

Matters

FALL 2017

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Interventional Cardiologist Rewarded through Research

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aniel Lee, MD, an interventional cardiologist at Bay Heart & Vascular with locations in Bay City, West Branch and Mount Pleasant, is among the top five enrollers in a trial studying the efficacy of an innovative stent. The LEADERS FREE II: BioFreedom™ Pivotal Study aims to confirm non inferiority of the BioFreedom™ Drug Coated Stent to the Gazelle Bare Metal Stent in high bleeding risk patients.

Dr. Lee describes the reason this study has generated excitement among heart and vascular specialists.

“Traditionally, someone receiving a drug-eluting stent required one year of blood thinners, aspirin and Plavix,” said Dr. Lee. “More recently that time is down to six months, but even six months of blood thinners can lead to bleeding complications in patients, especially if they are older and fragile. Also, if they need to have surgery before they’ve completed this dual antiplatelet therapy, they are at a higher risk of blood clots. The polymer used on the stent in the Leaders Free II study enables patients to only follow one month of aspirin and Plavix, which is great for our high risk patients or those needing surgery soon.”

Since he began his practice 18 years ago, Dr. Lee has been involved in clinical trials. His experience, reputation and ability to utilize the resources of the McLaren Center for Research and Innovation has led clinical trial sponsors such as that of the BioFreedom Pivotal Study, Biosensors Europe SA, to seek his participation. He points out the following rewards he has realized through his involvement in research.

Professional Recognition

Investigators who are among the top enrollers in studies could have the opportunity to share their experience and findings at professional events. If the study is published the top enroller is named on the paper. Both of these opportunities provide national or even international recognition for the physician group and the health system involved.

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Financial Benefits

When a medical device or drug, such as a new stent is the focus, the cost of the device is usually covered by the study sponsor, lowering the hospital's cost of the procedure.

Competitive Advantage

In the Bay area, as it is in many heavily populated areas, competition for health services is stiff. Dr. Lee noted that having innovative research offerings available helps gain an advantage over the competition.

"We want physicians to remember that we are the place that has the best options available. For example, when the first drug eluding stents were introduced, our practice was able to get these

for our patients two years before they were available to the public and give them great therapy that no one else could because we were involved in research."

Keeping the Passion Alive

Dr. Lee feels energized taking an active role in the evolution of cardiovascular medicine. He enjoys the professional connections he has made with leaders in the field through his involvement in research which includes and attending related conferences and meetings.

Anyone interested in finding out more about the clinical trials currently offered through McLaren Health Care may visit mclaren.org/research.

Why Clinical Trials Matter

By Majid Mughal, MD, FCCP, Interventional Cardiologist

Clinical drug trials matter because they can sometimes mean life or death for end of life patients suffering from an incurable disease or condition. Research studies and clinical drug trials are vital to even having a chance to extend the life of a terminal patient, while hopefully making them also feel more comfortable. As the Principal Investigator for two clinical drug studies (an initial study, followed by an extension of the first study) in which the condition being assessed currently has no approved drug or therapy treatment, I understand and support the use of clinical research.

In my initial study, RIN-PH-201 INCREASE, I am investigating the safety and efficacy of Inhaled Treprostinil in subjects with any of the following conditions: Pulmonary Hypertension due to Parenchymal Lung Disease, Pulmonary Hypertension associated with Interstitial Lung Disease or combined Pulmonary Fibrosis and Emphysema. Following this study, an extension study (RIN-PH-202) will be conducted to provide or continue to provide inhaled Treprostinil to eligible subjects who participated in the initial RIN-PH-201 (INCREASE) study. Both studies will also examine one's ability to exercise after taking the drug at different stages.

While it does not cure the condition, Treprostinil treats symptoms of pulmonary arterial hypertension (high blood pressure) in the main artery that carries blood from the heart's right ventricle to the lungs. When the blood vessels in the lungs become resistant to blood flow, the right ventricle must work harder to pump enough blood to the lungs. This results in symptoms such as chronic shortness of breath or chest pain with exertion; fainting or dizziness; swelling in your abdomen and legs; and extreme fatigue. Due to these symptoms being similar to those of the other conditions being examined in the study, we are hopeful that they will have the same effectiveness during our trials.

Most of the time patients are not aware of such drug trials, so conducting these studies spreads awareness to physicians who then advise their patients. As I stated previously, this is especially important for end of life patients who cannot wait for the FDA to approve a medication. Clinical trials allow these patients access to drugs and therapies without cost or waiting time, which is precisely why research matters and will continue to for years to come.



About Dr. Mughal

As the Greater Lansing area's only physician to be fellowship-trained in pulmonary hypertension, Dr. Mughal keeps busy treating patients at both McLaren Greater Lansing and McLaren Cardiovascular Group's Main Practice in Okemos. Along with two other Lansing physicians, Mughal became one of the first Investigators to launch the Research Site at McLaren Greater Lansing. Dr. Mughal also serves as a member of the McLaren Health Care Institutional Review Board.



EQUIP Corner

FDA Warning Letters and PI Oversight

By Patricia Ivery, QI and Education Specialist

Oversight of research conduct begins at the local level and culminates at the federal level. Locally, the principal investigator (PI) is accountable for overall study conduct which includes overseeing research trial activities delegated to appropriate research team members. At the federal level, research oversight is provided by the Food and Drug Administration (FDA) and Office of Human Research Protection (OHRP) under the Department of Health and Human Services (DHHS). Both OHRP and FDA can perform announced and unannounced inspections of clinical investigator sites. This article will focus on FDA inspections and warning letters that may be issued as a result of such inspections.

Why the FDA does perform inspections?

The FDA's Bioresearch Monitoring (BIMO) program performs onsite audits of FDA regulated research. These inspections are done to determine if the clinical investigators are operating in compliance with current FDA regulations and statutory requirements to protect human subjects and assure the quality, reliability and integrity of data. The FDA conducts routine, scheduled inspections of studies regularly. However, inspections may be conducted for a number of specific reasons, including:

- Complaint to the Agency about the conduct of the study at the site;
- In response to sponsor concerns or termination of the clinical site;
- History of non-compliance
- Request from an FDA review division

What happens after the inspection?

If deviations are found during the inspection, one of the following types of letters will be issued from the FDA to the clinical investigator:

1. Voluntary Action Indicated (VAI) Letter - issued when the FDA has observed no significant deviations from the regulations, but minor deficiencies have been identified and voluntary corrective action is sufficient.
2. Official Action Indicated (OAI) letter (a.k.a. Warning Letter) warning issued when serious deviations or non-compliance from applicable statutes and regulations. Prompt correction by the clinical investigator and a formal written response to the agency is required. Sometimes warning letters carry some type of sanctions, such as the FDA initiation of disqualification procedures of the clinical investigator

All warning letters publicly available and fully identify the PIs, the institution, and the violations incurred. Letters are posted publicly to keep the investigator community abreast of FDA concerns and findings.

Brown Bag Series

**Valid Informed Consent Education—
Using the Teach Back Method in the
Research Setting**

PART 1 • October 10, 2017 • 12:00 - 12:45 pm

PART 2 • October 17, 2017 • 12:00 - 12:45 pm
LIVE WEBINAR

Contact Markeda at (248) 484-4952
or markeda.richards@mclaren.org

Upcoming Education and Conferences

SOCRA 2017 Annual Conference
October 6 - 8, 2017 • Orlando, FL

**Public Responsibility in Medicine and
Research (PRIM&R)**
**2017 Advancing Ethical Research
Conference**

November 5 - 8, 2017 • San Antonio, TX

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Common reasons for the issuance of warning letters

The most common reason for investigator warning letters is failure to comply with commitments set forth in item 9 of the FDA Form 1572. The top FDA citations in warning letters for clinical investigators issued in 2016 were:

- Failure to ensure that the investigation was conducted according to the investigational plan, the signed agreement, applicable FDA regulations, to protect the rights, safety and welfare of subjects under investigator's care [21 CFR 312.60] and conditions of approval imposed by the IRB or FDA [21CFD 312.60]
- Failure to maintain adequate, accurate, and complete records that record all observations and other data pertinent to the investigation on each individual administered the investigational drug or employed as a control in the investigation [21 CFR 312.62(b)]

- Failure to ensure that informed consent was obtained in accordance with 21 CFR Part 50

Prevention

No one wants their name associated with serious non-compliance. The good news is that warning letters are the exception, rather than the norm. In 2016, out of 349 domestic investigators audited, only 7 received warning letters. There are 2 key things investigators use as measures of prevention:

1. Understand the implications of signing the FDA form 1572 and subsequently failing to honor the commitments and responsibilities as the PI of a federally-funded study or investigator-initiated study.
2. Conduct periodic self-audits of your study to validate compliance with applicable federal regulations, laws and institutional policies. If deficiencies are discovered corrections should be addressed in a corrective action preventative action plan (CAPA).

Resources for Researchers

View FDA warning letters since 2005

<https://www.fda.gov/iceci/enforcementactions/warningletters/default.htm>

FDA Guidance for Industry

Investigator Responsibilities – Protecting the Rights, Safety and Welfare of Study Subjects

Institution Policy

MHC_RP0125
– Investigator Responsibilities and MHC_RP0124 – Reporting to Regulatory Agencies and Institutional Officials
<http://www.mclaren.org/main/research-policies1.aspx>

QA/QI Review Self-Assessment Checklist (includes how to create a CAPA)

<http://www.mclaren.org/Uploads/Public/Documents/Corporate/QA-Self-Assessment-Tool.pdf>



Research Solutions

By Lana Gevorkyan, Corporate Director, Human Research Protections Program

The Research Solutions team has been very busy for the last few months developing a detailed implementation plan to support both oncology and non-oncology research across McLaren as part of the One McLaren project. The team has been meeting to discuss the design, build, testing, and implementation plan to support research at all McLaren subsidiaries, including KCI.

What's coming up?

The Research Solutions team will continue to work very closely over the next few months to standardize workflows for research across the system. This will allow research teams to use Cerner Millennium for patient access and research billing. The interim workflow solution will prepare research teams for the PowerTrials implementation scheduled for December 2018. As we move forward with the standardization of future workflows across the system and integrate research into Cerner Millennium, training will be provided to the research community. Please watch for a specific course schedule in the near future.

Our goal?

It is the goal of the Research Solutions team to standardize future state workflows as much as possible and to use Cerner Millennium by December 2017 in alignment with the Lansing Go Live date.



Resident's Corner

Quality Improvement vs. Research

Quality improvement (QI) activities are necessary in hospital operations, as they allow us to measure and improve the quality of care for patients. Much like research activities, QI activities involve systematic investigations and can involve human participants, making it difficult to differentiate between the two. Knowing some basic definitions is helpful when considering whether a project is research or QI:

- **Quality Improvement (QI)** - systematic, data-guided activities designed to bring about immediate improvements in health delivery in particular settings
- **Research** - a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalized knowledge.
- **Human Subjects Research** - any activity that meets the definition of "research" and involves "human subjects" as defined by either the Common Rule or FDA regulations.

Both research and quality improvement are systematic investigations that may involve human participants, however, they have very important differences. QI uses a hypothesis, reasoning, and similar analytical tools that are used in research, with the intent to investigate practices / procedures done in current routine medical care. Research, on the other hand, is designed to develop, test, and evaluate practices / procedures that are outside of that which is done in routine medical care. The table below outlines key similarities and differences:

	Human Subjects Research	Quality Improvement
Purpose	To develop or contribute to generalizable knowledge	To implement knowledge, assess a process or program as judged by currently accepted standards
Benefits	May or may not benefit current subjects; intended to benefit future patients	Directly benefits a process, system, or program; may or not benefit patients
Risks	May put subjects at risk	No increased risk to patients
Analysis	Statistically prove or disprove hypothesis	Compare a program, process, or system to established standards

The lines become even more blurred when we consider that some quality improvement activities are designed to simultaneously answer a research question and improve the quality of care. In such cases, regulations for the protection of subjects in research (45 CFR part 46) may apply and IRB review may be required. For this reason, MHC IRB requires that all projects be submitted for determination prior to implementation.

McLaren Residents Participate in Quality Improvement/Patient Safety Event

To meet Accreditation Council for Graduate Medical Education requirements at McLaren Flint, Internal medicine resident faculty QI teams joined the institutional Interdisciplinary Quality Improvement/Patient Safety Initiative. **Ahad**

Ayaz, MD a graduate of the internal medicine resident and his team Shikha Mishra, MD, Rowena Inocencio, MD, Farah AISabie, MD, Juan Gonzales, MD, with faculty mentor **Kavitha Kesari, MD**, were recognized for their presentation; which was one of the initiative project "Integrating Residents

- Faculty Team with Hospital Early Sepsis Interdisciplinary Quality Improvement (QI) Teams to Improve Sepsis Outcome" held in Troy in June. The event was organized by Dr. Robert Flora and Southeast Michigan Center for Medical Education. Three prizes in all were awarded at the resident level.



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What's New?

Clinical Research Associates Advisory Council

McLaren Health Care has embarked on an initiative to develop a Clinical Research Associate Advisory Council (CRAAC). The Council is for experienced and knowledgeable research associates (coordinators) to come together and function as a sounding board, discuss areas of concern and offer insight to senior leadership. The CRAAC will provide network opportunities and mentorship to those conducting research throughout McLaren Health Care. If you are interested in becoming part of the CRAAC or would like more information, please contact Jill George (jill.george@mclaren.org) or Patricia Ivery (patricia.ivery@mclaren.org).

Neurology Research Council

McLaren Health Care has embarked on an initiative to expand Neuroscience research. To guide this effort and bring forth quality opportunities, we are forming McLaren's Neuroscience Research Council (NRC).

The Neuroscience Research Council will function as the leadership body focusing on Neuroscience Research which will be part of the Neuroscience service line. In addition, the council will focus on strategic collaborations, funding opportunities and translational research advances.

Chaired by Dr. Aniel Majjhoo, the committee will commence in September of 2017 and meet bi-monthly.

HRPP Staff Member Presenting at 2017 Annual SOGRA Conference

Patricia Ivery RN, MSN, QI and Education Specialist for the Human Research Protection Program (HRPP) has been invited to be a presenter at the 26th Annual SOGRA Conference. This year's conference theme is "Promoting Excellence in Clinical Research" and will feature over 100 academic sessions, poster presentations, and exhibits. Patricia's presentation, "Quality Assessment of Research Conduct: Auditing Yourself Before They Do" will focus on looking at self-assessment in research conduct.



Quality Improvement vs. Research

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To submit a project that suspected to be QI, the investigator must submit a "Request for Determination Non-Human Subject Research" form, which is available on our website (<http://www.mclaren.org/main/research-irb1.aspx>) under the "Guidance for Investigators" tab. Once submitted, the IRB will determine whether or not the project is research involving human subjects and issue a determination letter to the investigator.

For more details regarding the IRB submission process, please visit our website or call the MHC IRB office at (248) 484-4950.

Karmanos Duo's Abstract Accepted for Presentation at Annual AACI Clinical Research Initiative Meeting

Congratulations to Cathy Galasso, RN, OCN, CCRP and Joanne Mancini, RN, CCRP, who recently had their abstract approved for both a poster and oral presentation at the 9th Annual AACI Clinical Research Initiative.

The abstract, titled "Implementing a Research Nurse Model for the Clinical Trials Office (CTO)" was also co-authored by Helen Peck, RN, MA, OCN, CCRP.

The group developed a CTO research nurse team model over a period of six years. The result was the research nurses were found to be an essential part of patient and investigator support, increased accrual and improved protocol compliance. This model has been in place for 10 years now and has expanded to the entire Karmanos network.

SoCRA Certification Earned

Congratulations to Karmanos Cancer Institute Research Coordinators, Jacqueline Brewer and Elizabeth Horvat for their recent SoCRA Certification!



Jacqueline Brewer



Elizabeth Horvat

Welcome Our New Corporate Director of Scholarly Inquiry

Carlos F. Ríos-Bedoya, PhD, has joined McLaren Health Care as Corporate Director of Scholarly Inquiry with McLaren Center for Research and Innovation. In his newly appointed position, Ríos-Bedoya will play a pivotal role in shaping many scholarly inquiry programs. His responsibilities will include: overseeing scholarly activity throughout the system, serving as Chair of System Committee of Scholarly Inquiry, Interface for collaborative scholarly activity with other institutions, and PhD support for McLaren Oakland and Macomb. In addition, he will oversee support provided by MS Clinical Research employees, provide higher level bio statistical and epidemiologic support, coordinate with MSUCOM SCS Scholarly Activity Consultation Service, and represent McLaren Health Care at SEMCME Research Committee.

Dr. Ríos-Bedoya earned his B.S. and M.P.H. at the University of Puerto Rico and received a Sc.D. in psychiatric epidemiology from Johns Hopkins University. Most recently he has served Michigan State University as both an Associate Professor for the Department of Family Medicine and as an Adjunct Associate Professor for the Department of Epidemiology & Biostatistics. In addition, he recently held the position of Research Associate Professor Chair for the Department of Internal Medicine at Hurley Medical Center.



He has published and presented numerous scholarly research studies with an emphasis on the assessment of a multitude of health care related topics including: substance abuse in both adolescents and adults, health promotion, disease prevention, behavioral intervention, as well as many intra-ethnic studies. He currently maintains memberships with the National Hispanic Science Network on Drug Abuse, the Society for Research on Nicotine and Tobacco, and the Research Society on Alcoholism.

Meet J. Quen Dickey Jr., DO

McLaren's Human Research Protections Program would like to welcome Dr. J. Quen Dickey Jr. to McLaren's Corporate IRB as one of the IRB members. Dr. Dickey brings a wealth of knowledge and expertise. Dr. Dickey is board certified in Internal Medicine, Cardiology, Critical Care, and Nuclear Cardiology. We are happy to have Dr. Dickey on Board.



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