DONOR INTERVENTION RESEARCH ACOT WORK GROUP

ACOT Meeting March 12-13, 2015

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Organ Quality Limits Transplant Outcomes

- Insufficient ideal donors; increase in DCD, marginal and expanded criteria donors
 - Donor quality defined by post-transplant outcomes according to risk of graft loss (patient death or need for retransplantation)
- Inferior organ quality engenders recipient morbidity and mortality

The Need for Innovation and Research in Donor Intervention and Treatment

- To increase the number of organs available for transplantation
 - Mitigate waiting list candidate morbidity and mortality
- To improve the quality of organs used for transplantation
 - Mitigate recipient morbidity and mortality

Obstacles to Research and Innovation in Deceased (Brain Dead) Donors

Scientific

Ethical

Logistical

Regulatory

Constituents:

Investigator

Donors / donor families

Donor hospitals

Organ Procurement Organizations

OPTN

Waiting list candidates

Transplant recipients / centers

Problem

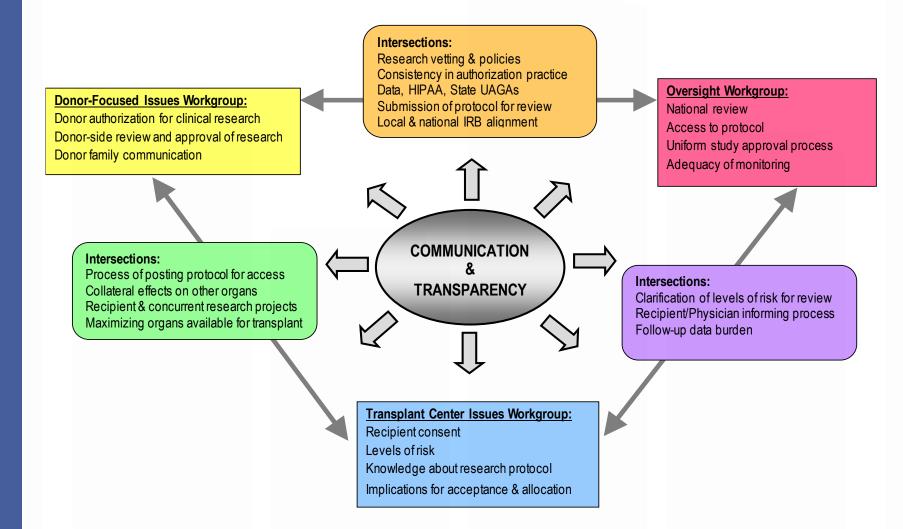
 Current infrastructure is inadequate to support effective donor intervention and treatment studies.

The magnitude and complexity of the challenges require guidelines/processes to facilitate the optimal design and safe execution of clinical trials in deceased donors.

Donor Intervention Research ACOT Work Group: Key Focus Areas

- Protocol and Oversight:
 - Key elements
 - Sharing
- Donor-Focused Issues:
 - Donor authorization for research
 - Ethical considerations
- Transplant Center/Recipient Issues:
 - Risk
 - Consent

Donor Intervention Research Issues Overview



Specific Actions to be Considered

Identify existing mechanisms, pathways, etc. and alternative pathways that could facilitate unique donor-related research activities

Donor Intervention Research ACOT Work Group: Key Focus Areas

- Protocol and Oversight:
 - Key elements
 - Sharing
 - Possibility of housing an IRB-type entity within the OPTN is under review and consideration
- Donor-Focused Issues:
 - Authorization for research
 - Ethical considerations
- Transplant Center/Recipient Issues:
 - Risk
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Donor Intervention Research ACOT Work Group

- Point of emphasis needs to be on big science with respect to guidance.
 - This strategy would allow the development of processes that capture all potential donor-related research activities.
- Complementary efforts are ongoing with IOM
 - Recent acknowledgement that there is funding for IOM planning meeting
 - Timeline for IOM study

Donor Intervention Research ACOT Work Group—Potential Protocol Process

Develop Proposal

Input: Personal observation; animal studies;

literature review

Responsibility: Researcher

Key Question: Research question examined

Develop Study Plan

Input: Colleagues; Research Consortium;

literature review

Responsibility: Researcher

Oversight: Researcher organization Key Question: Process and partners?

Resource OPO

INFO: Information elements needed by OPO

Scientific Merit Review

Input: Current or developed requirements *Responsibility:* Researcher submitted;

Committee review

Oversight: TBD (where committee is housed)

Key Question: Is study worth doing?

Resource SM:

Scientific Merit Review Process

Donor Intervention Research ACOT Work Group: Potential Protocol Process (cont.)

Human Subjects Review

Input: Guidance from OHRP, DIRB requirements *Responsibility*: Researcher submitted; DIRB

review

Oversight: DIRB, OHRP

Key Question: Does study demonstrate protection of human subjects?

Resource RISK:

Description of levels of risk to recipient

Allocation: Impact of allocation on protocol design and implementation; impact on non-targeted organs

Data and Safety Monitoring

Input: Standardized reporting process

Responsibility: Research team reporting; Board

monitoring and action Oversight: DSMB, OHRP

Key Questions: Does study protect subject? Are adverse events identified and mitigated?

Resource

DIRB/DSMB: Model elements for DIRB review and DSMB monitoring; centralized versus regional

Topics Addressed

- Donor-focused issues
 - Authorization under UAGA dual purpose of transplant and research
 - Standards for OPO review and participation
 - Donor hospital considerations
- Transplant-focused issues
 - Quantifying risk
 - Communicating info about protocol to accepting team – required elements
 - Informed consent of recipient or possible waiver of documentation of informed consent

Developing a Recommendation

- Points of Focus
 - Logistical Issues
 - Oversight/framework
- OHRP and request for secretarial waiver for IRB review
- Prioritization of donor-related research activities
 - HHS support system developments that facilitate donor intervention research
 - Decouple funding from process for research