RESEARCH *Matters*

SUMMER 2020

IN THIS ISSUE...

Association for the Accreditation of Human Research Protection Programs, Inc. — *Full* Accreditation

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RESEARCH AROUND McLAREN

CLINICAL RESEARCH CONDUCT DURING THE COVID-19 PANDEMIC

The impact of COVID-19 on clinical trials at McLaren has been immediate and unprecedented. A number of challenges became apparent overnight including travel bans, hospital visitation restrictions, and social distancing precautions, just to name a few. First and foremost, risk mitigation and precautionary strategies needed to protect our active research patients and front-line research staff were a crucial first step. Research operations at McLaren shifted immediately from in person contact with our patients, to completely remote patient interactions. Enrollment of new patients ceased in all studies that were not COVID-19 related. Investigational device use came to a halt with the hold on elective procedures. Our research staff and investigators began utilizing phone, telemedicine, video conferencing and other HIPAA compliant methods to conduct study assessments with our patients and collect the data that we could. We started shipping investigational drug to patient's homes or arranging drive-through pick up at the hospital door. All these operational changes present logistical issues for our on-site research staff to work through and ensure compliance and patient safety along the way. Regulatory staff were charged with reporting a multitude of changes in our operations to the IRB for each impacted study.

Unique challenges have presented for our study sponsors as well including missing data points, visits out of window, drug shipment delays and remote only data verification. This myriad of operational changes certainly has the potential to affect the overall outcome and success of the studies. Many sponsors are looking at and amending their study protocols to allow for better protocol adherence during the pandemic and beyond. Amendments might include modifying the number of protocol mandated in-person study visits, using home, remote or telemedicine visits and home health services for labs or non-invasive testing. These are all new ways forward for the clinical trials industry and trends that we may see well beyond the immediate COVID-19 pandemic.

McLaren has embarked on a number of COVID-19 related research projects and clinical trials. Opening these studies has pushed the envelope of what we currently know about study start-up. We have experienced outstanding teamwork and collaboration across the system to get these studies open and available to our patients on extreme timelines. We have come together to develop brand new consenting processes to ensure staff and patient safety and adherence to mandated precautions and other restrictions currently in place. We are working with investigators who are new to research with MCRI and having countless team meetings in virtual spaces. We are working through new processes of investigational drug dispensing from in-patient pharmacy and working closely with departments who have not participated in research before.

This is a very challenging yet exciting time for research at McLaren and across the world. The face of clinical research is changing before our eyes, and we don't yet know what to fully expect in a post-pandemic world. Technology is advancing quickly to meet the demands of our new work-space and the needs of our patients. Industry leaders are coming together regularly to brainstorm and blaze new trails for sites and sponsors alike. Creative thinking outside of the box will generate new and exciting ways forward for clinical research as an industry and keep McLaren's Center for Research and Innovation a competitive and cutting-edge research organization.

CONVALESCENT PLASMA AS A COVID-19 TREATMENT

Around the world, researchers and clinicians have shifted their focus to one subject: COVID-19. New treatments and trials are launching every day, all with the potential to stop coronavirus in its tracks. While we look forward to developments in fighting this pandemic, many are searching the past for possibilities.

Christopher Provenzano, MD

Case reports from the 1918 Spanish Flu describe the use of blood product transfusions in reducing risk for death and improving symptoms. Such treatments have been documented throughout the 20th century and, more recently, sophisticated transfusion techniques including the use of convalescent plasma, have been used in response to the outbreak of both Middle East Respiratory Syndrome coronavirus (MERS-CoV) and Ebola.

Patients who have fully recovered from COVID-19 have antibodies in their plasma that can attack the virus. This convalescent plasma is being evaluated as treatment for patients with serious or immediately life-threatening COVID-19 infections or those judged by a healthcare provider to be at high risk of progression to severe or life-threatening disease.

Although the efficacy of convalescent plasma has not yet been proven in clinical trials, many hope that it can be effective in treating patients with COVID-19. McLaren Health Care and Karmanos Cancer Institute are working collaboratively with Mayo Clinic and government partners to offer this expanded access treatment to our patient population. This treatment is available at all of our McLaren hospitals.

CONTINUED ON PAGE 9

ARE YOU INTERESTED IN BECOMING A RESEARCH PARTICIPANT?

For information on enrolling in a clinical trial please visit our website at https://www.mclaren.org/main/research-trials1.aspx . Here you will find a list of open enrolling studies at McLaren, including which hospital the research is being done at and contact information for each study.

We have enrolling studies for the following conditions (not a complete list):

- **Diabetes**
- **High Blood Pressure (Hypertension)**
- **Stroke**
- **Heart Attacks / Heart Failure / Heart Disease**
- **Kidney Diseases**
- **Lung Diseases**
- **Peripheral Artery Disease**
- **Carotid Artery Disease**
- **Mastectomy**
- **Various Cancers**
  - **Breast**
  - **Lung**
  - **Prostate**
  - **Multiple Myeloma**
- **Patients who underwent intracranial aneurysm coiling**
- **Drug study for patients with recent acute coronary syndrome**

For a complete list of conditions, please visit our website listed above.

RESEARCH AROUND McLAREN

MANUSCRIPTS ACCEPTED FOR PUBLICATION

Hybrid triad provides fracture plane stability in a computational model of a Pauwels Type III hip fracture
M. Cordeiro, S. Caskey, C. Frank, S. Martin, A. Srivastava & T. Atkinson. Computer Methods in Biomechanics and Biomedical Engineering. Received 20 Mar 2019, Accepted 02 Mar 2020, Published online: 11 Mar 2020

Pre-bending a Dynamic Compression Plate Significantly Alters Strain Distribution Near the Fracture Plane in the Mid-Shaft Femur, DOI: 10.1177/0954411920903875
Proceedings of the Institution of Mechanical Engineers. Part H, Journal of Engineering in Medicine. Jacob Ristow, Matthew Mead, Minal Cordeiro, James Ostrander, Theresa Atkinson, Patrick Atkinson

Frontal Crash Injury Metrics Are Below Mandated Limits for a Spica Casted Child Dummy in Currently Available Restraints, DOI: 10.1097/BPO.0000000000001477
Journal of Pediatrics Orthopedics. Angela C Collins, Sean Caskey, Jeffrey B Peck, Norman Walter, Theresa S Atkinson, Patrick J Atkinson

Injury metrics are altered in spica-casted versus non-casted child ATDs in side-impact collisions with door intrusion
Matthew Mead, Sean Caskey, Norman Walter, Patrick Atkinson, Theresa Atkinson & Angela C. Collins. Traffic Injury Prevention. Received 07 May 2019, Accepted 12 Apr 2020, Published online: 13 May 2020

We sincerely regret if we left out any fellow or resident, due to our publication deadline. Nevertheless, our congratulations to all of you that received any recognition for your scholarly activity work. We also would like to recognize faculty, program directors, and all medical education staff for their support and assistance. Without you, none of this would have been possible.

PRESENTATION AWARDS

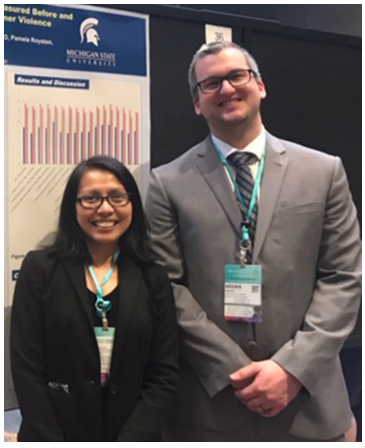
ACGME Residency: Improving Research Experiences for Medical Students
Dass, C., Ianitelli, M. and Brannan, G.D. 2nd Place. Poster presented at the AACOM Educating Leaders 2020 Virtual Conference. March 24-27, 2020.

Perceived Preparedness and Knowledge of Residents Measured Before and After a Resident Training in Domestic/Intimate Partner Violence
Burnell, M., Takov, V., Rummel, K., McMann, S., Royston, P., Brannan, GD. and Pawar, A. Poster presented at the 2020 ACGME Annual Educational Conference, February 28-29, 2020. San Diego, CA.

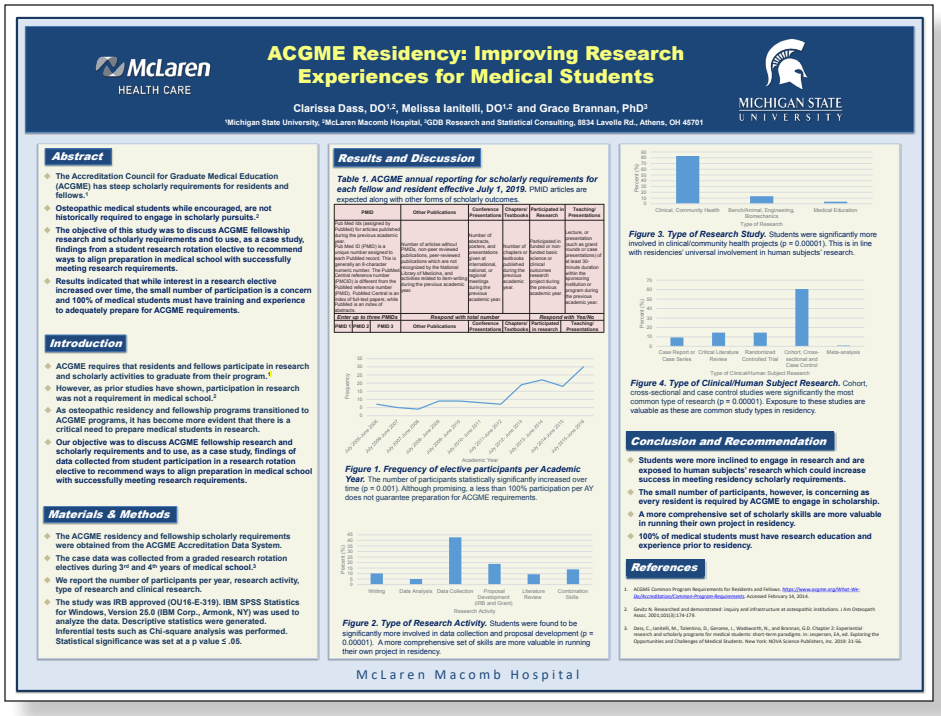
Clarissa Dass, MD

Improving Compliance Rates for Chemical and Physical Prophylaxis of Deep Vein Thrombosis Following Traumatic Events: A Quality Improvement Initiative
Fisher, P., Kohner, M., Gabriel-Champine, M. 3rd Place Overall. MSU's SCS Poster Day, May 20, 2020. East Lansing, MI.

Perceived Preparedness and Knowledge of Residents Measured Before and After a Resident Training in Domestic/Intimate Partner Violence
Dr. Kegan Rummel, McLaren Macomb General Surgery Resident, had a successful presentation at the 2020 ACGME Annual Educational Conference held February 28-29 in San Diego, CA. The poster was prepared in partnership with Dr. Mariah Burnell.



Grace Brannan, PhD, Macomb Research Advisor and Dr. Kegan Rummel, Macomb General Surgery Resident



MSU-FAME 2020 COMMUNITY RESEARCH FORUM

Congratulations to the winners of this year's Investigator of the Year award!

McLAREN FLINT
Faculty:
Andrew Champine, PsyD
Internal Medicine/Behavioral Medicine

Resident:
Arunima Dutta, MD
Internal Medicine

McLAREN BAY
Faculty:
Molly Gabriel-Champine, PhD
Family Medicine

Resident:
Jessica Gibson, DO
Family Medicine

McLAREN OAKLAND
Faculty:
Carl Shermetaro, DO
Otolaryngology

Resident:
Jason Kaplan, MD
Internal Medicine

RESEARCH AROUND McLAREN

THE ROAD TO 90

The following abstract will be presented at the 12th Annual Association of American Cancer Institute's Clinical Research Innovation Meeting in July 2020.

Authors: Kasha Donahue, BS, CCRP, Melissa Gorno, MS, CCRP, Sarah Bigelow, CCRP, Rachel Jarrard, PhD, Paige Dykema, BA, CCRP, Rajiv George, CCRP, Valerie Davis, BIS, CCRP, Veronica Gorden, BA, CCRP, Maureen Kelley, MSBMS, CCRP

Background

Study activation within 90 calendar days has been a priority for the Karmanos Cancer Institute (KCI) Clinical Trials Office (CTO) since the NCI Operational Efficiency Working Group (OEWG) directive was released in the 2000s. In early 2019, a task force was established to evaluate the activation process with a goal of modifying current workflows to maintain a consistent 90 day activation median for new studies. In order to make these changes, the task force recognized the need for institutional leadership support for interdepartmental workflow changes.

Goals

The primary goal was to decrease the activation timeline to 90 calendar days as defined by Protocol Review and Monitoring Committee (PRMC) submission to activation (open to accrual). Rate limiting steps needed to be defined and categorized by responsible department. In addition, the task force aimed to increase interdepartmental communication and collaboration.

Solutions

The CTO reviewed a diverse subset of the KCI study portfolio activated in 2018. The rate limiting steps were identified and included: receipt of required documents, consent preparation and review, Institutional Review Board (IRB) review, budget and contract review and Site Initiation Visit (SIV) requirements. Data related to these steps was used to develop recommendations and subsequently presented to institutional leadership. The presented recommendations were approved and introduced to the CTO as the "Road to 90" initiative in April 2019.

The following changes were implemented:

- Enforced receipt of necessary study documents prior to PRMC submission
- Amended consent, budget and contract study activation processes
- Expanded use of OnCore® task lists across departments to track key milestones
- Addition of two activation coordinators to facilitate communication and timely completion of required steps
- Streamlined and optimized the activation of protocols throughout the KCI Network
- Increased frequency of collaborative meetings with the local IRB to communicate newly defined goals and review progress
- Developed and revised policies and procedures to support this initiative

Outcome

The changes implemented resulted in a dramatic decrease in the CTO's monthly activation timeline (Attachment 1). Additionally, the initiative improved internal and external communication and collaboration. The "Road to 90" initiative has been adopted as an institutional goal and continues to be supported by leadership throughout the KCI Network. A welcome outcome that resulted from this initiative included a well-defined "Road Map" to support the activation of studies in the required timeframe. The addition of protocol activation coordinators allowed the CTO to globally track specific steps of activation using enhanced task lists within OnCore® and identify potential road blocks.

Lessons Learned

Optimal staffing levels and qualifications played a pivotal role in the success of the initiative. In addition, institutional leadership support has been abundant since the inception of the proposed process changes. Real time task list completion allowed for accurate tracking of activation metrics. These metrics provide the CTO with a plethora of data to aid in continued efforts to improve collaboration between all involved stakeholders. The CTO established specific timelines to successfully activate trials within 90 days; however, unanticipated sponsor delays continue to impact these efforts. The CTO continues to track these trends and review the robust data accordingly for continued process improvement.

RESEARCH AROUND McLAREN

DRUG STUDIED AT KARMANOS CANCER INSTITUTE ENTERS CLINICAL TRIALS FOR TREATMENT OF COVID-19

Asfar Azmi, PhD

Jeffrey Zonder, MD

An oral therapy that has been studied in laboratory experiments and clinical trials at the Barbara Ann Karmanos Cancer Institute, in partnership with Karyopharm Therapeutics Inc., has entered clinical trials for the treatment of COVID-19 and related viruses. The oral drug, selinexor (marketed as XPOVIO®), is currently approved at higher doses by the Food and Drug Administration (FDA) as a treatment for cancer patients with relapsed or refractory multiple myeloma. Asfar Azmi, PhD, assistant professor, co-leader, Tumor Biology and Microenvironment Research Program, Karmanos Cancer Institute and Wayne State University School of Medicine and director of pancreas cancer research initiatives led the Karmanos team that helped developed the drug.

Clinical trials exploring the use of selinexor in treating COVID-19 are underway at 40 locations internationally, including Karmanos Cancer Institute. Eligible participants must meet set criteria, which include confirmed laboratory diagnosis of SARS-CoV2, hospitalization with symptoms of severe infection, and consent to participate within the first 48 hours of hospitalization.

"The fascinating thing about this trial is that we are able to apply information learned about the drug's effect on tumor cell biology to the treatment of deadly viral infections using lower doses of the drug than we typically use to treat cancer," said Jeffrey Zonder, MD, who is the Principal Investigator (PI) for the trial at Karmanos. Zonder was also the PI for several previous trials studying the drug in multiple myeloma and a co-investigator on laboratory work and a clinical trial using the drug to treat Non-Hodgkin's Lymphoma.

Jeffrey Zonder, MD, leader of the Multiple Myeloma Multidisciplinary Team at Karmanos Cancer Institute, was interviewed by Russ McNamara on WDET, Detroit's NPR Station about this trial. To listen to the interview, visit karmanos.org/karmanos/news.

About Selinexor

Selinexor and related compounds can disrupt the movement of viral accessory proteins thereby blocking the replication of multiple viruses in vitro and in vivo. These drugs have also been shown to mediate anti-inflammatory and anti-viral effects, including suppression of respiratory infections in several animal models. Earlier studies showed that nuclear export inhibitors, such as selinexor, could retain SARS and MERS virus accessory proteins in the nucleus of host cells, thereby suppressing their virulence and pathogenicity. These findings have ushered the initiation of a global randomized clinical trial for low dose oral selinexor in hospitalized patients with severe COVID-19.

Dr. Azmi explained how the drug may work in treating COVID-19 and other viruses.

"Proteins move between different compartments of the cell, and their exact location is critical to their proper function," said Dr. Azmi. "Most of the genome surveillance and tumor suppressor proteins are exported out of the cell nucleus using an exporter called exportin 1 (XPO1). Every protein carries a barcode called nuclear export signal (NES) that is recognized by XPO1 causing the export of the cargo. XPO1

is hyperactivated in several pathologies including cancer and inflammation. This excessive XPO1 activity causes unusually high export and incorrect localization of tumor suppressors and genome surveillance proteins leading to their inactivation and tumor growth. Viruses that cause influenzas, H1N1 and SARs-COV2 similarly hijack the nuclear transport machinery. This makes XPO1 a vital component of viral replication and a valid therapeutic target."

"I am very proud that the work of our investigators is contributing to the fight against COVID-19. I congratulate the team in helping to develop a drug that is finding applications beyond cancer treatment," said Gerold Bepler, MD, PhD, president and CEO of Karmanos Cancer Institute.

In addition to the work conducted by Dr. Azmi's team, several other Karmanos investigators contributed to the development of the drug. These clinical investigators include Anthony Shields, MD, PhD; Elisabeth Heath, MD, FACP; Philip A. Philip, MD, PhD, FRCP; Ammar Sukari, MD; Erlene Seymour, MD; and Jeffrey Zonder, MD.

CONVALESCENT PLASMA AS A COVID-19 TREATMENT

CONTINUED FROM PAGE 3

According to Joseph Uberti, MD, PhD, division chief, Hematology and co-director, Bone Marrow & Stem Cell Transplant Program at Karmanos Cancer Institute, "(Convalescent plasma) is not proven for this disease, but we are trying to see if this is one way we can help overcome the bad outcomes in some of our patients. There is some information showing that people who have had a COVID-19 infection and recovered from it now have antibodies in their plasma which can help to treat the virus in somebody else."

There is preliminary data from a small group of patients from China showing that convalescent plasma may be effective in helping critically ill patients recover. Currently, a much larger study is underway at hundreds of hospitals across the country. Data from infused patients will be collected and analyzed to determine efficacy. As of June 1, this large study is underway at 2,396 sites with 7,157 physicians. 24,513 patients have been registered and 18,543 have received convalescent plasma.

At McLaren Health Care, the first COVID-19 convalescent plasma treatments started in late April. These were initially spearheaded by Dr. Franklin Rosenblat, Infectious Disease specialist at McLaren Oakland and Dr. Asif Alavi, Oncology and Hematology specialist at Karmanos Cancer Institute. The treatment for these patients includes a one-time plasma transfusion over the course of about an hour. Patients who received the transfusion will be monitored by physicians and included in the larger US study examining convalescent plasma transfusions.

The program at McLaren Health Care has grown rapidly since late April. Numerous physicians have ordered this investigational treatment for their sickest patients with hope of having a positive impact. Christopher Provenzano, MD, Director of the McLaren Macomb Internal Medicine Program, has chosen this treatment for many of his patients in an attempt to keep moderately ill patients from becoming critically ill. "Everyone has been affected in some way by COVID-19, and worldwide efforts to find treatment options have been inspiring. So, it is an honor and privilege to lead McLaren Macomb as part of the U.S. COVID Plasma Study sponsored by the Mayo Clinic," says Dr. Provenzano.

Safety data reported after the first 5,000 patients who were transfused revealed "no signal of toxicity beyond what is expected from plasma use in severely ill patients," according to Mayo reports. It has not yet been proven that this treatment will or will not help those with COVID-19 but this is one of the only treatments that we have at present. "Our hope is that COVID-19 convalescent plasma will be an effective antibody-based treatment for the virus," said Dr. Alavi.

While there is promise in the use of convalescent plasma, the treatment must overcome a major hurdle: availability of plasma. Donors must meet set criteria, including the requirement that they be 28 days post-recovery. This timeline, as well as hesitation among recovered patients, has created a long delay in the process.

"I clearly understand how patients might not want to do this because they have been through a lot with the COVID infection but … other patients may be treated successfully with this," said Dr. Uberti.

In coordination with the U.S. Food and Drug Administration (FDA), the Red Cross is seeking people who are fully recovered from the new coronavirus to sign up to donate plasma to help current COVID-19 patients. McLaren Health Care and Karmanos Cancer Institute are supporting this effort by connecting our patients to this important opportunity to help patients currently fighting the disease.

Individuals interested in donating plasma can find more information at: ***https://www.mclaren.org/main/red-cross-covid-19-plasma-donations*** *or* ***www.karmanos.org/DonateRedCross***

RESEARCH AROUND McLAREN

CLINICAL TRIALS DAY

Clinical Trials Day is celebrated internationally on May 20 of each year to commemorate the date that English surgeon Dr. James Lind began the first randomized clinical trial to combat scurvy in 1747. Dr. Lind's research took place on a British naval ship where he divided ill soldiers into six groups, provided each group with various dietary supplements, and was able to determine a positive connection between Vitamin C and scurvy. This clinical trial laid the foundation for modern clinical research.

Clinical Trials Day is a celebration of clinical research professionals and participants, by recognizing their contributions to public health and medicine. It is a well-deserved time out to honor those who make clinical trials possible and raise awareness of clinical trials in the community. Clinical Trials are research studies with human volunteers that are intended to add to overall medical knowledge. Behind every medication and medical intervention are thousands of patients that volunteered to participate in Clinical Trials. Without Clinical Trials, devastating diseases like polio would not be all but eradicated in the United States. Nor would we have seen a 50 percent decline in coronary artery mortality rates between 1980 and 2000. Clinical Research Professionals and patients are the unsung heroes in the development of new drugs, devices, biologics and treatments to improve the care of all Americans.

McLaren Health Care would like to take this time to thank our clinical research professionals for their tireless efforts to advance medical science, as well as improve the health and well-being of our patients. McLaren patients involved in clinical trials are often provided choices for their care beyond the standard available treatment. This care is coordinated and provided by our highly skilled clinical research professionals. At McLaren, research matters for our patients, our organization, and our physicians. Growing our research program gives our patients access to the latest clinical trials and the confidence that they are receiving the best treatments, proven by research conducted in our own hospitals, by physicians they know and trust.

Clinical Trials at McLaren Health Care are conducted by the McLaren Center for Research & Innovation and the Karmanos Cancer Institute.

KARMANOS REPORTS SUCCESSFUL NATIONAL CANCER INSTITUTE CORE GRANT VISIT

This year's visit was conducted virtually for the first time

After nearly 18 months of hard work and an almost 2,000-page grant application, Karmanos Cancer Institute is pleased to report that it had a successful core grant site visit on May 7, 2020.

This year's visit was unique due to its virtual format, in response to COVID-19. The National Institutes of Health (NIH) prohibited face-to-face peer review meetings and recommended alternative formats such as video conferencing and virtual meetings. Karmanos was one of the first four cancer centers to engage in a virtual visit.

Countless hours of rehearsal with Karmanos senior leadership were put on stage during the unique visit. At any one point, more than 60 participants were on the WebEx meeting, including a site review team of 15 expert peer reviewers and NCI leadership and staff.

The day started with special welcomes from Wayne State University President Dr. M. Roy Wilson; McLaren Health Care CEO Phil Incarnati; Chair of the Karmanos Cancer Institute Board of Directors Tim Monohan; and Peter Karmanos Jr. It was followed by presentations in all key review areas.

Karmanos leadership answered many questions while presenting the latest scientific achievements at the Institute. More importantly, reviewers were informed about the impact Karmanos has on its 46-county catchment area, which includes the 16-location Karmanos Network.

"The site visitors were very professional, and we are pleased to report that the visit was flawless; we have no complaints about the process," said Gerold Bepler, MD, PhD, president and CEO of Karmanos.

The next step in the process is the NCI Subcommittee-A review, which occurs in late July. After considering the written report of the site visit committee, the NCI Subcommittee-A provides a final merit evaluation and a budget recommendation for the Cancer Center Support Grant (CCSG) application in a Summary Statement.

Congratulations to the entire team for a successful site visit!

FACULTY, FELLOWS & RESIDENTS
SCHOLARLY ACTIVITY NEWS

Carlos F. Rios-Bedoya, ScD

CLARIFICATION: By the time this issue of Research Matters goes to press the IRB would still be transitioning to a new online application submission system called iRIS. As with almost everything, the COVID-19 pandemic has delayed the transitioning and implementation of the new IRB online application submission system. In the next part of this series I would be updating this section of the diagram/flowchart to describe the use of iRIS instead of eProtocol.

SCHOLARLY PROJECT STAGES EXPLAINED, PART 3

BY CARLOS F. RIOS-BEDOYA, ScD

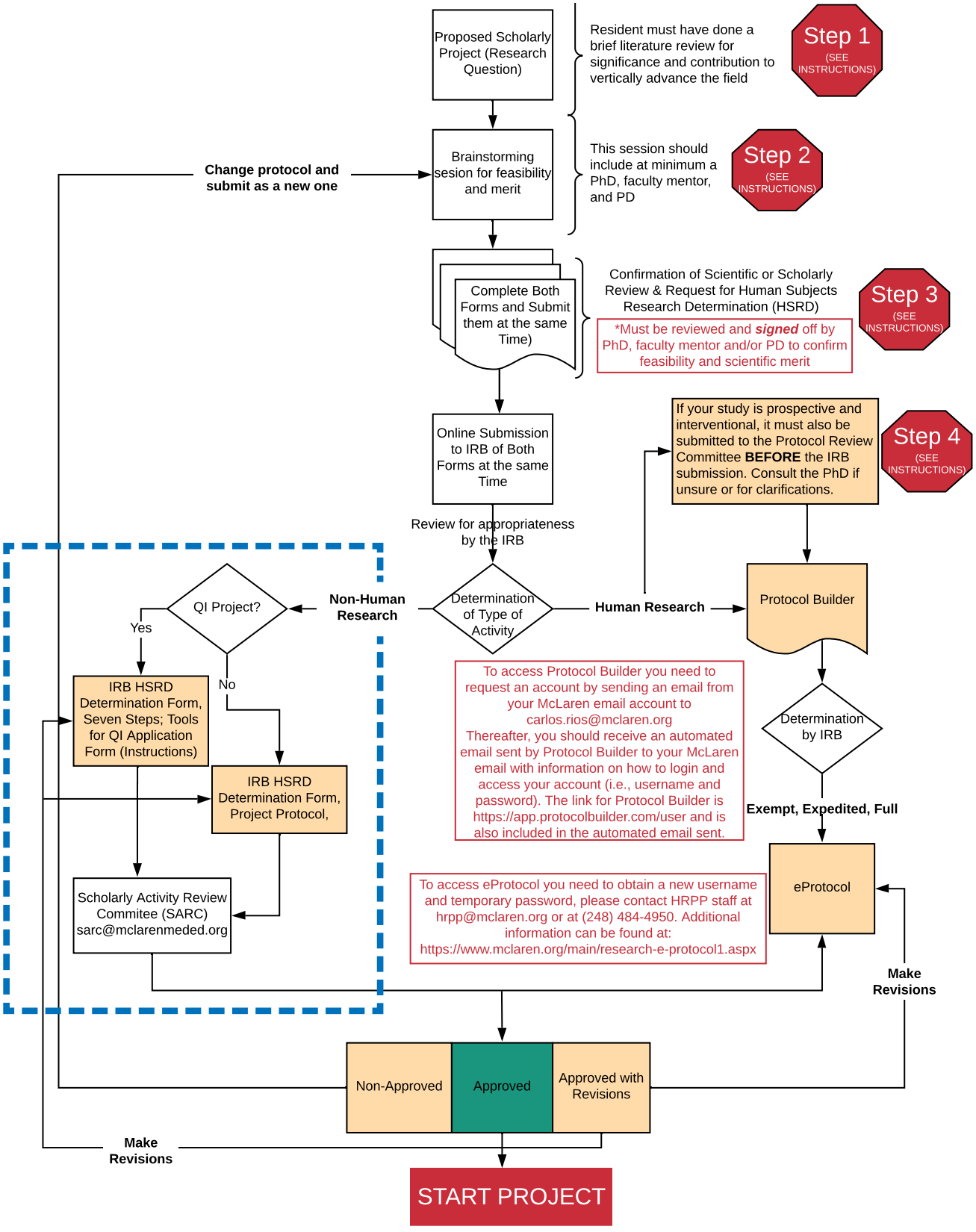
McLaren's Division of Scholarly Inquiry, in its efforts to encourage, promote, and support scholarly activity among residents/fellows and teaching physicians developed a scholarly project stages diagram/flowchart (Figure 1) more than two years ago. Over these past two years, it has been modified in response to suggestions and recommendations from residents/fellows and teaching physicians. The updated diagram/flowchart should serve as the roadmap for scholarly activity from its conception to its IRB/SARC approval. Even when residents/fellows, teaching physicians, and PhDs are aware of this diagram/flowchart, some misunderstanding seems to exist. Part 3 of this series will describe and explain the aim and purpose of the diagram/flowchart if the scholarly project is determined by the IRB as Non-Human Subjects Research (*see Figure 1 blowout section*).

Non-Human Research. The IRB sends a letter of determination to the Principal Investigator (PI) of the project informing the PI that, in this case, the proposed study has been determined that it **DOES NOT** meet the criteria for human subjects' research. The aim of this step is to guide residents/fellows to follow the non-human research path of the diagram/flowchart. The purpose of following this path is to begin writing the scholarly project protocol using either the Seven Steps; Tools for Quality Improvement (QI) Application form (if it is a QI project). For non-QI projects, the Research Plan for Secondary Analysis of Existing Data/Specimens form (projects using data already collected) or the Non-Human Subjects Research Form (neither QI nor secondary data analysis projects) should be completed. To determine what is the most appropriate form for the project, the resident/fellow should consult the PhD (your best friend in this process) assigned to each subsidiary. Thereafter, and in collaboration with the PhD, the resident/fellow must complete one of these forms and submit it, together with the IRB determination letter, to the Scholarly Activity Review Committee (SARC). These documents should be sent electronically to the SARC email (sarc@mclarenmeded.org).

Determination by SARC. The aim of this stage is for the SARC to evaluate the non-human research project for scientific rigor and feasibility. Once your proposal is received by the SARC, it goes through a quick administrative review for completeness and compliance with instructions. If the proposal moves forward, it is sent to two reviewers for comments and suggestions. Otherwise, it will be returned to the PI to revise the proposal and resubmit once the administrative findings have been addressed.

In Part 4 of this series I will describe and explain the aim and purpose of the diagram/flowchart if the scholarly project is approved, needs to be review and resubmit, or is rejected by the IRB/SARC. The diagram/flowchart presented and discussed in this article is available upon request to a PhD. In the Division of Scholarly Inquiry, we have a commitment and responsibility to promote, expedite, facilitate, and support scholarly activity productivity among McLaren residents, fellows, and teaching physicians. For additional information or questions contact Dr. Carlos F. Ríos-Bedoya at carlos.rios@mclaren.org.

Figure 1 Scholarly Project Stages



EQuIP CORNER

Andrea Klaver

UPCOMING RESEARCH EDUCATION

Virtual ACRP 2020: Workforce Development
ONLINE
June 25, 2020

MAGI's Clinical Research Cloud Conference 2020
ONLINE
June 22 – July 2, 2020

2020 SOCRA Annual Conference
Las Vegas, NV
September 25 – 27, 2020

MAGI's Clinical Research Conference – 2020 West
San Francisco, CA
November 15 – 18, 2020

BROWN BAG SERIES

Alternative Consenting: E-consenting and Telemedicine
July 7, 2020, 12:00 – 12:45
LIVE WEBINAR

Research Conflict of Interest
September 8, 2020, 12:00 – 12:45
LIVE WEBINAR

To register contact Andrea Klaver at (248) 484-4987 or andrea.klaver@mclaren.org.

CONDUCTING RESEARCH VISITS DURING THE COVID-19 PANDEMIC: CHOICES AND CHALLENGES

BY ANDREA KLAVER, MBA, CHRC

COVID-19 is not just altering our everyday life; the global coronavirus pandemic is also upending clinical research workflows. As health systems, universities, and other research systems across the country make the shift to go virtual, the McLaren Health Care (MHC) research staff are working to protect their research participants, staff, and their larger communities from risk of infection from COVID-19, in addition to preserving ongoing access to research which may provide essential support to participants in a fast-evolving landscape.

While COVID-19 is sure to slow most protocols, the area of research impacted most by the lack of face-to-face interaction may be study activities which involve bringing individuals or groups of people together in proximity – the study visit.

To alleviate the impact that the temporary pause on in-person methods might have on your research, you may want to consider alternative methods for visits as we endure the pandemic and know the challenges that may lie ahead.

Temporary Changes to your Research: Hit Pause or Go Virtual

Research teams that depend on face-to-face interaction to collect data or carry out research procedures will have the choice to place a study hold or continue their research with modifications – essentially, hit pause or go virtual.

If a study hold is placed, the Principal Investigator(s) can voluntarily hold all clinical research activities.

If the Principal Investigator(s) choose to continue their research with modifications, they may be implemented per MHC Policy without first obtaining IRB review and approval when the modification is necessary to eliminate apparent immediate hazards to the subject [45 CFR 46.108 (a)(3)(iii) and 21 CFR 56.108(a)(4)].

This allows for unavoidable, protocol-specific deviations as necessitated by the impact of the current COVID-19 public health emergency only.

For more details, see the McLaren Health Care Research Integrity web page at https://www.mclaren.org/main/research-integrity to review the Interim HRPP Policy on Human Subject Research During COVID-19 Pandemic linked on the page.

Continuing with Modifications: Telemedicine & HIPAA

The use of telemedicine technology for conducting clinical video visits limits the risk of infection of persons who would be exposed from an in-person consultation. The U.S. Department of Health and Human Services Office for Civil Rights (OCR) issued a Notice of Enforcement Discretion on March 17, 2020 which indicated that, during the COVID-19 national emergency, the OCR would not impose penalties for noncompliance with the regulatory requirements under the HIPAA Rules against health care providers who provide telehealth visits in good faith.

MHC offers secure platforms for telemedicine visits. To ensure the confidentiality and security of the telehealth video visit, it is important to ensure that both the provider and the patient are in a quiet and private setting and will not be interrupted.

Confidential patient information should not be recorded or stored on the computer or device used to conduct the visit, and, if using non-McLaren third party video chat applications such as Apple FaceTime to conduct visits, the patient should be notified of the potential privacy risks associated with the use of the application.

All available encryption and privacy modes, such as passwords, should be enabled whenever possible. Per the OCR Notice, the use of applications such as TikTok and Facebook Live were specifically prohibited since they are public-facing and present greater security concerns.

Managing Remote Study Visits and Data Collection

Privacy and confidentiality requirements remain critically important always, especially when conducting study visits remotely. Remember that the collection, transmission, and access to private identifiable information (PII) or protected health information (PHI) must comply with MHC and other policies for security of research data.

Do not store PII or PHI on unsecure devices in order to work remotely. Use McLaren-approved cloud services and VPN access while working at home instead of storing data directly on personal devices.

If making copies of physical research records or data (paper consent forms, case report forms, questionnaires/ surveys, etc.), secure all paper locally following HIPAA principles and return to the IRB-approved location as soon as is practical.

Challenges with Digital Literacy and Data Analysis

Addressing the digital literacy of study participants and research staff may be another issue. Depending on your research population, you might find that making the switch to virtual visits is either no big deal, or a significant investment of your time.

Should your study population feel uneasy using a virtual platform for their visits, there may be the potential for added stress on the part of the participant. Consequently, survey responses may be affected by the change of visit method, or even the types of health concerns that may be more prevalent during the pandemic.

Researchers should document when and how data were received and consider controlling for those differences. Research projects conducted prior to and continued throughout the pandemic must also account for changing methods in the middle, such as switching from in-person, pen and paper surveys conducted at study visits to online versions.

Difficulties with Alternative Visit Methods and FDA Guidance

As their guidance suggests, the Food and Drug Administration (FDA) understands that COVID-19 may impact clinical trial protocols. Challenges may be caused by quarantines, building or study site closures, travel limitations, or other issues, including COVID-19 infections of study personnel or study participants.

These issues might make it difficult to follow protocol-specific procedures, including the planned administration of study drugs or the use of investigational devices. Sticking to the schedule of study visits and laboratory or diagnostic testing may be affected, as well. Consequently, there may be unavoidable protocol deviations because of COVID-19 illness or infection control measures associated with the pandemic.

Overall, the FDA encourages investigators to follow the guidance of their local IRBs. At MHC, IRB policy-permitted deviations are typically submitted during continuing review. However, COVID-19 related protocol deviations should not be saved for the next continuing review, but instead submitted as they occur. It is acceptable to submit an aggregate of COVID-19 deviations on one Modification form.

Re-consenting is generally not necessary unless the changes to the research are such that the original consent is no longer valid.

Again, changes to minimize or eliminate immediate hazards or to protect the life and well-being of study participants may be implemented immediately, but the IRB must be alerted promptly.

The FDA Wants to Help Researchers

To assist with the alternative methods for in-person study visits necessary during the COVID-19 pandemic, the FDA has made its FDA MyStudies app (now COVID MyStudies) available as a free platform to obtain informed consent securely from eligible study patients when face-to-face contact is not possible or practical due to COVID-19 measures.

Obtaining informed consent virtually can help make sure clinical trials are not needlessly delayed during the pandemic. The FDA suggests and encourages investigators to consider using electronic methods of obtaining informed consent if possible.

If you are interested in using the COVID MyStudies app, contact the CDER Real-World Evidence Program at CDERMedicalPolicy-RealWorldEvidence@fda.hhs.gov and reference your pre-IND or IND number, if applicable.

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ANNOUNCEMENTS AND WHAT'S NEW

Andrea Klaver

Andrea Klaver, MBA, CHRC joined the McLaren Research Integrity department in February 2020 as the new Research Compliance, Quality Improvement, & Education Specialist. Andrea will provide on-going support and education to the research community at McLaren and its subsidiary hospitals to ensure compliance with applicable institutional, FDA, OHRP, HIPAA, and GCP requirements and guidelines. Andrea obtained her Bachelor of Science in Microbiology from Michigan State University and her MBA from Walsh College in Troy, MI. Andrea also holds her CHRC endorsement (Certified in Healthcare Research Compliance). Andrea has 14 years of research experience in biotechnology manufacturing and quality assurance, Alzheimer's and Parkinson's disease laboratory management, and compliance initiatives and research billing. Welcome Andrea!

Julie Thai, MD

Dr. Julie Thai, Family Medicine Resident at McLaren Flint, has been named 2020 Family Medicine Resident of the Year by the Michigan Academy of Family Physicians. According to her program director Dr. Prabhat Pokhrel, "she has set very high standards in many different areas for all of us, such as advocacy, scholarly activity, and just being a family physician in her heart." Please help us congratulate Dr. Thai.

EQUIP CORNER

CONDUCTING RESEARCH VISITS DURING THE COVID-19 PANDEMIC

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Doing What is Best for Participants

When it comes down to it, the question is whether the research visit is carried out in such a way that it changes the risk-benefit ratio outlined in the consent. The fundamental ethical principles outlined in the Belmont Report – autonomy, beneficence, and justice – should be considered when deciding the best course of action for study participants, prior to pausing all clinical activities or deciding to go virtual.

During the COVID-19 pandemic, this may include discussions about the risk of exposure to the disease and the latest information on disease transmission so that participants are able to make their own choices regarding study visits. It may also include the risks associated with delay or discontinuation of the study interventions, if applicable.

Keep Things in Perspective

The past few months have been upsetting, to say the least, for everyone. Our routines, personally and professionally, have been turned upside down with the introduction of COVID-19. We know all too well that sensitive research routines and protocols, especially, have been difficult to continue as they were.

However, it's important to remember that we're not the only ones in this situation and that normal research activities will eventually resume. In the meantime, alternative methods for in-person study visits can be arranged such that studies continue in a meaningful way while protecting study participants and minimizing difficulties.

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