School of Medicine

Eckhard U. Alt MD PhD
Professor of Medicine
Director of Cardiovascular Research
Heart and Vascular Institute
Department of Medicine

May the 1st 2019

To the Editors of the
World Journal of Stem Cells

Re: Manuscript WJSC 46609 "*Unmodified autologous stem cells at point of care for chronic myocardial infarction*" by A. Haenel, M. Ghosn, T. Karimi, J. Vykoukal, D. Shah, M. Valderrabano, D. Schulz, A. Raizner, C. Schmitz and E. Alt

Here: support by the Alliance of Cardiovascular Researchers (New Orleans, LA 70112, USA) to Mr. Alexander Haenel

The Editor who is handling our manuscript has stated that „*The approved grant application form(s) will be released online together with the manuscript in order for readers to obtain more information about the study and to increase the likelihood of subsequent citation. Our purpose of publishing the approved grant application form(s) is to promote efficient academic communication, accelerate scientific progress in the related field, and improve productive sharing of research ideas. In addition, a copy of the full approved grant application form(s), consisting of the information section and body section, should be provided to the BPG in PDF format*."

In this connection, we would like to make the following statement:

The Alliance of Cardiovascular Researchers (1010 Common St #1810, New Orleans, LA 70112, USA) (henceforth: „Alliance") is a medical research organization (U.S. National Taxonomy of Exempt Entities Code H43 [Specific Organ Research: Heart and Circulatory]; https://www.guidestar.org/profile/72-1502598) that supports heart and circulatory research. The Alliance does not make use of grant application forms. Rather, it supports on a case-by-case basis medical research based on approved IACUC/IRB protocols that are brought forward to the Alliance by individual researchers.

In the case of this project IACUC protocol No. AUP-0910-0019 / IS00000596 titled „Stem Cell Injection in a Myocardial Infarcted Pig Heart" by A. Raizner, E. Alt, D. Amish, M. Valderrabano, D. Schulz, J. Vykoukal and D. Shaw (except of D. Amish all of these colleagues are co-authors of Manuscript WJSC 46609) was approved by The Methodist Hospital Research Institute (Houston, TX 77030, USA) on January 05, 2011.

In the Fall of 2013, Mr. Alexander Haenel (at that time medical student at the University of Luebeck [Luebeck, Germany]; first author of Manuscript WJSC

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46609) met Dr. Eckhard U. Alt (senior author of Manuscript WJSC 46609) at a scientific conference in Germany. During this meeting Mr. Haenel expressed his interest in heart and circulatory research to Dr. Alt, and Dr. Alt introduced the aforementioned research project (based on approved IACUC protocol No. AUP-0910-0019 / IS00000596) to Mr. Haenel. Mr. Haenel and Dr. Alt agreed that Mr. Haenel shall come in the framework of a foreign student exchange to Tulane University (New Orleans, LA 70112, USA) where certain parts of the aforementioned research project were carried out under the supervision of Dr. Alt (after all animal experiments had been peformed at The Methodist Hospital Research Institute (Houston, TX, USA)). Then, Dr. Alt brought forward the approved IACUC protocol No. AUP-0910-0019 / IS00000596 to the Alliance; the Alliance approved funding (of a monthly stipend to Mr. Haenel from March 15, 2014 to March 15, 2015) on December 28, 2013; and Mr. Haenel obtained his J1 visa for performing this research at Tulane University on February 20, 2014.

We have uploaded the following documents to BPG (next pages of this file) when submitting revised manuscript WJSC 46609 titled "*Unmodified autologous stem cells at point of care for chronic myocardial infarction*" to the World Journal of Stem Cells:

- approved IACUC protocol No. AUP-0910-0019 / IS00000596 titled „*Stem Cell Injection in a Myocardial Infarcted Pig Heart*" by A. Raizner, E. Alt, D. Amish, M. Valderrabano, D. Schulz, J. Vykoukal and D. Shaw;
- the corresponding approval letter by James Davis, Ph.D., then IACUC Chair of The Methodist Hospital Research Institute (Houston, TX 77030, USA);
- a copy of Mr. Haenel's J1 visa; and
- the letter of funding by the Alliance of Cardiovascular Researchers.

Sincerely yours,

Eckhard Alt MD PhD

Alexander Haenel MD

Staff Identification

1. * Study Title:
   Stem Cell Injection in a Myocardial Infarcted Pig Heart
2. * Principal Investigator:
   Albert Raizner
3. * Primary Study Contact:

4. * Study Coordinator:
   Daryl Schulz
5. Please list staff who will be handling animals:
   Loading...

	Last Name	First Name					Date Created	Date Modified
			Title: Physician	**CITI Completion Date:** 5/27/2015	**CMP Orientation:**	**OHP Clearance:** 6/21/2011		
View	Raizner	Albert	**Years of experience working with animals:** **Responsibilities on this study:** **Please explain 'Other' Responsibilities on this study** **Relevant training and experience per species for the activities checked above and any non-surgical or surgical procedures to be performed on this protocol. (if none, who will train you?):**				8/16/2010	8/16/2010
View	Alt	Eckhard	**Title:** Sub investigator	**CITI Completion Date:** 4/22/2014	**CMP Orientation:** 12/30/2010	**OHP Clearance:** 3/5/2015	8/16/2010	8/16/2010

			Years of experience working with animals: **Responsibilities on this study:** **Please explain 'Other' Responsibilities on this study** **Relevant training and experience per species for the activities checked above and any non-surgical or surgical procedures to be performed on this protocol. (if none, who will train you?):**					
View	Dave	Amish	**Title:**	**CITI Completion Date:** 3/20/2018	**CMP Orientation:** 6/14/2010	**OHP Clearance:** 3/6/2019	8/16/2010	8/16/2010
			Years of experience working with animals: **Responsibilities on this study:** **Please explain 'Other' Responsibilities on this study** **Relevant training and experience per species for the activities checked above and any non-surgical or surgical procedures to be performed on this protocol. (if none, who will train you?):**					
View	Valderrabano	Miguel	**Title:** Division Head, Cardiac Electrophysiology	**CITI Completion Date:** 4/16/2018	**CMP Orientation:**	**OHP Clearance:** 3/29/2019	8/16/2010	8/16/2010
			Years of experience working with animals: **Responsibilities on this study:** **Please explain 'Other' Responsibilities on this study** **Relevant training and experience per species for the activities checked above and any non-surgical or surgical procedures to be performed on this protocol. (if none, who will train you?):**					

View	Schulz	Daryl	**Title:** Lab Manager	**CITI Completion Date:** 2/22/2018	**CMP Orientation:**	**OHP Clearance:** 2/20/2019	8/16/2010	8/16/2010
			Years of experience working with animals:					
			Responsibilities on this study:					
			Please explain 'Other' Responsibilities on this study					
			Relevant training and experience per species for the activities checked above and any non-surgical or surgical procedures to be performed on this protocol. (if none, who will train you?):					
View	Vykoukal	Jody	**Title:** Subinvestigator	**CITI Completion Date:** 10/25/2010	**CMP Orientation:** 12/1/2010	**OHP Clearance:** 12/14/2010	8/16/2010	8/16/2010
			Years of experience working with animals:					
			Responsibilities on this study:					
			Please explain 'Other' Responsibilities on this study					
			Relevant training and experience per species for the activities checked above and any non-surgical or surgical procedures to be performed on this protocol. (if none, who will train you?):					
View	Shah	Dipan	**Title:** Physician	**CITI Completion Date:** 1/18/2011	**CMP Orientation:** 1/14/2011	**OHP Clearance:** 4/30/2012	1/24/2011	1/24/2011
			Years of experience working with animals:					
			Responsibilities on this study:					
			Please explain 'Other' Responsibilities on this study					
			Relevant training and experience per species for the activities checked above and any non-surgical or surgical procedures to be performed on this protocol. (if none, who will train you?):					

6. Please list staff who will not be handling animals:

Last Name	First Name	Date Created	Date Modified
There are no items to display			

View: 2. Study Information

Current State: Expired

Date Entered State:1/5/2011 1:46 PM

ID:IS00000596

2. Study Information

1. * Lay Summary (Provide a brief statement understandable by someone with a high school education, with no acronyms or scientific jargon outlining the purpose and potential benefits of this research or project. Maximum of 250 words):
   Myocardial infarction (MI, heart attack) is characterized by reduced blood supply to the heart and loss of functioning cardiomyocytes (cells that form the heart muscle). After an MI, portions of the heart muscle will become necrotic (dead) and could progress to heart failure if not treated. One experimental treatment after an MI is the injection of stem cells into the affected heart muscle in order to regenerate heart tissue. Stem cells are found in all multi-cellular organisms and act as a repair system for the body, replenishing specialized cells like muscle cells (myocytes). Bone marrow is commonly used as a source of stem cells, however, adult stem cells are also found in other tissues, including fat (adipose) tissue. Stem cells recovered from fat tissue are termed adipose tissue-derived stem cells (ASCs). In previous animal studies, we showed that delivery of ASCs into infarcted heart muscles results in improved cardiac function. In this study, we propose to evaluate the effectiveness of delivering ASCs into an infarcted pig heart muscle through a collection of blood vessels that receive deoxygenated blood from the heart muscle known as the coronary sinus. The cardiac function will then be assessed several weeks after treatment. This is

a straightforward and unique way to deliver the stem cells to the heart that could potentially be highly effective and that could be easily adapted to clinical use if successful.

2. * Is this a 3 yr Resubmission of an approved protocol? ○ ○ Yes ◉ ◉ **No**

   If yes, What progress have you made within the past three years?

   Previous AUP#: **New Question**

View: 3. Funding

Current State: Expired

Date Entered State:1/5/2011 1:46 PM

ID:IS00000596

3. Funding

1. * Please select the appropriate funding source for your animal research:

Funding Type	Description
Non-Profit or Foundation	

2.

3. 1.1 Please attach a copy of your grant research plan here.

Name	Version
There are no items to display	

4.
5.

1.2 Who is the PI for the Grant?

1.3 If Other, please name:

6. Sponsor:

If not listed, please type the name of the sponsor below:

Address:

City:

State:

ZipCode:

Country:

Phone:

7. Other Sponsors:

Name	Category	Website	E-Mail
There are no items to display			

8. Select your Office of Sponsored Projects ID for this research:

Name	Principal Investigator	Status
There are no items to display		

9. Other Sponsor Information:

View: 4. Research Procedures Summary

Current State: Expired

Date Entered State:1/5/2011 1:46 PM

ID:IS00000596

4. Research Procedures Summary

1. * Provide your overall purpose and objectives for the study. Include a brief description of what will happen to the animals. Give a timeline of events including when agents will be administered, when procedures will be conducted, and study

endpoints:
The primary goal of this project is to evaluate the effectiveness of adipose tissue-derived stem cells (ADCs) in regenerating functional myocytes in a porcine model of myocardial infarction. We propose using ventriculargraphy, cardiac MRI, electro-anatomical mapping and ventricular vulnerability testing to evaluate the autotransplantation and compare it to control animals that will receive saline injection instead of the stem cells.

The flow of the study for both test and control animals will be:
1. Create myocardial infarction
2. 4-6 weeks later, inject stem cells or saline
3. 4 weeks later , evaluate ventricular function/termination

1. Myocardial infarction induction:

The animal is prepped and a cardiac catheterization is performed as described in section 6.13. Blood may be obtained for baseline blood workup. Using coronary angiography, a suitable location is selected in the left anterior descending coronary artery (LAD) distal to the major diagonal branch of the LAD. Being distal to the diagonal branch will create a more focal MI and increase the chances of survival during and after the creation of the MI. A properly sized coronary angioplasty balloon is advanced over a coronary guide wire to the selected section of the LAD and is inflated for 3 hours. This type of MI induction has been successfully performed by Dr. Alt in several porcine studies. The animal is closely watched for arrhythmias and is treated with antiarrhythmic drugs should they occur. After 3 hours of inflation time, the balloon is deflated and post-MI angiograms and ventriculargrams are performed. The catheters and sheaths are removed and the animal is recovered as described in section 6.13. No cardiac MRI or electro-anatomical mapping is performed during this procedure.

2. Adipose harvest and stem cell administration: Performed at 5 weeks +/- 7 days post-MI.

The animal is transported with security personnel to Cardiac MRI in the Endovascular Suite of the Radiology Department via an IACUC approved route. The Cardiac MRI room is located on the 2nd floor of the Main Building of TMH in room MB251.The animal is prepped and placed under general anesthesia before transportation as described in Section 6.13. Gadolinium is infused through the IV and a post-MI cardiac MRI is performed. After the MRI, the animal is transported with security personnel to the 6th floor vivarium for extubation and recovery, or taken directly to the pre-clinical catheterization lab (F642) for the 2nd catheterization.
Note: Cardiac MRI is performed by Dr. Dipan Shah outside of normal working hours. If possible the MRI procedure will be coordinated with the catheterization procedure to eliminate the need for additional sedation and general anesthesia.

The animal is prepped for cardiac catheterization as described in section 6.13. Blood may be obtained for post-MI blood workup. Adipose tissue is removed from the animal, placed in a sterile specimen container, covered with a sterile towel and delivered down the hall to room F650 where it is processed under a laminar air flow hood to retrieve the stem cells as described in section 6.13 and in an uploaded protocol in section 4.1. Stem cell isolation is performed by Dr. Alt's molecular pathology team who are specially trained and have performed the isolation process many times with human and porcine adipose tissue. During the isolation process, coronary angiography and left ventriculargraphy is performed. An electro-anatomical map of the left ventricle (LV) is performed by Dr. Valderrabano and/or Dr. Dave. A guide catheter is placed in a venous sheath and is advanced to the coronary sinus (CS) over a guide wire. Once in place in the CS, an angioplasty balloon is advanced over the wire and positioned in the distal portion of the coronary sinus that receives deoxygenated blood from the area of the infarcted heart muscle. The balloon is inflated, the wire is removed, and the stem cells are injected through the wire lumen. Normal saline will be injected in the same manner for the control animals. 1.0 X 106 stem cells/kg in 10 ml saline is infused at a rate of ~ 0.25 ml/s. The catheters and sheaths are removed and the animal is recovered as described in section 6.13.

3. Terminal procedure: 4 weeks after stem cell administration.

The animal is transported with security personnel to Cardiac MRI in the Endovascular Suite of the Radiology Department via an IACUC approved route. The animal is prepped and placed under general anesthesia before transportation as described in Section 6.13. Gadolinium is infused through the IV and a post-MI cardiac MRI is performed. After the MRI, the animal is transported with security personnel to the 6th floor vivarium for extubation and recovery, or taken directly to the pre-clinical catheterization lab (F642) for the 2nd catheterization.
The animal is prepped for cardiac catheterization as described in section 6.13. Blood may be obtained for post-stem cell administration blood workup. Coronary angiography and left ventriculargraphy is performed. An electro-anatomical map of the left ventricle (LV) is performed by Dr. Valderrabano and/or Dr. Dave. Ventricular vulnerability testing is performed by placing a bipolar pacing catheter through a venous sheath to the right ventricle. Programmed stimulation protocol for the induction of ventricular arrhythmias is performed using a train of 8 S1 stimuli (interval 500 and 400 ms) and up to three extra-stimuli applied from the right ventricular apex and right ventricular out-flow tract. Ventricular cycle length will be measured at 1 and 10 seconds via the right ventricular mapping catheter. The catheters are removed and the animal is euthanized. The heart and select organs are explanted to retrieve the anatomical specimens needed for histology. The animal carcass is disposed of in accordance to CMP standard operating procedure.

Amendment 6:In this amendment, fat will be harvested during the first surgical procedure in 3-4 animals, prior to induction of the infarction, so that adipose tissue derived cells can be prepared and labeled for re-administration during a second surgical period. The adipose-tissue derived stem cells will be transfected to produce EGFP (Enhanced Green Fluorescent Protein),

mCherry (a red fluorescent protein), or Luciferase (an enzyme that catalyzes the bioluminescent oxidation of Luciferin substrate) using a non-viral, transposon-mediated gene transfer approach developed by Dr. Richard Behringer at MD Anderson Cancer Center (paper included as attachment). After four weeks, we will have stable, antibiotic-selected cultures of marker protein expressing cells from each pig, sufficient in number for reinjection. The Luciferase labeling has the benefit that we can exactly and quantitatively determine by injection of Luciferin the presence of living cells over time.

Four to six weeks after the initial induction of the infarction, the labeled stem cells will be administered during the second surgical procedure. This is the same typical second procedure as we currently perform, with the exception that no adipose tissue will be harvested since this will have been done during the first surgical period. As the primary purpose of this experimental subset is to better understand engraftment and proliferation of the therapeutic stem cell dose, we do not anticipate performing extensive functional assessments using methods such as MRI or electroanatomical mapping since, for this follow-up the coronary angiograms and the ventriculograms before and after the induction of the infarction will be sufficient.

The pigs will be followed-up for four to six weeks after the injection of cells, at that time another angiogram and a ventriculogram will be performed. At the end of the study the heart will be taken out for histology and molecular work-up. An epi-fluorescent microscope is used to visualize the engrafted fluorescent proteins on histology sections. Assessment of the various factors will be done as far as differentiation of the labeled stem cells to cardiomyocyte its concerns, the replication rate, doubling rate, apoptosis rate as indicated by markers such as Ki-67, Troponin-T, Troponin-I, Alpha Actinin, Smooth - Muscle Actin, and others. We also will study if the injected cells will engraft and differentiate to vessels, to express extracellular matrix by the respective immunuhistochemistry assessment as published and described by our group previously.

Example:

- Day 0 - Acquire mice from vendor and allow 3 day acclimation period.
- Day 3 - Feed them a high fat diet for 3 months measuring weights weekly.
- @ 2 months, each group will receive 1 of 4 concentrations of drug x.
- @ Day 30, 60, and 90, time points we will draw blood.

2. * Provide your humane endpoints for each of the experiments listed in #1 including euthanasia criteria.

3. Diagrams/Flowcharts:

Name	Version
Behringer Article	0.01

5.

View: 5. Animal Species/Strain/Number

Current State: Expired

Date Entered State:1/5/2011 1:46 PM

ID:IS00000596

5. Animal Species/Strain/Number

1. * Why are you using animals for these experiments as opposed to alternative methods?
   Live animals are needed to achieve our research goals. No non-animal substitute can replicate the myocardial infarction and subsequent heart failure required to evaluate the regenerative properties of the stem cells.
2. In the table, list the species, strain, clinically relevant phenotype, quantity you are requesting per strain, and indicate if you are using the animals for experimentation or breeding:

Species				Date Created	Date Modified
Pigs	**Strain:** Domestic	**Clinically Relevant phenotype (Example: Eventual Paralysis)** null **Purpose of these animals? (Breeding, experiments, etc):** null **Total number of this strain requested:** 16	**Total Number of animals requested per species:** 16	8/25/2010	8/25/2010

		Rationale for using this species/strain: null			
Pigs	**Strain:** Domestic	**Clinically Relevant phenotype (Example: Eventual Paralysis)** null **Purpose of these animals? (Breeding, experiments, etc):** null **Total number of this strain requested:** 6 **Rationale for using this species/strain:** null	**Total Number of animals requested per species:** 6	5/18/2011	5/18/2011
Pigs	**Strain:** Domestic	**Clinically Relevant phenotype (Example: Eventual Paralysis)** null **Purpose of these animals? (Breeding, experiments, etc):** null **Total number of this strain requested:** 6 **Rationale for using this species/strain:** null	**Total Number of animals requested per species:** 6	8/5/2011	8/5/2011
Pigs	**Strain:** Domestic	**Clinically Relevant phenotype (Example: Eventual Paralysis)** null	**Total Number of animals requested per**	11/19/2011	11/19/2011

		Purpose of these animals? (Breeding, experiments, etc): null **Total number of this strain requested:** 4 **Rationale for using this species/strain:** null	**species:** 4			
Pigs	**Strain:** Domestic	**Clinically Relevant phenotype (Example: Eventual Paralysis)** null **Purpose of these animals? (Breeding, experiments, etc):** null **Total number of this strain requested:** 3 **Rationale for using this species/strain:** null	**Total Number of animals requested per species:** 3		3/29/2012	3/29/2012

3.

Species	Strain	# Requested
Pigs	Domestic	35

4.

5. * Why do you need this number of animals?
Previous studies involving various treatments in myocardial infarcted swine demonstrate that 6-8 animals per group has consistently been sufficient to detect statistically significant differences between a treated group and a control group with 80% probability where $p<0.05$ is taken as significant.

Amendment 4: Our experiments on the first group of 8 animals produced early deaths in 3 animals. One animal died during the MI procedure, one animal died 2 weeks after the MI, and one animal had a degenerative bone abnormality of the front leg that

required the animal to be euthanized. This amendment would replace the 3 animals lost in the first 8 studies and add 3 animals to the second group of 8 animals in the event of early deaths.

Amendment 5: After completion and termination of the 1st set of animals, 2 animals were excluded from the protocol requiring an amendment to add more animals in order to complete the study. One was excluded because the stem cell injection was performed differently than the others, and one had developed what appeared to be hypertrophic cardiomyopathy, making the post-procedure data useless.
Also after review of our outcomes so far, we have a better understanding of how many animals will be needed to complete the study. Below is an overview and rationale for the number of animals we are requesting.
Of the 22 animals approved (protocol and Amendment 4), 21 animals have been used for the study as of this amendment. 5 animals had early death after MI, 1 died from complications during the stem cell surgery and 2 were excluded after termination as noted above. Of the 13 animals left, 4 have been terminated and deemed acceptable for the study and 9 are in various stages of the study. If the 9 animals alive are included in the final study numbers, we would need 3 more animals to complete the study. Considering a 25% mortality rate after MI, we request 4 animals in order for 3 to survive the MI induction. Also in anticipation of future animal exclusions due to circumstances revealed after termination, we would anticipate needing 3 additional animals for a total of 7 animals to complete the study. We have 1 animal left on the protocol; therefore we are requesting 6 animals for Amendment 5.
As a note on the excluded animals, we were able to utilize some of the data obtained, especially from the MRI and cardiac mapping analysis.

AMENDMENT 6 : The additional 3-4 animals will be used to assess engraftment and proliferation of transplanted cells using the already established chronic MI model. These data will supplement that from the earlier groups, and thus a reduced number of animals is required for this component of the study. All animals will be injected with labled cells. Four animals are requested to ensure that this substudy yields at least triplicate data due to a possible 25% mortality rate.

Amendment 7: After a comprehensive review of the data from all experiments in 19 animals that survived to the endpoint, we would like to add 3 more animals to the stem cell protocol to replace 3 animals our data concluded received up to five times less the number of stem cells. Improvements in processing the adipose tissue have yielded many times more stem cells than in our earlier experiments. The earlier experiments still gave us valuable MI, mapping and MRI data, however, for us to achieve statistical significance with groups that received comparable amounts of stem cells we are requesting these additional animals.

6. Document Collection:

Name	Version
There are no items to display	

7.

View: 6. External Site Use and Transportation

Current State: Expired

Date Entered State:1/5/2011 1:46 PM

ID:IS00000596

6. External Site Use and Transportation

1. * Will the animals be transported to a location outside the vivarium? **Yes** No

   NOTE: Animal use outside of the 3rd or 4th floor vivarium requires IACUC inspection/approval. Please contact Maya Justilian to arrange the inspection. Prior to inspection, all areas must be ready for animal use.
2. Why do you have to take the animals outside the vivarium?
   Angiographic imaging and electro-anatomic mapping can only be performed in the Pre-clinical Catheterization Laboratory in room F642. Cardiac MRI can only be performed in the cardiac MRI suite located on the 2nd floor of the Main building of The Methodist Hospital.
3. Where are you taking the animals? **New Question**

4. Attach the relevant cleaning SOP for the area:

Name	Version
There are no items to display	

5.
6. How will you contain the animals during transport?
   Transportation to the catheterization lab is performed while the animal is under general anesthesia. A special cart is used to transport the covered animal.
   Transportation to the cardiac MR suite is also performed under general anesthesia. The animal is transported on a special cart and is performed after hours with security clearance.
7. What is the specific route you will take to move the animals from the vivarium to the location?
   Transportation to the catheterization lab is through a secured hallway that connects the 6th floor vivarium to the lab.
   Transportation to the cardiac MR suite is detailed in the IACUC approve route which has been uploaded in section 4.1

View: 7. Animal Disposition

Current State: Expired

Date Entered State:1/5/2011 1:46 PM

ID:IS00000596

7. Animal Disposition

1. Indicate what you will do with the animal at the end of the study: (One of the below 3 options must be checked)

   Euthanasia: Complete the table below (Please use these links, TMHRI Euthanasia of Large Animal Procedure, TMHRI Euthanasia of Rodents Procedure, to reference recommended agents with dosing information): CMP will administer euthanasia on all USDA covered species.

	Species	Primary Method	Agent	Dosage	Route of Administration.Route	Method of Verification of Death
View	Pigs	IV injection of Pentobarbital/Phenytoin combination administered by CMP staff in conjunction with isoflorane overdose.	Beuthanasia or Euthasol	1 ml/10 lbs BW		
View	Pigs	Intravenous injection of KCL administered by CMP staff in conjunction with isoflorane overdose	Potassium Chloride	2 meq/kg		

1. Euthanasia: Does the above deviate from the AVMA guidelines (Example: Cervical Dislocation without anesthesia)?: ○ Yes ◉ **No**
   - a. If Yes. Justification (Proficiency demonstration is required)

☐ Transfer to another AUP

2. Please provide the AUP #(s) these animals will be transferred to:

☐ Death without euthanasia is planned for this study? Death without euthanasia is highly discouraged.

3. **Give a detailed justification for the use of "Death as an Endpoint":**

☐

View: Research Procedures Checklist

Current State: Expired

Date Entered State:1/5/2011 1:46 PM

ID:IS00000596

Research Procedures Checklist

1. Research Procedures: (Please check all procedures to be performed in this protocol)

Name	Description
Substance/Agent Administration	Any substance which will be administered to animals, including topical substances. Excludes agents listed in the non-surgical procedures, surgical procedures, tissue/cell administration, or radiation exposure
Animal Exposure: Radiation	This should be selected any time you will expose an animal to radiation.
Food/Water Regulation	Includes any variation in the frequency or amount of food or water given for research purposes, this does not include fasting for pre- surgical prep. Example: An animal normally fed ad libitum, is restricted to twice daily. Food and Fluid Regulation
Fluid (Blood, urine, saliva, etc)/Specimen Collection combination	Select this for all peri-mortem specimen collection, fluid or tissue collection.
Surgical Procedure	
Specimen Collection	

View: 11. Alternatives to Painful/Distressful Procedures

Current State: Expired

Date Entered State:1/5/2011 1:46 PM

ID:IS00000596

11. Alternatives to Painful/Distressful Procedures

1. * What steps have you taken to reduce the number of animals you will use in this study? (Ex: Power analysis, in vitro work, improving technique, prior experience, literature, etc)
   We will use only the minimal number of animals it takes to prove a statistical significance between test and control data. This number will be determined by examining the animal numbers of previous MI and stem cell animal studies performed by Dr. Alt and other investigators that have achieved statistical significance in test vs.control data.
2. * What steps have you taken to reduce the amount of pain or distress experienced by the animals? Ex: Improving techniques, analgesia/anesthesia regimen, etc)
   All laboratory animal users will comply with institutional and federal guidelines and regulations to assist them in carrying out their responsibilities for the humane care and use of animals in research projects. The Policy of Humane Care and Use of Laboratory Animals, and the Guide for the Care and Use of Laboratory Animals are available in the laboratory for training purposes. The principle investigator for this project is appropriately trained to perform all experimental manipulations described by this protocol in accordance to the ethical standards described by federal regulations. The investigator gives unqualified assurance that ALL laboratory personnel will receive high quality training to minimize animal discomfort.the pain producing procedures have been modified by the addition of analgesics. In addition, this protocol incorporates a multimodal analgesic regimen and all meds are given pre-emptively to prevent ramp up.
3. Literature Search for alternatives to painful or distressful procedures and whether this is duplicative research or not. (*Required for pain category D or E only*.) This search is required to evaluate the possibilities of reduction, refinement, and reuse according to Federal requirements.

   3.1 Name of databases searched (Please search more than 1):
   Pubmed

* 3.2. Date of the search: From: 8/18/2010 - * To:

* 3.3. What keywords were used?
stem cell administration, porcine, adipose tissue-derived cells, coronary sinus injection, myocardial infarction, heart failure

* 3.4. Summarize the types of articles found and how they relate to your study:
Several articles are published regarding stem cell administration in animals for MI and heart failure in an attempt to regenerate myocytes and improve ventricular function after an MI. Many of the articles were published by Dr. Alt. There are no studies utilizing fresh adipose tissue-derived stem cells and administering them to the myocardium via the coronary sinus.

* 3.5 Were there any alternatives to painful or distressful procedures found? ○ ○ Yes ◉ ◉ **No**

3.5.1 If yes, please provide justification for not using the alternatives found:

4. * Does this project duplicate any previous research? ○ ○ Yes ◉ ◉ **No**

   4.1. If yes, please explain.

View: Substance/Agent Administration

Current State: Expired

Date Entered State:1/5/2011 1:46 PM

ID:IS00000596

Substance/Agent Administration

1. Any substance which will be administered to animals for experimental purposes, including topical substances. Excludes agents listed in the pain assessment section (surgical and non-surgical), tumor tissue/cells, or radiation exposure

	Agent Name			Date Created	Date Modified
View	Eptifibatide (Integrillin)	**Type of Agent:**:	null		
		Species you will administer it to:	Pigs		
		Dose:	180 mcg/kg		
		Frequency:	Once		
		Duration of Administration?			
		Route of administration:			
		if other route, list:			
		Is it Pharmaceutical Grade?:			
		If using a non-pharmaceutical grade agent, please provide justification for its use:			
		Per the MSDS or the BIMBL, is this agent considered Hazardous to humans?:			
		What is the danger to Humans?:			
		Do you have a procedure in your Laboratory Specific Safety Manual for the use of this agent?:			
		What is the frequency and duration of observation of animals post administration?:			
		What clinical signs may be seen due to administration of this agent?:			

What criteria are used to determine the need for treatment or euthanasia? :

If treatment is required, how will you treat these clinical signs?:

Are there any special requirements for animal disposal?:

How will you notify animal care personnel of the hazards associated with this agents?:

Exposure Management:

What precautions will you take during the administration of the agent? :

What special handling should be used post administration? Are there any risks to animal care personnel? What should they be aware of in handling animals associated with these agents?:

Is there any special training required for animal care personnel?:

What precautions will you take during necropsy/specimen collection? :

Do you have an HSC protocol?:

If Yes, please select HSC:

Do you have an IBC protocol?:

If Yes, please select IBC:

View Plavix

Type of Agent::	null
Species you will administer it to:	Pigs
Dose:	225 mg
Frequency:	daily

Duration of Administration?

Route of administration:

if other route, list:

Is it Pharmaceutical Grade?:

If using a non-pharmaceutical grade agent, please provide justification for its use:

Per the MSDS or the BIMBL, is this agent considered Hazardous to humans?:

What is the danger to Humans?:

Do you have a procedure in your Laboratory Specific Safety Manual for the use of this agent?:

What is the frequency and duration of observation of animals post administration?:

What clinical signs may be seen due to administration of this agent?:

What criteria are used to determine the need for treatment or euthanasia? :

If treatment is required, how will you treat these clinical signs?:

Are there any special requirements for animal disposal?:

How will you notify animal care personnel of the hazards associated with this agents?:

Exposure Management:

What precautions will you take during the administration of the agent? :

	What special handling should be used post administration? Are there any risks to animal care personnel? What should they be aware of in handling animals associated with these agents?:	
	Is there any special training required for animal care personnel?:	
	What precautions will you take during necropsy/specimen collection? :	
	Do you have an HSC protocol?:	
	If Yes, please select HSC:	
	Do you have an IBC protocol?:	
	If Yes, please select IBC:	
	Type of Agent::	null
	Species you will administer it to:	Pigs
	Dose:	50 mg
	Frequency:	as needed for ventricular arrythmias
	Duration of Administration?	
View	Amiodarone **Route of administration:**	
	if other route, list:	
	Is it Pharmaceutical Grade?:	
	If using a non-pharmaceutical grade agent, please provide justification for its use:	
	Per the MSDS or the BIMBL, is this agent considered Hazardous to humans?:	
	What is the danger to Humans?:	

Do you have a procedure in your Laboratory Specific Safety Manual for the use of this agent?:

What is the frequency and duration of observation of animals post administration?:

What clinical signs may be seen due to administration of this agent?:

What criteria are used to determine the need for treatment or euthanasia? :

If treatment is required, how will you treat these clinical signs?:

Are there any special requirements for animal disposal?:

How will you notify animal care personnel of the hazards associated with this agents?:

Exposure Management:

What precautions will you take during the administration of the agent? :

What special handling should be used post administration? Are there any risks to animal care personnel? What should they be aware of in handling animals associated with these agents?:

Is there any special training required for animal care personnel?:

What precautions will you take during necropsy/specimen collection? :

Do you have an HSC protocol?:

If Yes, please select HSC:

Do you have an IBC protocol?:

If Yes, please select IBC:

View Omnipaque

Type of Agent::	null
Species you will administer it to:	Pigs
Dose:	100 - 250 ml
Frequency:	as needed to visualize vascular anatomy
Duration of Administration?	
Route of administration:	
if other route, list:	
Is it Pharmaceutical Grade?:	
If using a non-pharmaceutical grade agent, please provide justification for its use:	
Per the MSDS or the BIMBL, is this agent considered Hazardous to humans?:	
What is the danger to Humans?:	
Do you have a procedure in your Laboratory Specific Safety Manual for the use of this agent?:	
What is the frequency and duration of observation of animals post administration?:	
What clinical signs may be seen due to administration of this agent?:	
What criteria are used to determine the need for treatment or euthanasia? :	

If treatment is required, how will you treat these clinical signs?:

Are there any special requirements for animal disposal?:

How will you notify animal care personnel of the hazards associated with this agents?:

Exposure Management:

What precautions will you take during the administration of the agent? :

What special handling should be used post administration? Are there any risks to animal care personnel? What should they be aware of in handling animals associated with these agents?:

Is there any special training required for animal care personnel?:

What precautions will you take during necropsy/specimen collection? :

Do you have an HSC protocol?:

If Yes, please select HSC:

Do you have an IBC protocol?:

If Yes, please select IBC:

View Eptifibatide (Integrillin)

Type of Agent::	null
Species you will administer it to:	Pigs
Dose:	2 mcg/kg/min
Frequency:	as needed
Duration of Administration?	
Route of administration:	

if other route, list:

Is it Pharmaceutical Grade?:

If using a non-pharmaceutical grade agent, please provide justification for its use:

Per the MSDS or the BIMBL, is this agent considered Hazardous to humans?:

What is the danger to Humans?:

Do you have a procedure in your Laboratory Specific Safety Manual for the use of this agent?:

What is the frequency and duration of observation of animals post administration?:

What clinical signs may be seen due to administration of this agent?:

What criteria are used to determine the need for treatment or euthanasia? :

If treatment is required, how will you treat these clinical signs?:

Are there any special requirements for animal disposal?:

How will you notify animal care personnel of the hazards associated with this agents?:

Exposure Management:

What precautions will you take during the administration of the agent? :

What special handling should be used post administration? Are there any risks to animal care personnel? What should they be aware of in handling

	animals associated with these agents?:	
	Is there any special training required for animal care personnel?:	
	What precautions will you take during necropsy/specimen collection? :	
	Do you have an HSC protocol?:	
	If Yes, please select HSC:	
	Do you have an IBC protocol?:	
	If Yes, please select IBC:	
	Type of Agent::	null
	Species you will administer it to:	Pigs
	Dose:	1.25 mg
	Frequency:	daily
	Duration of Administration?	
	Route of administration:	
	if other route, list:	
View Bisoprolol	**Is it Pharmaceutical Grade?**:	
	If using a non-pharmaceutical grade agent, please provide justification for its use:	
	Per the MSDS or the BIMBL, is this agent considered Hazardous to humans?:	
	What is the danger to Humans?:	
	Do you have a procedure in your Laboratory Specific Safety Manual for the use of this agent?:	

What is the frequency and duration of observation of animals post administration?:

What clinical signs may be seen due to administration of this agent?:

What criteria are used to determine the need for treatment or euthanasia? :

If treatment is required, how will you treat these clinical signs?:

Are there any special requirements for animal disposal?:

How will you notify animal care personnel of the hazards associated with this agents?:

Exposure Management:

What precautions will you take during the administration of the agent? :

What special handling should be used post administration? Are there any risks to animal care personnel? What should they be aware of in handling animals associated with these agents?:

Is there any special training required for animal care personnel?:

What precautions will you take during necropsy/specimen collection? :

Do you have an HSC protocol?:

If Yes, please select HSC:

Do you have an IBC protocol?:

If Yes, please select IBC:

View Ampicillin

Type of Agent::	null
Species you will administer it to:	Pigs
Dose:	250 mg
Frequency:	every 12 hours
Duration of Administration?	
Route of administration:	
if other route, list:	
Is it Pharmaceutical Grade?:	
If using a non-pharmaceutical grade agent, please provide justification for its use:	
Per the MSDS or the BIMBL, is this agent considered Hazardous to humans?:	
What is the danger to Humans?:	
Do you have a procedure in your Laboratory Specific Safety Manual for the use of this agent?:	
What is the frequency and duration of observation of animals post administration?:	
What clinical signs may be seen due to administration of this agent?:	
What criteria are used to determine the need for treatment or euthanasia? :	
If treatment is required, how will you treat these clinical signs?:	
Are there any special requirements for animal disposal?:	

How will you notify animal care personnel of the hazards associated with this agents?:

Exposure Management:

What precautions will you take during the administration of the agent? :

What special handling should be used post administration? Are there any risks to animal care personnel? What should they be aware of in handling animals associated with these agents?:

Is there any special training required for animal care personnel?:

What precautions will you take during necropsy/specimen collection? :

Do you have an HSC protocol?:

If Yes, please select HSC:

Do you have an IBC protocol?:

If Yes, please select IBC:

View Enoxoparin

Type of Agent::	null
Species you will administer it to:	Pigs
Dose:	0.5 mg/kg
Frequency:	as needed
Duration of Administration?	
Route of administration:	
if other route, list:	
Is it Pharmaceutical Grade?:	

If using a non-pharmaceutical grade agent, please provide justification for its use:

Per the MSDS or the BIMBL, is this agent considered Hazardous to humans?:

What is the danger to Humans?:

Do you have a procedure in your Laboratory Specific Safety Manual for the use of this agent?:

What is the frequency and duration of observation of animals post administration?:

What clinical signs may be seen due to administration of this agent?:

What criteria are used to determine the need for treatment or euthanasia? :

If treatment is required, how will you treat these clinical signs?:

Are there any special requirements for animal disposal?:

How will you notify animal care personnel of the hazards associated with this agents?:

Exposure Management:

What precautions will you take during the administration of the agent? :

What special handling should be used post administration? Are there any risks to animal care personnel? What should they be aware of in handling animals associated with these agents?:

Is there any special training required for animal care personnel?:

What precautions will you take during necropsy/specimen collection? :

Do you have an HSC protocol?:

If Yes, please select HSC:

Do you have an IBC protocol?:

If Yes, please select IBC:

Type of Agent::	null
Species you will administer it to:	Pigs
Dose:	0.05-0.1 mmol/kg
Frequency:	once

Duration of Administration?

Route of administration:

if other route, list:

Is it Pharmaceutical Grade?:

View Gadolinium

If using a non-pharmaceutical grade agent, please provide justification for its use:

Per the MSDS or the BIMBL, is this agent considered Hazardous to humans?:

What is the danger to Humans?:

Do you have a procedure in your Laboratory Specific Safety Manual for the use of this agent?:

What is the frequency and duration of observation of animals post administration?:

What clinical signs may be seen due to administration of this agent?:

What criteria are used to determine the need for treatment or euthanasia? :

If treatment is required, how will you treat these clinical signs?:

Are there any special requirements for animal disposal?:

How will you notify animal care personnel of the hazards associated with this agents?:

Exposure Management:

What precautions will you take during the administration of the agent? :

What special handling should be used post administration? Are there any risks to animal care personnel? What should they be aware of in handling animals associated with these agents?:

Is there any special training required for animal care personnel?:

What precautions will you take during necropsy/specimen collection? :

Do you have an HSC protocol?:

If Yes, please select HSC:

Do you have an IBC protocol?:

If Yes, please select IBC:

View Aspirin

Type of Agent::	null
Species you will administer it to:	Pigs
Dose:	325 mg
Frequency:	daily

Duration of Administration?

Route of administration:

if other route, list:

Is it Pharmaceutical Grade?:

If using a non-pharmaceutical grade agent, please provide justification for its use:

Per the MSDS or the BIMBL, is this agent considered Hazardous to humans?:

What is the danger to Humans?:

Do you have a procedure in your Laboratory Specific Safety Manual for the use of this agent?:

What is the frequency and duration of observation of animals post administration?:

What clinical signs may be seen due to administration of this agent?:

What criteria are used to determine the need for treatment or euthanasia? :

If treatment is required, how will you treat these clinical signs?:

Are there any special requirements for animal disposal?:

How will you notify animal care personnel of the hazards associated with this agents?:

Exposure Management:

What precautions will you take during the administration of the agent? :

What special handling should be used post administration? Are there any risks to animal care personnel? What should they be aware of in handling animals associated with these agents?:

Is there any special training required for animal care personnel?:

What precautions will you take during necropsy/specimen collection? :

Do you have an HSC protocol?:

If Yes, please select HSC:

Do you have an IBC protocol?:

If Yes, please select IBC:

View Plavix

Type of Agent::	null
Species you will administer it to:	Pigs
Dose:	75 mg
Frequency:	daily

Duration of Administration?

Route of administration:

if other route, list:

Is it Pharmaceutical Grade?:

If using a non-pharmaceutical grade agent, please provide justification for its use:

Per the MSDS or the BIMBL, is this agent considered Hazardous to humans?:

What is the danger to Humans?:

Do you have a procedure in your Laboratory Specific Safety Manual for the use of this agent?:

What is the frequency and duration of observation of animals post administration?:

What clinical signs may be seen due to administration of this agent?:

What criteria are used to determine the need for treatment or euthanasia? :

If treatment is required, how will you treat these clinical signs?:

Are there any special requirements for animal disposal?:

How will you notify animal care personnel of the hazards associated with this agents?:

Exposure Management:

What precautions will you take during the administration of the agent? :

What special handling should be used post administration? Are there any risks to animal care personnel? What should they be aware of in handling animals associated with these agents?:

Is there any special training required for animal care personnel?:

What precautions will you take during necropsy/specimen collection? :

Do you have an HSC protocol?:

If Yes, please select HSC:

Do you have an IBC protocol?:

If Yes, please select IBC:

View Nitroglycerin

Type of Agent::	null
Species you will administer it to:	Pigs
Dose:	200 mcg
Frequency:	as needed
Duration of Administration?	
Route of administration:	
if other route, list:	
Is it Pharmaceutical Grade?:	
If using a non-pharmaceutical grade agent, please provide justification for its use:	
Per the MSDS or the BIMBL, is this agent considered Hazardous to humans?:	
What is the danger to Humans?:	
Do you have a procedure in your Laboratory Specific Safety Manual for the use of this agent?:	
What is the frequency and duration of observation of animals post administration?:	
What clinical signs may be seen due to administration of this agent?:	
What criteria are used to determine the need for treatment or euthanasia? :	
If treatment is required, how will you treat these clinical signs?:	
Are there any special requirements for animal disposal?:	

How will you notify animal care personnel of the hazards associated with this agents?:

Exposure Management:

What precautions will you take during the administration of the agent? :

What special handling should be used post administration? Are there any risks to animal care personnel? What should they be aware of in handling animals associated with these agents?:

Is there any special training required for animal care personnel?:

What precautions will you take during necropsy/specimen collection? :

Do you have an HSC protocol?:

If Yes, please select HSC:

Do you have an IBC protocol?:

If Yes, please select IBC:

View Aspirin

Type of Agent::	null
Species you will administer it to:	Pigs
Dose:	500 mg
Frequency:	once during cath procedures
Duration of Administration?	
Route of administration:	
if other route, list:	
Is it Pharmaceutical Grade?:	

If using a non-pharmaceutical grade agent, please provide justification for its use:

Per the MSDS or the BIMBL, is this agent considered Hazardous to humans?:

What is the danger to Humans?:

Do you have a procedure in your Laboratory Specific Safety Manual for the use of this agent?:

What is the frequency and duration of observation of animals post administration?:

What clinical signs may be seen due to administration of this agent?:

What criteria are used to determine the need for treatment or euthanasia? :

If treatment is required, how will you treat these clinical signs?:

Are there any special requirements for animal disposal?:

How will you notify animal care personnel of the hazards associated with this agents?:

Exposure Management:

What precautions will you take during the administration of the agent? :

What special handling should be used post administration? Are there any risks to animal care personnel? What should they be aware of in handling animals associated with these agents?:

Is there any special training required for animal care personnel?:

	What precautions will you take during necropsy/specimen collection? :	
	Do you have an HSC protocol?:	
	If Yes, please select HSC:	
	Do you have an IBC protocol?:	
	If Yes, please select IBC:	
	Type of Agent::	null
	Species you will administer it to:	Pigs
	Dose:	22 mg/kg
	Frequency:	every 2 hours
	Duration of Administration?	
	Route of administration:	
	if other route, list:	
View Cefazolim	**Is it Pharmaceutical Grade?**:	
	If using a non-pharmaceutical grade agent, please provide justification for its use:	
	Per the MSDS or the BIMBL, is this agent considered Hazardous to humans?:	
	What is the danger to Humans?:	
	Do you have a procedure in your Laboratory Specific Safety Manual for the use of this agent?:	
	What is the frequency and duration of observation of animals post administration?:	

What clinical signs may be seen due to administration of this agent?:

What criteria are used to determine the need for treatment or euthanasia? :

If treatment is required, how will you treat these clinical signs?:

Are there any special requirements for animal disposal?:

How will you notify animal care personnel of the hazards associated with this agents?:

Exposure Management:

What precautions will you take during the administration of the agent? :

What special handling should be used post administration? Are there any risks to animal care personnel? What should they be aware of in handling animals associated with these agents?:

Is there any special training required for animal care personnel?:

What precautions will you take during necropsy/specimen collection? :

Do you have an HSC protocol?:

If Yes, please select HSC:

Do you have an IBC protocol?:

If Yes, please select IBC:

View Enoxoparin

Type of Agent:: null

Species you will administer it to: Pigs

Dose: 1 mg/kg

Frequency: once

Duration of Administration?

Route of administration:

if other route, list:

Is it Pharmaceutical Grade?:

If using a non-pharmaceutical grade agent, please provide justification for its use:

Per the MSDS or the BIMBL, is this agent considered Hazardous to humans?:

What is the danger to Humans?:

Do you have a procedure in your Laboratory Specific Safety Manual for the use of this agent?:

What is the frequency and duration of observation of animals post administration?:

What clinical signs may be seen due to administration of this agent?:

What criteria are used to determine the need for treatment or euthanasia? :

If treatment is required, how will you treat these clinical signs?:

Are there any special requirements for animal disposal?:

How will you notify animal care personnel of the hazards associated with this agents?:

Exposure Management:

What precautions will you take during the administration of the agent? :

What special handling should be used post administration? Are there any risks to animal care personnel? What should they be aware of in handling animals associated with these agents?:

Is there any special training required for animal care personnel?:

What precautions will you take during necropsy/specimen collection? :

Do you have an HSC protocol?:

If Yes, please select HSC:

Do you have an IBC protocol?:

If Yes, please select IBC:

View Lidocaine

Type of Agent::	null
Species you will administer it to:	Pigs
Dose:	50-100 mg
Frequency:	as needed for ventricular arrythmias

Duration of Administration?

Route of administration:

if other route, list:

Is it Pharmaceutical Grade?:

If using a non-pharmaceutical grade agent, please provide justification for its use:

Per the MSDS or the BIMBL, is this agent considered Hazardous to humans?:

What is the danger to Humans?:

Do you have a procedure in your Laboratory Specific Safety Manual for the use of this agent?:

What is the frequency and duration of observation of animals post administration?:

What clinical signs may be seen due to administration of this agent?:

What criteria are used to determine the need for treatment or euthanasia? :

If treatment is required, how will you treat these clinical signs?:

Are there any special requirements for animal disposal?:

How will you notify animal care personnel of the hazards associated with this agents?:

Exposure Management:

What precautions will you take during the administration of the agent? :

What special handling should be used post administration? Are there any risks to animal care personnel? What should they be aware of in handling animals associated with these agents?:

Is there any special training required for animal care personnel?:

What precautions will you take during necropsy/specimen collection? :

	Do you have an HSC protocol?:	
	If Yes, please select HSC:	
	Do you have an IBC protocol?:	
	If Yes, please select IBC:	
	Type of Agent::	null
	Species you will administer it to:	Pigs
	Dose:	100-300 mcg/min/kg
	Frequency:	as needed for arrythmias
	Duration of Administration?	
	Route of administration:	
	if other route, list:	
	Is it Pharmaceutical Grade?:	
View Lidocaine	**If using a non-pharmaceutical grade agent, please provide justification for its use:**	
	Per the MSDS or the BIMBL, is this agent considered Hazardous to humans?:	
	What is the danger to Humans?:	
	Do you have a procedure in your Laboratory Specific Safety Manual for the use of this agent?:	
	What is the frequency and duration of observation of animals post administration?:	
	What clinical signs may be seen due to administration of this agent?:	

What criteria are used to determine the need for treatment or euthanasia? :

If treatment is required, how will you treat these clinical signs?:

Are there any special requirements for animal disposal?:

How will you notify animal care personnel of the hazards associated with this agents?:

Exposure Management:

What precautions will you take during the administration of the agent? :

What special handling should be used post administration? Are there any risks to animal care personnel? What should they be aware of in handling animals associated with these agents?:

Is there any special training required for animal care personnel?:

What precautions will you take during necropsy/specimen collection? :

Do you have an HSC protocol?:

If Yes, please select HSC:

Do you have an IBC protocol?:

If Yes, please select IBC:

View luciferin

Type of Agent::	null
Species you will administer it to:	Pigs
Dose:	150 mg/kg
Frequency:	once

Duration of Administration?

Route of administration:

if other route, list:

Is it Pharmaceutical Grade?:

If using a non-pharmaceutical grade agent, please provide justification for its use:

Per the MSDS or the BIMBL, is this agent considered Hazardous to humans?:

What is the danger to Humans?:

Do you have a procedure in your Laboratory Specific Safety Manual for the use of this agent?:

What is the frequency and duration of observation of animals post administration?:

What clinical signs may be seen due to administration of this agent?:

What criteria are used to determine the need for treatment or euthanasia? :

If treatment is required, how will you treat these clinical signs?:

Are there any special requirements for animal disposal?:

How will you notify animal care personnel of the hazards associated with this agents?:

Exposure Management:

What precautions will you take during the administration of the agent? :

What special handling should be used post administration? Are there any risks to animal care personnel? What should they be aware of in handling animals associated with these agents?:

Is there any special training required for animal care personnel?:

What precautions will you take during necropsy/specimen collection? :

Do you have an HSC protocol?:

If Yes, please select HSC:

Do you have an IBC protocol?:

If Yes, please select IBC:

2. Additional Documents:

Name	Version
There are no items to display	

3.

View: 13. Animal Exposure: Radiation

Current State: Expired

Date Entered State:1/5/2011 1:46 PM

ID:IS00000596

13. Animal Exposure: Radiation

1. * Do you have an RSC protocol?: ○ ○ Yes ○ ○ No

   If Yes, please select RSC Protocol:

2. Isotope Use:

	Isotope		Date Created	Date Modified
	Species::	Pigs		
	Dose to be administered:	to effect		
	Frequency of exposure:	as needed		
	Room/Location of Exposure:			
	Time Period for Decay:			
	Location for Decay:			
	List any special housing required post exposure:			
View	**Is any special waste disposal required?:**		8/24/2010	8/24/2010
	How will you notify animal care personnel of the hazards associated with this agents?::			
	Are there any special precautions staff should take when handling the animals?:			
	If yes, who will train them?:			
	What clinical signs may be seen due to this radiation exposure?:			

If treatment is required, how will you treat these clinical signs?:

What criteria are used to determine the need for treatment or euthanasia?::

3. Equipment Use:

Equipment	Date Created	Date Modified
There are no items to display		

View: 15. Food or Water Regulation

Current State: Expired

Date Entered State:1/5/2011 1:46 PM

ID:IS00000596

15. Food or Water Regulation

1. * Food or Water Restrictions: Food and Fluid Regulation.docx

Change in amount or frequency of water or food			Date Created	Date Modified
Food	**Species:**:	Pigs	8/24/2010	8/24/2010

Duration of food or water regulation:	12 hours prior to surgery
Describe the change to the amount or frequency of food or water given::	
Why do you have to regulate the food /water?	Standard operating procedure for procedure performed under general anesthesia.
What are the frequency, duration and method of observation of the animals during the food/water regulation?	Any change in appearance, vomiting or self injury related to hunger.
What clinical signs may be seen due to the food/water regulation?	Hunger, irritability
What criteria are used to determine the need for treatment or euthanasia?	
If treatment is required, how will you treat these clinical signs?	

Current State: Expired

Date Entered State:1/5/2011 1:46 PM

ID:IS00000596

21. Fluid (blood, urine, saliva, etc)/Specimen Collection

1. Fluid/Specimen Collection: TMHRI Blood Collection Policy

	Species	Fluid/Specimen	Collection Method	Frequency	Volume per event	Disposal	Specimen/Fluid Storage Location	Date Modified	Date Created
View		Blood	Drawn from introducer sheath	once per each catheterization	10-20 ml			8/24/2010	8/24/2010

Current State: Expired

Date Entered State:1/5/2011 1:46 PM

ID:IS00000596

Final Page

You have completed the application!

Applications may only be submitted to the IACUC by the Principal Investigator.

Step 1: Check ‘Submit to PI’ to alert the PI that the application is ready for his/her review and submission.

Step 2: Click ‘Finish’ to save and exit the application.

You can track the ongoing status of your submission by logging into the study workspace.

Please contact the IACUC with any questions or concerns.
Maya Justilian MMJustilian@houstonmethodist.org 713-441-7887

IS00000596

NOTIFICATION OF IACUC COMMITTEE DECISION

January 5, 2011

From:	James Davis, Ph.D. TMHRI IACUC Chair
To:	Albert Raizner
CC:	Amish Dave Eckhard Alt Miguel Valderrábano Daryl Schulz
Re:	AUP-0910-0019 IS00000596 Stem Cell Injection in a Myocardial Infarcted Pig Heart

The above numbered protocol was reviewed by the Institutional Animal Care and Use Committee. The protocol has been **APPROVED** for the following period:

1/5/2011 through 1/4/2014

Renewal of this study is required on an annual basis.

Please note that prior to starting any experiments it is your responsibility to give a copy of this document to all research personnel involved in the project and to discuss the project with each employee. Any changes to the protocol must be approved by the IACUC before the changes can take place.

Sincerely,

James Davis, Ph.D.

The Methodist Hospital Research Institute
6565 Fannin Street
Houston, TX 77030
713-441-1261

U.S. Department of State

CERTIFICATE OF ELIGIBILITY FOR EXCHANGE VISITOR (J-1) STATUS

OMB APPROVAL NO.1405-0119
07/31/2014
ESTIMATED BURDEN TIME: 45 min
*See Page 2

N0010973365

J-1

1. Family Name: Haenel
First Name: Alexander
Middle Name:
Gender: MALE

Date of Birth (mm-dd-yyyy): 12-26-1988
City of Birth: Oberhausen
Country of Birth: GERMANY
Citizenship Country Code: GM
Citizenship Country: GERMANY

Legal Permanent Residence Country Code: GM
Legal Permanent Residence Country: GERMANY
Position Code: 214
Position: UNIVERSITY GRADUATE STUDENTS

Primary Site of Activity: Tulane University Health Sciences Center
Section of Cardiology
1430 Tulane Ave. SL-48
New Orleans, LA 70112

2. Program Sponsor: Tulane University
Program Number: P-1-00284

Participating Program Official Description:
PROFESSOR; RESEARCH SCHOLAR; SHORT-TERM SCHOLAR; STUDENT ASSOCIATE; STUDENT BACHELORS; STUDENT DOCTORATE; STUDENT INTERN; STUDENT MASTERS; STUDENT NON-DEGREE

Purpose of this form: Begin new program; accompanied by number (0) of immediate family members.

3. Form Covers Period:
From (mm-dd-yyyy): 03-10-2014
To (mm-dd-yyyy): 03-31-2015

4. Exchange Visitor Category: RESEARCH SCHOLAR
Subject/Field Code: 51.1401
Subject/Field Code Remarks: EV will research the role of mesenchymal stem cells in cardiac remodeling and their poten

5. During the period covered by this form, the total estimated financial support (in U.S. $) is to be provided to the exchange visitor by:
Alliance of Cardiovascular Researchers : $31,250.00
Total : $31,250.00

6. U.S. DEPARTMENT OF STATE / DHS USE OR CERTIFICATION BY RESPONSIBLE OFFICER OR ALTERNATE RESPONSIBLE OFFICER THAT A NOTIFICATION COPY OF THIS FORM HAS BEEN PROVIDED TO THE U.S. DEPARTMENT OF STATE (INCLUDE DATE).

7. Elizabeth Nazar
Name of Official Preparing Form

Alternate Responsible Officer
Title

Tulane University
6823 St. Charles Ave.
New Orleans, LA 70118
Address of Responsible Officer or Alternate Responsible Officer

504-865-5208
Telephone Number

Signature of Responsible Officer or Alternate Responsible Officer

01-22-2014
Date (mm-dd-yyyy)

8. Statement of Responsible Officer for Releasing Sponsor (FOR TRANSFER OF PROGRAM)
Effective date (mm-dd-yyyy): _____. Transfer of this exchange visitor from program number _____ sponsored by _____ to the program specified in item 2 is necessary or highly desirable and is in conformity with the objectives of the Mutual Educational and Cultural Exchange Act of 1961, as amended.

Signature of Responsible Officer or Alternate Responsible Officer

Date (mm-dd-yyyy) of Signature

PRELIMINARY ENDORSEMENT OF CONSULAR OR IMMIGRATION OFFICER REGARDING SECTION 212(e) OF THE IMMIGRATION AND NATIONALITY ACT AND PL 94-484, AS AMENDED (see item 1(a) of page 2).

The Exchange Visitor in the above program:

1. [X] Not subject to the two-year residence requirement.
2. [ ] Subject to two-year residence requirement based on:
   A. [ ] Government financing and/or
   B. [ ] The Exchange Visitor Skills List and/or
   C. [ ] PL 94-484 as amended

(ALL USAID PARTICIPANTS G-2-00263 AND ALL ALIEN PHYSICIANS SPONSORED BY P-3-04510 ARE SUBJECT TO THE TWO-YEAR HOME RESIDENCE REQUIREMENT)

Andrew Berdy
Name
Vice Consul of the United States of Am
Title

Signature of Consular or Immigration Officer

02/20/2014
Date (mm-dd-yyyy)

THE U. S. DEPARTMENT OF STATE RESERVES THE RIGHT TO MAKE FINAL DETERMINATION REGARDING 212 (e).

TRAVEL VALIDATION BY RESPONSIBLE OFFIC
(Maximum validation period is 1 year*)

*EXCEPT: Maximum validation period is up to 6 months for Short-Scholars and 4 months for Camp Counselors and Summer Work/Tra

(1) Exchange Visitor is in good standing at the present time

Date (mm-dd-yyyy)

Signature of Responsible Officer or Alternate Responsible

(2) Exchange Visitor is in good standing at the present time

Date (mm-dd-yyyy)

Signature of Responsible Officer or Alternate Responsible

EXCHANGE VISITOR CERTIFICATION: I have read and agree with the statement in item 2 on page 2 of this document.

Signature of Applicant

Frankfurt
Place

02/20/20
Date (mm-dd-yyy

2019
011

ALLIANCE OF CARDIOVASCULAR RESEARCHERS

December 28, 2013

TO WHOM IT MAY CONCERN

This is to certify that Mr. Alexander Haenel has been elected by the Alliance of Cardiovascular Researchers for a sponsored research stipend.

He will be supported by a monthly stipend of USD 2500.- from March 15 2014 to March 15 2015 through the funds of the Alliance of Cardiovascular Researchers.

He will spend his educational research associate time at the research labs at Tulane University under the supervision of Prof. Dr. Eckhard Alt and Dr. Reza Izadpanah.

Regards

Gunter Koller
-President-

Alliance of Cardiovascular Researchers

1010 COMMON STREET
SUITE 1810
NEW ORLEANS, LA 70112