

***** NOTICE OF GRANT AWARD *****
RESEARCH PROJECT COOPERATIVE AGREEMENT Issue Date:03/08/2004
Department of Health and Human Services
National Institutes of Health

NATIONAL CENTER FOR COMPLEMENTARY & ALTERNATIVE MEDICINE

Grant Number: 5 U01 AT001156-02 (Revised)
Principal Investigator: LAMAS, GERVASIO A MD
Project Title: Trial to Assess Chelation Therapy (TACT)

DIRECTOR OF RESEARCH
MT SINAI MED CTR OF FLORIDA, INC
4300 ALTON ROAD
MIAMI BEACH, FL 33140
MIAMI BEACH, FL
UNITED STATES

Budget Period: 03/01/2003 - 02/29/2004
Project Period: 08/15/2002 - 02/28/2007

Dear Business Official:

The National Institutes of Health hereby revises this award (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to MOUNT SINAI MEDICAL CENTER (MIAMI BEACH) in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 31 USC 6305 & 6306 and is subject to terms and conditions referenced below.

Acceptance of this award including the Terms and Conditions is acknowledged by the grantee when funds are drawn down or otherwise obtained from the grant payment system.

Award recipients are responsible for reporting inventions derived or reduced to practice in the performance of work under this grant. Rights to inventions vest with the grantee organization provided certain requirements are met and there is acknowledgement of NIH support. In addition, recipients must ensure that patent and license activities are consistent with their responsibility to make unique research resources developed under this award available to the scientific community, in accordance with NIH policy. For additional information, please visit <http://www.iedison.gov>.

If you have any questions about this award, please contact the individual(s) referenced in the information below.

Sincerely yours,

George Tucker
Grants Management Officer
NATIONAL CENTER FOR COMPLEMENTARY & ALTERNATIVE MEDICINE

See additional information below

SECTION I - AWARD DATA - 5 U01 AT001156-02 (Revised)

AWARD CALCULATION (U.S. Dollars):

| | |
|---------------------------------------|--------------|
| Salaries and Wages | \$487,492 |
| Personnel Costs | \$487,492 |
| Consultant Services | \$18,000 |
| Equipment | \$9,992 |
| Supplies | \$18,337 |
| Travel Costs | \$200,448 |
| Other Costs | \$150,490 |
| Consortium/Contractual Cost | \$11,649,425 |
| Federal Direct Costs | \$12,534,184 |
| Federal F&A Costs | \$556,598 |
| APPROVED BUDGET | \$13,090,782 |
| Less Unobligated Balance | \$5,431,109 |
| TOTAL FEDERAL AWARD AMOUNT | \$7,659,673 |
| AMOUNT OF THIS ACTION (FEDERAL SHARE) | +\$0 |

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project, is as follows.

| | |
|----|-------------|
| 03 | \$8,284,710 |
| 04 | \$4,202,788 |
| 05 | \$3,482,267 |

FISCAL INFORMATION:

CFDA 93.213

Number:

EIN

Document Number: UIAT01156A

| | | | | |
|-------------|------------|------------|------------|-----------|
| IC/ CAN / | FY2003 / | FY2004 / | FY2005 / | FY2006 |
| AT/8424951/ | 4,659,673/ | 5,284,710/ | 1,202,788/ | 482,267 |
| HL/8424300/ | 3,000,000/ | 3,000,000/ | 3,000,000/ | 3,000,000 |

NIH ADMINISTRATIVE DATA:

PCC: 10 / OC: 41.4P /Processed: TUCKERG 040304 0401

SECTION II - PAYMENT/HOTLINE INFORMATION - 5 U01 AT001156-02 (Revised)

For Payment and HHS Office of Inspector General Hotline Information,
see the NIH Home Page at
<http://grants.nih.gov/grants/policy/awardconditions.htm>

SECTION III - TERMS AND CONDITIONS - 5 U01 AT001156-02 (Revised)

This award is based on the application submitted to, and as approved by, the NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

- a. The grant program legislation and program regulation cited in this Notice of Grant Award.
- b. The restrictions on the expenditure of federal funds in appropriations acts, to the extent those restrictions are pertinent to the award.
- c. 45 CFR Part 74 or 45 CFR Part 92 as applicable.
- d. The NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget period.
- e. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

□

(see NIH Home Page at
<http://grants.nih.gov/grants/policy/awardconditions.htm> for certain references cited above.)

Carry over of an unobligated balance into the next budget period requires Grants Management Officer prior approval.

This award provides support for one or more NIH defined Phase III clinical trials. The NIH Policy for research supported as an NIH Phase III Clinical Trial has been amended in Section II.B. of the NIH Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research - Amended October 2001
http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm.

A description of plans to conduct analyses, as appropriate, by sex/gender and racial/ethnic groups must be included in clinical trial protocols. Cumulative subject accrual and progress in conducting subset analyses must be reported to NIH in the annual Progress Reports. Final analyses of sex/gender and racial/ethnic differences must be reported in the required Final Progress Report or Competitive Renewal Applications (or Contract Renewals/Extensions) as stated in Section II.B. of the Guidelines.

Treatment of Program Income:
Additional Costs

SECTION IV - ADDITIOANL TERMS AND CONDITIONS

5 U01 AT-01156-02 (Revision #2)
DR. GERVASIO LAMAS

REVISION(S)

- 1) INTERIM PROGRESS REPORT: Due to the receipt of a satisfactory Interim Progress Report, previously awarded but restricted funds in the amount of \$5,106,449 (4,929,531 Direct; 202,450 F/A) are released and available for expenditure.
- 2) HUMAN SUBJECT RESEARCH INFORMATION: Based on the receipt of a valid certification of IRB approval, the restriction on the use of human subjects has been rescinded.

The following terms and conditions cited on previous NGA still apply and are listed below *** for reference.

CARRYOVER INFORMATION: This revised award authorizes a carryover of \$5,431,109 (\$5,176,675 direct costs and \$254,434 associated facilities and administrative costs) in unexpended funds from the 01 year to be used in the 02 year for: the purposes requested in Dr. Lamas's letters dated 5/28/03. The carryover is subject to the availability of the funds. If the actual balance as reported on the 01 year Financial Status Report is less than \$5,431,109 the carryover authorization is reduced accordingly.

These funds are restricted and may not be used for any other purpose without the written prior approval of the National Center for Complementary and Alternative Medicine (NCCAM). These funds are not available for carryover under expanded Authorities or the Federal Demonstration Partnership without the written prior approval of the NCCAM.

ADDITIONAL FUNDS INFORMATION: The progress report has been received and reviewed. The additional total costs of \$39,715 requested is not approved. The request does not have appropriate scientific justification. NCCAM staff have determined that there is sufficient

□

flexibility within the awarded grant budget to permit the research to proceed as originally proposed. The travel category has been reduced by this amount and the total cost has been awarded at the previous commitment level.

PROJECT PERIOD REQUIREMENT: This is the 2 year of a 5 year project period. Continuation of funding for the 02 year will require that the grantee satisfactorily address, by 7/15/2003, a plan to expedite clinical site IND approvals and complete staff training in a timely manner as identified in the Interim progress report. Should the progress report be deficient, the total project period may be reduced.

PARTICIPANT RECRUITMENT REQUIREMENT: Future NCCAM support for this study is contingent upon adequate participant recruitment based on: target patient accrual. The PI is responsible for providing projected milestones. These milestones will be established by NIH Staff prior to the initiation of data collection. In the event that actual recruitment fall significantly below projected recruitment numbers as defined in the agreed upon milestones, NCCAM may consider withholding future support and/or negotiating an orderly phase out of this study.

FUNDING DETERMINATION INFORMATION: Specific budget categories are based on target patient accrual of 2,372 & have been determined using the type 5 application categories. Total costs are limited and will not exceed the \$7,659,673 provided in this award.

FACILITIES AND ADMINISTRATIVE COST CALCULATION REQUIREMENT & INFORMATION: F/A costs could not be verified and have been arbitrary awarded using the original awarded amount. The grantee must submit a revised checklist paged demonstrating based and rate calculations. Base of 8,722 has been arbitrarily determined from the consortium category and used to reach the Total Cost of the commitment base. Resulting funds of \$5,495 (8,722 x 63%) are restricted pending a revised checklist & description of F/A cost calculations.

REVISED BUDGET SUBMISSION REQUIREMENT: An itemized categorical budget for years 3 through 5 is required to be submitted to Victoria Carper by 7/15/2003. The budget and all supporting documentation must be countersigned by an appropriate institutional business official.

HUMAN SUBJECTS RESEARCH RESTRICTION: This provisional award is issued subject to the following condition:

NOTICE: Under governing regulations, Federal funds administered by the department of Health and Human Services may not be expended for research involving human subjects and individuals may not be enrolled in research a any site, domestic or foreign, that does not have an Office for Human Research Protections (OHRP)-approved Assurance to comply with the requirements of 45 CFR Part 46 to protect human subjects and an Institutional Review Board (IRB) approval of the research that satisfies the requirements of 45 CFR Part 46.

The present award is being made without currently valid certification of IRB approval for this project with the following restriction: Only activities, which do not directly involve human subjects (i.e., are clearly severable and independent from those activities that do involve human subjects) may be conducted pending acceptance by the National Center of Complementary and Alternative Medicine (NCCAM) of certification of IRB approval. The certification of IRB approval must be submitted within 30 days of the issue date of this award.

If the certification of IRB approval has not been received and accepted by the NCCAM within the 30-day period, the award may be suspended and/or terminated. No funds may be drawn down from the payment system and no obligations may be made against federal funds for any research involving human subjects in this project until NCCAM has accepted the certification of IRB approval.

HUMAN SUBJECTS RESEARCH IRB REQUIREMENT: To avoid possible lapse in future support, the annual Institutional Review Board review and approval for this project should be scheduled several months prior to the beginning date of the award and be submitted with the continuation

□
application. No funds may be drawn down and no obligations may be made against federal funds for the period not covered by a valid IRB approval.

HUMAN SUBJECTS RESEARCH EDUCATION REQUIREMENT: Documentation of the Required Education in the Protection of Human Subject Research Participants for: Danielle Hollar & other new Key Personnel's Names. Information regarding this requirement can be found at the following

websites: <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html>. <http://grants.nih.gov/grants/news.htm>.

PATIENT CARE RESTRICTION: All funds associated with patient care activities are restricted and are not available for expenditure pending final protocol review and approval by DSMB.

Any unobligated funds resulting from these restrictions must be reported and identified on the Financial Status Report and may not be carried over for any purpose without the prior approval of the NCCAM Staff. Should the status of these restricted funds change, notification will occur via the issuance of a revised NGA.

NIH FUNDING ACKNOWLEDGEMENT REQUIREMENT: Grantees are required to place an acknowledgement of NIH grant support and a disclaimer, as appropriate, on any publication written or published with such support and, if feasible, on any publication reporting the results of, or describing, a grant-supported activity. An acknowledgment shall be to the effect that:

"This publication was made possible by Grant Number ___ from the National Center for Complementary and Alternative Medicine (NCCAM) or "the project described was supported by Grant Number ___ from the National Center for Complementary and Alternative Medicine" and "Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NCCAM, or the National Institutes of Health."

Grant recipients presenting NCCAM-sponsored research at scientific, professional, and consumer meetings are asked to acknowledge the publicly funded support they receive. A copy of the NCCAM Grantee Acknowledgement slide in PowerPoint is available at: nccam.nih.gov/research/information for grantees.

CO-FUNDING INFORMATION: This award includes total costs funds of \$3,000,000 provided by the National Heart Lung and Blood Institute (NHLBI).

CONSORTIUM/CONTRACTUAL COST INFORMATION: This award includes funds for consortium activities that will be provided with this award. Consortia are to be established and administered in accordance with the NIH Grants Policy Statement.

This award includes total costs funding of \$6,886,606 for the following consortium:

Omnicom \$57,000
Clinical Sites: \$2,794,216 RESTRICTED
DUKE University: 1,573,831
Brigham & Women's Hospital Clinical Events \$50,725
Quantum/Central Pharm. \$2,302,489
Quest/Central Lab. \$99,624

Remaining unidentified consortium funds of: \$8,721 are restricted.

FINANCIAL STATUS REPORT REQUIREMENTS: NIH recipients are reminded of the following requirements:

Financial Status Report (FSR) (Standard Form 269 or 269A, whichever is applicable) must be submitted to NIH within 90 calendar days after the last day of each budget period. For consortium partner arrangements, institutions must stipulate in agreements the deadlines for submitting

reports to the prime.

Recipients that submit reports at the 3-month mark will be considered out of compliance if that period exceeds 90 calendar days. Recipients are encouraged to report in advance of the deadline as a good business practice as well as to facilitate the timely submission of progress and invention reports. FSRs should be accurate at the time of submission, with revisions made rarely, only to provide updated information. Revisions should not be used as a mechanism to correct routinely incomplete or erroneous FSRs.

FSR's (OMB 269, which can be found at: <http://www.whitehouse.gov/omb/grants/#forms>) should be submitted electronically to the Office of Financial Management, NIH. Non-electronic reports may be mailed to:
Government Accounting Branch
Office of Financial Management
National Institutes of Health
31 Center Drive, Room B1B05A
MSC 2050
Bethesda, MD 20892-2050

Failure to submit these required reports, when due, may result in the imposition of special award provision or the withholding of support for other eligible projects or activities involving the grantee organization or the individual responsible for the delinquency.

CARRYOVER REQUIREMENT: The progress report states a sizeable estimated unobligated balance. This grant requires a formal written carryover request. The FSR from year 1 is due to NIH by 5/31/2003. The carryover request must be received by 6/30/2003. Carryover requests must be completed following the NCCAM Carryover Guidelines sent under separate cover by Victoria Carper on 3/31/2003 to Dr. Lamas, D. Hollar & V. Martini.

PROGRAM OFFICIAL CONTACT INFORMATION: The program official responsibilities for this award have changed. If you have any questions regarding the scientific, programmatic and technical aspects of this project, please contact:

Richard Nahin, Ph.D., MPH Email: nahinr@mail.nih.gov Phone: 301-496-7801

TERMS INFORMATION: Terms and conditions which were listed on the previous NGA and still applicable are incorporated by subtitle listed below ***. Refer to original NGA dated 08/08/2002 for a complete description of terms and conditions.

PUBLICATIONS REQUIREMENT

ANNUAL PROGRESS REPORTS REQUIREMENT

PERSONNEL COSTS INFORMATION

ESCALATION INFORMATION

ADDITIONAL RFA TERMS AND CONDITIONS: This award is being issued according to the guidelines and requirements in RFA AT-01-004, entitled EDTA CHELATION THERAPY FOR CORONARY ARTERY DISEASE.

Richard Nahin, Program Official
Phone: (301)-496-7801 Email: nahinr@od.nih.gov Fax: (301) 435-6549

Victoria Carper, Grants Specialist
 Phone: 301-594-9102 Email: vp8g@nih.gov Fax: 301-480-3621

SPREADSHEET

GRANT NUMBER: 5 U01 AT001156-02 (Revised)

P.I.: LAMAS, GERVASIO A
 INSTITUTION: MOUNT SINAI MEDICAL CENTER (MIAMI BEACH)

□

| | YEAR 02 | YEAR 03 | YEAR 04 | YEAR 05 |
|------------------------|------------|-----------|-----------|-----------|
| | ===== | ===== | ===== | ===== |
| Salaries and Wages | 487,492 | | | |
| Personnel Costs | 487,492 | | | |
| Consultant Services | 18,000 | | | |
| Equipment | 9,992 | | | |
| Supplies | 18,337 | | | |
| Travel Costs | 200,448 | | | |
| Other Costs | 150,490 | | | |
| Consortium/Contractual | 11,649,425 | | | |
| Cost | | | | |
| | | | | |
| TOTAL FEDERAL DC | 12,534,184 | 7,997,047 | 3,972,048 | 3,245,544 |
| | | | | |
| TOTAL FEDERAL F&A | 556,598 | 287,663 | 230,740 | 236,723 |
| TOTAL COST | 13,090,782 | 8,284,710 | 4,202,788 | 3,482,267 |

| | YEAR 02 | YEAR 03 | YEAR 04 | YEAR 05 |
|-----------------|---------|---------|---------|---------|
| | ===== | ===== | ===== | ===== |
| F&A Cost Rate 1 | 63.00% | 63.00% | 63.00% | 63.00% |
| F&A Cost Base 1 | 470,903 | 456,608 | 366,254 | 375,751 |
| | | | | |
| F&A Costs 1 | 296,669 | 287,663 | 230,740 | 236,723 |
| | | | | |
| F&A Cost Rate 2 | 63.00% | | | |
| F&A Cost Base 2 | 8,722 | | | |
| | | | | |
| F&A Costs 2 | 5,495 | | | |
| | | | | |
| F&A Cost Rate 3 | 63.00% | | | |
| F&A Cost Base 3 | 403,864 | | | |
| | | | | |
| F&A Costs 3 | 254,434 | | | |

.....END OF NGA.....

***** NOTICE OF GRANT AWARD *****
RESEARCH PROJECT COOPERATIVE AGREEMENT Issue Date:07/11/2003
Department of Health and Human Services
National Institutes of Health

NATIONAL CENTER FOR COMPLEMENTARY & ALTERNATIVE MEDICINE

Grant Number: 5 U01 AT001156-02 (Revised)
Principal Investigator: LAMAS, GERVASIO A MD
Project Title: Trial to Assess Chelation Therapy (TACT)

DIRECTOR OF RESEARCH
MT SINAI MED CTR OF FLORIDA, INC
4300 ALTON ROAD
MIAMI BEACH, FL 33140
UNITED STATES

Budget Period: 03/01/2003 - 02/29/2004
Project Period: 08/15/2002 - 02/28/2007

Dear Business Official:

The National Institutes of Health hereby revises this award (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to MOUNT SINAI MEDICAL CENTER (MIAMI BEACH) in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 31 USC 6305 & 6306 and is subject to terms and conditions referenced below.

Acceptance of this award including the Terms and Conditions is acknowledged by the grantee when funds are drawn down or otherwise obtained from the grant payment system.

Award recipients are responsible for reporting inventions derived or reduced to practice in the performance of work under this grant. Rights to inventions vest with the grantee organization provided certain requirements are met and there is acknowledgement of NIH support. In addition, recipients must ensure that patent and license activities are consistent with their responsibility to make unique research resources developed under this award available to the scientific community, in accordance with NIH policy. For additional information, please visit <http://www.iedison.gov>.

If you have any questions about this award, please contact the individual(s) referenced in the information below.

Sincerely yours,

Victoria Carper

Grants Management Officer
NATIONAL CENTER FOR COMPLEMENTARY & ALTERNATIVE MEDICINE

See additional information below

□□

SECTION I - AWARD DATA - 5 U01 AT001156-02 (Revised)

AWARD CALCULATION (U.S. Dollars):

| | |
|---------------------------------------|--------------|
| Salaries and Wages | \$487,492 |
| Personnel Costs | \$487,492 |
| Consultant Services | \$18,000 |
| Equipment | \$9,992 |
| Supplies | \$18,337 |
| Travel Costs | \$200,448 |
| Other Costs | \$150,490 |
| Consortium/Contractual Cost | \$11,649,425 |
| Federal Direct Costs | \$12,534,184 |
| Federal F&A Costs | \$556,598 |
| APPROVED BUDGET | \$13,090,782 |
| Less Unobligated Balance | \$5,431,109 |
| TOTAL FEDERAL AWARD AMOUNT | \$7,659,673 |
| AMOUNT OF THIS ACTION (FEDERAL SHARE) | +\$0 |

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project, is as follows.

| | |
|----|-------------|
| 03 | \$8,284,710 |
| 04 | \$4,202,788 |
| 05 | \$3,482,267 |

FISCAL INFORMATION:

CFDA 93.213

Number:

EIN

Document Number: U1AT01156A

| IC/ | CAN / | FY2003 | / | FY2004 | / | FY2005 | / | FY2006 |
|-------------|-------|------------|---|------------|---|------------|---|-----------|
| AT/8424951/ | | 4,659,673/ | | 5,284,710/ | | 1,202,788/ | | 482,267 |
| HL/8424300/ | | 3,000,000/ | | 3,000,000/ | | 3,000,000/ | | 3,000,000 |

NIH ADMINISTRATIVE DATA:

PCC: 10 / OC: 41.4P /Processed: PUTPRUSHV 030711 0119

SECTION II - PAYMENT/HOTLINE INFORMATION - 5 U01 AT001156-02 (Revised)

For Payment and HHS Office of Inspector General Hotline Information,

see the NIH Home Page at
<http://grants.nih.gov/grants/policy/awardconditions.htm>

SECTION III - TERMS AND CONDITIONS - 5 U01 AT001156-02 (Revised)

This award is based on the application submitted to, and as approved by, the NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

-
- a. The grant program legislation and program regulation cited in this Notice of Grant Award.
- b. The restrictions on the expenditure of federal funds in appropriations acts, to the extent those restrictions are pertinent to the award.
- c. 45 CFR Part 74 or 45 CFR Part 92 as applicable.
- d. The NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget period.
- e. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.
-

(see NIH Home Page at
<http://grants.nih.gov/grants/policy/awardconditions.htm> for certain references cited above.)

Carry over of an unobligated balance into the next budget period requires Grants Management Officer prior approval.

This award provides support for one or more NIH defined Phase III clinical trials. The NIH Policy for research supported as an NIH Phase III Clinical Trial has been amended in Section II.B. of the NIH Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research - Amended October 2001
http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm.

A description of plans to conduct analyses, as appropriate, by sex/gender and racial/ethnic groups must be included in clinical trial protocols. Cumulative subject accrual and progress in conducting subset analyses must be reported to NIH in the annual Progress Reports. Final analyses of sex/gender and racial/ethnic differences must be reported in the required Final Progress Report or Competitive Renewal Applications (or Contract Renewals/Extensions) as stated in Section II.B. of the Guidelines.

Treatment of Program Income:
Additional Costs

SECTION IV - ADDITIOANL TERMS AND CONDITIONS
5 U01 AT-01156-02 Revision # 1
DR. GERVASIO LAMAS

CARRYOVER INFORMATION: This revised award authorizes a carryover of \$5,431,109 (\$5,176,675 direct costs and \$254,434 associated facilities and administrative costs) in unexpended funds from the 01 year to be used in the 02 year for: the purposes requested in Dr. Lamas's letters dated 5/28/03. The carryover is subject to the availability of the funds. If the actual balance as reported on the 01 year Financial Status Report is less than \$5,431,109 the carryover authorization is

reduced accordingly.

These funds are restricted and many not be used for any other purpose without the written prior approval of the National Center for Complementary and Alternative Medicine (NCCAM). These funds are not available for carryover under expanded Authorities or the Federal Demonstration Partnership without the written prior approval of the NCCAM.

TERMS OF AWARD INFORMATION: All previous terms and conditions still applicable are incorporated by subtitle listed below ***. Refer to NGA dated: 4/02/2003 for a complete description of terms and conditions.

ADDITIONAL FUNDS INFORMATION: The progress report has been received and reviewed. The additional total costs of \$39,715 requested is not approved. The request does not have appropriate scientific justification. NCCAM staff have determined that there is sufficient flexibility within the awarded grant budget to permit the research to proceed as originally proposed. The travel category has been reduced by this amount and the total cost has been awarded at the previous commitment level.

□ FUNDING RESTRICTION: Although total costs of: \$7,659,673 have been provided, funds representing (33 %) of the total funds awarded \$2,553,224 (\$2,427,978 Direct; 99,714 F/A) are authorized at this time to provide support for 4 months. Remaining funds of \$5,106,448 are restricted and may not be expended or rebudgeted without the prior written approval from the NCCAM awarding unit.

INTERIM PROGRESS REPORT RESTRICTION: Due to scientific/administrative

□

concerns regarding the conduct of this project, funds representing (67 %) of the total funds awarded \$5,106,449 (4,929,531 Direct; 202,450 F/A) are restricted and may not be rebudgeted without the prior written approval from the NCCAM awarding unit. These funds are unavailable for expenditure pending review and approval of:

-An Interim progress report covering the period of: 01/01/2003 through 6/31/2003.

-The report should include proposed recruitment milestones, scheduling of staff training and description of efforts to obtain clinical site IND approvals.

The Interim report is due by: 07/15/2003, must be countersigned by an institutional business official and may be electronically submitted via email to vp8g@nih.gov or faxed to (301) 480-1552 attention: Victoria Carper

Any unobligated funds resulting from this restriction must be reported and identified on the Financial Status Report and may not be carried over for any purpose without the prior approval of the NCCAM Staff. Should the status of these restricted funds change, notification will occur via the issuance of a revised Notice of Grant Award (NGA).

PROJECT PERIOD REQUIREMENT: This is the 2 year of a 5 year project period. Continuation of funding for the 02 year will require that the grantee satisfactorily address, by 7/15/2003, a plan to expedite clinical site IND approvals and complete staff training in a timely manner as identified in the Interim progress report. Should the progress report be deficient, the total project period may be reduced.

PARTICIPANT RECRUITMENT REQUIREMENT: Future NCCAM support for this study is contingent upon adequate participant recruitment based on: target patient accrual. The PI is responsible for providing projected milestones. These milestones will be established by NIH Staff prior to the initiation of data collection. In the event that actual recruitment fall significantly below projected recruitment numbers as defined in the agreed upon milestones, NCCAM may consider withholding future support and/or negotiating an orderly phase out of this study.

FUNDING DETERMINATION INFORMATION: Specific budget categories are based on target patient accrual of 2,372 & have been determined using the type 5 application categories. Total costs are limited and will not exceed the \$7,659,673 provided in this award.

FACILITIES AND ADMINISTRATIVE COST CALCULATION REQUIREMENT & INFORMATION: F/A costs could not be verified and have been arbitrary awarded using the original awarded amount. The grantee must submit a revised checklist paged demonstrating based and rate calculations. Base of 8,722 has been arbitrarily determined from the consortium category and used to reach the Total Cost of the commitment base. Resulting funds of \$5,495 (8,722 x 63%) are restricted pending a revised checklist & description of F/A cost calculations.

REVISED BUDGET SUBMISSION REQUIREMENT: An itemized categorical budget for years 3 through 5 is required to be submitted to Victoria Carper by 7/15/2003. The budget and all supporting documentation must be countersigned by an appropriate institutional business official.

HUMAN SUBJECTS RESEARCH RESTRICTION: This provisional award is issued subject to the following condition:

NOTICE: Under governing regulations, Federal funds administered by the department of Health and Human Services may not be expended for research involving human subjects and individuals may not be enrolled in research a any site, domestic or foreign, that does not have an Office for Human Research Protections (OHRP)-approved Assurance to comply with the requirements of 45 CFR Part 46 to protect human subjects and an Institutional Review Board (IRB) approval of the research that satisfies the requirements of 45 CFR Part 46.

The present award is being made without currently valid certification of IRB approval for this project with the following restriction: Only activities, which do not directly involve human subjects (i.e., are

clearly severable and independent from those activities that do involve human subjects) may be conducted pending acceptance by the National Center of Complementary and Alternative Medicine (NCCAM) of certification of IRB approval. The certification of IRB approval must be submitted within 30 days of the issue date of this award.

If the certification of IRB approval has not been received and accepted by the NCCAM within the 30-day period, the award may be suspended and/or terminated. No funds may be drawn down from the payment system and no obligations may be made against federal funds for any research involving human subjects in this project until NCCAM has accepted the certification of IRB approval.

HUMAN SUBJECTS RESEARCH IRB REQUIREMENT: To avoid possible lapse in future support, the annual Institutional Review Board review and approval for this project should be scheduled several months prior to

the beginning date of the award and be submitted with the continuation application. No funds may be drawn down and no obligations may be made against federal funds for the period not covered by a valid IRB approval.

HUMAN SUBJECTS RESEARCH EDUCATION REQUIREMENT: Documentation of the Required Education in the Protection of Human Subject Research Participants for: Danielle Hollar & other new Key Personnel's Names. Information regarding this requirement can be found at the following websites: <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html>. <http://grants.nih.gov/grants/news.htm>.

PATIENT CARE RESTRICTION: All funds associated with patient care activities are restricted and are not available for expenditure pending final protocol review and approval by DSMB.

Any unobligated funds resulting from these restrictions must be reported and identified on the Financial Status Report and may not be carried over for any purpose without the prior approval of the NCCAM Staff. Should the status of these restricted funds change, notification will occur via the issuance of a revised NGA.

DELAYED START DATE AWARDS INFORMATION: This award has been issued after the budget period start date of 3/1/2003 due to the NCCAM's late receipt of required late documentation; however, the expiration date of the budget period remains unchanged 02/28/2003. Allowable preaward costs may be charged to this award, in accordance with the conditions outlined in the NIH Grants Policy Statement (March 2001) and with institutional requirements for prior approval.

CURRENT AND FUTURE YEAR LEVELS INFORMATION: The attached summary of budget calculations for the future years is shown in total costs. In accordance with the October 27, 1995 NIH Guide announcement and NIH implementation, future year recommended levels are shown as total costs (the sum of direct plus facilities and administrative costs). Adjustments to facilities and administrative costs (increases or decreases in rate or base changes) will not routinely be made for future year awards.

NIH FUNDING ACKNOWLEDGEMENT REQUIREMENT: Grantees are required to place an acknowledgement of NIH grant support and a disclaimer, as appropriate, on any publication written or published with such support and, if feasible, on any publication reporting the results of, or describing, a grant-supported activity. An acknowledgment shall be to the effect that:

"This publication was made possible by Grant Number ___ from the National Center for Complementary and Alternative Medicine (NCCAM) or "the project described was supported by Grant Number ___ from the National Center for Complementary and Alternative Medicine" and "Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NCCAM, or the National Institutes of Health."

Grant recipients presenting NCCAM-sponsored research at scientific, professional, and consumer meetings are asked to acknowledge the

publicly funded support they receive. A copy of the NCCAM Grantee Acknowledgement slide in PowerPoint is available at: nccam.nih.gov/research/information for grantees.

CO-FUNDING INFORMATION: This award includes total costs funds of \$3,000,000 provided by the National Heart Lung and Blood Institute (NHLBI).

CONSORTIUM/CONTRACTUAL COST INFORMATION: This award includes funds for consortium activities that will be provided with this award. Consortia are to be established and administered in accordance with the NIH Grants Policy Statement.

This award includes total costs funding of \$6,886,606 for the following consortium:

Omnicom \$57,000
Clinical Sites: \$2,794,216 RESTRICTED
DUKE University: 1,573,831
Brigham & Women's Hospital Clinical Events \$50,725
Quantum/Central Pharm. \$2,302,489
Quest/Central Lab. \$99,624

Remaining unidentified consortium funds of: \$8,721 are restricted.

FINANCIAL STATUS REPORT REQUIREMENTS: NIH recipients are reminded of the following requirements:

Financial Status Report (FSR) (Standard Form 269 or 269A, whichever is applicable) must be submitted to NIH within 90 calendar days after the last day of each budget period. For consortium partner arrangements, institutions must stipulate in agreements the deadlines for submitting reports to the prime.

Recipients that submit reports at the 3-month mark will be considered out of compliance if that period exceeds 90 calendar days. Recipients are encouraged to report in advance of the deadline as a good business practice as well as to facilitate the timely submission of progress and invention reports. FSRs should be accurate at the time of submission, with revisions made rarely, only to provide updated information. Revisions should not be used as a mechanism to correct routinely incomplete or erroneous FSRs.

FSR's (OMB 269, which can be found at: <http://www.whitehouse.gov/omb/grants/#forms>) should be submitted electronically to the Office of Financial Management, NIH. Non-electronic reports may be mailed to:
Government Accounting Branch
Office of Financial Management
National Institutes of Health
31 Center Drive, Room B1B05A
MSC 2050
Bethesda, MD 20892-2050

Failure to submit these required reports, when due, may result in the imposition of special award provision or the withholding of support for other eligible projects or activities involving the grantee organization or the individual responsible for the delinquency.

CARRYOVER REQUIREMENT: The progress report states a sizeable estimated unobligated balance. This grant requires a formal written carryover request. The FSR from year 1 is due to NIH by 5/31/2003. The carryover request must be received by 6/30/2003. Carryover requests must be completed following the NCCAM Carryover Guidelines sent under separate cover by Victoria Carper on 3/31/2003 to Dr. Lamas, D. Hollar & V.

Martini.

PROGRAM OFFICIAL CONTACT INFORMATION: The program official responsibilities for this award have changed. If you have any questions regarding the scientific, programmatic and technical aspects of this project, please contact:

□

Richard Nahin, Ph.D., MPH Email: nahinr@mail.nih.gov Phone: 301-496-7801

TERMS INFORMATION: Terms and conditions which were listed on the previous NGA and still applicable are incorporated by subtitle listed below ***. Refer to original NGA dated 08/08/2002 for a complete description of terms and conditions.

PUBLICATIONS REQUIREMENT

ANNUAL PROGRESS REPORTS REQUIREMENT

PERSONNEL COSTS INFORMATION

ESCALATION INFORMATION

ADDITIONAL RFA TERMS AND CONDITIONS: This award is being issued according to the guidelines and requirements in RFA AT-01-004, entitled EDTA CHELATION THERAPY FOR CORONARY ARTERY DISEASE.

Richard Nahin, Program Official
Phone: (301)-496-7801 Email: nahinr@od.nih.gov Fax: (301) 435-6549

Victoria Carper, Grants Specialist
Phone: 301-594-9102 Email: vp8g@nih.gov Fax: 301-480-3621

SPREADSHEET

GRANT NUMBER: 5 U01 AT001156-02 (Revised)

P.I.: LAMAS, GERVASIO A
INSTITUTION: MOUNT SINAI MEDICAL CENTER (MIAMI BEACH)

| | YEAR 02 | YEAR 03 | YEAR 04 | YEAR 05 |
|------------------------|------------|-----------|-----------|-----------|
| | ===== | ===== | ===== | ===== |
| Salaries and Wages | 487,492 | | | |
| Personnel Costs | 487,492 | | | |
| Consultant Services | 18,000 | | | |
| Equipment | 9,992 | | | |
| Supplies | 18,337 | | | |
| Travel Costs | 200,448 | | | |
| Other Costs | 150,490 | | | |
| Consortium/Contractual | 1,649,425 | | | |
| Cost | | | | |
| | | | | |
| TOTAL FEDERAL DC | 12,534,184 | 7,997,047 | 3,972,048 | 3,245,544 |
| | | | | |
| TOTAL FEDERAL F& | 556,598 | 287,663 | 230,740 | 236,723 |
| TOTAL COST | 13,090,782 | 8,284,710 | 4,202,788 | 3,482,267 |

YEAR 02 YEAR 03 YEAR 04 YEAR 05

| | | | | |
|-----------------|---------|---------|---------|---------|
| F&A Cost Rate 1 | ===== | ===== | ===== | ===== |
| F&A Cost Base 1 | 63.00% | 63.00% | 63.00% | 63.00% |
| | 470,903 | 456,608 | 366,254 | 375,751 |
| F&A Costs 1 | | | | |
| | 296,669 | 287,663 | 230,740 | 236,723 |
| F&A Cost Rate 2 | | | | |
| F&A Cost Base 2 | 63.00% | | | |
| | 8,722 | | | |
| F&A Costs 2 | | | | |
| | 5,495 | | | |
| F&A Cost Rate 3 | | | | |
| F&A Cost Base 3 | 63.00% | | | |
| | 403,864 | | | |
| F&A Costs 3 | | | | |
| | 254,434 | | | |

.....END OF NGA.....

***** NOTICE OF GRANT AWARD *****
 RESEARCH PROJECT COOPERATIVE AGREEMENT Issue Date:04/02/2003
 Department of Health and Human Services
 National Institutes of Health

NATIONAL CENTER FOR COMPLEMENTARY & ALTERNATIVE MEDICINE

Grant Number: 5 U01 AT001156-02
 Principal Investigator: LAMAS, GERVASIO A MD
 Project Title: Trial to Assess Chelation Therapy (TACT)

DIRECTOR OF RESEARCH
 MT SINAI MED CTR OF FLORIDA, INC
 4300 ALTON ROAD
 MIAMI BEACH, FL 33140
 UNITED STATES

Budget Period: 03/01/2003 - 02/29/2004
 Project Period: 08/15/2002 - 02/28/2007

Dear Business Official:

The National Institutes of Health hereby awards a grant in the amount of \$7,659,673 (see "Award Calculation" in Section I) to MOUNT SINAI MEDICAL CENTER (MIAMI BEACH) in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 31 USC 6305 & 6306 and is subject to terms and conditions referenced below.

Acceptance of this award including the Terms and Conditions is

acknowledged by the grantee when funds are drawn down or otherwise obtained from the grant payment system.

Award recipients are responsible for reporting inventions derived or reduced to practice in the performance of work under this grant. Rights to inventions vest with the grantee organization provided certain requirements are met and there is acknowledgement of NIH support. In addition, recipients must ensure that patent and license activities are consistent with their responsibility to make unique research resources developed under this award available to the scientific community, in accordance with NIH policy. For additional information, please visit <http://www.iedison.gov>.

If you have any questions about this award, please contact the individual(s) referenced in the information below.

Sincerely yours,

Victoria Carper
Grants Management Officer
NATIONAL CENTER FOR COMPLEMENTARY & ALTERNATIVE MEDICINE

See additional information below

□□

SECTION I - AWARD DATA - 5 U01 AT001156-02

AWARD CALCULATION (U.S. Dollars):

| | |
|-----------------------------|-------------|
| Salaries and Wages | \$316,214 |
| Personnel Costs | \$316,214 |
| Consultant Services | \$12,000 |
| Supplies | \$10,000 |
| Travel Costs | \$86,569 |
| Other Costs | \$46,120 |
| Consortium/Contractual Cost | \$6,886,606 |
| Federal Direct Costs | \$7,357,509 |
| Federal F&A Costs | \$302,164 |
| APPROVED BUDGET | \$7,659,673 |
| TOTAL FEDERAL AWARD AMOUNT | \$7,659,673 |

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project, is as follows.

| | |
|----|-------------|
| 03 | \$8,284,710 |
| 04 | \$4,202,788 |
| 05 | \$3,482,267 |

FISCAL INFORMATION:

CFDA 93.213

Number:

Document Number: U1AT01156A

| IC/ | CAN | / | FY2003 | / | FY2004 | / | FY2005 | / | FY2006 |
|-------------|------------|---|------------|---|------------|---|-----------|---|--------|
| AT/8424951/ | 4,659,673/ | | 5,284,710/ | | 1,202,788/ | | 482,267 | | |
| HL/8424300/ | 3,000,000/ | | 3,000,000/ | | 3,000,000/ | | 3,000,000 | | |

NIH ADMINISTRATIVE DATA:

PCC: 2 / OC: 41.4P /Processed: PUTPRUSHV 030331 0502

SECTION II - PAYMENT/HOTLINE INFORMATION - 5 U01 AT001156-02

For Payment and HHS Office of Inspector General Hotline Information, see the NIH Home Page at <http://grants.nih.gov/grants/policy/awardconditions.htm>

SECTION III - TERMS AND CONDITIONS - 5 U01 AT001156-02

This award is based on the application submitted to, and as approved by, the NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

- a. The grant program legislation and program regulation cited in this Notice of Grant Award.
- b. The restrictions on the expenditure of federal funds in appropriations acts, to the extent those restrictions are pertinent to the award.
- c. 45 CFR Part 74 or 45 CFR Part 92 as applicable.
- d. The NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget period.
- e. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

(see NIH Home Page at <http://grants.nih.gov/grants/policy/awardconditions.htm> for certain references cited above.)

□

Carry over of an unobligated balance into the next budget period requires Grants Management Officer prior approval.

This award provides support for one or more NIH defined Phase III clinical trials. The NIH Policy for research supported as an NIH Phase III Clinical Trial has been amended in Section II.B. of the NIH Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research - Amended October 2001 http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm.

A description of plans to conduct analyses, as appropriate, by sex/gender and racial/ethnic groups must be included in clinical trial protocols. Cumulative subject accrual and progress in conducting subset analyses must be reported to NIH in the annual Progress Reports. Final

analyses of sex/gender and racial/ethnic differences must be reported in the required Final Progress Report or Competitive Renewal Applications (or Contract Renewals/Extensions) as stated in Section II.B. of the Guidelines.

Treatment of Program Income:
Additional Costs

SECTION IV - ADDITIONAL TERMS AND CONDITIONS
5 U01 AT-01156-02
DR. GERVASIO LAMAS

ADDITIONAL FUNDS INFORMATION: The progress report has been received and reviewed. The additional total costs of \$39,715 requested is not approved. The request does not have appropriate scientific justification. NCCAM staff have determined that there is sufficient flexibility within the awarded grant budget to permit the research to proceed as originally proposed. The travel category has been reduced by this amount and the total cost has been awarded at the previous commitment level.

FUNDING RESTRICTION: Although total costs of: \$7,659,673 have been provided, funds representing (33 %) of the total funds awarded \$2,553,224 (\$2,427,978 Direct; 99,714 F/A) are authorized at this time to provide support for 4 months. Remaining funds of \$5,106,448 are restricted and may not be expended or rebudgeted without the prior written approval from the NCCAM awarding unit.

INTERIM PROGRESS REPORT RESTRICTION: Due to scientific/administrative concerns regarding the conduct of this project, funds representing (67 %) of the total funds awarded \$5,106,449 (4,929,531 Direct; 202,450 F/A) are restricted and may not be rebudgeted without the prior written approval from the NCCAM awarding unit. These funds are unavailable for expenditure pending review and approval of:

-An Interim progress report covering the period of: 01/01/2003 through 6/31/2003.

-The report should include proposed recruitment milestones, scheduling of staff training and description of efforts to obtain clinical site IND approvals.

The Interim report is due by: 07/15/2003, must be countersigned by an institutional business official and may be electronically submitted via email to vp8g@nih.gov or faxed to (301) 480-1552 attention: Victoria Catper

Any unobligated funds resulting from this restriction must be reported and identified on the Financial Status Report and may not be carried over for any purpose without the prior approval of the NCCAM Staff. Should the status of these restricted funds change, notification will occur via the issuance of a revised Notice of Grant Award (NGA).

PROJECT PERIOD REQUIREMENT: This is the 2 year of a 5 year project period. Continuation of funding for the 02 year will require that the

grantee satisfactorily address, by 7/15/2003, a plan to expedite clinical site IND approvals and complete staff training in a timely manner as identified in the Interim progress report. Should the progress report be deficient, the total project period may be reduced.

PARTICIPANT RECRUITMENT REQUIREMENT: Future NCCAM support for this

study is contingent upon adequate participant recruitment based on: target patient accrual. The PI is responsible for providing projected milestones. These milestones will be established by NIH Staff prior to the initiation of data collection. In the event that actual recruitment fall significantly below projected recruitment numbers as defined in the agreed upon milestones, NCCAM may consider withholding future support and/or negotiating an orderly phase out of this study.

FUNDING DETERMINATION INFORMATION: Specific budget categories are based on target patient accrual of 2,372 & have been determined using the type 5 application categories. Total costs are limited and will not exceed the \$7,659,673 provided in this award.

FACILITIES AND ADMINISTRATIVE COST CALCULATION REQUIREMENT & INFORMATION: F/A costs could not be verified and have been arbitrary awarded using the original awarded amount. The grantee must submit a revised checklist paged demonstrating based and rate calculations. Base of 8,722 has been arbitrarily determined from the consortium category and used to reach the Total Cost of the commitment base. Resulting funds of \$5,495 (8,722 x 63%) are restricted pending a revised checklist & description of F/A cost calculations.

REVISED BUDGET SUBMISSION REQUIREMENT: An itemized categorical budget for years 3 through 5 is required to be submitted to Victoria Carper by 7/15/2003. The budget and all supporting documentation must be countersigned by an appropriate institutional business official.

HUMAN SUBJECTS RESEARCH RESTRICTION: This provisional award is issued subject to the following condition:

NOTICE: Under governing regulations, Federal funds administered by the department of Health and Human Services may not be expended for research involving human subjects and individuals may not be enrolled in research a any site, domestic or foreign, that does not have an Office for Human Research Protections (OHRP)-approved Assurance to comply with the requirements of 45 CFR Part 46 to protect human subjects and an Institutional Review Board (IRB) approval of the research that satisfies the requirements of 45 CFR Part 46.

The present award is being made without currently valid certification of IRB approval for this project with the following restriction: Only activities, which do not directly involve human subjects (i.e., are clearly severable and independent from those activities that do involve human subjects) may be conducted pending acceptance by the National Center of Complementary and Alternative Medicine (NCCAM) of certification of IRB approval. The certification of IRB approval must be submitted within 30 days of the issue date of this award.

If the certification of IRB approval has not been received and accepted by the NCCAM within the 30-day period, the award may be suspended and/or terminated. No funds may be drawn down from the payment system and no obligations may be made against federal funds for any research involving human subjects in this project until NCCAM has accepted the certification of IRB approval.

HUMAN SUBJECTS RESEARCH IRB REQUIREMENT: To avoid possible lapse in future support, the annual Institutional Review Board review and approval for this project should be scheduled several months prior to the beginning date of the award and be submitted with the continuation application. No funds may be drawn down and no obligations may be made against federal funds for the period not covered by a valid IRB approval.

HUMAN SUBJECTS RESEARCH EDUCATION REQUIREMENT: Documentation of the Required Education in the Protection of Human Subject Research Participants for: Danielle Hollar & other new Key Personnel's Names.

Information regarding this requirement can be found at the following websites: <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html>. <http://grants.nih.gov/grants/news.htm>.

PATIENT CARE RESTRICTION: All funds associated with patient care activities are restricted and are not available for expenditure pending final protocol review and approval by DSMB.

Any unobligated funds resulting from these restrictions must be reported and identified on the Financial Status Report and may not be carried over for any purpose without the prior approval of the NCCAM Staff. Should the status of these restricted funds change, notification will occur via the issuance of a revised NGA.

DELAYED START DATE AWARDS INFORMATION: This award has been issued after the budget period start date of 3/1/2003 due to the NCCAM's late receipt of required late documentation; however, the expiration date of the budget period remains unchanged 02/28/2003. Allowable preaward costs may be charged to this award, in accordance with the conditions outlined in the NIH Grants Policy Statement (March 2001) and with institutional requirements for prior approval.

CURRENT AND FUTURE YEAR LEVELS INFORMATION: The attached summary of budget calculations for the future years is shown in total costs. In accordance with the October 27, 1995 NIH Guide announcement and NIH implementation, future year recommended levels are shown as total costs (the sum of direct plus facilities and administrative costs). Adjustments to facilities and administrative costs (increases or decreases in rate or base changes) will not routinely be made for future year awards.

NIH FUNDING ACKNOWLEDGEMENT REQUIREMENT: Grantees are required to place an acknowledgement of NIH grant support and a disclaimer, as appropriate, on any publication written or published with such support and, if feasible, on any publication reporting the results of, or describing, a grant-supported activity. An acknowledgment shall be to the effect that:

"This publication was made possible by Grant Number ___ from the National Center for Complementary and Alternative Medicine (NCCAM) or "the project described was supported by Grant Number ___ from the National Center for Complementary and Alternative Medicine" and "Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NCCAM, or the National Institutes of Health."

Grant recipients presenting NCCAM-sponsored research at scientific, professional, and consumer meetings are asked to acknowledge the publicly funded support they receive. A copy of the NCCAM Grantee Acknowledgement slide in PowerPoint is available at: nccam.nih.gov/research/information for grantees.

CO-FUNDING INFORMATION: This award includes total costs funds of \$3,000,000 provided by the National Heart Lung and Blood Institute (NHLBI).

CONSORTIUM/CONTRACTUAL COST INFORMATION: This award includes funds for consortium activities that will be provided with this award. Consortia are to be established and administered in accordance with the NIH Grants Policy Statement.

This award includes total costs funding of \$6,886,606 for the following consortium:

Omnicom \$57,000
Clinical Sites: \$2,794,216 RESTRICTED
DUKE University: 1,573,831
Brigham & Women's Hospital Clinical Events \$50,725
Quantum/Central Pharm. \$2,302,489
Quest/Central Lab. \$99,624

Remaining unidentified consortium funds of: \$8,721 are restricted.

FINANCIAL STATUS REPORT REQUIREMENTS: NIH recipients are reminded of the following requirements:

Financial Status Report (FSR) (Standard Form 269 or 269A, whichever is applicable) must be submitted to NIH within 90 calendar days after the last day of each budget period. For consortium partner arrangements, institutions must stipulate in agreements the deadlines for submitting reports to the prime.

Recipients that submit reports at the 3-month mark will be considered out of compliance if that period exceeds 90 calendar days. Recipients are encouraged to report in advance of the deadline as a good business practice as well as to facilitate the timely submission of progress and invention reports. FSRs should be accurate at the time of submission, with revisions made rarely, only to provide updated information. Revisions should not be used as a mechanism to correct routinely incomplete or erroneous FSRs.

FSR's (OMB 269, which can be found at: <http://www.whitehouse.gov/omb/grants/#forms>) should be submitted electronically to the Office of Financial Management, NIH. Non-electronic reports may be mailed to:
Government Accounting Branch
Office of Financial Management
National Institutes of Health
31 Center Drive, Room B1B05A
MSC 2050
Bethesda, MD 20892-2050

Failure to submit these required reports, when due, may result in the imposition of special award provision or the withholding of support for other eligible projects or activities involving the grantee organization or the individual responsible for the delinquency.

CARRYOVER REQUIREMENT: The progress report states a sizeable estimated unobligated balance. This grant requires a formal written carryover request. The FSR from year 1 is due to NIH by 5/31/2003. The carryover request must be received by 6/30/2003. Carryover requests must be completed following the NCCAM Carryover Guidelines sent under separate cover by Victoria Carper on 3/31/2003 to Dr. Lamas, D. Hollax & V. Martini.

PROGRAM OFFICIAL CONTACT INFORMATION: The program official responsibilities for this award have changed. If you have any questions regarding the scientific, programmatic and technical aspects of this project, please contact:

Richard Nahin, Ph.D., MPH Email: nahinr@mail.nih.gov Phone: 301-496-7801

TERMS INFORMATION: Terms and conditions which were listed on the previous NGA and still applicable are incorporated by subtitle listed below ***. Refer to original NGA dated 08/08/2002 for a complete description of terms and conditions.

PUBLICATIONS REQUIREMENT

ANNUAL PROGRESS REPORTS REQUIREMENT

PERSONNEL COSTS INFORMATION

ESCALATION INFORMATION

ADDITIONAL RFA TERMS AND CONDITIONS: This award is being issued according to the guidelines and requirements in RFA AT-01-004, entitled EDTA CHELATION THERAPY FOR CORONARY ARTERY DISEASE.

Christine M Goertz, Program Official

Phone: (301) 402-1030 Email: goertz@mail.nih.gov Fax: (301) 480-3621

Victoria Carper, Grants Specialist

Phone: 301-594-9102 Email: vp8g@nih.gov Fax: 301-480-3621

□

SPREADSHEET

GRANT NUMBER: 5 U01 AT001156-02

P.I.: LAMAS, GERVASIO A

INSTITUTION: MOUNT SINAI MEDICAL CENTER (MIAMI BEACH)

| | YEAR 02 | YEAR 03 | YEAR 04 | YEAR 05 |
|-----------------------------|-----------|-----------|-----------|-----------|
| | ===== | ===== | ===== | ===== |
| Salaries and Wages | 316,214 | | | |
| Personnel Costs | 316,214 | | | |
| Consultant Services | 12,000 | | | |
| Supplies | 10,000 | | | |
| Travel Costs | 86,569 | | | |
| Other Costs | 46,120 | | | |
| Consortium/Contractual Cost | 6,886,606 | | | |
| TOTAL FEDERAL DC | 7,357,509 | 7,997,047 | 3,972,048 | 3,245,544 |
| TOTAL FEDERAL F& | 302,164 | 287,663 | 230,740 | 236,723 |
| TOTAL COST | 7,659,673 | 8,284,710 | 4,202,788 | 3,482,267 |

| | YEAR 02 | YEAR 03 | YEAR 04 | YEAR 05 |
|-----------------|---------|---------|---------|---------|
| | ===== | ===== | ===== | ===== |
| F&A Cost Rate 1 | | | | |
| F&A Cost Base 1 | 63.00% | 63.00% | 63.00% | 63.00% |
| | 470,903 | 456,608 | 366,254 | 375,751 |
| F&A Costs 1 | | | | |
| | 296,669 | 287,663 | 230,740 | 236,723 |
| F&A Cost Rate 2 | | | | |

| | |
|-----------------|--------|
| F&A Cost Base 2 | 63.00% |
| | 8,722 |
| F&A Costs 2 | |
| | 5,495 |

.....END OF NGA.....

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

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) | | | | | | 12,000 |
| EQUIPMENT (Itemize) | | | | | | |
| LCD Projector | | | | | | 4,000 |
| SUPPLIES (Itemize by category) | | | | | | |
| copier supplies | | | | | | |
| fax supplies | | | | | | |
| paper | | | | | | 10,000 |
| TRAVEL | | | | | | |
| Yearly Meetings (\$90,700); CCC Travel (\$23,606) | | | | | | 114,306 |
| PATIENT CARE COSTS | | | | | | |
| INPATIENT 0 | | | | | | 0 |
| OUTPATIENT 0 | | | | | | 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) | | | | | | 46,120 |
| 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 PERIOD | FROM 03/01/2003 | THROUGH 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

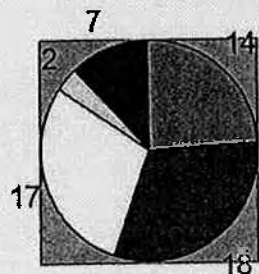
First Investigators Meeting – July 10-13, 2003

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 |

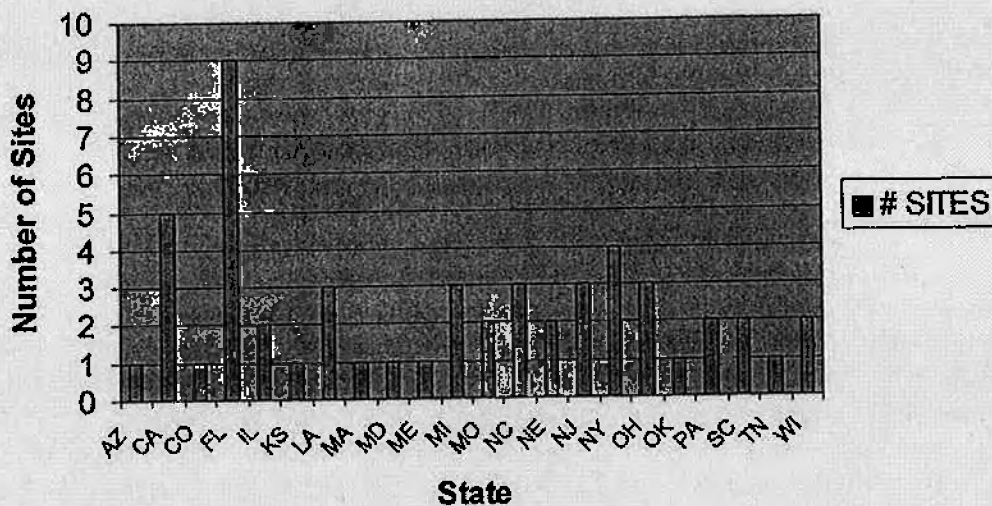
The figure below, titled "TACT Investigators Meeting – July 10-13, 2003: Types of Clinical Sites," illustrates the number of each of four types of sites that attended the first Investigators Meeting. The second figure, titled "TACT Investigators Meeting – July 10-13, 2003: Geographic Location of Clinical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

***** NOTICE OF GRANT AWARD *****
RESEARCH PROJECT COOPERATIVE AGREEMENT Issue Date:02/07/2005
Department of Health and Human Services
National Institutes of Health

NATIONAL CENTER FOR COMPLEMENTARY & ALTERNATIVE MEDICINE

Grant Number: 5 U01 AT001156-03 (Revised)
Principal Investigator: LAMAS, GERVASIO A MD
Project Title: Trial to Assess Chelation Therapy (TACT)

DIRECTOR OF RESEARCH
MT SINAI MED CTR OF FLORIDA, INC
4300 ALTON ROAD
MIAMI BEACH, FL 33140
MIAMI BEACH, FL
UNITED STATES

Budget Period: 03/01/2004 - 02/28/2005
Project Period: 08/15/2002 - 02/28/2007

Dear Business Official:

The National Institutes of Health hereby revises this award (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to MOUNT SINAI MEDICAL CENTER (MIAMI BEACH) in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 31 USC 6305 & 6306 and is subject to terms and conditions referenced below.

Acceptance of this award including the Terms and Conditions is acknowledged by the grantee when funds are drawn down or otherwise obtained from the grant payment system.

Award recipients are responsible for reporting inventions derived or reduced to practice in the performance of work under this grant. Rights to inventions vest with the grantee organization provided certain requirements are met and there is acknowledgement of NIH support. In addition, recipients must ensure that patent and license activities are consistent with their responsibility to make unique research resources developed under this award available to the scientific community, in accordance with NIH policy. For additional information, please visit <http://www.iedison.gov>.

If you have any questions about this award, please contact the individual(s) referenced in the information below.

Sincerely yours,

George Tucker
Grants Management Officer
NATIONAL CENTER FOR COMPLEMENTARY & ALTERNATIVE MEDICINE

See additional information below

SECTION I - AWARD DATA - 5 U01 AT001156-03 (Revised)

AWARD CALCULATION (U.S. Dollars):

| | |
|---------------------------------------|--------------|
| Salaries and Wages | \$466,315 |
| Personnel Costs | \$466,315 |
| Consultant Services | \$23,016 |
| Equipment | \$6,219 |
| Supplies | \$23,739 |
| Travel Costs | \$148,070 |
| Other Costs | \$126,586 |
| Consortium/Contractual Cost | \$13,551,110 |
| Federal Direct Costs | \$14,345,055 |
| Federal F&A Costs | \$495,111 |
| APPROVED BUDGET | \$14,840,166 |
| Less Unobligated Balance | \$10,556,545 |
| TOTAL FEDERAL AWARD AMOUNT | \$4,283,621 |
| AMOUNT OF THIS ACTION (FEDERAL SHARE) | +\$0 |

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project, is as follows.

04 \$5,202,788
05 \$5,482,267

FISCAL INFORMATION:

CFDA 93.213

Number:

Document Number: U1AT01156A

| IC/ CAN / | FY2004 / | FY2005 / | FY2006 |
|-------------|------------|------------|-----------|
| AT/8424951/ | 3,283,621/ | 1,202,788/ | 1,482,267 |
| HL/8424300/ | 1,000,000/ | 4,000,000/ | 4,000,000 |

NIH ADMINISTRATIVE DATA:

PCC: 10 / OC: 41.4P /Processed: TUCKERG 050204 0348

SECTION II - PAYMENT/HOTLINE INFORMATION - 5 U01 AT001156-03 (Revised)

For Payment and HHS Office of Inspector General Hotline Information,
see the NIH Home Page at
<http://grants.nih.gov/grants/policy/awardconditions.htm>

SECTION III - TERMS AND CONDITIONS - 5 U01 AT001156-03 (Revised)

This award is based on the application submitted to, and as approved by, the NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

- a. The grant program legislation and program regulation cited in this Notice of Grant Award.
- b. The restrictions on the expenditure of federal funds in appropriations acts, to the extent those restrictions are pertinent to the award.
- c. 45 CFR Part 74 or 45 CFR Part 92 as applicable.
- d. The NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget period.
- e. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

(see NIH Home Page at
<http://grants.nih.gov/grants/policy/awardconditions.htm> for certain references cited above.)

Carry over of an unobligated balance into the next budget period requires Grants Management Officer prior approval.

This award provides support for one or more NIH defined Phase III clinical trials. The NIH Policy for research supported as an NIH Phase III Clinical Trial has been amended in Section II.B. of the NIH Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research - Amended October 2001
http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm.

A description of plans to conduct analyses, as appropriate, by sex/gender and racial/ethnic groups must be included in clinical trial protocols. Cumulative subject accrual and progress in conducting subset analyses must be reported to NIH in the annual Progress Reports. Final analyses of sex/gender and racial/ethnic differences must be reported in the required Final Progress Report or Competitive Renewal Applications (or Contract Renewals/Extensions) as stated in Section II.B. of the Guidelines.

Treatment of Program Income:
Additional Costs

SECTION IV - ADDITIONAL TERMS AND CONDITIONS
5 U01 AT-01156-03

DR. GERVASIO LAMAS
Revision #6

CARRYOVER:

This revised award authorizes a carryover of \$10,545,988 in "other" direct costs in unexpended funds from the -02 year to be used in the -03 year. This transfer will cover future grant costs related to the trials.

REVISION INFORMATION:

Revised Notice of Grant Award (NGA) issued to provide carryover funds. Supersedes NGA issued 02/01/2005. All previous terms and conditions are still applicable.

CARRYOVER:

This revised award authorizes a carryover of \$10,557 in "other" direct costs in unexpended funds from the -02 year to be used in the -03 year. This transfer will cover future grant costs related to the trials.

REVISION INFORMATION:

Revised Notice of Grant Award (NGA) issued to provide carryover funds. Supersedes NGA issued 09/10/2004. All previous terms and conditions are still applicable.

PREVIOUS TERMS AND CONDITIONS:

This award has been revised to reflect future year budget adjustments by the National Center for Complementary and Alternative Medicine and the National Heart, Lung and Blood Institute. Total Costs were adjusted accordingly. Supersedes Notice of Grant Award (NGA) issued 9/6/2004.

DELAYED START DATE AWARDS INFORMATION: This award has been issued after the budget period start date, however, the expiration date of the budget period remains unchanged (02/28/05). Allowable preaward costs may be charged to this award, in accordance with the conditions outlined in the NIH Grants Policy Statement (March 2001) and with institutional requirements for prior approval.

□

HUMAN SUBJECTS RESEARCH INFORMATION: See page 62 of the NIH Grants Policy Statement (rev. 03\01) for specific requirements related to the protection of human subjects, which are applicable to and a term and condition of this award. This information is available online at the following NIH website: .

Notice: Under governing regulations, Federal funds administered by the department of Health and Human Services may not be expended for research involving human subjects and individuals may not be enrolled in research a any site, domestic or foreign, that does not have an Office for Human Research Protections (OHRP)-approved Assurance to comply with the requirements of 45 CFR Part 46 to protect human subjects and an Institutional Review Board (IRB) approval of the research that satisfies the requirements of 45 CFR Part 46.

It is the grantee institution's responsibility (1) to ensure that all sites engaged in research involving human subjects have an appropriate OHRP-approved Assurance and an IRB approval of the research consistent with 45 CFR Part 46 and (2) to retain documentation of compliance with the requirements of 45 CFR Part 46. The list of institutions with approved Assurances and information on and instructions for submitting and negotiating a Federal wide Assurance of Protection for Human Subjects are available at the OHRP website:

().

No funds may be drawn down from the payment system and no obligations may be made against Federal funds for research involving human subjects at any site engaged in such research for any period not covered by an OHRP-approved Assurance and an IRB approval consistent with 45 CFR Part 46.

Failure to comply with the above requirements may result in suspension and/or termination of this award, withholding of support, audit disallowances, and/or other appropriate action.

PARTICIPANT RECRUITMENT REQUIREMENT: Future NCCAM support for this study is contingent upon adequate participant recruitment based on: target patient accrual. The PI is responsible for providing projected milestones. These milestones will be established by NIH Staff prior to the initiation of data collection. In the event that actual recruitment fall significantly below projected recruitment numbers as defined in the agreed upon milestones, NCCAM may consider withholding future support and/or negotiating an orderly phase out of this study.

PATIENT CARE RESTRICTION: All funds associated with patient care activities are restricted and are not available for expenditure pending final protocol review and approval by DSMB.

Any unobligated funds resulting from these restrictions must be reported and identified on the Financial Status Report and may not be carried over for any purpose without the prior approval of the NCCAM Staff. Should the status of these restricted funds change, notification will occur via the issuance of a revised NGA.

FUNDING DETERMINATION INFORMATION: Specific budget categories are based on target patient accrual of 2,372 & have been determined using the type 5 application categories. Total costs are limited and will not exceed the \$8,284,710 provided in this award.

FACILITIES AND ADMINISTRATIVE (F&A) COST CALCULATION INFORMATION: In accordance with the grantee's negotiated F&A cost rate agreement dated 1/03/01, total F&A costs applicable to this award have been reduced from \$287,663 to \$286,574. F&A costs have been recalculated due to the grantee's non-exclusion of equipment costs (\$1,728) in the F&A base amount used to calculate the F&A costs.

NIH FUNDING ACKNOWLEDGEMENT REQUIREMENT: Grantees are required to place an acknowledgement of NIH grant support and a disclaimer, as appropriate, on any publication written or published with such support and, if feasible, on any publication reporting the results of, or describing, a grant-supported activity. An acknowledgment shall be to the effect that:

□

"This publication was made possible by Grant Number ___ from the National Center for Complementary and Alternative Medicine (NCCAM) or "the project described was supported by Grant Number ___ from the National Center for Complementary and Alternative Medicine" and "Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NCCAM, or the National Institutes of Health."

Grant recipients presenting NCCAM-sponsored research at scientific, professional, and consumer meetings are asked to acknowledge the

publicly funded support they receive. A copy of the NCCAM Grantee Acknowledgement slide in PowerPoint is available at: nccam.nih.gov/research/information for grantees.

CO-FUNDING INFORMATION: This award includes total costs funds of \$3,000,000 provided by the National Heart Lung and Blood Institute (NHLBI).

OVERCOMMITMENT INFORMATION: A review of other support information provided in the pending application for this project indicates that with the award of this project, Dr. Daniel Mark's effort commitment may exceed 100%. If applicable, the awardee is responsible both for eliminating this over commitment (and any other over commitment of effort) and for obtaining appropriate prior approval(s) in accordance with NIH and institutional policy requirements.

INFORMATION REQUIREMENT: The following information must be submitted within 30 days of the issue date of this award.

- Consortium cost information which includes the name of each institution and funds provided for that institution.
- Biographical Sketch for Jamie Zimmerman

CONSORTIUM/CONTRACTUAL COST INFORMATION: This award includes funds for consortium activities in the amount of \$7,540,439 that will be provided with this award. Consortia are to be established and administered in accordance with the NIH Grants Policy Statement.

FINANCIAL STATUS REPORT REQUIREMENTS: NIH recipients are reminded of the following requirements:

Financial Status Report (FSR) (Standard Form 269 or 269A, whichever is applicable) must be submitted to NIH within 90 calendar days after the last day of each budget period. For consortium partner arrangements, institutions must stipulate in agreements the deadlines for submitting reports to the prime.

Recipients that submit reports at the 3-month mark will be considered out of compliance if that period exceeds 90 calendar days. Recipients are encouraged to report in advance of the deadline as a good business practice as well as to facilitate the timely submission of progress and invention reports. FSRs should be accurate at the time of submission, with revisions made rarely, only to provide updated information. Revisions should not be used as a mechanism to correct routinely incomplete or erroneous FSRs.

FSR's (OMB 269, which can be found at: <http://www.whitehouse.gov/omb/grants/#forms>) should be submitted electronically to the Office of Financial Management, NIH. Non-electronic reports may be mailed to:

Government Accounting Branch
Office of Financial Management
National Institutes of Health
31 Center Drive, Room B1B05A
MSC 2050
Bethesda, MD 20892-2050

Failure to submit these required reports, when due, may result in the imposition of special award provision or the withholding of support for other eligible projects or activities involving the grantee organization

□

or the individual responsible for the delinquency.

TERMS INFORMATION: Terms and conditions, which were listed on the previous NGA and still applicable, are incorporated by subtitle listed below ***. Refer to original NGA dated 08/08/2002 for a complete description of terms and conditions.

PUBLICATIONS REQUIREMENT

ANNUAL PROGRESS REPORTS REQUIREMENT

PERSONNEL COSTS INFORMATION

ESCALATION INFORMATION

ADDITIONAL RFA TERMS AND CONDITIONS: This award is being issued according to the guidelines and requirements in RFA AT-01-004, entitled EDTA CHELATION THERAPY FOR CORONARY ARTERY DISEASE.

PROGRAM OFFICIAL CONTACT INFORMATION: The program official responsibilities for this award have changed. If you have any questions regarding the scientific, programmatic and technical aspects of this project, please contact:

SPECIALIST CONTACTS INFORMATION: If you have any questions regarding the negotiation, award, administration of this project and for interpretation of Grants Administration policies and provisions, the grants management contact is:

Richard Nahin, Program Official
Phone: (301)-496-7801 Email: nahinr@od.nih.gov Fax: (301) 435-6549

Debera Campbell, Grants Specialist
Phone: 301-594-8738 Email: campbelde@mail.nih.gov Fax: 301-480-1552

SPREADSHEET

GRANT NUMBER: 5 U01 AT001156-03 (Revised)

P.I.: LAMAS, GERVASIO A
INSTITUTION: MOUNT SINAI MEDICAL CENTER (MIAMI BEACH)

| | YEAR 03 | YEAR 04 | YEAR 05 |
|------------------------|------------|-----------|-----------|
| | ===== | ===== | ===== |
| Salaries and Wages | 466,315 | | |
| Personnel Costs | 466,315 | | |
| Consultant Services | 23,016 | | |
| Equipment | 6,219 | | |
| Supplies | 23,739 | | |
| Travel Costs | 148,070 | | |
| Other Costs | 126,586 | | |
| Consortium/Contractual | 13,551,110 | | |
| Cost | | | |
| | | | |
| TOTAL FEDERAL DC | 14,345,055 | 4,972,048 | 5,245,544 |
| | | | |
| TOTAL FEDERAL F&A | 495,111 | 230,740 | 236,723 |
| TOTAL COST | 14,840,166 | 5,202,788 | 5,482,267 |

| | YEAR 03 | YEAR 04 | YEAR 05 |
|------------------|---------|---------|---------|
| □F&A Cost Rate 1 | 63.00% | 63.00% | 63.00% |
| F&A Cost Base 1 | 785,891 | 366,254 | 375,751 |
| F&A Costs 1 | 495,111 | 230,740 | 236,723 |

.....END OF NGA.....

***** NOTICE OF GRANT AWARD *****
 RESEARCH PROJECT COOPERATIVE AGREEMENT Issue Date:02/04/2005
 Department of Health and Human Services
 National Institutes of Health

NATIONAL CENTER FOR COMPLEMENTARY & ALTERNATIVE MEDICINE

Grant Number: 5 U01 AT001156-03 (Revised)
 Principal Investigator: LAMAS, GERVASIO A MD
 Project Title: Trial to Assess Chelation Therapy (TACT)

DIRECTOR OF RESEARCH
 MT SINAI MED CTR OF FLORIDA, INC
 4300 ALTON ROAD
 MIAMI BEACH, FL 33140
 MIAMI BEACH, FL
 UNITED STATES

Budget Period: 03/01/2004 - 02/28/2005
 Project Period: 08/15/2002 - 02/28/2007

Dear Business Official:

The National Institutes of Health hereby revises this award (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to MOUNT SINAI MEDICAL CENTER (MIAMI BEACH) in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 31 USC 6305 & 6306 and is subject to terms and conditions referenced below.

Acceptance of this award including the Terms and Conditions is acknowledged by the grantee when funds are drawn down or otherwise obtained from the grant payment system.

Award recipients are responsible for reporting inventions derived or reduced to practice in the performance of work under this grant. Rights to inventions vest with the grantee organization provided certain

Type 5

Department of Health and Human Services
Public Health ServicesReview Group Type Activity Grant Number
U01 AT01156-03

Grant Progress Report

Total Project Period
From: 08/15/2002 Through: 02/28/2007Requested Budget Period:
From: 03/01/2004 Through: 02/28/2005

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

EIN

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 Yes

6a. Research Exempt

 No Yes

6b. Human Subjects Assurance No.

#A00000176

7. VERTEBRATE ANIMALS

 No Yes

7a. If "Yes," IACUC approval Date

If Exempt ("Yes" in 6a):

Exemption No.

6c. NIH-Defined Phase III

Clinical Trial No Yes

7b. Animal Welfare Assurance No.

If Not Exempt ("No" in 6a):

IRB approval date

 Full IRB or Expedited Review

8. COSTS REQUESTED FOR NEXT BUDGET PERIOD

8a. DIRECT

\$7,997,047

8b. TOTAL

\$8,284,710

9. INVENTIONS AND PATENTS

 No YesIf "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

2/1/03

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

12-1-03

| DETAILED BUDGET FOR NEXT BUDGET PERIOD - DIRECT COSTS ONLY | | FROM 03/01/04 | THROUGH 02/28/05 | GRANT NUMBER 1 U01 AT01156-03 | | |
|--|------------------------|------------------------|---------------------|--------------------------------------|-----------------|--------------------|
| 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 |
| Danielle Hollar, Ph.D. | Project Director | 12 | | 74,100 | 0 | 74,100 |
| Steven Hussein, MD | Clinical Manager | 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 |
| Jamie Zimmerman, MPH | Research Assistant | 12 | | 28,500 | 0 | 28,500 |
| Renea Moss | Admin. Assistant | 12 | | 24,800 | 0 | 24,800 |
| SUBTOTALS → | | | | | 0 | 261,980 |
| CONSULTANT COSTS | | | | | | |
| Martin Dayton, DO (\$6,000); Ted Rozema, MD (\$6,000), Regulatory Consultant (\$3,000) | | | | | | 15,000 |
| EQUIPMENT (Itemize) | | | | | | |
| Copier | | | | | | 1,728 |
| SUPPLIES (Itemize by category) | | | | | | |
| copier supplies | | | | | | |
| fax supplies | | | | | | |
| paper | | | | | | 10,000 |
| TRAVEL | | | | | | |
| Yearly Meetings (\$125,000); CCC Travel (\$26,134) | | | | | | 151,134 |
| PATIENT CARE COSTS | | | | | | |
| INPATIENT 0 | | | | | | 0 |
| OUTPATIENT 0 | | | | | | 0 |
| ALTERATIONS AND RENOVATIONS (Itemize by category) | | | | | | |
| OTHER EXPENSES (Itemize by category) | | | | | | |
| Telecommunications (\$7,572.00) | | | | | | |
| Audiovisual (\$2,704); Postage (\$6,490); Advertisements (0) | | | | | | 18,766 |
| SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD | | | | | | \$456,608 |
| CONSORTIUM/CONTRACTUAL COSTS | | | | | | |
| DIRECT COSTS | | | | | | \$7,540,439 |
| FACILITIES AND ADMINISTRATIVE COSTS | | | | | | 287,663 |
| TOTAL DIRECT COSTS FOR NEXT PROJECT PERIOD (Item 9a, Face Page) | | | | | | \$7,997,047 |

BUDGET JUSTIFICATION

GRANT NUMBER
1 U01 AT01156-03

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.

There has been sub-category rebudgeting among the subcontractors described below.

Central Pharmacy: Specifically, the Central Pharmacy is receiving more funding to account for separate shipments of vitamin supplies to sites.

Omnicom: Additional funds were added to the OmniComm budget line to cover costs related to the creation of a workflow system for shipping and tracking vitamins and vitamin placebos.

Central Lab: Additional funds were added to the Central Lab budget line to cover costs related to measuring high sensitivity C-reactive protein levels (Cardio-CRP) 3 times for each patient. The Cardio-CRP test is more expensive than general CRP test, but is required in order to be able to understand the effect of Chelation therapy, if any, on this important inflammatory marker, as specified in the original RFA.

| CURRENT BUDGET PERIOD | FROM | THROUGH |
|-----------------------|------------|------------|
| | 03/01/2003 | 02/29/2004 |

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

Consultant Costs: A pharmacy regulatory consultant has been added to the budget. This consultant will assist with ongoing regulatory requirements of the FDA Investigational New Drug Application (IND) and other pharmacy regulatory issues.

Equipment: Currently, computers and a printer are being purchased to meet the needs of the TACT CCC. Expenses will show up by the end of year 2.

Supplies: Expenditures of supplies are lower than expected due to delay in activating clinical sites.

Travel: The number of clinical sites that will attend the Second Investigators' Meeting, planned for Spring 2004, will be significantly higher than the number that attended the first meeting. Consequently, the budget category for this expense has been increased, and expenses will be deducted in 2004. A carryover request will be forthcoming.

Other expenses: Postage funds for Year 1 will be used as part of payment for the 2nd Investigators Meeting. Audiovisual expenses were incurred during the First 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. However, advertising will take place during the rest of Year 2 and throughout Year 3.

Consortium: Because patient enrollment has been slower than expected, there have been few expenditures for the central lab, clinical units, or the Clinical Events Committee (Brigham & Women's) as of November 2003. These expenses will be incurred during year 3 as the number of enrolled patients increases. A carryover request will be forthcoming.

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 | | POSITION TITLE | | |
|---|----------------------------------|----------------|----------------|--|
| 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 | |
| | | | | |

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.

No new sketches are required at this time.

| | | |
|---|---|----------------------------------|
| PROGRESS REPORT SUMMARY | | GRANT NUMBER 1 U01 AT01156-03 |
| 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 | <input checked="" type="checkbox"/> No Change Since Previous Submission | <input type="checkbox"/> Change |
| B. Vertebrate Animals (Complete Item 7 on the Face Page) | | |
| Use of Vertebrate Animals | <input type="checkbox"/> No Change Since Previous Submission | <input type="checkbox"/> 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 TACT CCC since the last reporting period (July 2003).

Charles H. Hennekens, MD, DrPH (Co-Principal Investigator): Dr. Hennekens resigned from TACT.

Jamie Zimmerman, MPH (Research Assistant): Jamie Zimmerman has been added to the CCC as a full-time Research Assistant (base salary of

| | |
|---------------|--------|
| Institutional | % |
| Page Set | Effort |

 FTE). Her principle 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. She reports to the Project Director.

Is it anticipated that an estimated unobligated balance (including prior year carry over) will be greater than 25 percent of the current year's total budget?

Yes, an unobligated balance (including prior year approved carry over) will be greater than 25% of the current year's total budget principally due to slower than expected patient enrollment. A carryover request will be forthcoming.

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 because the study only began enrolling patients in September 2003.

c. Significance

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

d. Plans

Milestones accomplished:

d.1. IND Application Requirements

The TACT Clinical Coordinating Center (CCC) submitted 1572s and CVs for Site Investigators to the FDA according to IND Application requirements. A plan has been operationalized to ensure that subsequent submissions of these documents occur on a monthly basis.

In accordance with the IND Application requirements, the TACT Pharmacy submitted pharmaceutical samples of required study medications to Guidelines Laboratory, of Miramar, FL. Testing continues based on the laboratory schedule outlined in the IND Application, with results being maintained on site at the TACT Pharmacy.

d.2. Site Activation

Based on the current rate of patient enrollment per site, it is predicted that the number of clinical sites needed to meet TACT enrollment goals will be much higher than originally expected. Accordingly, clinical site recruitment continues. To date, four sets of clinical sites are in various stages of site activation. These sets of sites are described below.

First Set of Sites

As of November 27, 2003, 30 of 58 clinical sites that attended the First Investigators Meeting are regulatory compliant and approved to enroll. Six sites are located in academic centers, 9 are cardiology practices, 14 are chelation practices, and 1 is a research institute. These clinical sites are screening and enrolling patients at this time (patient enrollment is described later in this section of the report).

Second Set of Sites

During the fall of 2003, an additional 110 potential clinical sites were invited to begin the regulatory process for site activation. Clinical sites that complete the regulatory process by early February 2004 will be invited to attend the Second Investigators Meeting planned for Spring 2004.

Third Set of Sites

Also during the fall of 2003, approximately 25 potential clinical sites with experience in other cardiovascular clinical trials directed by Dr. Lamas were invited to begin the regulatory process for site activation. Clinical sites that complete the regulatory process by early February 2004 will be invited to attend the Second Investigators Meeting planned for Spring 2004.

Fourth Set of Sites

Approximately 70 attendees of the American College for Advancement in Medicine (ACAM) visited the TACT information booth during the November 19-21, 2003 annual conference. Currently, approximately 12 of these attendees are completing the TACT application materials. Upon approval by the TACT Steering Committee, these sites will be invited to begin the final set of regulatory requirements for site activation and to attend the Spring 2004 meeting if their regulatory requirements are met.

d.3. TACT Contractors**The Pharmed Group**

On November 7, 2003 a contract was executed between the CCC and The Pharmed Group for the provision of vitamins at below production cost for the term of the trial.

d.4. Clinical Site IRB Approvals

As mentioned in previous submissions, Sterling Institutional Review Board (IRB) serves as the central IRB for TACT. Thus far, 48 clinical sites have received IRB approval.

Central IRB – Sterling Institutional Review Board

As of November 27, 2003, 30 clinical sites have been approved by Sterling Institutional Review Board.

Local IRBs

As of November 27, 2003, 18 clinical sites have been approved by local institutional review boards.

d.5. Enrollment Update

Patient randomization began September 10, 2003, and the first infusion occurred September 12, 2003. The table below presents the demographics of the patient population, as of November 27, 2003.

| 32 Patients (as of November 27, 2003) | University Center (n) | Cardiology Practice (n) | Chelation Practice (n) | Totals (n) |
|--|--------------------------------------|--|---------------------------------------|-----------------------|
| Gender: | | | | |
| Female | 1 | 3 | 4 | 8 |
| Male | 0 | 12 | 12 | 24 |
| Race/Ethnicity: | | | | |
| Asian | - | - | - | 0 |
| Black | - | - | - | 0 |
| Hawaii | - | - | - | 0 |
| White | 1 | 15 | 16 | 32 |
| Age: | | | | |
| 50-54 | - | 2 | 2 | 4 |
| 55-59 | 1 | 4 | 2 | 7 |
| 60-64 | - | 3 | 2 | 5 |
| 65-69 | - | 1 | 4 | 5 |
| 70-74 | - | 1 | 5 | 6 |
| 75-79 | - | 1 | 2 | 3 |
| 80+ (oldest: 82) | - | 2 | - | 2 |
| State: | | | | |
| CA | - | - | 7 | 7 |
| FL | - | 2 | - | 2 |
| LA | - | - | 2 | 2 |
| ME | - | 5 | - | 5 |
| NC | 1 | 2 | - | 3 |
| NY | - | 6 | - | 6 |
| SC | - | - | 7 | 7 |

Enrollment is slower than projected. The principal reasons for slower patient enrollment have been:

- 1] The final protocol was not approved until May 29, 2003.
- 2] The study binder and CRF's were approved June 27, 2003.
- 3] Vitamins and their placebos were received on September 3, 2003.
- 4] Regulatory approval for sites has been slower than anticipated. There are 9 specific regulatory steps required to be approved to enroll in TACT. Of 58 sites that attended the initial investigators' meeting in July 10-13, 2003, only 30 have completed regulatory requirements and are ready to enroll. Thus, the median time to gain approval for the group is 11 weeks and rising. The principal delays have been with IRBs, particularly local, University-based IRBs, and with the contract to carry out TACT.
- 5] Once sites are approved, they are finding that enrollment is more difficult than anticipated due to the patient burden required by the study.
- 6] The public relations campaign planned by the NCCAM Communications office has been delayed, of necessity, since not enough sites are ready, but this has compounded slow enrollment.
- 7] Enrollment is slower than projected. The principal reason, however, is delay in activating new sites. For example, the very first date that enrollment could occur, due to drug delivery, was September 3, or 3 months ago. If, to be realistic, we assume a 4-week lag after approval for screening, consent, and scheduling before the first enrollment, then the randomization rate is 0.9 patients per site per month, very similar to our original projections. Thus, CCC activities to improve enrollment are geared towards increasing site approval, as well as assisting sites with screening and enrollment advice.

The TACT CCC expects that the following solutions put into place will speed enrollment:

- 1] An additional research assistant, Jamie Zimmerman, MPH, was employed to assist sites with fulfilling initial regulatory requirements, and an additional one will be employed within the month.
- 2] Dr. Lamas and colleagues have stepped up efforts to move sites through the regulatory process with frequent telephone and email contact with PIs.
- 3] Mount Sinai, the grantee institution, has provided more flexibility with contractual variations relating to levels of malpractice insurance coverage for subcontracting PIs.
- 4] Efforts to identify additional potential sites have been stepped up – over 100 sites have expressed interest since the initial investigators' meeting and are beginning to move through the regulatory process.
- 5] Coordinators' conference calls have been instituted so that successful sites may speak with less successful ones to learn strategies for success.

As shown in the table above, the number of minority patients in the population is low. Sites that would be expected to have a high minority patient base, however, have not yet started enrolling, and the previously planned NCCAM public relations campaign in Spanish has not yet been launched. The trial management remains committed to enrolling an ethnically diverse population, and optimistic that we can do so.

GRANT NUMBER
1 U01 AT01158-03

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 \$ 456,608 x Rate applied 63 % = F&A costs \$ 287,663

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.):

PERSONNEL REPORT

GRANT NUMBER
1 U01 AT01156-03

Place this form at the end of the signed original copy of the application. Do not duplicate.

Pr. 2

| Senior Investigator | Participating Institution | Role | % Effort |
|--|--|---------------------------|----------|
| Hollar, Danielle PhD <i>Replaced by Jamie Zimmerman, Approved by PO.</i> | Mount Sinai Medical Center 4300 Alton Rd Miami Beach, FL 33140 | Project Director | |
| ✓ Hussein, Steven MD <i>(Has replaced Dr. Alan Ackerman)</i> | Mount Sinai Medical Center 4300 Alton Rd Miami Beach, FL 33140 | Clinical Manager | |
| ✓ Lamas, Gervasio MD | Mount Sinai Medical Center 4300 Alton Rd Miami Beach, FL 33140 | Principal Investigator | |
| ✓ Lee, Kerry PhD | Duke Clinical Research Institute Box 3300 Durham, NC 27715 | Co-Principal Investigator | |
| ✓ Mark, Daniel MD * | Duke Clinical Research Institute Box 3300 Durham, NC 27715 | Co-Principal Investigator | |

Changes in Personnel

Dr. Charles Hennekens
Dr. Rachel Eidelman
Dr. Alan Ackerman

% Effort

- Resigned and will not be replaced
- No longer working on the grant
- Replaced by Dr. Steven Hussein

Targeted/Planned Enrollment Table

This report format should NOT be used for data collection from study participants.

Study Title: Trial To Assess Chelation Therapy**Total Planned Enrollment:** 2372

| TARGETED/PLANNED ENROLLMENT: Number of Subjects | | | |
|--|-------------------|--------------|--------------|
| Ethnic Category | Sex/Gender | | |
| | Females | Males | Total |
| Hispanic or Latino | 57 | 133 | 190 |
| Not Hispanic or Latino | 655 | 1528 | 2182 |
| Ethnic Category Total of All Subjects* | 712 | 1660 | 2372 |
| Racial Categories | | | |
| American Indian/Alaska Native | 7 | 17 | 24 |
| Asian | 14 | 33 | 47 |
| Native Hawaiian or Other Pacific Islander | 14 | 33 | 47 |
| Black or African American | 85 | 199 | 285 |
| White | 591 | 1378 | 1969 |
| Racial Categories: Total of All Subjects * | 712 | 1660 | 2372 |

*The "Ethnic Category Total of All Subjects" must be equal to the "Racial Categories Total of All Subjects."

PHS 2590 OTHER SUPPORT

Provide active support for all key personnel. Other Support includes all financial resources, whether Federal, non-Federal, commercial or institutional, available in direct support of an individual's research endeavors, including but not limited to research grants, cooperative agreements, contracts, and/or institutional awards. Training awards, prizes, or gifts do not need to be included.

There is no "form page" for other support. Information on other support should be provided in the format shown below, using continuation pages as necessary. Include the principal investigator's name at the top and number consecutively with the rest of the Grant Progress Report. The sample below is intended to provide guidance regarding the type and extent of information requested. For information pertaining to the use of and policy for other support, see "Policy and Additional Guidance" in the PHS 398 instructions.

Lamas, Gervasio A. MD

ACTIVE

Private Source

12/01/01 - 12/31/03

\$550,000

The major goal is to evaluate the effects of three different doses of Bayer aspirin on levels of C-Reactive Protein in Post-Menopausal women who initiate hormone replacement therapy.

Private Source

(Lamas)

1/10/99 - present

\$500,000

Advanced Elements of Pacing Trial (ADEPT)

The major goal is to determine how effective the dual sensor rate modulation and automatic mode switching features in the Kappa 400 are in improving patients' quality of life.

Overlap: None

RO1 HL 62509-01A1 (Hochman)

12/1/99 - 11/30/06

NIH/NHLBI

\$15,000,000

Occluded Artery Trial (OAT)

Co-Chairman

The major goal is to evaluate if the late reestablishment of blood flow to the artery that caused the heart attack will decrease clinical events and improve the quality of life.

Overlap: None

R01 HL 72906 (Rashba)

9/1/02 - 8/31/06

NIH/NHLBI

\$900,000

Electrophysiologic effects of late PCI (OAT-EP)

Co-Chairman

The major goal is to characterize the effects of late PCI of occluded IRAs on the most prognostically important and clinically relevant noninvasive markers of vulnerability to malignant ventricular arrhythmias: heart rate variability, T wave variability and signal averaged electrocardiography.

Overlap: None

U01HL49804

12/1/98 - 9/30/01

NIH/NHLBI

\$11,000,000

Mode Selection Trial (MOST)

Clinical benefits of dual versus single chamber pacing.

Overlap: None

PHS 2590 OTHER SUPPORT (continued)

1 U01 AT01156-01 (Lamas, PI)
NIH/NHLBI
Trial to Assess Chelation Therapy (TACT)

08/15/2002-02/28/2007
\$30,000,000

The major goal of the Trial to Assess Chelation Therapy is to determine whether an intensive course of EDTA chelation, will reduce major adverse coronary events in patients with coronary artery disease who have recovered from a prior myocardial infarction.

Lee, Kerry L.

ACTIVE

HL55297(Lee)
NIH/NHLBI

5/1/97-4/30/03
\$3,856,583 (total costs)

Data Coordinating Center for the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT)

The objective of this project is to provide the Statistical and Data Coordinating Center for the multicenter randomized clinical trial of prophylactic amiodarone or implantable defibrillator therapy versus conventional heart failure therapy in patients with Class II or Class III heart failure and a reduced ejection fraction.

(Lee)

5/1/97-4/30/03

Private Support

\$3,400,000

0%

Data Coordinating Center for the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT)

This grant provides additional support for the SCD-HeFT trial to cover study materials, expenses for investigator/coordinator meetings, and the payments to sites for enrolling and following the study patients.

1R01HL69015-01 (Lee)
NIH/NHLBI

1/1/02-12/31/08
\$2,965,075 (Total Direct Costs)

STICH (Surgical Treatment for Ischemic Heart Failure Trial)

This grant supports the Statistical and Data Coordinating Center for the STICH trial. The study is a multicenter, international, randomized trial in patients with clinical heart failure and left ventricular dysfunction who have coronary artery disease amenable to surgical revascularization.

1R01HL63747 (O'Connor, Christopher)
NIH/NHLBI

9/30/2002-9/29/2007
\$30,179,911 Total Direct Cost

HF-ACTION (A CHF Trial Investigating Outcomes of Exercise Training)

This grant supports the Coordinating Center for the multi-center HF-ACTION trial. The objective of this trial is to assess whether exercise training improves clinical outcomes for heart failure patients.

1 U01-AT01156 (Lamas, G.A.)
NIH/NCCAM/NHLBI/Mt Sinai
Trial to Assess Chelation Therapy (TACT)


8/15/02 - 2/28/07
\$1,879,530 (Year 1 Total Costs)

% Effort

PHS 2590 OTHER SUPPORT (continued)

Duke Clinical Research Institute (under leadership of Dr. Lee) is a subcontractor to Mt. Sinai Medical Center to provide the Statistical and Data Coordinating Center for this trial. The study is a multicenter, randomized clinical trial of chelation therapy in patients with a prior myocardial infarction.

1 U01-HL67972 (Bardy, Gust) 9/30/02 - 8/31/07
NIH/NHLBI/Seattle Institute for Cardiac Research \$430,245 (Year 1 Total Costs)
Home Automatic External Defibrillator Trial - H.A.T.

 80 Total

Duke Clinical Research Institute (under leadership of Dr. Lee) is a subcontractor to the Seattle Institute for Cardiac Research to provide statistical services and perform economic and quality of life analyses for this trial. The study is a multicenter, randomized clinical trial to assess the effects of home use of automatic external defibrillators in reducing mortality in patients with a prior anterior myocardial infarction.

OVERLAP

No overlap exists at this time.

Mark, Daniel B.

ACTIVE

U01 HL55496 (Mark, Daniel B.; PI) 05/01/2003-04/30/2004
NIH/NHLBI \$232,764
Economics & Quality of Life in SCD-HeFT (1-yr ext)



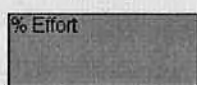
The objective of this project is to establish an Economics and Quality of Life Coordinating Center for SCD-HeFT, a multi-center clinical trial of prophylactic amiodarone or implantable defibrillator therapy versus conventional heart failure therapy in 2500 patients with Class II or Class III congestive heart failure (CHF) and an ejection fraction $\leq 35\%$. This is a one-year extension of the initial project.

U01 HL62257 (Mark, Daniel B.; PI) 09/01/1999-08/31/2004
NIH/NHLBI \$222,225
Economics and Quality of Life in the Occluded Artery Trial (OAT)



The objective of this study is to establish an Economics and Quality of Life Coordinating Center for the Occluded Artery Trial, a multi-center, randomized trial of late (3-42 days) percutaneous revascularization versus standard medical therapy in 3200 asymptomatic high-risk acute myocardial infarction (MI) survivors and who are found at diagnostic catheterization to have an occluded infarct related artery. Cost, cost effectiveness, and health-related quality of life are secondary endpoints.

U01 HL69011 (Mark, Daniel B.; PI) 01/01/2002-12/31/2008
NIH/NHLBI \$208,533
Economics and Quality of Life Core Laboratory in Surgical Treatment of Ischemic Heart Failure (STICH)

 % Effort

The major goal of this substudy of the Surgical Treatment of Heart Failure Trial is to determine cost effectiveness and health-related quality of life of CABG +/- ventricular reconstruction versus medical therapy.

PHS 2590 OTHER SUPPORT (continued)

1R01 HL69081-01 (Newman, Mark; PI) 12/01/2001-11/30/2005
NIH \$393,123
Peri-Operative Interventional Neuroprotection Trial: POINT

The major goal of this project is to determine the impact of magnesium administration to therapeutic serum levels on short- and long-term neurocognitive function after cardiac surgery evaluated by preoperative and postoperative neurocognitive and neurologic testing.

1R01 HL54780 (Barefoot, John; PI) 08/01/2000-07/31/2004
NIH/NHLBI \$225,000
Hostility, depression, social environment, and CHD risk

The major goal of this study is to identify interactions among psychosocial risk factors and demographic variables that affect the risk of cardiovascular disease.

R01 HS013345-01 (Eisenstein, Eric L.; PI) 09/12/2002-08/31/2004
AHRQ \$227,777
Dialysis Facility Management

The goal of this study is to define the impact of dialysis facility characteristics on dialysis patient mortality, morbidity, and total medical costs.

1U01 HL66530 (Mark, Daniel B.; PI) 08/15/2002-08/14/2007
NIH/NHLBI \$86,478
Economics and Quality of Life in the Trial to Assess Chelation Therapy (TACT)

The major goal of the Trial to Assess Chelation Therapy is to determine whether an intensive course of EDTA chelation, administered over 18 months, will reduce major adverse coronary events in patients with coronary artery disease who have recovered from a prior myocardial infarction. The objective of this project is to assess the secondary endpoints of cost effectiveness and health-related quality of life of the treatment strategies being tested in TACT.

U01 HL67972-01 (Bardy Gust; PI) 10/01/2002-08/30/2007
NIH/NHLBI \$1,965,243
Home Automatic External Defibrillator Trial (HAT)

The major objective of this study is to conduct a randomized clinical trial of automatic external defibrillator therapy, provided by spouses or other family members, superimposed on the local emergency medical system vs. the local emergency medical system in 3400 survivors of anterior myocardial infarction. Duke University will act as subcontractor to Seattle Institute for Cardiac Research for this trial. Duke will provide data management and statistical services for the trial, as well as performing economic and quality of life analyses.

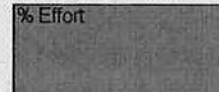
PHS 2590 OTHER SUPPORT (continued)

5 U18 HS10548-05 (Kramer, Judith; PI)
NIH/AHCPR
DCRI Cardiovascular CERT Research Center

09/30/2003-09/29/2007
\$519,480



The main objective of this project is to investigate clinical therapeutics in cardiovascular medicine at Duke's DCRI by providing vision, leadership, and direction to translate clinical findings into improved medical practice.



Private Source

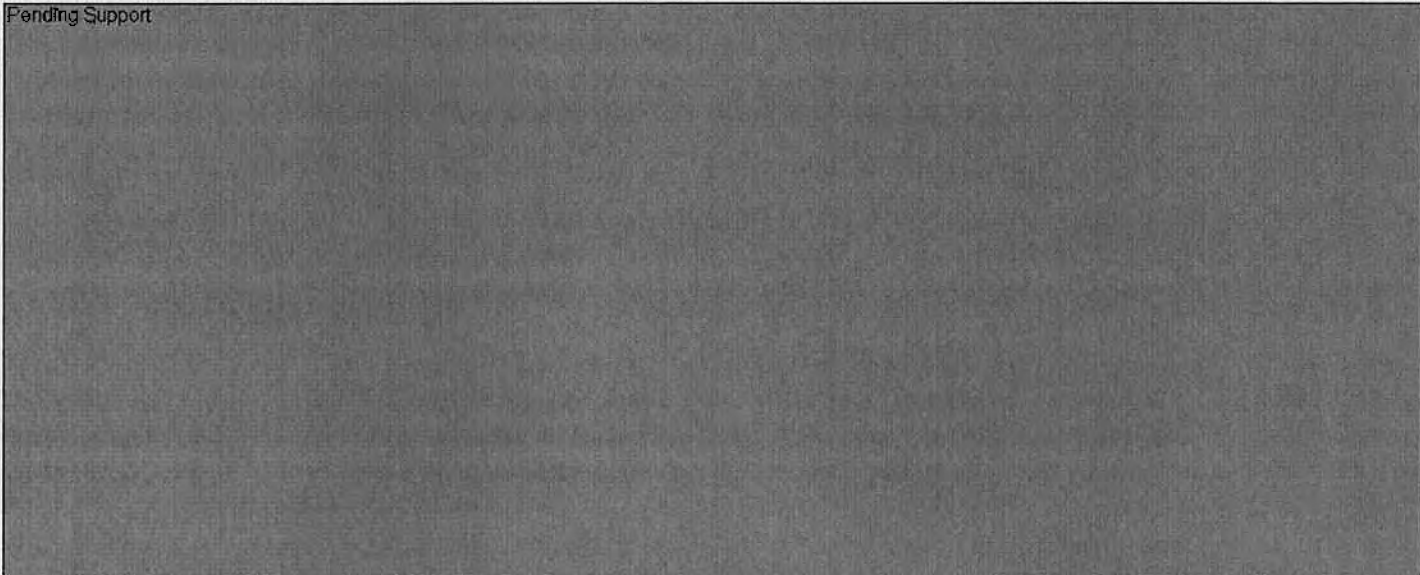
(Mark, Daniel B.; PI)

02/10/1998-12/31/2005

Treating to New Targets (TNT) Economics Substudy

The objective of this substudy of the TNT clinical trial is to determine cost effectiveness of lowering LDL-C beyond the currently accepted minimum targets for patients at high risk for developing coronary heart disease.

Pending Support



TACT CLINICAL COORDINATING CENTER BUDGET

Y2006-2007

Year 5

| Name | Position | Appointment | Effort | Salary | Salary Requested | Fringe Rate | Fringe Total | Salary Total | | |
|---|----------------------|-------------|----------|---------------------------|------------------|-------------|--------------|-------------------------|----------------------------|-----------------------|
| Gervasio Lamas MD | Study Chairman | 12 | % Effort | Institutional Base Salary | \$64,480 | 0 | \$0.00 | \$ | 64,480 | |
| Charles Hennekens MD DrPH | Co-PI | 12 | | | \$64,480 | 0 | \$0.00 | \$ | 64,480 | |
| Danielle Hollar PhD | Project Director | 12 | | | \$74,100 | 0 | \$0.00 | \$ | 74,100 | |
| TBN | Clinical Coordinator | 12 | | | \$38,995 | 0 | \$0.00 | \$ | 38,995 | |
| Virginia Martini BS | Admin Coordinator | 12 | | | \$41,600 | 0 | \$0.00 | \$ | 41,600 | |
| TBN | Research Assistant | 12 | | | \$28,500 | 0 | \$0.00 | \$ | 28,500 | |
| TBN | Research Assistant | 12 | | | \$28,500 | 0 | \$0.00 | \$ | 28,500 | |
| Ophelia Stephens | Admin Assistant | 12 | | | \$24,800 | 0 | \$0.00 | \$ | 24,800 | |
| | | | | | | | | Total Salaries | \$365,455 420017 | |
| Consultants | | | | Salary | | | | | | |
| Martin Dayton DO | | | | \$3,000 | | | | | \$6,000 6000 | |
| Theodore Rozema MD | | | | \$3,000 | | | | | | |
| Equipment | | | | | | | | | Total equipment | \$0 |
| Supplies | | | | | | | | | Total supplies | \$10,000 10000 |
| copier supplies | | | | | | | | | | |
| fax supplies | | | | | | | | | | |
| paper | | | | | | | | | | |
| Travel | | | | | | | | | Total Travel | \$20,171 20171 |
| Yearly meetings | | | | \$0 | | | | | | |
| CCC travel | | | | \$20,171 | | | | | | |
| Patient care costs | | | | | | | | | Total Patient Costs | \$0 |
| Telephone | | | | \$7,019 | | | | | | |
| Pagers | | | | \$1,170 | | | | | | |
| Audiovisual | | | | \$2,925 | | | | | | |
| Postage | | | | \$7,019 | | | | | | |
| Advertisement | | | | \$0 | | | | | | |
| | | | | | | | | Total other (A) | \$18,133 18133 | |
| Consortium/ contractual costs | | | | | | | | | | |
| Direct costs | | | | | | | | | | |
| • DCRI | | | | \$1,107,018 | | | | | | |
| OmniComm | | | | \$60,200 | | | | | | |
| Brigham and Women's | | | | \$45,647 | | | | | | |
| Clinical units | | | | \$2,561,760 | | | | | | |
| Central Pharmacy | | | | \$0 | | | | | | |
| Central Lab | | | | \$0 | | | | | | |
| Pharmed | | | | \$150,000 | | | | | | |
| Total direct costs | | | | \$3,924,625 | | | | | | |
| Indirect costs | | | | | | | | | | |
| DCRI | | | | \$585,782 | | | | | | |
| Brigham and Women's | | | | \$11,412 | | | | | | |
| Total indirect costs | | | | \$597,194 | | | | | | |
| | | | | | | | | Total Consortium | \$4,521,819 2679313 | |
| TOTAL DIRECT COSTS YEAR 5 ==> | | | | | | | | \$4,941,578 | | |
| COST BASE FOR CALCULATING INDIRECT | | | | | | | | \$413,759 | | |
| INDIRECT COST | | | | | | | | 0.63 \$260,668 | | |
| TOTAL COST | | | | | | | | \$5,202,246 | | |