include: provision of pancreas slices, hand-picking islets for distribution by size, acquisition of matching donor biomaterials to provide to the network (such as pancreatic exocrine tissue and/or ducts, spleen, lymph nodes), or access to unique donor populations for pancreas recovery. Additionally, provide any ideas that could expand the IIDP researcher base and/or increase the placement of islets and related tissues to the research community.

**3. Prior Experience in Isolating Human Islets**

Provide prior human islet isolation experience data accomplished over the past 5 years as specified by IIDP in the application table (e.g., number of IEQ isolated, number of isolations performed, number of IEQ shipped to other investigators, etc.)

**4. Current Organ Procurement Organizations Relationships**

Upload a list of OPOs that have agreed to serve the IIC, including the number of pancreata projected to be procured each year based on current OPO relationships.

**5. Investigator Qualifications: (up to 500 words)**

Provide evidence to support your background of appropriate expertise in islet biology and the ability to provide high quality services to the IIDP and its affiliated diabetes research community.

**6. Letters of Recommendations: (up to 5 and uploaded)**

## Section VI. Application Review Information

### VI-1. Criteria

Only the criteria described below will be considered in the RFP review process. Consistent with IIDP practices, all applications submitted will be evaluated for scientific and technical merit using external peer review using NIH scoring conventions (Priority Scores: 1-10).

#### Overall Assessment

Reviewers will provide an overall impact score to reflect their assessment of the likelihood that the project will exert a sustained and important contribution to the IIDP program.

#### Scored Individual Review Criteria

Reviewers will consider each of the review criteria below in the determination of merit and give a separate score for each. An application does not need to be strong in all categories to be judged likely to have major scientific impact as reflected in the overall assessment.

- **Overall strategy and prior experience:** Is the scope of activities proposed by the IIC appropriate to meet the needs of the IIDP? Does the IIC team have a documented record of excellence in providing resources to the diabetes research community, and the requisite expertise to oversee a successful IIC?
- **Management Plan, Personnel and Available Infrastructure:** Are the management plan and named personnel well-suited to execute the aims and goals of the IIC? Are methods described to ensure that all personnel are adequately trained to perform activities described? Is there a plan for periodic evaluation/requalification of technical personnel? Are there appropriate plans in place for Quality Assurance/Quality Control of products, and to assure timeliness of responses to needs?
- **Approach:** Are the overall strategy, methodology, and procedures well-reasoned and appropriate to accomplish the goals of the IIC? Does the description of the IIC Workflow, Capacity, Procurement, Shipping, Cost Recovery and Data Handling practices ensure that the IIC will be able to provide high quality resources to the IIDP community? Are potential problems, alternative strategies, and benchmarks for success presented? Does the IIC present unique opportunities that may enhance the IIDP program in the future?
- **Environment:** Will the institutional environment contribute to the probability of success? Are the institutional support, equipment, and other physical resources available to the investigator adequate for the project proposed?

### VI-2. Review and Selection Process

- Applications will be evaluated for scientific and technical merit by external peer reviewers convened by the IIDP using the stated review criteria.
- As part of the scientific peer review:
  - All applications will receive a written critique.
  - Appeals of the IIDP peer review process **will NOT** be accepted for applications submitted in response to this funding opportunity.
- Following initial peer review, recommended applications will receive a second level of review by the IIDP External Scientific Panel. Final funding decisions will be made by the IIDP, with consideration of the following:
  - Scientific and technical merit of the proposed project as determined by scientific peer review.
  - Relevance of the proposed project to program priorities.

### VI-3. Anticipated Announcement and Award Dates

- After peer review and secondary review of the applications are complete, applicants will be notified by the IIDP as to final decisions by May 31, 2023.