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Geoffrey Lomax DrPH

Senior Science Officer

CIRM Scientific and Medical Accountability Standards Working Group

January 5, 2023 South San Francisco

CIRM
CALIFORNIA'S STEM CELL AGENCY

Mission Statement

OUR MISSION

Accelerating world class science to deliver transformative regenerative medicine treatments in an equitable manner to a diverse California and world

Presentation Aims

CIRM Medical and Ethical Standards Working Group (SWG)

- Provide an Overview of SWG Charge and History
- Identify Contemporary Ethics-Policy Topics

Standards Working Group Charge

Recommend to the ICOC standards for all medical, socioeconomic, and financial aspects of clinical trials and therapy delivery to patients, including, among others, standards for safe and ethical procedures for obtaining materials and cells for research and clinical efforts for the appropriate treatment of human subjects in medical research.

The California Stem Cell Research, Treatments, and Cures Initiative of 2020 (Proposition 14)

SWG Membership

Proposition 14 Specifies SWG Membership:

- Five ICOC Patient Advocate or Nurse Members
- Nine MDs/scientists with stem cell / gene therapy expertise
- Four medical ethicists (one appointed co-chair)
- Chairperson of the ICOC (one appointed co-chair)

Standards Working Group History

Foundational Standards (2005-2006)

- Standards Requiring Review and Oversight of Human Gamete and Embryo Research
- Generally Aligned with Standards Adopted by the National Academy of Sciences (NAS)
- First Formal Codification of Stem Cell Research Oversight Committees

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Evaluation & Amendments (2007-2010)

- On Site Compliance Evaluation and Awardee Feedback
- Three Workshops Involving Institutional Officials (ESCRO Committees 2007, 2008 and 2010)
- Ongoing Interaction with NAS Embryonic Stem Cell Research Oversight

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iPSC Consent & Banking (2009-2011)

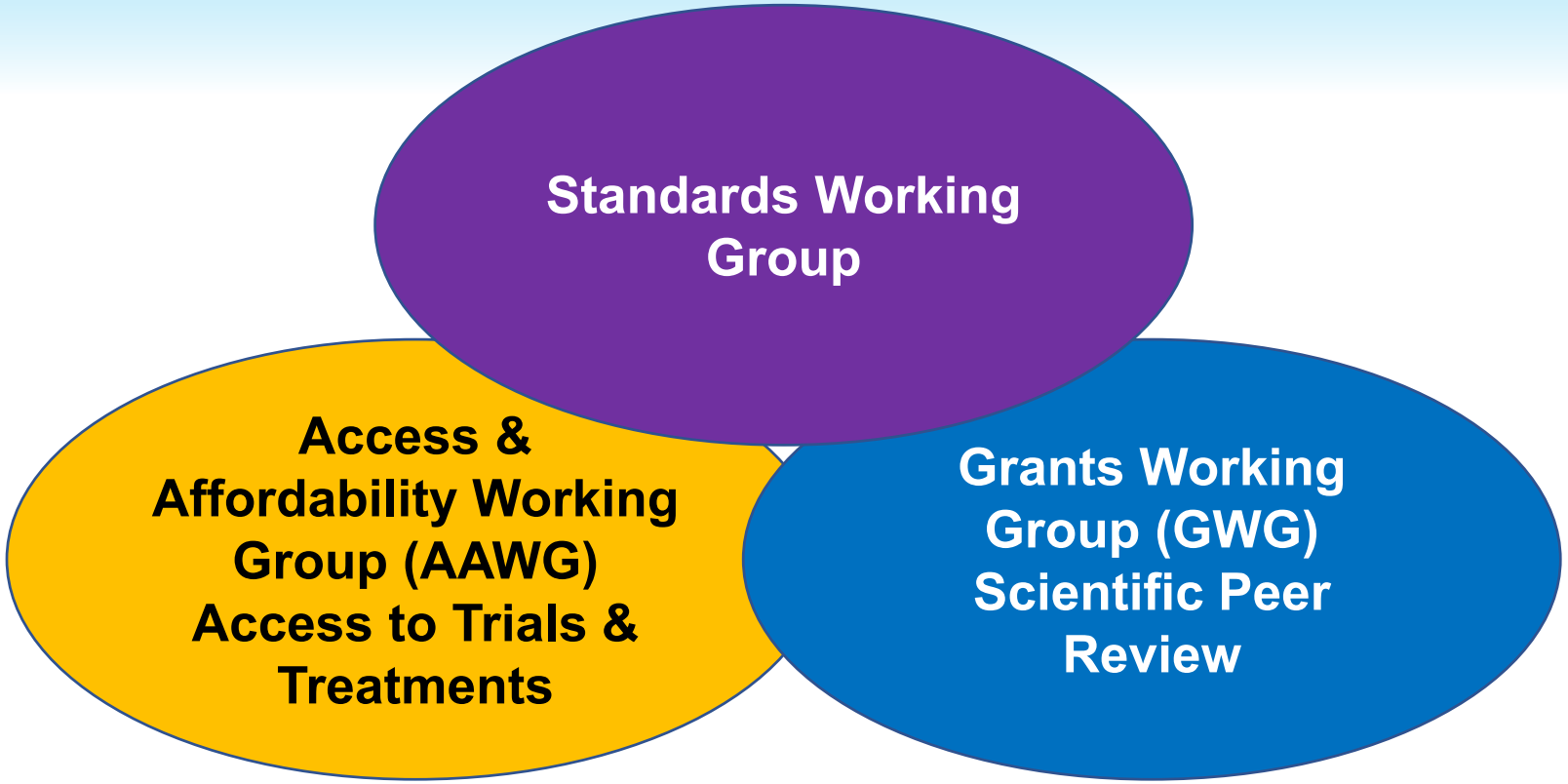
- Model Consent for iPSC Derivation, Banking and Distribution
- Template Utilized in Seven Tissue Collection Awards
- Continues to be Recognized as a Robust Consent Template for iPSC Research

Contemporary Topics in Stem Cell Research

- NAS Human Genome Editing Initiative
- Embryo Model Systems (NAS, 2020)
- Human Neural Organoids (NAS, 2021)
- Blastocyst Complementation
- Unauthorized Treatments | Stem Cell Clinics

Questions relating to the review and oversight of these techniques have arisen from CIRM awardees and during CIRM's strategic planning process

SWG Interacts With CIRM Programs



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Ben Huang

Associate General Counsel

CIRM Scientific and Medical Accountability Standards Working Group

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Presentation Aims

CIRM Medical and Ethical Standards Working Group (SWG)

- Brief overview of SWG bylaws
- Brief overview of Non-ICOC Conflict of Interest

Standards Working Group Duties

The duties of the SWG shall include the following:

(a) Recommend to the ICOC scientific, medical and ethical standards and modifications to existing standards;

(b) Recommend to the ICOC standards for all medical, socioeconomic, diversity, and financial aspects of clinical trials and therapy development and delivery to patients, including among others, standards for equitable access to therapies and safe and ethical procedures for obtaining materials and cells for research and clinical efforts for the appropriate treatment of human subjects in medical research consistent with paragraph (2) of subdivision (b) of Section 125290.35, and to ensure compliance with patient privacy laws.

(c) Make recommendations to the ICOC on the oversight of funded research to ensure compliance with the standards above;

(d) Regularly advise the ICOC, the Scientific and Medical Research Funding Working Group, and the Scientific and Medical Research Facilities Working Group on relevant ethical and regulatory issues.

SWG Co-Chairs

SWG bylaws specifies Co-Chair requirement:

The ICOC shall appoint a Patient Advocate Member of the SWG to serve as Co-Chair of the SWG. In addition, the ICOC shall appoint a Scientist/Clinician Member or an Ethicist Member of the SWG to serve as Co- Chair.

SWG Meetings

The SWG shall meet in public session except for discussions related to matters involving patient privacy or the review of a complaint regarding an investigator's or institution's compliance with medical or ethical standards adopted by the ICOC, and discussion of other matters that may be considered in closed session under the Bagley-Keene Open Meeting Act or under Health & Safety Code section 125290.30.

SWG Quorum

Sixty-five percent of the SWG members who are eligible to vote shall constitute a quorum of the SWG. All actions of the SWG shall be taken by a majority vote of a quorum of members.

SWG Conflict of Interest (non-ICOC)

Non-ICOC Members of the Standards Working Group are precluded from deriving direct financial benefit from the CIRM through grants, loans or contracts and from acting as a Principal Investigator on any CIRM-funded grant.

A conflict of interest exists when there is a financial or other interest that significantly impairs the individual's objectivity or that creates an unfair advantage for any person, institution or company. A non-ICOC member has a conflict of interest when any financial interest identified in subdivision (b) of this regulation is the subject of a decision before the working group

SWG Financial Interest Conflict of Interest

b) Disclosure: A non-ICOC working group member has a financial interest in and must disclose confidentially and under penalty of perjury the following:

(1) All California-based academic or non-profit research institutions from which Standard Working Group members, their spouses, or others with whom a member has a common financial interest, receive current income of $5,000 or more;

(2) All biotechnology and pharmaceutical companies from which members, their spouses, or others with whom a member has a common financial interest, receive current income or other benefit or investments of $5,000 or more; and

(3) All real property interests in California of $5,000 or more (including real estate interests and interests in intellectual property such as patents and copyrights) held by members, their spouses, or others with whom a member has a common financial interest

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Alpha Clinic Network Sites

Alpha Clinic Network Value Proposition

CLINICAL PLATFORMS	THERAPY DEVELOPMENT	ACCESS INCLUSIVITY
CGT Delivery Tools	GMP Processing	Patient Registries
Research Coordination	Genomics	Community Engagement Platforms
Regulatory Expertise & Network MOUs	Gene Editing Tools and Technologies	Patient Navigation
Multi Site Startup		

NETWORK OFFERINGS

TRAINING EDUCATION WORKFORCE DEVELOMENT

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Medical Affairs and Policy Team

A new department within CIRM tasked with developing CIRM's Roadmap for Access and Affordability in coordination with the AAWG, and responsible for post-marketing research, outcomes, registries, real world evidence, health economics and policy.

Five major workstreams:

- Alpha Clinics
- Access and Affordability Working Group
- Standards Working Group
- Community Care Centers of Excellence
- Patient Support Program

Roadmap to Access & Affordability Strategies - Examples

DELIVER A ROADMAP FOR ACCESS AND AFFORDABILITY OF REGENERATIVE MEDICINE FOR ALL CALIFORNIA PATIENTS

Facilitate Reimbursement and Limit Patient Expenses	Support New Payer Models	Address State Policy Issues	Expand Clinical Infrastructure
Patient Support Services	Engagement with Payers	Creation and/or endorsement of new State policy for C&GT	Alpha Clinics and CCCE
Alpha Site Coordination and Alignment	Performance Based Models	Treatment across state lines	Patient and post-marketing Registries, RWE, HEOR
Patient Navigator at CCCEs	Introduce New Payer Mechanisms for Orphan Products	Inpatient vs. Outpatient reimbursement	Accelerate Advocacy at community level; Medical Education
Coverage Analysis, Insurance Support, Co-Pay Assistance, Access and Appeals	Risk Pools/Coalition Partners	Align to Gov Plan on Office of Health and Affordability	State and Federal authorized treatment centers

What Barriers Must be Overcome to Achieve Broad, Equitable Access to Regenerative Medicines?

CULTURAL AND SOCIAL DETERMINANTS

- Lower enrollment for minorities [2]
- Socioeconomic status, unemployment, education [4,5]
- Population size/geography [6,7]
- Stigma of disease [8,9]

INFORMATIONAL

- Physician low referral rate [10]
- Medical mistrust and misinformation about regenerative medicine [11]

LOGISTICAL

- Lack reliable transportation [12,13]
- Language[14]
- Work or childcare requirements [11]

FINANCIAL

- Cost of regenerative medicines (gene or cell therapies) and insurance benefits may include high copays and lifetime benefit [15]

ABILITY-BASED

- Participation is limited for elderly,[16] adolescent and young adult,[17] and disabled patients[18,19]

Purpose of CIRM's Patient Support Program

Cell and gene therapy trials are becoming more demanding on patients and require additional support beyond routine costs for patients and their families

New Patient Assistance Programs have emerged to address bottlenecks associated with gene therapy/gene edited trials

The objective is to launch a Patient Support Program (PSP) to provide logistical and financial support to patients seeking to enroll in clinical trials. The overall aim is to improve access and retention in clinical trials with an emphasis on underserved populations

Patient Support Program is one component of the 5-year Strategic Plan to create a roadmap for Access and Affordability

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Discussion: Education and Consent Considerations

What are the opportunities within CIRM programs – clinical trial awards, clinical research infrastructure (Alpha Clinics & future community care centers) and Patient Support Program promote robust patient education, consent and inclusion of under-represented populations?

Are there tools or resources that could enhance the education and consent process?

Are there ethics-policy research needs?

Are there specific needs or opportunities to support under-represented populations?

What opportunities can be developed within a patient support program?

Overview CIRM Regulations

CIRM Scientific and Medical Accountability Standards Working Group

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Overview CIRM Medical and Ethical Standards and Future Considerations

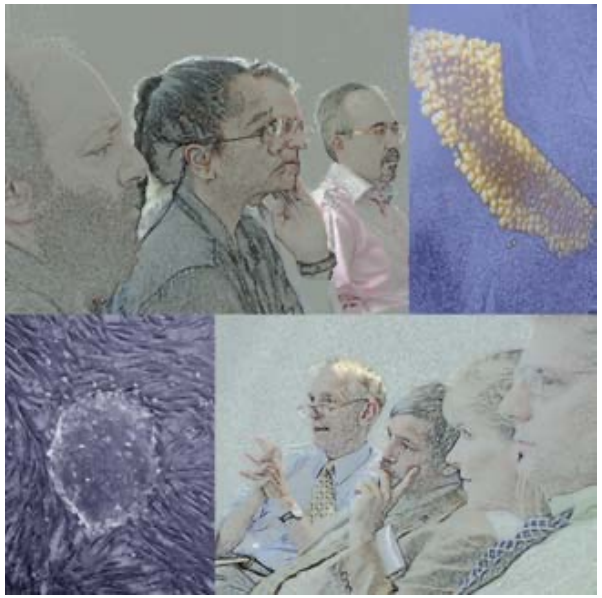
OPEN ACCESS Freely available online

PLoS MEDICINE

Policy Forum

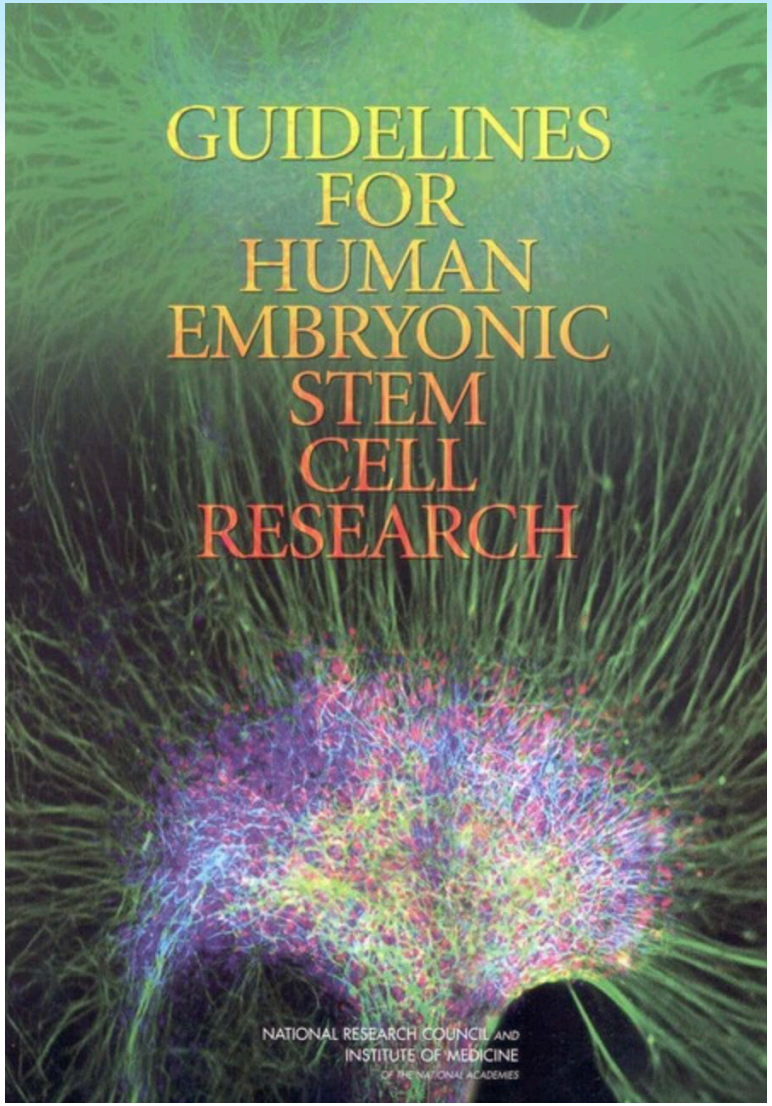
Responsible Oversight of Human Stem Cell Research: The California Institute for Regenerative Medicine's Medical and Ethical Standards

Geoffrey P. Lomax*, Zach W. Hall, Bernard Lo



Policy Framework

- Modeled after the NAS Guidelines for Human Embryonic Stem Cell Research
- Designed to address activities not covered by federal policy (e.g. embryo research, hESC derivation and utilization)



Scope

- These regulations apply to CIRM-funded projects or activities.
- However, California adopted **guidelines** in 2006 (SB 1260) applying similar policy to all research

Important Restrictions

- **Reiterates Proposition 71 & 14 restrictions:**
  - On human reproductive cloning
  - The culture of an intact human embryo or SCNT product beyond 12 days
- **Consistent with NAS Guidelines and/or recommendations:**
  - The introduction of human stem cells into primate embryos
  - The **breeding** of animals into which human pluripotent stem cells have been introduced
  - The use of **genetically modified** human embryos (CRISPR) for reproductive purposes

CIRM Requires Oversight of Human Embryo Research

- **Adopts the ESCRO Committee Framework**
  - Review and approval of protocols involving the oocytes or embryos
  - Review and approval of blastocyst complementation studies or introduction of neural progenitor cells into the brain of non-human animals
  - Includes additional requirement for research involving oocytes

Contemporary Topics in Stem Cell Research

- NAS Human Genome Editing Initiative
- Embryo Model Systems (NAS, 2020)
- Human Neural Organoids (NAS, 2021)
- Blastocyst Complementation
- Genetic Data Sharing and Privacy
- Unauthorized Treatments or High-cost Stem Cell Clinics
- Cord Blood Banking

Questions relating to the review and oversight of these techniques have arisen from CIRM awardees and during CIRM's strategic planning process