INFORMED CONSENT
Trial to Assess Chelation Therapy (TACT)

YOU ARE ASKED TO READ THE FOLLOWING FORM TO MAKE SURE THAT YOU COMPLETELY UNDERSTAND WHAT WILL HAPPEN IF YOU AGREE TO TAKE PART IN THIS RESEARCH STUDY. SIGNING THIS FORM MEANS THAT THE STUDY HAS BEEN EXPLAINED TO YOU AND THAT YOU GIVE YOUR PERMISSION TO TAKE PART. THE FEDERAL GOVERNMENT REQUIRES YOUR APPROVAL IN WRITING BEFORE YOU TAKE PART IN ANY RESEARCH STUDY. IT IS IMPORTANT THAT YOU KNOW WHAT WILL TAKE PLACE AND WHAT RISKS ARE INVOLVED BEFORE YOU DECIDE WHETHER OR NOT TO TAKE PART IN THIS STUDY.

1. Why is this research study being done?

You are being asked to take part in a research study to test the effectiveness of chelation therapy for patients who have survived a heart attack. Chelation therapy, as used in this study, consists of up to 40 treatments through a vein in your arm (infusion) of a solution of vitamins and dissolved materials that are thought to bind specific toxic elements circulating in your blood. These elements, known as heavy metals, include iron, copper, and calcium, and may contribute to the development of heart disease. Although the Food and Drug Administration has not approved chelation therapy as an effective treatment for heart disease, chelation therapy has been practiced in the community for many years. The present clinical practice of chelation therapy also involves the use of high-dose antioxidant vitamins, minerals, and nutritional supplements taken by mouth. However, like with chelation therapy, there is no evidence that these supplements are beneficial for patients like you. The Trial to Assess Chelation Therapy (TACT) will test chelation solution versus a placebo (inactive) salt-water solution, and high-dose vitamins and minerals taken by mouth versus low-dose.

This research is being carried out because many people each year receive chelation therapy, and vitamin and mineral supplements, even though there is no reliable evidence of their effectiveness.

2. How many people will take part in the research study?

TACT will involve 2372 patients like you at up to 150 clinical centers.

3. How long will I be in the research study?

Your participation in the study will include up to 28 months of treatment and 5 years of follow-up.

4. What will happen in the research study?

If you agree to take part in this study, you will be scheduled for a screening visit. During this visit, a complete medical history and a simple physical examination will be performed. We will also obtain samples of your blood (two tablespoonfuls) to check your blood cell counts as well as your kidney and liver function. You will be asked questions about how you rate your health, about your activities, how you are feeling emotionally and some questions about your working status, education, and income. We expect this screening visit to take about 90 minutes to carry out. Once the laboratory tests are complete, you will be contacted by the research staff and told whether you are eligible, and, if so, asked to schedule your first infusion visit.

The research staff will call for a treatment assignment and you will be assigned randomly by a computer (by chance) to one of four groups:

You will be assigned to one of these four possible treatment assignments:

Chelation solution + High-dose supplements	Chelation placebo + High-dose Supplements	Chelation solution + Low-dose supplements	Chelation placebo + Low-dose supplements

All patients, including yourself, will receive a total of 40 infusions, beginning with one treatment per week for 30 weeks, followed by an additional 10 treatments given approximately once every 2 weeks to once every 2 months. It will take up to 28 months to complete all the required treatments. Each treatment consists of receiving the solution slowly through a needle in your vein. The needle will be inserted by trained medical personnel under sterile conditions and each infusion will last for 3 hours. You will have blood drawn for laboratory tests during 10 of your visits. Each time, you will have approximately 1 tablespoonful of blood drawn. During each visit, you will be asked how you feel, and whether you have had any symptoms. In addition, the research staff will ask you whether you have had any new heart problems or hospitalizations, and will measure your blood pressure and perform a simple physical exam. Because of the time of the infusions, you should count on being at the clinic for at least 5 hours. If you live far away from your doctor's office, you may spend a lot of time traveling back and forth.

If you are assigned to the chelation group you will intravenously receive a mixture that is a standard mixture established by the American College for Advancement in Medicine.

The components are:

Additive	Role of Additive
Up to 3 grams of EDTA	Chelating agent
2 grams of magnesium chloride	To reduce local discomfort and replace losses
100 mg of procaine HCL	To reduce local discomfort
2500 units of heparin	To reduce local inflammation of veins
7 grams of ascorbate	Anti-oxidant
2 mEq KCl	To replace losses
840 mg sodium bicarbonate	To act as a buffer and reduce discomfort
250mg pantothenic acid	For anti-oxidant properties
100mg of thiamine	For anti-oxidant properties
100mg of pyridoxine	To replace chelation losses

Because chelation therapy may also remove important vitamins and other nutritional elements needed by the body, all patients, including yourself, will be required to take vitamins and nutritional supplements. These supplements will be taken on a daily basis. You will be assigned by chance to receive either high-dose vitamin supplements or low-dose vitamin supplements. Neither you nor the research staff will know to which group you have been assigned. On the day of actual infusion, you will be asked to take these supplements 3-5 hours after the infusion to avoid the possibility of the supplements being removed by the chelation therapy. We will ask you to bring these supplements with you to every infusion visit, to ensure that you are taking them as required.

The high dose vitamin and mineral schedule consists of the following to be taken twice daily:

High Dose Regimen (Taken twice daily)	Total amount you will take compared to the recommended Daily Value
Vitamin A (as fish liver oil and beta-carotene)	10 times
Vitamin C (as calcium ascorbate, magnesium ascorbate and potassium ascorbate)	40
Vitamin D_3 (as cholecalciferol)	_
Vitamin E (as d-alpha tocopheryl succinate and d-alpha tocopheryl acetate)	27
Vitamin K_1 (as phytonadione)	1 _
Thiamin (vitamin B_1) (as thiamin mononitrate)	134
Niacin (as niacinamide and niacin)	20

Vitamin B_6 (as pyridoxine hydrochloride)	50
Folate (as folic acid)	4
Vitamin B_{12} (as cyanocobalamin)	34
Biotin	2
Pantothenic acid (as d-calcium pantothenate)	80
Calcium (as calcium citrate and calcium ascorbate)	Same
Iodine (from kelp)	2
Magnesium (as magnesium aspartate, magnesium ascorbate and magnesium amino acid chelate)	2 _
Zinc (as zinc amino acid chelate)	$2\ ^2/_3$
Selenium (as selenium amino acid chelate)	6
Copper (as copper amino acid chelate)	2
Manganese (as manganese amino acid chelate)	20
Chromium (as chromium polynicotinate)	$3\ ^1/_3$
Molybdenum (as molybdenum amino acid chelate)	4
Potassium (as potassium aspartate and potassium ascorbate)	Less than _
Choline (as choline bitartrate)	There is no Daily Value established for these supplements.
Inositol	
PABA (as para-amino benzoic acid)	
Boron (as boron aspartate and boron citrate)	
Vanadium (as vanadyl sulfate)	
Citrus Bioflavonoids	

All patients assigned to the high-dose set of vitamins will additionally receive a low-dose set of vitamins to be taken once daily. This low-dose schedule is presented in the table below. Patients assigned to the low-dose schedule also take this low-dose set of vitamins and minerals once daily:

Low-Dose Regimen (Taken once daily)	**Total amount you will take compared to the recommended Daily Value**
Vitamin B6(as pyridoxine hydrochloride)	12 _ times
Zinc (as zinc gluconate)	$1\ ^2/_3$
Copper (as copper gluconate)	Same
Manganese (as manganese gluconate)	7 _
Chromium (as chromium picolinate)	Less than _
These supplements are taken in an olive oil based gel capsule.	

In order to make sure patients and their physicians are "blinded" to which group you have been assigned, all patients assigned to the low-dose group will be taking additional placebo pills that are identical to those that the high-dose group is taking. You will be required to take these pills and capsules, up to 12 per day, for the duration of the study.

After the initial enrollment visit, research staff from the Coordinating Center at the Duke Clinical Research Institute may contact you by telephone at 6 months, 1 year and 2 years to ask questions about how you are doing. They will ask if there are any changes in how you feel, in your ability to perform your daily activities, or in your working status. Not everyone in the study will answer these questions. This group of 1000 patients will be chosen by chance. If you are chosen, the information will allow us to understand the effects of the chelation and vitamins on the quality and economics of patients' lives. You will also be asked about any hospitalizations, heart procedures or doctor visits you may have had between study visits to help better understand the costs of your illness. All of these data will be analyzed using coded information without your name or other identifiable information publicized. The calls will take about 15-25 minutes.

After the 40 infusion visits have been completed, research staff from Mount Sinai Medical Center/Miami Heart Institute will call you every 3 months to find out how you are doing and whether you have had any heart problems since the last call. If you have been hospitalized during the follow-up period, it will be necessary for you to sign a release so we can have access to your medical records. In addition, you will be asked to return for a visit each year and at the end of the study. At each visit, you will be asked questions about your medical condition and you will be asked to have an electrocardiogram (ECG) of your heart.

If you are a woman and are able to become pregnant, you are not eligible to participate in this study.

5. Are there any risks or discomforts?

This treatment may cause the side effects listed below. However, there may be some side effects that we cannot predict.

EDTA, or ethylenediamine tetraacetate, is approved for use by the FDA as a treatment for lead poisoning but not for coronary artery disease. It binds heavy metals like lead, copper, and iron, and allows them to be excreted in the urine. EDTA rarely may cause allergies, kidney problems, or if given too quickly may cause low calcium, muscular spasms, heart rhythm problems, and low blood pressure that might be serious. You will be monitored carefully for these side effects. The infusion will be monitored closely so it does not go in too quickly, and your blood pressure will be checked before, during, and after the infusion. If your kidney function is not good, you will not be allowed to

participate in the study. If your kidney function gets worse during the infusions, then the dose of EDTA will be reduced, or the infusions will be stopped. As part of monitoring your kidney function, you will need to inform your study physician if you do not urinate for 12 hours. You may develop flu-like symptoms such as low-grade fevers, sneezing, muscle and joint aches, headaches and watery eyes. These symptoms usually occur 4 to 8 hours after receiving the infusion. These symptoms are usually seen when high doses of EDTA are given, or if the infusion rate is too rapid. Patients with diabetes have been reported to develop low blood sugar during the infusion. For this reason, if you are diabetic, we will ask you to snack before the infusion, and monitor you for symptoms of low blood sugar.

During the infusions, you may experience a "burning-like" sensation at the site of the infusion, or through the vein. Certain medications (such as magnesium and a local anesthetic) are added to the solution to reduce this discomfort.

EDTA has the ability to remove certain vitamins and minerals that are needed by your body. You will be provided with supplements to be taken by mouth that will replace these elements. Although the risk of removal of these minerals is small, this can cause symptoms such as fatigue, dry skin, tingling sensation in your hands and feet, a skin rash, diarrhea, and constipation. EDTA also may reduce the effectiveness of some of the medications you are taking.

As described earlier, magnesium chloride and potassium chloride are included in the infusion solution. Magnesium and potassium are essential salts that are components of all cells in the body. Potassium can cause burning at the site where the intravenous line is placed. However, there are no other likely side effects expected from the doses to be infused.

Vitamins B1, B6, pantothenic acid, and vitamin C also are included in the infusion solution. These essential vitamins have no significant side effects. However, vitamin C is being used at a higher dose than usual.

Heparin, also included in the infusion solution, is a commonly used blood thinner that is used to prevent clotting of the vein used for the intravenous infusion. The principal side effect of heparin at the doses used in this study is an allergy that could lead to bleeding or blood clots. You will be closely monitored for this, and the heparin will be stopped if an allergy seems to occur.

Procaine, also included in the infusion solution, is a local anesthetic that will prevent stinging or discomfort during the intravenous infusions. The main side effect is the possibility of allergy. Sodium bicarbonate is a naturally occurring substance that increases the ability of the kidney to excrete impurities. It is included in the infusion solution.

If your heart is weak, you may be at risk of developing fluid in your lungs as a result of the heart's inability to tolerate the amount of fluid that will be infused. People who already have a history of decreased heart function will be at greater risk. If you have had fluid in your lungs due to a weak heart within the last 6 months, you will not be permitted to participate in the study.

Since chelation therapy is given intravenously, you will have some discomfort at the needle puncture site. There is also a risk of bruising, swelling, and redness developing at the site of the intravenous infusion. Rarely, a serious blood infection may develop that would require antibiotic treatment. It will be important for you to report any pain, swelling, or redness at the site of the needle punctures, as well as any fever or chills, so you may be promptly treated. You may also experience these discomforts when having your blood drawn.

The anti-oxidant vitamin, mineral, and nutrient supplements taken by mouth are generally well-tolerated, taken by millions of people, and have low risks of serious side effects. Beta carotene, however, one of the supplements used, has been associated with a higher rate of cancer in patients who smoke. Smokers are not eligible to participate in this study, and it is important that you not start smoking while you are participating.

Finally, there does remain the risk of serious unanticipated side effects that we cannot predict, because this type of study has never been carried out in so many patients.

For more information about risks and discomforts not listed here, or if you have any questions, ask the researcher or contact Cardiology Research at (305) 674-2162.

6. Are there benefits to taking part in this research study?

If you agree to take part in this study, there may or may not be direct medical benefit to you. We hope the information learned from this study will benefit other patients with coronary artery disease in the future.

7. What other choices do I have if I don't take part in this research study?

If you do not take part in this study, your other cardiac treatments as directed and recommended by your doctor will not be affected. You should use standard medicines for heart attack patients whether or not you participate in this research study.

8. Will I need to pay for the tests and procedures?

You or your insurance company will not be billed for any study-related procedures. They will be provided to you without cost. Should you have a complication of chelation therapy that requires medication or hospitalization, the study and/or its researchers will

be unable to pay for those costs, and you and/or your insurance company will be responsible for the costs resulting from the complication.

9. Will I receive payment for taking part in this study?

You will not be paid to participate in this study.

10. What about confidentiality?

Your role in this research study as well as any information that might identify you with this study (records) will remain confidential to the extent permitted by law. However, the following parties may review your study and medical records without your permission, or the permission of your legal representative, as they deem necessary:

Department of Health and Human Services (DHHS),
United States Food and Drug Administration (FDA),
Duke Clinical Research Institute (DCRI),
Mount Sinai Medical Center of Florida, Inc. including its Institutional Review Board, authorized employees and/or designated agents

All of the above groups are bound to hold this information confidential. Although every effort will be made to keep your information confidential, absolute confidentiality cannot be guaranteed. Your personal information may be disclosed if required by law. The results of this study may be published; however, you will not be identified in these publications.

Organizations that may inspect and/or copy your research records for quality assurance and data analysis include groups such as the National Institutes of Health.

11. Is there compensation for research related injury?

Financial compensation for research-related injury or loss of wages is not available; however, necessary emergency medical care will be provided at Mount Sinai Medical Center. You will be responsible for all costs of this care if not covered by your insurance company.

12. Who can answer my questions?

If you do not understand anything related to this study or have an injury, illness or problem related to your taking part in this study, please contact:

Gervasio A. Lamas, MD
Mount Sinai Medical Center/Division of Cardiology
(305) 674-2162

For questions about your rights as a research participant, contact the Coordinator of the MOUNT SINAI MEDICAL CENTER Institutional Review Board (which is a group of people who review the research to protect your rights) at (305) 674-2790.

13. What are my rights if I take part in this research study?

Taking part in this study is voluntary. You may choose not to take part or may leave the study at any time. Leaving the study will not result in any penalty or loss of benefits to which you are entitled. This will not affect your continued medical care and treatment by your doctor. Your doctor may ask you to leave this study if he/she feels it is appropriate or necessary. Your doctor will notify you if this should occur. This in no way will affect your continued medical care and treatment by your physician. Should you decide to discontinue your study participation early, you are asked to contact Geravsio A Lamas, MD to arrange for final study visit procedures. In addition your participation in this study may be terminated by the investigator or by the sponsor without regard to your consent if either party believes it to be in your best interest. Such conditions may include, but are not limited to, a serious adverse reaction, a worsening of your condition, or lack of cooperation on your part.

A Data Safety and Monitoring Board, an independent group of experts, will be reviewing the information from this research throughout the study. We will tell you about the new information from this or other studies that may affect your health, welfare, or willingness to stay in this study.

The results of this study may be published ; however, you will not be identified in these publications.

14. I HAVE READ THIS INFORMED CONSENT FORM AND HAVE BEEN GIVEN THE OPPORUNITY TO DISCUSS AND ASK QUESTIONS ABOUT THIS RESEARCH STUDY. I HAVE ALSO RECEIVED A COPY OF THIS INFORMED CONSENT FORM AND AGREE TO PARTICIPATE.

Printed Name, Address & Telephone No of Participant:

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Signature of Participant Date

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Printed Name of Witness Date Signature of Witness Date

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Signature of Principal Investigator Date
or Designated Representative