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LLU *clinical trials*

Looking to the Future

Contributed by Linda Wu, Director — Clinical Trial Center

In the February issue of *Notes from the President*, Dr. Hart raises a strategic question that the CTC and many clinical research stakeholders have been contemplating for some time. For the past two years that the CTC has been working alongside clinical researchers, we have observed firsthand the challenges of maturing clinical research as an institution. With increasing regulatory complexity and decreasing federal research funding, clinical research today is expensive, highly competitive, and requires the highest caliber research teams and facilities. The answer to the strategic question will drive the future development of clinical research on campus.

In 2011, there were 60 new clinical trials, prospective in design with therapeutic intent. Of these 60 new trials, 76% were industry-sponsored, 12% were Investigator initiated and the remaining 12% were cooperative group trials. For non-interventional studies in 2010 and 2011, there were 154 expedited-review human studies, most of which were chart review, data collection, and observational studies with 65% driven by school of medicine (SOM) investigators and 73 exempt-reviewed human studies, mostly chart review, survey and questionnaire studies with 90% driven by SOM investigators. These statistics indicate that the majority of our clinically-related research is non-interventional and with those that are interventional, only a small percentage (12%) is LLU investigator initiated studies.

Searching through Thomson Reuters *Web of Science*®, our institution has about 1,178 records of publication in peer review journals from 2010 and 2011. Twenty five percent (25%) of these records are authored by clinical faculty with approximately 65% journal articles, 25% meeting abstracts and 10% review, letter or editorial materials.

In an effort towards further development of clinical research, the Dean of SOM has begun a brainstorming taskforce comprised of key clinical investigators within the SOM. The first meeting was held to target our current clinical trial challenge-subject enrollment. With collective knowledge, experience and insight, root causes were discussed with possible solutions. The group exchanged solutions in areas of physician engagement, coordinator quality, infrastructure, leadership and the need to build a clinical research culture that embeds research as part of clinical service. These invaluable suggestions will be considered as we continue to develop clinical research in our institution.

As for now, CTC continues to partner with all members of the clinical research community to build excellence in clinical research. For our ongoing studies, CTC is privileged to facilitate the management of studies with several departments. This partnership also provides good insight for CTC to identify areas of need and provide services accordingly. The recent coordinator toolbox training was one example which was designed with hands on information and practical exercise. We hope to develop more training sections to target needs in the future.

The mission of the Clinical Trial Center is to facilitate clinical trial processing in order to foster and promote the clinical trial enterprise within the institution. As we ponder deeper around the question of research development, the CTC remains committed and enthusiastic about building research excellence with our research stakeholders.

Clinical Trial Coordinator Toolbox

A valuable, collaborative experience!

Contributed by Amy L. Casey, MBA, CCRP
Assistant Director of Clinical Trial Contracts, CTC

On Friday February 24th 30 clinical research coordinators and professionals embarked on an educational adventure unlike any offered at Loma Linda before. The Clinical Trial Coordinator Toolbox was designed with a specific focus on study and patient management which highlighted subject management, study advertising, patient recruitment and retention strategies.

It was truly a collaborative and interactive workshop where stories were shared amongst the group and coordinator successes and challenges were expressed.

Coordinators and professionals across all disciplines were present which made for a diverse group. Some of the departments present were: Pediatrics, Ophthalmology, Maternal-Fetal medicine, Internal Medicine, Transplant, Anesthesiology, Dermatology and Neurology. The coordinators across the multiple departments were able to meet and interact with one another which in turn gathered a sense of "coordinator community" within the workshop.

Lila Dalton, Associate Director of the Clinical Trial Center and Mary Ann Nyc, Regulatory Coordinator in the Clinical Trial Center, expertly guides the attendees through the sessions. Their slides were well laid out and they passed out very useful sample forms and resources for the coordinators to reference in their everyday work.

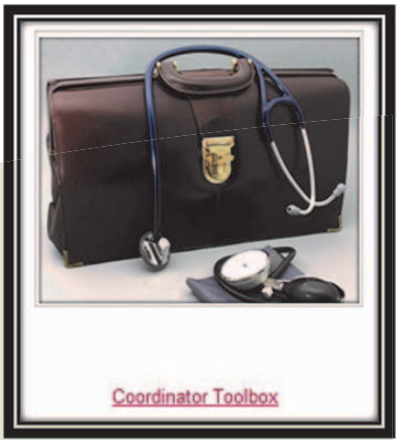
The workshop was broken up into 4 sessions: Regulatory Document Management, Recruitment and Prescreening, Subject Management: Screening and Subject Management: Enrollment through Close-Out

One particular interactive session occurred in the morning during the Regulatory Document Management session. The room was divided into teams to compete against one another to create what would ultimately be a sample regulatory binder which allowed every participant to leave with a useful tool that adds to every coordinators arsenal. The participants were quite competitive and were eager to win.

The toolbox was extremely well received as demonstrated by the evaluation form given to the participants. The lowest average score on the five point scale was a 4.9! The rating for the toolbox overall was a five across the board from all participants. One participant stated that what was most helpful about the toolbox was "learning about all of the resources and tools available to help things run smoother and maintain organization". Another participant added that "both speakers expressed not only knowledge, but a passion for what they spoke about". The Clinical Trial Center has already received requests to hold another toolbox workshop in the future so be on the lookout for further details.

You can now access electronic forms and templates from the Coordinator Toolbox Training on the CTC Website from any LLU Computer (or logged on remotely from home).

Go to "For Clinical Researchers; Useful Guides & Forms, then click on the "Coordinator Toolbox" link.



Adverse Event Policies & System Update

New Clarity Regarding Which Ones to Report

Contributed by JR Krausz, JD, CIP, CCRP
Research Education Coordinator, Research Integrity

It is easy to understand *why* adverse event reporting is necessary. Despite the many safeguards (careful study design, regulatory controls, IRB review, etc.), risk is never eliminated. Although not all studies carry equal risks for subjects, in the aggregate, there remain innumerable ways for human subjects (upon whom research depends) to experience harms of diverse kinds. Monitoring the occurrence of adverse events allows corrective measures to be taken. AE's surveillance is also an important way to verify whether the risks of participation match what IRB judged them to be at the time of study approval.

Unfortunately, the simple idea of AE reporting has become ambiguous and tangled for researchers to fulfill in practice. One big reason is the lack of harmonization among the many regulators and stakeholders (DHHS, FDA, other Federal agencies, sponsors, IRB, State government, Loma Linda University, etc.) who place different, often inconsistent mandates on researchers regarding what to report, to whom, and when. The nature of research also means initial results or occurrences may not be easily interpreted. This can make it challenging to render judgment about AE causality, whether the AE was expected, and whether or not serious.

Further, for multi-center studies the long-standing requirement for investigators to independently evaluate and submit to IRB reports of AE's occurring at other institutions has flooded the system with information of questionable value, yet consumed substantial investigator and staff resources that could be more productively employed.

Fortunately, government and others have come to recognize these issues over the last few years and made important changes to both regulation and guidance documents in this area. Accordingly, last December Loma Linda also approved new Adverse Event reporting policies and procedures. Research Affairs also developed innovative enhancements to its current systems and tools to help investigators achieve reporting compliance with more precision and typically with less effort.

Here are some of the important benefits to look forward to from an investigator's perspective:

- For every applicable study, IRB will provide unambiguous and specific instruction (in the form of an "AE reporting matrix"), regarding which adverse events need to be reported.
- For multi-center, sponsored clinical studies that utilize either a data safety monitor board (DSMB) or data monitoring committee (DMC), Loma Linda investigators will no longer have to routinely evaluate and report to our IRB all the AE's occurring at other, external sites. (Those few requiring study changes directed by the DSMB or DMC will still be reported.)
- Principal Investigators (or qualified investigators to whom AE surveillance has been appropriately delegated) have responsibility to classify the AE; but once done, new system elements can capture that assessment in a way that allows coordinators or other support staff to "take it from there." Using the tools, the coordinator can easily determine which AE's are reportable to Loma Linda's IRB, and only enter those that must be into the computer.
- The new system's procedures are uniform, even though the specifics of each study are not. Adhering to the simplified procedures guarantees cross-the board compliance with the different regulatory authorities because "harmonization" of the reporting rules has been built-in to the system.

The changes to the AE reporting policies and system are being rolled-out already as this article is published. A new on-line training course accessible through the "OWL" portal is coming very soon. A training session for your department or other aggregation of personnel can also be arranged by contacting J.R. at Extension 87463, or email jrkrausz@llu.edu.

Engagement: The Key to Successful Recruitment in Clinical Trials

Contributed by Lila Dalton, Associate Director at the Clinical Trial Center

Recruiting for clinical trials is a constant challenge for even the most experienced Principal Investigators and study coordinators. Understanding the challenge of recruitment requires identifying the barriers and challenges and then identifying ways to overcome them. The fact that many primary care physicians, surgeons, and other members of the healthcare team do not encourage their patients to consider participation in clinical trials contributes to low enrollment. Results from one study showed that a recommendation by their physician was the primary factor influencing patients' decisions to enroll in a trial.[1] Obtaining the support of the primary healthcare team is an important factor to increasing enrollment. In addition to lack of primary care physician and healthcare team support, the misconceptions about human subject research continue to create resistance toward clinical trials. An engaged PI and study coordinator are the primary element to the success of clinical trials and effective recruitment at a site. It is essential that the study team present a positive image, be honest and respectful, and be engaged.

So what does the engaged PI look like? An engaged PI is well versed on the research protocol, provides protocol training and encouragement to both the clinical and research teams, and is committed to the success of the clinical trial. A primary role of the PI is to lead the regular research team meetings to discuss the details of the study at the site. An important purpose of the team meeting is to discuss recruitment, enrollment, and the status of currently enrolled subjects. The team meeting is an opportune time to encourage team involvement and develop recruitment strategies. Enlisting the support of referring physicians and healthcare team is another role of the PI that has a direct impact on recruitment. Direct communication between the primary physician and the PI or physician referral letters can be used to gain this support. This also sends a clear message to the clinical team, the research team, and the sponsor that the PI believes in the research and is actively engaged.

The coordinator's role in recruitment cannot be underestimated. The engaged coordinator shares the PI's commitment to the success of the clinical trial. This requires the coordinator to have full knowledge of the study protocol, Good Clinical Practice, and the institution's research policies. Potential subjects need to have the ability to connect directly with a member of the research team to have questions answered or fears addressed. The PI is simply not available to serve that role, so the coordinator becomes an essential team member. The availability of the coordinator is important; however it is not enough to simply be "available". The coordinator supports the success of the study at the site through active recruitment and positive engagement. Effective recruitment is an active process and a primary role of the coordinator. The active coordinator uses whatever resources available to identify potential subjects. This may include screening clinic schedules, querying databases, or identifying nursing staff that may assist with identifying subjects. The coordinator is the subject's advocate and should be dedicated to helping the subject understand the details of the clinical trial and guide them through their participation from consent to study completion. The coordinator's engagement will demonstrate to the subject and the clinical team the importance of the clinical trial they are being asked to support.

The engaged research team supports successful recruitment, however there is key member of the team that has not yet been identified: the subject. It is important that the patient who has been identified as a potential subject in a clinical trial be treated with respect and appreciation to facilitate engagement. Patient or subject engagement requires "communication with the patient, or clinical trial subject on the patient's terms."[2] Successful patient or subject engagement may require an additional commitment of time and resources, both of which are becoming more limited.[2] Many potential subjects are lost at the consenting stage of clinical trials; by utilizing technology and increasing communication time, we increase the likelihood of successful recruitment and increased engagement. Patient engagement is a challenge in many areas of healthcare, so what can we learn from the methods being used to improve engagement between healthcare providers and the patients? Technology may be the key; technology cannot and should not replace personal interaction but rather enhance it.[2]

Leveraging technology to encourage increased communication between healthcare providers and patients has been proven effective in actively engaging patients in their own healthcare.[2] Technology can be equally as effective for patient recruitment and increasing communication between subjects or potential subjects in clinical trials and the PI or coordinator. Perhaps the use of the study sponsor's website for referrals or prescreening; if the sponsor does not provide a website or centralized recruitment, they may provide study recruitment tools or subject education tools; consider posting these on approved websites. Text messages may be used to remind subjects of scheduled appointments and e-mail may be utilized to confirm the subject's understanding of the consent and confirming scheduled visits. By offering alternative methods of communication, the research team engages research subjects in the clinical trial on the subject's terms, therefore increasing the likelihood of compliance.

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irb corner

Contributed by Anu Diekmann, Sponsored Research Analyst at Sponsored Research

Get to Know Your IRB Chair

Rhodes "Dusty" Rigsby, MD, MBA has been Chair of the IRB since 2002. He is also an Associate Professor and Assistant Dean of LLU's School of Medicine, and Loma Linda's mayor since 2010.

1. As IRB Chair, what do you think is your most significant contribution to the protection of human subjects?

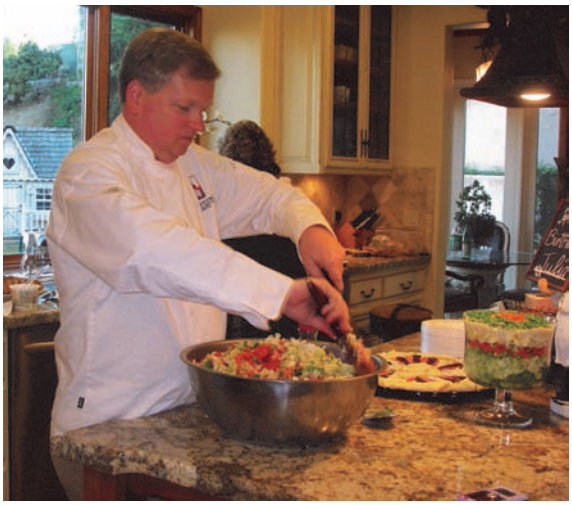
I like to think my biggest contribution at LLU is to keep the review process user-friendly so everyone can feel good about doing what's right.

2. What are 3 helpful hints you can give investigators/coordinators to streamline the IRB review process?

    1. *Follow the online instructions and templates.*
    2. *Respond rapidly to corrections from the IRB.*
    3. *Whenever in doubt, ask for help.*

3. What is the most rewarding aspect of being IRB Chair?

    Working with so many interesting and delightful people in Loma Linda's research community.



4. Do you see any similarities between being IRB Chair and the Mayor of Loma Linda?

    Yes. Keeping everyone happy is impossible. I endeavor in each realm to dissatisfy only a minority of people at any one time. If I lose a majority, I'm outta there!

5. What are some of your favorite books?

    Candide, for its humor and philosophy; Cold Mountain, for its language; Flatland, for its perspective.

6. You are a wonderful gourmet chef. Explain your approach to cooking. What is currently your favorite dish to make?

    I approach cooking like a chemistry experiment, trying to perfect a dish by trial and error and educated guesswork. My current favorite is vegetable stew.

Engagement: The Key to Successful Recruitment in Clinical Trials

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Time is a key component to increasing a subject's understanding, increasing enrollment, and retention. Respect of the subject's and clinical team's time will go a long way toward bringing them into the research team. A prime example of this is the consenting process, which takes quite a bit of time, can be overwhelming to the potential research subject, and often takes place in less than ideal situations. In ideal settings, the PI or coordinator would have both the time and tools they need to thoroughly review the protocol and allow time for the potential subject to absorb what he or she is committing to. When subjects have been given the time to consider the impact of participating in the clinical trial and connect with the research team, it opens the door for engagement.

Engagement is the key to success in clinical trials. Much can be learned from the patient engagement programs currently in use in the healthcare environment. By increasing the use of technology to increase awareness of clinical trials and to increase communication with the subject, the retention of subjects on studies may increase. In addition, by expanding the concept of the research team to include not only the principal investigator and coordinators but also referring physicians, health care teams, and subjects, engagement is increased and therefore enrollment will increase.

1 Kinney AY, Richards C, Vernon SW, Vogel VG. The effect of physician recommendation on enrolment in the Breast Cancer Chemoprevention Trial. Prev Med. 1998; 27(5 Pt 1): 713-719.

2 Safran, C. Patient engagement is a challenge across all of healthcare. The Monitor. April 2012; 26(2): 29-33.

coordinator's corner

Hello, I am so happy to be able to write this corner that is for us, the Study Coordinators here at Loma Linda University. Each publication I will be giving some tidbits of information to you that I think might be useful. Keep in mind that this is not anything life altering or earth shattering, but I am hoping you may pick up something to apply to your everyday life as a Study Coordinator.

As a coordinator I strive to:

- Serve as an advocate for my research subjects
- Work directly with prospective and enrolled subjects, and their families as needed
- Manage a GREAT deal of paperwork, electronic correspondence and data
- Report any findings to the PI, sponsor, IRB and other regulatory authorities
- Communicate with all members of the research team regarding the study, the research subjects and any items related to the conduct of the research study

These are just a few of the things we do every day to keep our studies up and running. Remember, you are a valuable member to your PI, study team and to your families that are helping us with our research. Until next time remember…

"Never go to a doctor's office whose plants die."

Cindy Kronbeck, LVN
Clinical Trial Center Study Coordinator

Share with us! Send your tips and/or questions to clinicaltrials@llu.edu for the next edition of Coordinator's Corner!

Congratulations!

The Clinical Trial Center would like to extend enthusiastic congratulations to the Cardiology Research Division. They have reached their initial enrollment goal of 60 subjects. Congratulations!

We would also like to extend enthusiastic congratulations to Physical Medicine & Rehabilitation. Dr. Brandstater's team received the bronze award for enrollment in January. Congratulations!

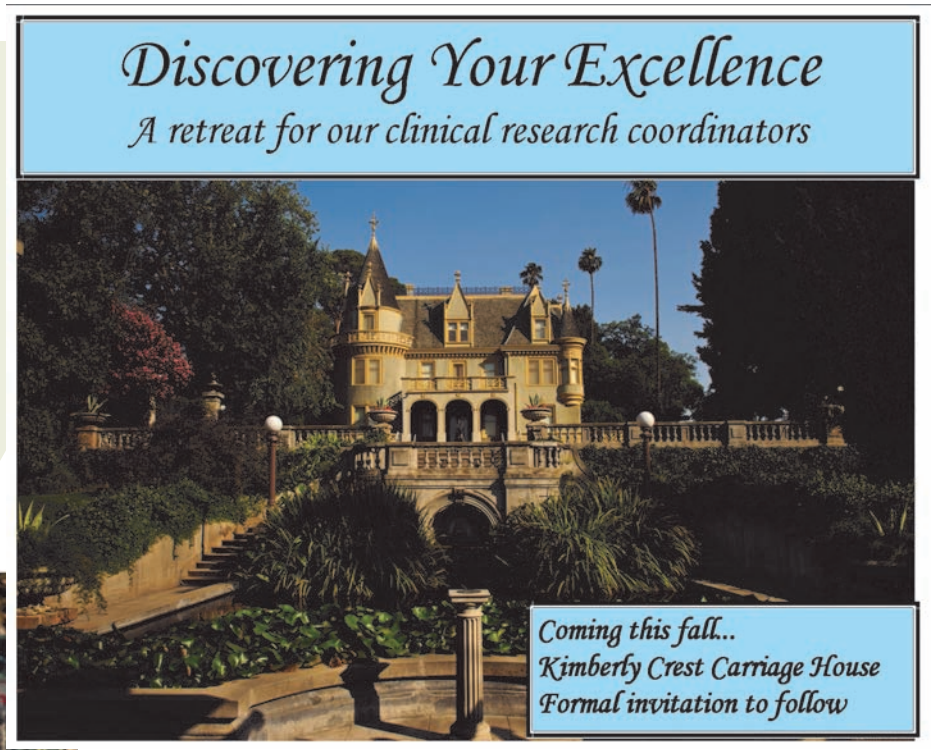
Congratulations to Dr. Torres! The Department of Dermatology was recently granted IRB approval for a new study investigating the use of Vismodegib as adjunctive therapy to Mohs Surgery in the treatment of Basal Cell Carcinoma with Industrial Grant Support funding close to one million dollars.

Anesthesiology research deserves a round of applause for enrolling 43 out of 50 subjects since their study opened for enrollment in January. Congratulations!

Thank you for your continued dedication to transform lives through clinical research.

Researcher's Resources

Your toolbox is only useful if you fill it with the right things. Here are some ideas…



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http://www.socra.org/html/SoCRA_Annual_Conference.htm

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