At-a-Glance

- **Proposal to clarify islet allocation protocol**

- **Policy Affected: Policy 3.8.1.6 (Islet Allocation Protocol)**

- **Pancreas Transplantation Committee**

- **Summary of proposal**
  The proposed revisions clarify the process for the allocation of islets. Additionally, the proposed revisions establish criteria for when islet candidates can be listed at an active status.

- **Affected groups**
  Pancreas Islet Program Transplant Administrators, Pancreas Islet Transplant Coordinators, Pancreas Islet Program Directors, Pancreas Candidates, Pancreas Transplant Surgeons, Pancreas Transplant Physicians, Pancreas Islet Transplant Social Workers, Pancreas Islet Transplant Data Coordinators

- **Specific requests for comment**
  1. Are the criteria for an islet candidate to be eligible for active status reasonable?
  2. Are the requirements for the re-allocation of islets clear?

  Please consider and comment on the entire proposal. Please do not feel limited to the focused questions. They are meant only to point out key issues within the proposal that may be of specific interest to some readers.

Proposal to clarify islet allocation protocol

Policy Affected: Policy 3.8.1.6 (Islet Allocation Protocol)

Pancreas Transplantation Committee

Summary and Goals of the Proposal:

The purpose of the revisions to the islet allocation protocol is to clarify the existing islet allocation protocol policy language. The proposed revisions:

- Define when a candidate is medically suitable for an islet transplant,
- Set criteria for when a candidate can be listed as active on the pancreas islet waiting list,
- Increase efficiency and access for candidates on the islet waiting list to receive an offer,
- Clarify the process for re-allocating islets, and
- Explain what documentation a transplant center must maintain to demonstrate compliance with this policy.

Background and Significance of the Proposal:

At its March 14, 2008 meeting, the Pancreas Transplantation Committee was concerned that the current islet allocation policy language is ambiguous because it does not define when a candidate is medically suitable for an islet transplant, and it allows a program to accept an unlimited number of pancreata for islet infusion for a candidate without that candidate ever receiving an islet infusion. Current OPTN/UNOS policy allows a candidate to remain on the waiting list until he/she has had three islet infusions. The Committee reviewed data that showed that at least one center had accepted an unusually large number of pancreata for islets for a candidate over a two year period without that candidate receiving three infusions. In such a case, a candidate could remain at the top of the waiting list indefinitely and act as a magnet for pancreas offers.

The Committee discussed whether limits should be placed on the number of pancreata for islets that a program can accept for a particular candidate without that candidate receiving an infusion. The Committee recognized that not every pancreas allocated for islet isolation will yield enough islets for infusion for a candidate. The Pancreas Committee and the Membership and Professional Standards Committee(MPSC) have both reviewed this situation.

Another aspect of the current islet allocation policy is that once a pancreas is allocated to, and accepted for, a candidate, a center can potentially re-allocate the isolated islets to another candidate if the transplant center determines that the islets are not medically suitable for the intended candidate. The current language does not clearly state the requirements for organ sharing that are specified in other OPTN/UNOS policies. The Committee stated the need for all islet offers to be made through UNOS and only to candidates who are registered at a UNOS approved islet program and who are active on the waiting list. The Committee formed a subcommittee to reassess and draft language to clarify islet allocation policy.

The Islet Allocation Protocol Subcommittee met in August 2008 to develop revisions to islet allocation protocol. The revised policy language addresses the following areas:

- The definition of medical suitability,

- A definition of when an islet candidate can be active on the waiting list and can accrue waiting time,
- A definition of when an islet candidate must be listed as inactive,
- An outline of the documentation the center must maintain to verify that the candidate is eligible for active status,
- The process for re-allocating islets,
- A statement of what documentation the center must maintain to demonstrate that an islet preparation was not medically suitable for the candidate to whom the pancreas was allocated, and
- A restatement of the specific UNOS policies that apply to organ allocation.

The Committee sent the proposed revisions to the principal investigators of the NIH-supported Clinical Islet Transplant (CIT) Consortium. The CIT principal investigators were supportive of the revisions and provided feedback. The Committee has considered their suggestions in developing the policy language that appears at the end of this document.

The Pancreas Transplantation Committee met on September 12, 2008 to vote to send the proposed revisions to islet allocation protocol out for public comment.

The Policy Oversight Committee reviewed this proposal on September 16, 2008, and was supportive of the proposed revisions. (7- Support, 0- Oppose, 0- Abstain)

Supporting Evidence and/or Modeling:

If approved by the Board, the requirements for candidates to be active on the pancreas islet waiting list will be:
- That the candidate is insulin dependent **or**
- That the candidate is insulin independent and has an HbA1c value greater than 6.5 %.

Regarding the requirements for insulin dependence, the subcommittee reviewed for guidance the existing criteria in the Investigational New Drug Application (IND) for the NIH-funded CIT trials that consider a successsful transplant to be when candidate is able to titrate off insulin therapy for at least one week and have an HbA1c value of 6.5% or less.

Other supporting evidence for the active status criteria of requiring HbA1c to be less than or equal to 6.5% comes from the American Diabetes Association's Standards of Medical Care in Diabetes (2008)[1]. According to these standards, "lowering A1C to an average of ~7% has clearly been shown to reduce microvascular and neuropathic complications of diabetes and, possibly, macrovascular disease. Therefore, the A1C goal for nonpregnant adults in general is <7%." The subcommittee chose 6.5% as the cut-off for active status because it is consistent with all the evidence reviewed.

The Standards of Medical Care in Diabetes also state that diabetic patients should have an HbA1c test twice a year if they are meeting treatment goals. Patients who do not have good glycemic control should be tested quarterly. Therefore, the policy requires that centers must update the candidate's HbA1c value in the candidate's record at least every six months.

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[1] American Diabetes Association (ADA). Standards of medical care in diabetes. V. Diabetes care. Diabetes Care 2008 Jan;31(Suppl 1):S16-24.

Expected Impact on Program Goals, Strategic Plan, and Adherence to OPTN Final Rule:

This proposal addresses two strategic plan goals. First, the clarification of the policy language addresses the strategic goal of improving compliance with policies to protect patient safety and preserve public trust. By making the policy easier to understand, these policy revisions make it easier for centers to comply with the policy. Second, by adding criteria for active status, these revisions refine allocation policies. By requiring candidates that have good glycemic control (defined as insulin independence with an HbA1c value of 6.5% or less) to be listed as inactive, the policy gives candidates who need an islet transplant to attain good glycemic control priority over candidates who already have good glycemic control.

Plan for Evaluating the Proposal:

The goals of these policy revisions are:

- To verify that active candidates are appropriate for islet infusions,
- To increase efficiency and access for candidates on the islet waiting list to receive an offer by:
    - Defining listing criteria for active candidates, and
    - Monitoring the activity of centers that accept pancreata for islets and the fate of those acceptances, and
- To improve compliance with islet allocation protocol by clarifying policy language.

In order to evaluate whether the policy change has met these goals, the Pancreas Transplantation Committee will review the following data six months after implementation:

- The number of islet offers that have been accepted for candidates in the six months before and after the policy change, and
- The number of offers that candidates have accepted with and without receiving an infusion.

This data will show whether the policy change has decreased the possibility of a program accepting a potentially unlimited number of islet offers for a candidate without that candidate ever receiving an islet infusion. The Committee will continue to review this data annually for three years and upon request. The Committee will also review any available feedback on this policy from the islet transplantation community.

Additional Data Collection:

For active candidates who are insulin <u>dependent</u>:
This proposal requires that transplant centers document the candidate's current insulin status every six months in the candidate's record.

For active candidates who are insulin <u>independent</u>:
This proposal requires that transplant centers document the candidate's current insulin status and HbA1c level every six months in the candidate's record.

If the transplant center wishes to move a candidate from an inactive to an active status, the transplant center must document the candidate's insulin status and HbA1c level in the candidate's record before the candidate can be listed as active. If the candidate is insulin independent and does not have an HbA1c value greater than 6.5%, then the candidate cannot be listed as active.

This data collection meets the data collection principle of determining if institutional members are complying with policy. UNOS Staff can use the documentation in the candidate's record of his/her insulin status and HbA1c level to determine whether the candidate is eligible for active status and whether the center has listed the candidate correctly in UNet℠. This proposal does not require any additional data to be entered into UNet℠.

Expected Implementation Plan:

Islet Waiting List Status

If approved by the Board, transplant centers will need to determine if their islet candidates qualify for active status according to the new policy language. If the candidate is not eligible for active status, the center will need to set the candidate to inactive in UNet℠. If the candidate is eligible for active status, the transplant center will need to document in the candidate's record every six months:

- That the candidate is currently insulin dependent

OR

- That the candidate has had an HbA1c test in the past 6 months, and
- That the most recent HbA1c test had a value of greater than 6.5%, and
- That the candidate is insulin independent.

The transplant center will need to document the same information above to move a candidate from inactive to active status.

Islet Allocation

If approved by the Board, transplant centers will need to determine if an islet preparation is medically suitable for the candidate for whom the center accepted the islets, as defined by the center's IND. The center must document whether the islets were medically suitable or unsuitable, and, if unsuitable, the reason the islets were medically unsuitable for the candidate.

If the transplant center wishes to re-allocate the islets, it must offer the islets to the next medically suitable candidate covered by its IND, based on waiting time in compliance with OPTN/UNOS policies. The center must maintain documentation of this re-allocation process.

This proposal will not require programming in UNet℠.

Communication and Education Plan:

If approved by the Board of Directors, the transplant community will receive information regarding new policy language via the Policy Notice that follows each Board meeting. Additionally, pancreas islet programs will receive a targeted e-mail explaining the policy change, outlining what they will be expected to do, and providing information on where to direct questions. There will also be information included in the UNOS Update briefly describing the policy change.

Communication Activities			
Type of Communication	**Audience(s)**	**Deliver Method(s)**	**Timeframe**
Policy Notice (summary of all policy changes approved by the board in a PDF format)	Transplant Coordinators, Transplant Surgeons, Transplant Physicians, Transplant Center Program Directors, Transplant Administrators	Electronic (email sent from the UNOS Communications mailbox)	30 days after the board approves the change.
Targeted e-mail	Pancreas Islet Program Directors, Pancreas Islet Primary Surgeons, Pancreas Islet Transplant Coordinators	Electronic (email sent from the UNOS Communications mailbox)	Upon implementation
Short blurb in the UNOS Update to appear next to the Pancreas Transplantation Committee profile	All primary and secondary readers of the UNOS Update	Delivery by mail as well as online access to Update story	TBD

Monitoring and Evaluation:

Transplant centers will be expected to comply with all requirements stated in Policy 3.8, its subsections, and other policy and bylaws requirements applicable to pancreas islet transplantation. UNOS Department of Evaluation and Quality (DEQ) Staff will evaluate member compliance with this policy.

How members will be expected to comply with this policy

Transplant centers will be expected to:

- Maintain documentation of the center's islet product release criteria contained in the center's Investigational New Drug (IND) application,
- Document if the islets are suitable for the candidate for whom the pancreas was accepted after isolating the islets, including the reason the islets were not suitable for the intended candidate,
- Maintain documentation that islets were re-allocated according to policy if, after isolation, the islets are unsuitable for the intended candidate,
- Document the candidate's current insulin status in the candidate's record every six months,
- Document the candidate's HbA1c level in the candidate's record every six months if the candidate is insulin independent,
- List candidates for pancreas islet transplantation according to the requirements of active status and inactive status stated in policy and keep the candidate's listing status current in UNet℠,

- Remove a candidate from the waiting list within 24 hours of the candidate receiving his or her third pancreas islet infusion, and
- Present documentation to the OPTN upon request.

How the OPTN will evaluate member compliance with this policy
The OPTN currently monitors member compliance with the existing requirements of Policy 3.8 during site surveys of OPOs and as part of the allocation review process. UNOS staff will forward potential violations of this policy to the OPTN/UNOS Membership and Professional Standards Committee (MPSC) for review. If these revisions are approved and implemented, then UNOS staff will incorporate the new and modified requirements into monitoring procedures.

The OPTN also monitors all complaints. Any complaint received that has the potential to be a policy or bylaw violation is forwarded to the MPSC If the MPSC identifies the need for clarification, education, or additional changes related to this policy, the MPSC will forward its recommendation to the OPTN/UNOS Pancreas Transplantation Committee.

Please note: the MPSC performs confidential medical peer review, and any recommendations or information reported to the Pancreas Transplantation Committee could only be reported as aggregate (i.e. non-identified, not case specific) data.

Policy Proposal:

At its September 2008 meeting, the Pancreas Transplantation Committee voted to send the following language out for public comment (10-Support, 0-Oppose, 0-Abstain):

3.8.1.~~5~~6 Islet Allocation Protocol. Allocation of pancreata for islet transplantation shall be to the most medically suitable candidate based upon need and transplant candidate length of waiting time. After~~If after~~ islet processing is completed, the transplant center will determine if the islet preparation is medically ~~un~~suitable for the candidate. Medical suitability is defined as meeting the islet transplant center's islet product release criteria contained in the center's Investigational New Drug (IND) application, as approved by the FDA. The center must document whether the islets are medically suitable or medically unsuitable for the candidate for whom the center accepted the islets. If the islets are medically unsuitable for the candidate, the center must also document the reason the islets were medically unsuitable for the candidate. This documentation must be maintained and submitted upon request.

If the transplant center determines that the islets are medically unsuitable for the candidate for whom the center accepted the islets, the islets from that pancreas will be reallocated to a medically suitable candidate at a transplant center covered by the same IND, based upon waiting time. The transplant center that accepted the islets on behalf of the original candidate is responsible for documenting:

- to which candidate the center re-allocated the islets, and
- that the center re-allocated the islets to the medically suitable candidate covered by the same IND who had the most waiting time.

The transplant center must maintain this documentation and submit it upon request. ~~to the next most suitable candidate within the OPO that the Investigational New Drug (IND) application allows~~.

Islet allocation must abide by all applicable OPTN/UNOS policies, including but not limited to:

- Policy 3.2.1 (Mandatory Listing of Potential Recipients), which states that all candidates who are potential recipients of deceased donor organs must be on the Waiting List,
- Policy 3.2.1.4 (Prohibition for Organ Offers to Non-Members), which stipulates that organ offers cannot be made to non-member centers,
- Policy 3.2.4 (Match System Access), which requires that organs only be allocated to candidates who appear on a match run,
- Policy 6.4.1 (Exportation), which states that the exportation of organs from the United States or its territories is prohibited unless a well documented and verifiable effort, coordinated through the Organ Center, has failed to find a suitable recipient for that organ on the Waiting List.

~~The purpose of this policy is to allow for the application of medical judgment and to avoid islet wastage. The outcomes of this allocation policy will be reported to the Board by the Kidney & Pancreas Transplantation Committee within three years.~~

Waiting Time

A candidate is eligible to accrue waiting time:

- while listed in an active or inactive status; and
- until the candidate has received a maximum of three islet infusions.

Waiting time ~~shall~~will begin when a candidate is placed on Waiting List. Waiting time will end when the candidate is removed from the waiting list. Waiting time will accrue for a candidate until he/she has received a maximum of three islet infusions or the transplant center removes the candidate from the waiting list, whichever is the first to occur. If the candidate is still listed at this time or subsequently added back to the Waiting List, waiting time will start anew.

One point will be assigned to the candidate waiting for the longest period with fractions of points assigned proportionately to all other candidates, according to their relative waiting time. For example, if there are 75 candidates waiting for islets, the candidate waiting the longest would receive 1 point (75/75 x 1 = 1). A person with the 60th longest time of waiting would be assigned 0.2 points (75-60)/75 x 1 = 0.2). The calculation of points is conducted separately for each geographic (local, regional and national) level of islet allocation. The local points calculation includes only candidates on the local Waiting List. The regional points calculation includes only candidates on the regional list, without the local candidates. The national points calculation includes all candidates on the national list excluding all candidates listed on the Host OPO's local or regional waiting list~~. Candidates shall continue to accrue waiting time while registered on the Waiting List as inactive.~~

Active and Inactive Status

A candidate is **not** eligible for active status if the candidate:

- Is insulin independent **and**
- Has an HbA1c value of less than or equal to 6.5%.

The transplant center is responsible for keeping the candidate's listing status current in UNet^{SM}.

If the candidate is listed as active and is insulin dependent, the transplant center must maintain documentation in the candidate's record of his/her current insulin status. To retain active status for an insulin dependent candidate, the transplant center must document in the candidate's record every six months that the candidate is currently insulin dependent.

If the candidate is listed as active and is insulin independent, the transplant center must maintain documentation in the candidate's record of his/her insulin status and HbA1c level with the date of the HbA1c test. To retain active status for an insulin independent candidate, the transplant center must document in the candidate's record every six months:

- That the candidate has had an HbA1c test within the past six months with a result of greater than 6.5%, **and**
- That the candidate is insulin independent.

The transplant center must use the most recent HbA1c value when determining whether the candidate is eligible for active status.

If a candidate's clinical condition changes, and the candidate is no longer eligible for active status, the transplant center must change the candidate's status in UNet^{SM} within 72 hours of the transplant center's knowledge of this candidate's clinical change. The transplant center must maintain documentation in the candidate's record of when the center learned of this clinical change. If a transplant center wishes to list an inactive candidate as active, the transplant center must have documentation that the candidate had the appropriate HbA1c level and insulin status in the past six months. The transplant center must present any documentation required by this policy to the OPTN upon request.

Removal from the Waiting List

The transplant center must remove the candidate from the waiting list within 24 hours of the candidate receiving his/her third islet infusion.