

Department of Health and Human Services
Public Health ServicesReview Group Type Activity Grant Number
1 U01 AT001156-02

Grant Progress Report

Total Project Period
From: 08/15/2002 Through: 02/28/2007Requested Budget Period:
From: 03/01/03 Through: 02/29/04

1. TITLE OF PROJECT

Trial to Assess Chelation Therapy (TACT)

2a. PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR
(Name and address, street, city, state, zip code)Gervasio A. Lamas, MD
Mount Sinai Medical Center
4300 Alton Rd; Suite 207A
Miami Beach, FL 33140

3. APPLICANT ORGANIZATION

(Name and address, street, city, state, zip code)
Mount Sinai Medical Center of Florida, Inc.
4300 Alton Road
Miami Beach, FL, 33140

2b. E-MAIL ADDRESS

TACTNIH@aol.com

4. ENTITY IDENTIFICATION NUMBER

EN [REDACTED]

2c. DEPARTMENT, SERVICE, LABORATORY, OR EQUIVALENT

Medicine

5. TITLE AND ADDRESS OF ADMINISTRATIVE OFFICIAL

William Abraham, Ph.D., Director of Research
4300 Alton Road
Miami Beach, FL
33140

2d. MAJOR SUBDIVISION

Cardiology

E-MAIL: Abraham@msmc.com

6. HUMAN SUBJECTS

No	6a. Research Exempt	6b. Human Subjects Assurance No.
Yes	No Yes	#A00000176

If Exempt ("Yes" in 6a):	6c. NIH-Defined Phase III
Exemption No.	Clinical Trial No <input checked="" type="checkbox"/> Yes

If Not Exempt ("No" in 6a):	<input checked="" type="checkbox"/> Full IRB or
IRB approval date	Expedited Review

7. VERTEBRATE ANIMALS

No	7a. If "Yes," IACUC approval Date
Yes	

7b. Animal Welfare Assurance No.

8. COSTS REQUESTED FOR NEXT BUDGET PERIOD

8a. DIRECT \$ 4,464,704 8b. TOTAL \$4,776,325

9. INVENTIONS AND PATENTS

No	Yes	If "Yes," Previously Reported
		Not Previously Reported

10. PERFORMANCE SITE(S) (Organizations and addresses)

Mount Sinai Medical Center
4300 Alton Rd
Miami Beach, FL 33140Duke Clinical Research Institute
Box 3300
Durham, NC 2771511a. PRINCIPAL INVESTIGATOR
OR PROGRAM DIRECTOR (Item 2a)

Gervasio A. Lamas, MD

TEL 305-674-2162

FAX 305-674-3970

11b. ADMINISTRATIVE OFFICIAL
NAME (Item 5)

William Abraham, Ph.D.

TEL 305-674-2790

FAX 305-674-2198

11c. NAME AND TITLE OF OFFICIAL SIGNING FOR APPLICANT
ORGANIZATION (Item 14)

NAME Paul Katz, MD

TITLE Vice President

TEL 305-674-2633

FAX 305-674-2007

E-MAIL pkatz@msmc.com

12. Corrections to Page 1 Face Page

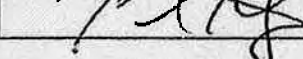
13. PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR ASSURANCE: I certify that the statements herein are true, complete and accurate to the best of my knowledge. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. I agree to accept responsibility for the scientific conduct of the project and to provide the required progress reports if a grant is awarded as a result of this application.

SIGNATURE OF P/VPD NAMED IN 2a.
(In ink. "Per" signature not acceptable.)

DATE

7/18/03

14. APPLICANT ORGANIZATION CERTIFICATION AND ACCEPTANCE: I certify that the statements herein are true, complete and accurate to the best of my knowledge, and accept the obligation to comply with Public Health Services terms and conditions if a grant is awarded as a result of this application. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties.

SIGNATURE OF OFFICIAL NAMED IN
11c. (In ink. "Per" signature not acceptable.)

DATE

7-18-03

Principal Investigator: Lamas, Gervasio A.

DETAILED BUDGET FOR NEXT BUDGET PERIOD – DIRECT COSTS ONLY		FROM 03/01/2003	THROUGH 02/29/2004	GRANT NUMBER 1 U01 AT001156-02		
PERSONNEL (Applicant organization only)		TYPE APPT. (months)	% EFFORT ON PROJ.	DOLLAR AMOUNT REQUESTED (omit cents)		
NAME	ROLE ON PROJECT			SALARY REQUESTED	FRINGE BENEFITS	TOTALS
Gervasio A. Lamas, MD	Principal Investigator	12	% Effort	64,480	0	64,480
Charles H. Hennekens, MD, DrPH	Co-PI	12		64,480	0	64,480
Danielle Hollar, Ph.D.	Project Director	12		74,100	0	74,100
Steven Hussein, MD	Clinical Coordinator	12		0	0	0
Virginia Martini, BS	Admin. Coordinator	12		41,600	0	41,600
Matt Shields, BS	Research Assistant	12		28,500	0	28,500
TBN	Research Assistant	12	95	14,250	0	28,500
Ophelia Stephens	Admin. Assistant	12	% Effort	24,800	0	24,800
SUBTOTALS				312,210	0	312,210
CONSULTANT COSTS						
Martin Dayton, DO (\$6,000); Ted Rozema, MD (\$6,000)						
EQUIPMENT (Itemize)						
LCD Projector						
SUPPLIES (Itemize by category)						
copier supplies						
fax supplies						
paper						
TRAVEL						
Yearly Meetings (\$90,700); CCC Travel (\$23,606)						
PATIENT CARE COSTS		INPATIENT 0				
		OUTPATIENT 0				
ALTERATIONS AND RENOVATIONS (Itemize by category)						
OTHER EXPENSES (Itemize by category)						
Telecommunications (\$6,240); Pagers (\$1,040)						
Audiovisual (\$2,600); Postage (\$6,240); Advertisements (\$30,000)						
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD					\$498,636	
CONSORTIUM/CONTRACTUAL COSTS		DIRECT COSTS		3,434,112		
		FACILITIES AND ADMINISTRATIVE COSTS		531,956		
TOTAL DIRECT COSTS FOR NEXT PROJECT PERIOD (Item 9a, Face Page)					\$4,464,704	

BUDGET JUSTIFICATIONGRANT NUMBER
1 U01 AT001156-02

Provide a detailed budget justification for those line items and amounts that represent a significant change from that previously recommended. Use continuation pages if necessary.

Following pre-release of funds discussions with NCCAM and NHLBI, the scope of TACT increased in order to improve statistical power. The sample size was increased from 1600 to 2372 (a 48% increase) without an increase in cost. The number of performance sites increased from 50 to 120 (a 140% increase) without an increase in cost.

CURRENT BUDGET PERIODFROM
03/01/2003THROUGH
02/29/2009

Explain any estimated unobligated balance (including prior year carryover) that is greater than 25% of the current year's total budget.

Equipment: There has been a slight delay in deducting the expenses for the purchase of a laptop computer; hence this expense will show up in the near future.

Supplies: Funds for a copier will be expended in Year 2. Also, because of the delay in activating clinical sites, expenditures of supplies has been less than expected, but will be expended during the current year.

Travel: The Investigators Meeting occurred recently (July 10-13, 2003), hence travel funds will be deducted very soon.

Other expenses: The categories "telephones" and "pagers" have been combined into a broader category of "telecommunications" that includes expenses for multifunctional devices that incorporate cell phone, pager, and email functionality. Postage funds for Year 1 will be used as part of payment for the Investigators Meeting. Audiovisual expenses were incurred during the recent Investigators Meeting and will be deducted in the near future. No advertisement funds were expended during Year 1 because clinical sites were not activated during this time.

Consortium: Because no patients have been enrolled up to this point, there have been no expenditures for the central lab, clinical units, or the Clinical Events Committee (Brigham & Women's). The Pharmacy was paid approximately five percent of their budget in order to prepare for trial start-up. DCRI will be invoicing the CCC within the near future for work completed during year 1. No indirect costs have been billed by the consortia.

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel in the order listed for Form Page 2.
Follow the sample format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Steven Husseln, MD		POSITION TITLE Clinical Coordinator	
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
The Stamford Hospital, Stamford, CT	Residency	July 1998- June 2001	Internal Medicine Residency (PGY I - III)
Ross University School of Medicine, Dominica, West Indies	MD	1998	Medicine
State University of New York at Stony Brook, Stony Brook, NY	BS	1992	Biochemistry

NOTE: The Biographical Sketch may not exceed four pages. Items A and B (together) may not exceed two of the four-page limit. Follow the formats and instructions on the attached sample.

Professional Experience

- 2002-present University of California at San Francisco/San Francisco Veterans Affairs Medical Center, San Francisco, CA
Congestive Heart Failure Fellow
- July 2001 - June 2002 The Stamford Hospital, Stamford, CT
House Physician & Columbia University Clinical Instructor
- July 1992 - June 1993 State University of New York at Stony Brook, Department of Anesthesiology, Stony Brook, NY
Electron Microscopist

Publications

Husseln SJ, Teerlink JR. Novel Pharmacologic Therapy of Heart Failure, Curr Treat Options Cardiovasc Med. 2003 Aug;5(4):321-335.

LoPachin RM Jr, Lehning EJ, Stack EC, Husseln SJ, Saubermann AJ. Journal Neurochemistry 1994 Dec; 63 (6); 2266 - 2278, 2,5 Hexanedione alters elemental composition and water content of rat peripheral nerve myelinated axons.

Principal Investigator: Lamas, Gervasio A.

PROGRESS REPORT SUMMARY		GRANT NUMBER 1 U01 AT01156-02
PERIOD COVERED BY THIS REPORT		
PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR Gervasio A. Lamas, MD	FROM 03/01/2003	THROUGH 02/29/2004
APPLICANT ORGANIZATION Mount Sinai Medical Center		
TITLE OF PROJECT (Repeat title shown in Item 1 on first page) Trial to Assess Chelation Therapy (TACT)		
A. Human Subjects (Complete Item 6 on the Face Page) Involvement of Human Subjects	No Change Since Previous Submission	Change
B. Vertebrate Animals (Complete Item 7 on the Face Page) Use of Vertebrate Animals	No Change Since Previous Submission	Change

SEE PHS 2590 INSTRUCTIONS.

Has there been a change in the support of key personnel since the last reporting period?

The following represent organizational changes in the CCC designed to permit an efficient management of TACT, given its greatly enlarged scope and responsibilities. All these changes have been made without an increase in total cost.

Danielle Hollar, PhD (Project Director): Dr. Hollar's position title has changed in order to reflect her leadership role and organizational changes in the CCC.

Matt Shields, BA (Research Assistant): Matt Shields has replaced Adam Williams as a research assistant for TACT. He will work on the trial for ^{EFFORT} (July 2003 to June 2004), bracketing grant years 2 and 3, at ^{FTE} FTE, with a base salary of ^{ESBUDGET}. His principal duties are to assist in identifying clinical sites; assisting clinical sites with IRB applications, FWA applications, and the completion of regulatory documents; collecting and storing regulatory documents; assisting with literature searches and protocol revisions; assisting with IRB issues for the CCC, and assisting with the coordination of sub-contracts and ancillary studies. He reports to the Project Director.

Based on the amount of activity required for supporting clinical sites and ensuring the collection, storage, and updating of trial regulatory documents, the CCC has added a second research assistant to the TACT budget at the base salary of \$30,000. This addition is budget neutral due to the fact that Drs. Rachel Eidelman and Alan Ackermann (Project Co-Leaders during the Year 1 of TACT and the first half of Year 2) are no longer working on the trial.

Rachel Eidelman, MD (Project Co-Leader) and **Alan Ackermann, DO (Project Co-Leader)** are no longer working on TACT.

Steven Hussein, MD (Clinical Coordinator): Dr. Hussein will be assisting with TACT. No salary is requested for Dr. Hussein because he is being supported by a Fellowship grant from MSMC. His principal responsibilities will focus on clinical aspects of TACT:

1. Training and then assisting clinical units with the clinical management of TACT patients.
2. Training and then assisting clinical units with patient recruitment strategies.
3. Training and then assisting clinical units with patient retention strategies.
4. Responding to clinical inquiries from clinical units.
5. Triaging difficult clinical calls to a more senior clinician when appropriate, especially Dr. Lamas or Dr. Hennekens.
6. Participating on the weekly Operations Committee calls.
7. ~~Participating on the Steering Committee as an ex-officio member.~~

Interim Progress Report Summary

a. Specific Aims

The specific aims of the Trial to Assess Chelation Therapy (TACT) remain the same as listed in the original award.

b. Studies and Results

No results have been obtained. This is a double-blind trial and results are not expected until the end.

c. Significance

As mentioned above, no results have been obtained thus far.

d. Plans

Milestones accomplished:

d.1. TACT Protocol, Study Materials, and IND Application Protocol

The TACT Protocol was approved by the Data Safety Monitoring Board (DSMB) May 29, 2003.

Informed Consent Form

The TACT Informed Consent Form (available in English and Spanish) was approved by the Data Safety Monitoring Board (DSMB) May 29, 2003.

TACT Study Binder

The TACT Study Binder was approved by NCCAM and NHLBI June 27, 2003.

Internet Case Report Form (ICRF)

The TACT Internet Case Report Form (ICRF) was approved by NCCAM and NHLBI June 27, 2003.

IND Application

The TACT Clinical Coordinating Center (CCC) received acknowledgement of receipt of the IND application on April 24, 2003. According to the letter from the FDA, the IND application was received on February 21, 2003.

The first set of pharmaceutical samples was sent to the laboratory the week of July 7, 2003. This first set of labs was sent for product/chemical validation. Subsequent shipments will be sent once randomization commences, and results will be provided to the FDA as quickly as possible.

d.2. TACT Contractors

Contracts with five organizations were completed. Each organization will complete a specific component of the trial.

Brigham and Women's Hospital

The CCC and Brigham Women's Hospital finalized a contract on June 3, 2003

Duke Clinical Research Institute

The contract between the CCC and the Duke Clinical Research Institute (DCRI) was executed in June 2003.

The Pharmed Group

The CCC and The Pharmed Group established an arrangement for the provision of vitamins at below cost for the term of the trial. No funds will be expended until the final contract is signed (date expected: August 2003).

OmniComm Systems, Inc.

The CCC and OmniComm Systems, Inc. finalized a contract on February 5, 2003.

Quest Diagnostics Incorporated

The CCC and Quest Diagnostics Inc. finalized a contract on June 25, 2003.

Quantum Healthcare Consultants, Inc.

The CCC and Quantum Healthcare Consultants, Inc. finalized a contract on February 14, 2003.

d.3. Staff Training

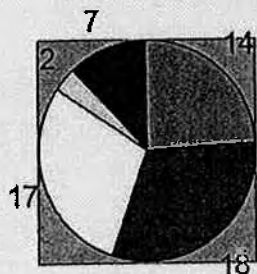
First Investigators Meeting – July 10-13, 2003

Fifty-seven TACT clinical sites attended the first Investigators Meeting July 10-13 in Sunny Isles Beach, FL. These sites comprise the first set of sites to be activated, with the goal of randomization beginning the first week of September 2003. Sites received training on the following topics:

<u>Topic</u>	<u>Presenter</u>
Overview of Complementary and Alternative Medicine, NCCAM Communications Plan	NCCAM
Study Protocol and Regulatory Requirements	CCC
TACT Study Materials, Electronic Data Capture, Start-up, Randomization Process, Clinical Events, Adverse and Serious Adverse Events, HIPAA and Good Clinical Practices, EQOL Sub-Study, and Data Collection	DCRI
TACT Statistical Plan	
TACT Laboratory	Quest Diagnostics Incorporated
TACT Pharmacy	Quantum Healthcare Consultants, Inc.
TrialMaster (electronic data capture software) Including hands on computer lab sessions	OmniComm Systems, Inc.
Discussions about Chelation Therapy	TACT Consultants
Discussions about Evidence-based Post-MI Care	CCC

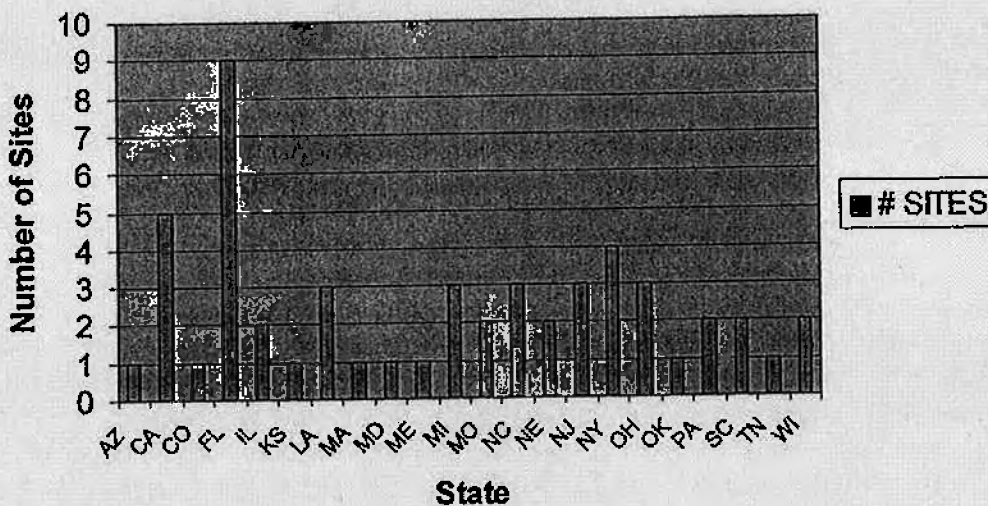
The figure below, titled "TACT Investigators Meeting – July 10-13, 2003: Types of Clinical Sites," illustrates the number of each of four types of sites that attended the first Investigators Meeting. The second figure, titled "TACT Investigators Meeting – July 10-13, 2003: Geographic Location of Clinical Sites," illustrates the geographic locations of sites that attended the first Investigators Meeting.

**TACT Investigators Meeting – July 10-13, 2003:
Types of Clinical Sites
(58 Total)**



- Academic
- Cardiology
- Chelation
- Research Institute
- Not Determined

**TACT Investigators Meeting – July 10-13, 2003:
Geographic Location of Clinical Sites
(68 Total)**



During the first Investigators Meeting, the following committees met:

- TACT Steering Committee
- TACT Executive Committee
- TACT Publications, Presentations, and Ancillary Studies Committee

Principal Investigator: Lamas, Gervasio A.

The Executive Committee is reviewing the organization and mandate of the Public Information Committee.

The second Investigators Meeting will be held in late September or October 2003. Approximately 50 clinical sites will attend this training.

d.4. Clinical Site IRB Approvals

As typical in this type of clinical trial, a two-tiered process has been initiated for helping sites get IRB approvals. The CCC has contracted with Sterling Institutional Review Board to serve as the central IRB for TACT. Local IRBs will be used in cases where they exist.

Central IRB – Sterling Institutional Review Board

Thirty-one TACT clinical sites that attended the first Investigators Meeting will use a central IRB called Sterling IRB. The TACT protocol, informed consent forms (English and Spanish versions), advertisements (print and radio), and required application forms were sent to Sterling for review in June 2003. Sterling requested revisions, which were made by the CCC, and returned to Sterling the first 2 weeks of July 2003. As of July 14, 2003, five sites have been approved by Sterling.

Local IRBs

Twenty-seven TACT clinical sites that attended the first Investigators Meeting will use a local IRB. The TACT protocol, informed consent forms (English and Spanish versions), advertisements (print and radio), and in some instances, the Investigators Brochure, were sent to all sites for submission to their local IRBs on June 3, 2003.

d.4. Proposed Recruitment Milestones

Overall projections for TACT patient recruitment for the next three years are as follows:

<u>TACT Grant Year</u>	<u>Number of Patients</u>
2	474
3	712
4	1186

The commitment to enrolling an ethnically and racially diverse patient population that represents the demographics of the United States has not changed.

Principal Investigator: Lamas, Gervasio A.

GRANT NUMBER
1 U01 AT01156-02

CHECKLIST

1. PROGRAM INCOME (See Instructions.)

All applications must indicate whether program income is anticipated during the period(s) for which grant support is requested. If program income is anticipated, use the format below to reflect the amount and source(s).

Budget Period	Anticipated Amount	Source(s)

2. ASSURANCES/CERTIFICATIONS (See Instructions.)

The following assurances/certifications are made and verified by the signature of the Official Signing for Applicant Organization on the Face Page of the application. Descriptions of individual assurances/ certifications are provided in Section III of the PHS 398. If unable to certify compliance, where applicable, provide an explanation and place it after this page.

•Human Subjects •Research Using Human Embryonic Stem Cells •Research on Transplantation of Human Fetal Tissue •Women and Minority Inclusion Policy •Inclusion of Children Policy •Vertebrate Animals

•Debarment and Suspension •Drug- Free Workplace (applicable to new [Type 1] or revised [Type 1] applications only); •Lobbying •Non-Delinquency on Federal Debt •Research Misconduct •Civil Rights (Form HHS 441 or HHS 690); •Handicapped Individuals (Form HHS 641 or HHS 690) •Sex Discrimination (Form HHS 639-A or HHS 690) •Age Discrimination (Form HHS 680 or HHS 690); •Recombinant DNA and Human Gene Transfer Research •Financial Conflict of Interest (except Phase I SBIR/STTR) •STTR ONLY: Certification of Research Institution Participation.

3. FACILITIES AND ADMINISTRATIVE (F&A) COSTS

Indicate the applicant organization's most recent F&A cost rate established with the appropriate DHHS Regional Office, or, in the case of for-profit organizations, the rate established with the appropriate PHS Agency Cost Advisory Office.

F&A costs will *not* be paid on construction grants, grants to Federal organizations, grants to individuals, and conference grants. Follow any additional instructions provided for Research Career Awards, Institutional National Research Service Awards, Small Business Innovation Research/Small Business Technology Transfer Grants, foreign grants, and specialized grant applications.

DHHS Agreement: 12/21/2000

No Facilities and Administrative Costs Requested.

No DHHS Agreement, but rate established with _____

Date _____

CALCULATION*

Entire proposed budget period: Amount of base \$ 494,636 x Rate applied 63 % = F&A costs \$ 311,621
Add to total direct costs from Form Page 2 and enter new total on Face Page, Item 8b.

***Check appropriate box(es):**

Salary and wages base

Modified total direct cost base

Other base (Explain)

Off-site, other special rate, or more than one rate involved (Explain)

Explanation (Attach separate sheet, if necessary.):