RAC Reviews and Investigator and Institutional Responses

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June 2003 RAC Meeting

"That the RAC request OBA staff to develop a mechanism whereby in response to our review of amendments, investigators and their IRBs and IBCs are requested to respond to our suggestions and comments, and that the RAC be informed about those responses."

Initial RAC Review

- Within 15 working days of receipt of a complete submission the RAC recommends whether a protocol requires additional in-depth review and public discussion.
- In either case, a letter with the results of the RAC review is sent to the Principal Investigator, Sponsor, Chairs of the IRB and IBC, and other relevant Federal Agencies.

Completion of RAC Review Process of New Protocols

1.) receipt by the Principal Investigator(s) a letter from NIH OBA indicating the submission does not warrant in-depth public RAC review and discussion; or

2.) receipt by the Principal Investigator(s) of a letter from the NIH OBA after public RAC review that summarizes key comments and recommendations (if any).

- Initial RAC Review Process Completed
- Ongoing Reporting Requirements

NIH Guidelines: Appendix M-I-C Reporting Requirements

- M-I-C-1: Initiation of Clinical Investigation
- M-I-C-2: Additional Clinical Trial Sites
- M-I-C-3: Annual Reports
- M-I-C-4: Safety Reporting

OBA website: **http://www4.od.nih.gov/oba/**

NIH OBA
Processing of Information

- All submissions are reviewed by OBA Staff for completeness and categorized by type of submission.
- The substance of all submissions are reviewed by OBA Staff and summarized quarterly.
- All summaries are presented to RAC members and selected submissions may require further discussion at public RAC meetings quarterly or at specially convened meetings.

Data Management Sub-Group of the RAC

- Initiation of Clinical Trial ("20-day responses")
- PI or Site Change
- Status of the Protocol Changes or Updates
- Annual Reports
- Protocol Amendments
- Other types of communications (e.g., IRB and IBC communications, animal studies)

AMENDMENTS AND UPDATES TO HUMAN GENE TRANSFER PROTOCOLS

December 2003

ID #	Letter Date	Protocol #	Amendment Description
		0101-452	**A Multicenter, Randomized, Double-Blind, Placebo Controlled, Dose-Response Study to Evaluate the Efficacy and Safety of Ad5.1FGF-4 in Patients with Stable Angina. Sponsor: Berlex Laboratories.**
1028	03/03/2003		*PI or Site Change:* Appendix M-I-C-2 *Protocol Change:* *Status Change:* *Annual Update:* Appendix M-I-C-3 *Other:*

After Data Management Team Review

- PI invited to present the amendment to the RAC at a public meeting.
- Amendment mentioned at public RAC meeting .
- Discussed at public RAC meeting and RAC makes recommendations at the meeting.
- Discussed at public RAC meeting and a letter with RAC concerns sent to the PI with copies to the IRB and IBC.

Recent Examples

- Protocol 371-Kathy High and Mark Kay presented rationale for protocol amendment at December 2001 RAC Meeting.
- Protocol 453-March 2003 RAC meeting-concern about amendment lead to a letter sent to the PI, Sponsor, FDA, and the IRB and IBCs of all 5 trial sites.
- Dr. Deisseroth will present an amendment to Protocol 419 today.

Mechanism is in Place

NIH OBA and the RAC

- Primary relationship is with the Investigator and the IBC.
- Final IBC approval can only be after the RAC review process is complete.
- Letters are sent to IRB and we welcome communications from IRBs.

Opportunities for Education and Outreach

- Many sites do communicate with NIH OBA and the RAC and this serves to inform the field.
- IBCs and IRBs are welcome to communicate to the RAC via NIH OBA any questions or feedback of a generalizable nature which would be applicable to more than just that one protocol.

Recent IRB/IBC Outreach Efforts

- February 2003 – "The Future Face of IBCs:Evolving Roles and Responsibilities, Upcoming Challenges and Opportunities" in San Diego (co-sponsored with ABSA, ARENA, OLAW)
- April 2003 – "Medical Research Summit" – Clinical research administrators
- April 2003 – Annual Meeting of the Association of Clinical Research Professionals

Outreach Efforts, continued

- October 2003-ABSA-American Biological Safety Association Annual Meeting in Philadelphia
- December 2003- Annual Meeting of ARENA (Applied Research Ethics National Association) and PRIM&R (Public Responsibility in Medicine and Research)
- Ongoing - Ad hoc education and outreach (OBA_NEWS listserv, BIOSAFTY listserv, articles, brochures)

Webcasts:
www.webconferences.com

NIH OBA Website:
www4.od.nih.gov/oba/

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M-I-C-1: Initiation of the Clinical Investigation

- No later than 20 working days after enrollment of the first research participant, PI must submit:
  - Copies of Approved Informed Consent document, IRB/IBC Approved Protocol, IRB and IBC approval letters, written summary of responses to RAC recommendations., FDA changes, NIH Grant numbers, IND number, date of trial initiation.