NIH RAC Design Working Group

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RAC Design Working Group

- Dave DeMets co-chair
- Nancy King co-chair
- Terry Kwan (Boston)
- Bernie Lo (UCSF)
- David Harrington (Harvard)
- Susan Ellenberg (FDA/CBER)
- Laurence Friedman (NHLBI)
- James Neaton (U Minn)

RAC Design Working Group

- Greg Podsakoff (USC)
- Cynthia Rask (FDA/CBER)
- Marcel Salive (Center for Medicare & Medicaid)
- H James Williams (Univ Utah)
- Cheryl McDonald (NIH/OBA)
- Alex Rakowski (NIH/OBA)

Design WG Process

- Teleconference, Nov 2003
- Bethesda Meeting, Feb 2004
- Design Draft developed May 2004
- Summer Interns
  - Tiffany Scharschmidt (UCSF)
  - Dan Lipton (U Virginia – NIH)
- RAC Preliminary Report Sept 2004

Three Components

- Draft Design Guidelines
- "Review" of RAC Review
  - Tiffany Scharschmidt & Bernie Lo
- "Review" of Informed Consents
  - Daniel Lipton & Cheryl McDonald
- Need to integrate 3 pieces

Overview of Design Draft

- **No single design is possible**
  - **Varied disease areas**
  - **Varied methods of gene transfer**
  - **Various design stages**
- **Each protocol should address a series of issues**
- **Draft identifies several issues**

Design Issues

- Rationale for protocol
- What is the question or goal?
- What outcomes will be measured?
- What population and why?
- Basic experimental design and sample size justification
- Analysis plan
- What will be learned to help in the design of the next trial

X	n = 5	n = 10	n = 15	n = 20	n = 25	n = 30
0	0.0 (0.0, 52.2)	0.0 (0.0, 30.9)	0.0 (0.0, 21.8)	0.0 (0.0, 16.8)	0.0 (0.0, 13.7)	0.0 (0.0, 11.6)
1	20.0 (0.5, 71.6)	10.0 (0.3, 44.5)	6.7 (0.2, 31.9)	5.0 (0.1, 24.9)	4.0 (0.1, 20.4)	3.3 (0.1, 17.2)
2	40.0 (5.3, 85.3)	20.0 (2.5, 55.6)	13.3 (1.7, 40.5)	10.0 (1.2, 31.7)	8.0 (1.0, 26.0)	6.7 (0.8, 22.1)
3	60.0 (14.7, 94.7)	30.0 (6.7, 65.2)	20.0 (4.3, 48.1)	15.0 (3.2, 37.9)	12.0 (2.5, 31.2)	10.0 (2.1, 26.5)
4	80.0 (28.4, 99.5)	40.0 (12.2, 73.8)	26.7 (7.8, 55.1)	20.0 (5.7, 43.7)	16.0 (4.5, 36.1)	13.3 (3.8, 30.7)
5	100.0 (47.8, 100.0)	50.0 (18.7, 81.3)	33.3 (11.8, 61.6)	25.0 (8.7, 49.1)	20.0 (6.8, 40.7)	16.7 (5.6, 34.7)
6		60.0 (26.2, 87.8)	40.0 (16.3, 67.7)	30.0 (11.9, 54.3)	24.0 (9.4, 45.1)	20.0 (7.7, 38.6)
7		70.0 (34.8, 93.3)	46.7 (21.3, 73.4)	35.0 (15.4, 59.2)	28.0 (12.1, 49.4)	23.3 (9.9, 42.3)
8		80.0 (44.4, 97.5)	53.3 (26.6, 78.7)	40.0 (19.1, 63.9)	32.0 (15.0, 53.5)	26.7 (12.3, 45.9)

Informed Consent Issues

- **Project**
  - **Dan Lipton – summer intern**
  - **Supervised by Cheryl McDonald**
- **Results Presented by Terry Kwan**

Informed Consent Issues

- Reviewed 43 protocols from past two years
- Asked questions about following 11 consent form descriptions
- Objectives of study
- Research vs available treatment
- Gene transfer procedures
- Dose escalation if appropriate

Informed Consent Issues

- Potential benefits
- Potential risks and discomforts
- Conditions for trial termination
- Financial costs for participation
- PI financial conflicts
- Physician contact information
- Dealing with emergencies

RAC Review Issues

- **Summer Project**
  - **Tiffany Scharschmidt – summer intern**
  - **Supervised by Bernard Lo**
- **Results Presented by Tiffany Scharschmidt**