AST | AMERICAN SOCIETY OF TRANSPLANTATION

Research in Deceased Donors:

Advancing science while maintaining public trust

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UCSF

CEOT CUTTING EDGE OF TRANSPLANTATION

TRANSPLANT SUMMIT 2020

BALANCING EQUITY AND UTILITY IN THE FACE OF AN ORGAN SHORTAGE

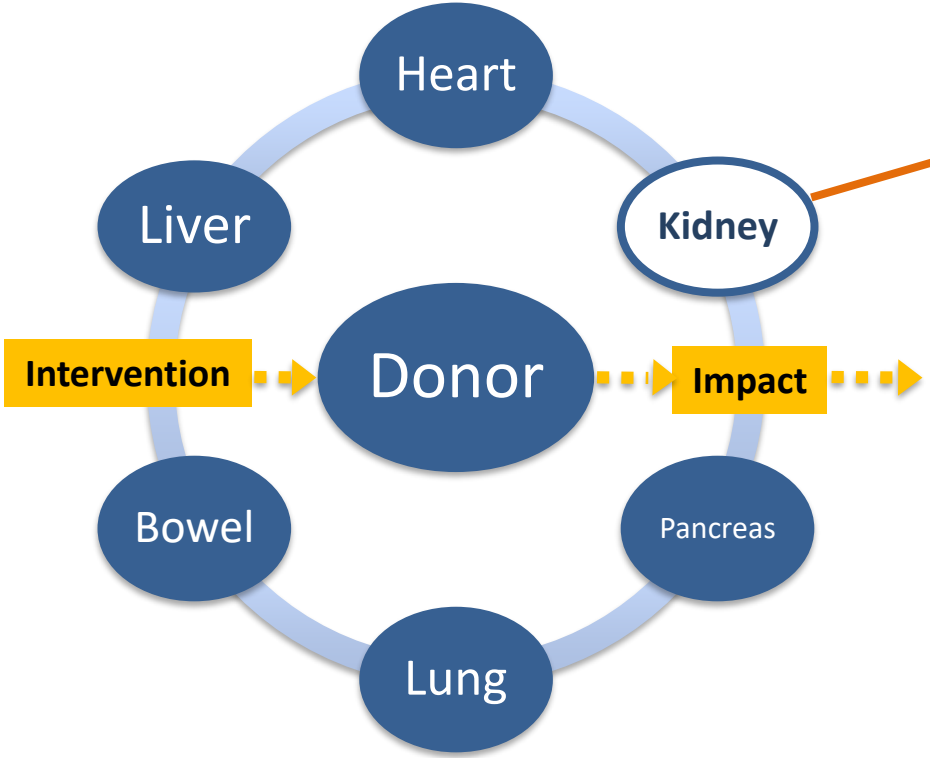
Disclosures

- None relevant to today's presentation

Learning Objectives

- Explain why donor intervention research represents a paradigm shift with respect to informed consent and human subjects' protection.
- Analyze whether and how the requirements for informed consent might map to recipients of organs from donors exposed to donor intervention research.
- Identify options for regulatory compliance if and when full informed consent is not possible.

Research in Deceased Donors: A Paradigm Shift



Non-human subjects

Donor hospitals

Intervention

Impact

Research recipients

Human subjects

- Waitlist candidates
- Transplant recipients

Bystander recipients

Advocacy Timeline

Feng AJT

Abt AJT

2/10 **5/13**

5/10 **8/12**

ASTS, AST, AOPO, ODRC, HRSA, ODTA

ACOT

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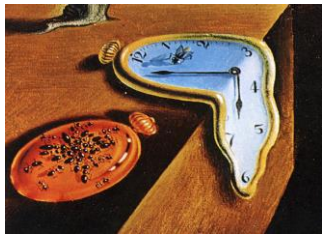

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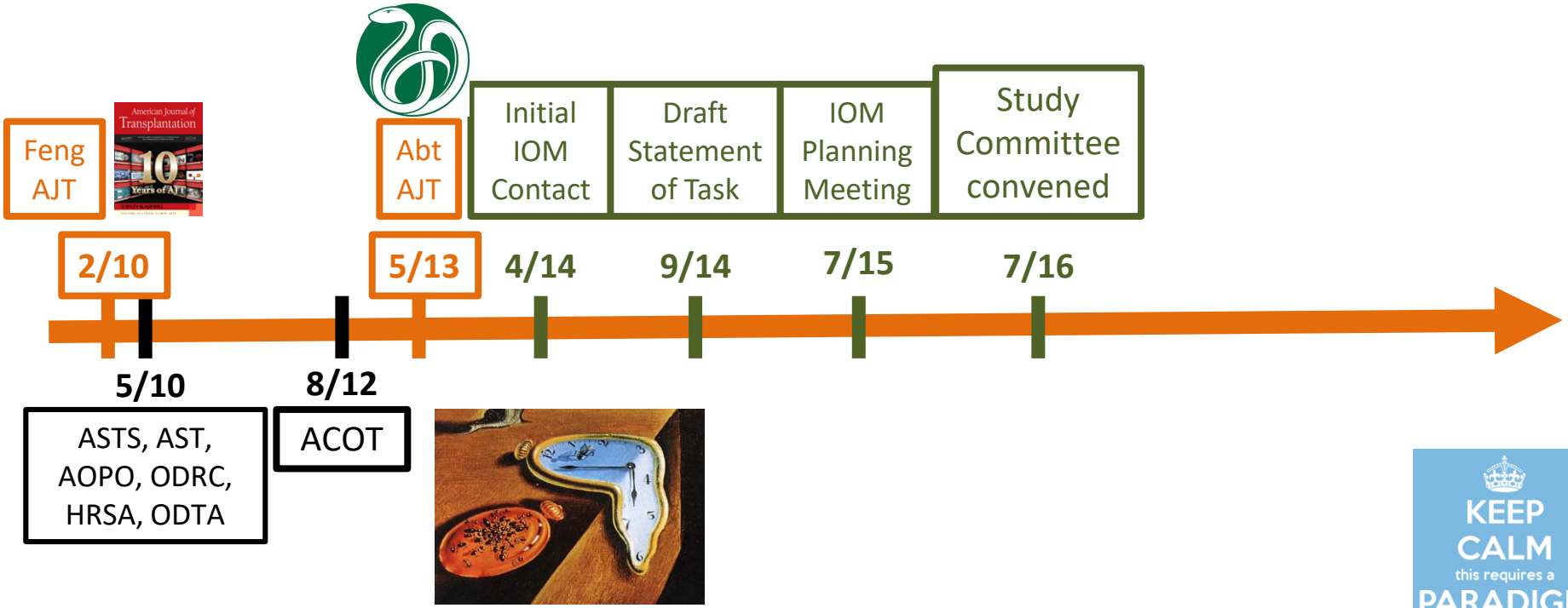

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Initial IOM Contact

Draft Statement of Task

IOM Planning Meeting

Study Committee convened

2/10 **5/13** **4/14** **9/14** **7/15** **7/16**

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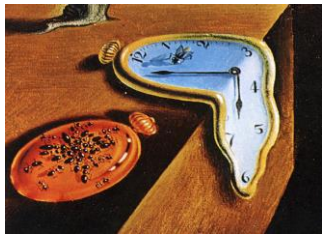

9/15

DIREP: National oversight mechanism

HRSA

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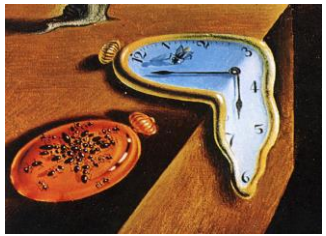

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OHRP → SACHRP

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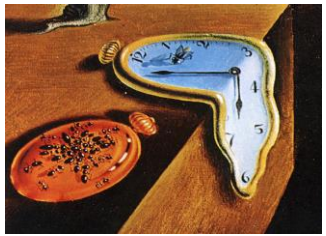

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The NAM Report

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March 5–7, 2020 | Arizona Biltmore | Phoenix, AZ

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NAM affirmed the importance of DIR

This report seeks to **enable** organ donor intervention research to move forward, within appropriate ethical, legal, and regulatory limits, in order to save more lives, to improve the quality of lives, and to fully honor the gifts of organs for both current and future transplant recipients.

James F. Childress, *Chair*
Committee on Issues in Organ Donor Intervention Research

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DONOR-BASED ISSUES

INFORMED CONSENT

NATIONAL OVERSIGHT

⇒ 6 GOALS Associated Recommendations

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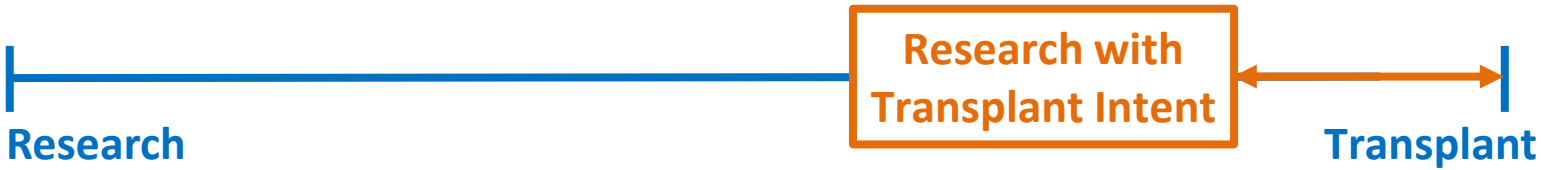
Donor-based Goals

- Improve transparency and public trust in the organ donation process for research followed by transplantation.
- Improve coordination and sharing of information about donor preferences
- Clarify legal guidance on organ donation for the purpose of research followed by transplantation

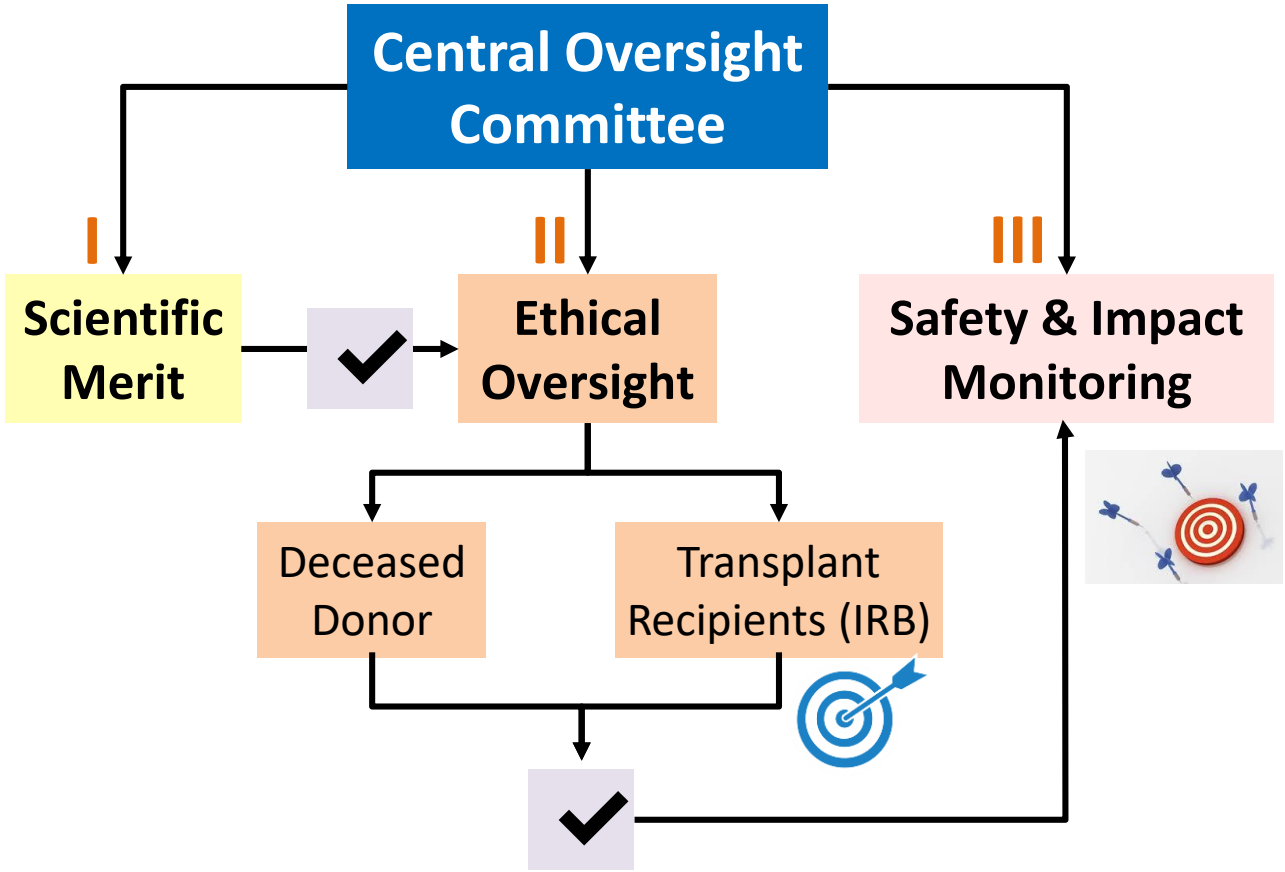


National Oversight Goals

- Establish centralized management and oversight of organ DIR to ensure equitable, transparent, and high-quality research
- Promote transparency regarding organ DIR and enable the implementation, tracking, and analysis of organ DIR to improve transplant outcomes

NAM affirmed oversight model proposed by Direp (HRSA)

- 3 functional pillars



The NAM report concluded that **recipients of organs** that have been subjected to research interventions, and whose organs are now being studied for their function, efficacy, and safety, should be treated as **research subjects.**

Informed Consent Goal

Promote informed consent for participation in DIR that is compatible with the logistical complexities of transplantation.

Informed Consent Recommendations

- Implement a protocol to educate transplant candidates about the possibility of receiving offers for organs exposed to DIR
- Implement a protocol for informed consent
  - **Consider a “two-step” process**

Informed consent: THE LAW

CFR Title 45: Public Welfare; DHHS

Part 46: Protection of Human Subjects

46.116: General requirements for informed consent

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Selected elements of informed consent

- Explanation of purposes of research and expected duration of participation
- Description of the procedures; identification of experimental procedures
- Description of any reasonably foreseeable risks or discomforts
- Description of any benefits to the subject or to others which may reasonably be expected from the research
- Disclosure of appropriate alternative procedures or courses of treatment
- Statement that participation is voluntary …
  - *Seek such consent only under circumstances that provide the prospective subject or the representative* ***sufficient opportunity to consider*** *whether or not to participate and* ***that minimize the possibility of coercion or undue influence.***

Will the 2-stage consent work?

- 1st consent conversation is **IN**sufficient to meet the regulatory requirements for research informed consent.
- 2nd consent conversation is likely so short and time-constrained that there is **IN**adequate time to meet the traditional ethical and regulatory requirements for information, comprehension, and voluntariness.

Secretary's Advisory Committee for Human Research Protections (SACHRP)

OHRP specifically asked SACHRP to provide recommendations regarding the NAM's recommendations about obtaining research informed consent from the recipients of the organs.

https://www.hhs.gov/ohrp/sachrp-committee/index.html

Secretary's Advisory Committee for Human Research Protections (SACHRP)

OHRP specifically asked SACHRP to provide recommendations regarding the NAM's recommendations about obtaining research informed consent from the recipients of the organs.

SACHRP's recommendations will inform HHS action, including the advisability of issuing guidance concerning the proper application of the HHS regulations for human subjects research protections to DDIR and whether a **Secretarial waiver** of certain regulatory requirements should be explored with respect to such research.

https://www.hhs.gov/ohrp/sachrp-committee/index.html

OHRP
Office for Human Research Protections

OHRP posed 10 questions to SACHRP including:

- How practicable would it be for investigators to implement the 2-stage consent process proposed by the NAM?
  - Specifically, is the 2nd step of the proposed consent process **feasible to implement** given that it would occur at the time the organ is being offered to the transplant candidate?
- Would the 2-step process, taken as a whole, **satisfy the regulatory criteria** for informed consent? If not, what would need to be included, and what circumstances would make regulatory compliance challenging?

And … raised consideration of waivers

Department or Agency Waivers of Regulatory Requirements:

Is a **Secretarial waiver** necessary or appropriate for any DDIR?

- If so, please describe the scope of such a waiver, including which regulatory requirements should be waived, and whether the waiver should include alternate procedures to be followed.
- Would such waiver be necessary or appropriate if informed consent were required for all DDIR (i.e., if an IRB determined that the current regulatory requirements would not allow informed consent to be waived or altered for such research)?

OHRP
Office for Human Research Protections

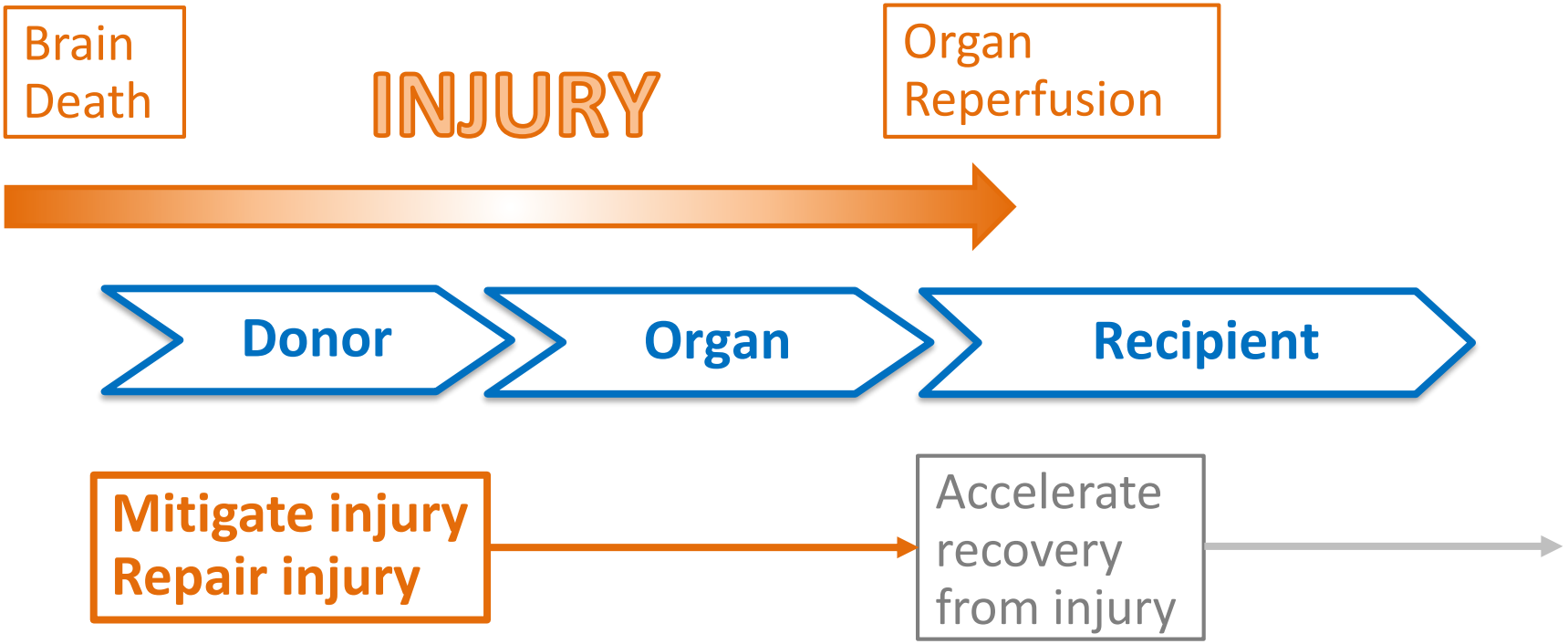
What is a secretarial waiver?

Unless otherwise required by law, department or agency heads may **waive the applicability of some or all of the provisions of this policy to specific research activities** or classes of research activities otherwise covered by this policy, ***provided the alternative procedures to be followed are consistent with the principles of the Belmont Report.***

Yet another complexity: The FDA

- The mechanism of a Secretarial waiver is not available for FDA regulated research.
- FDA has 2 available exceptions for informed consent
  - CFR Title 21: Food and Drug; Part 50: Protection of Human Subjects
  - §50.23 Applies to an individual participant's circumstances
  - §50.24 Applies to research under emergency circumstances
- SACHRP considering whether and how FDA approaches might be applicable to DIR
  - Can a broad interpretation allow an approach to fit?

Is all of this trouble worth it?



Donor intervention can be very effective!

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Therapeutic Hypothermia in Deceased Organ Donors and Kidney-Graft Function

Claus U. Niemann, M.D., John Feiner, M.D., Sharon Swain, M.S.N., R.N., Scott Bunting, R.R.T., Melissa Friedman, M.S.N., R.N., Megan Crutchfield, M.P.H., Kristine Broglio, M.S., Ryutaro Hirose, M.D., John P. Roberts, M.D., and Darren Malinoski, M.D.

So where are we, one decade later?

- Clarity how to adequately fulfill human subjects' protection
- Expert and comprehensive national oversight mechanism
- Vigorous advocacy to emphasize the tremendous need for donor intervention research to enhance the quality and increase the quantity of organs available for transplantation

Grateful Acknowledgements

- Laura and John Arnold Foundation
- ASTS
- AST
- AASLD
- AOPO
- Gift of Life
- NKF
- One Legacy
- TTS

- **P. Abt**
- C. Niemann

- HRSA: DoT/ACOT
- OHRP
- SACHRP
- NIAID
- NIDDK
- NHLBI