Clinical Research

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Featured Topic: Penn Clinical Research Management System (CRMS)

The Penn CRMS is an enterprise-wide Velos, Inc. based 21 CFR Part 11 compliant system that incorporates capabilities that enable full audit trails and wherein security is supported by individual user accounts requiring specific training and permissions. The Penn CRMS can be utilized by Penn as a data capture system for local or multisite trials. Permissions within the system can be configured for local users as well as users from external sites, and for view only by monitors, and sponsors. The Penn CRMS facilitates study operations and reduces costs by enabling remote monitoring and/or virtual signatures. Existing Electronic Case Report Forms (eCRFs) can be imported into Penn CRMS from other systems such as REDCap. Notifications and alerts can be generated as emails from within the system to appropriate parties. Robust financial features are also available for budget building, milestone tracking, automated invoicing and payment reconciliation. The system can also be used to generate Institutional, Departmental, PI and study level metrics.

Important Perelman School of Medicine (PSOM) Standard Operating Procedures (SOPs) for Clinical Research can be found at https://www.med.upenn.edu/clinicalresearch/policies-procedures-and-guidance.html#OperationalResearchTechnologySOPs8. PSOM requires registration in and use of Penn CRMS for all applicable studies per SOP 400 "CRMS Requirements". In addition to protocol registration in Penn CRMS, patient level research association in Penn CRMS is also required for applicable studies. In the Department of Orthopaedic Surgery, the Clinical Research Team completes the Penn CRMS registration on behalf of the surgeon PI as part of our routine services. For studies that are set up with a workflow that engages Penn Chart, patient registration in Penn CRMS is seamless as the two systems are linked. Many studies do not require use of Penn Chart in their workflow. In these cases, the Orthopaedic Surgery CRC or McKay Lab Teams complete direct patient level research association. It is therefore critical that all surgeon PIs ensure that at least one Orthopaedic Surgery CRC are designated as Study Contacts in the Penn IRB system and that the OS CRC is appropriately engaged in all aspects of the research including exempt studies.

As of this writing, Penn Orthopaedics has 77 studies with an Active/Pre-Active Status out of the 214 studies registered in the Penn CRMS (Table 1). There are 75 studies with an active status and 2 studies ready to launch.

Since Penn CRMS initiation, the Orthopaedic Surgery CRCs and the McKay Laboratory Teams have completed the association of 16,826 patients to our portfolio of 214 studies according to 21 different enrollment categories as shown in Table 2. It is important to note that enrollment criteria for any study must be obeyed and just over 60% of patients pre-screened for study participation (10,247) are not or are not yet enrolled due to the following dispositions: active decline of participation (1534), incomplete participation status (169 (identified, interested, in pre-screening activities)) or not meeting full eligibility criteria (8543).

Table 1 Penn CRMS Utilization for Penn Orthopaedic Surgery

Penn Ortho (by Responsible Org)	Count
4607 - CC-Cancer Center	1
4373 - OS-Clinical Research	202
4374 - OS-McKay Laboratories	11
Studies Registered	**214**
Registered Closed Studies (all Orgs)	**137**
4607 - CC-Cancer Center	0
4373 - OS-Clinical Research	34
4374 - OS-McKay Laboratories	7
Open/Recruiting (Active)	**41**
4607 - CC-Cancer Center	0
4373 - OS-Clinical Research	34
4374 - OS-McKay Laboratories	0
Closed to Accrual (Still Active)	**34**
4607 - CC-Cancer Center	0
4373 - OS-Clinical Research	2
4374 - OS-McKay Laboratories	0
Pre-Open (Pending Active)	**2**
Total Active/Pre-Active Studies	**77**

Among those patients who do enroll (6,579), 5,471 individuals have achieved a "completed" status either through actually completing all protocol milestones (4,988) or for any 1 of 11 dispositions related to study withdrawal/discontinuation (483). The remaining 1,108 patients have 1 of 4 Active Statuses (Active Follow-Up, Active on Study, Consented/Enrolled, and Long-term Follow-up). Orthopaedic Surgery CRCs and the McKay Laboratory Teams continue to ensure the performance of visit scheduling, study procedures, data capture, research billing review, and Adverse Event monitoring. As most of the Orthopaedic Surgery studies require multi-year commitments from the participants, completion of all study activities can take as long as 5 to 10 years after the last participant is enrolled. The study commitment duration is a critical consideration in the development of study budgets and logistical planning for any new study both for the success of that study and in relation to the overall study burden on the Department. At this writing, Penn Orthopaedics is ranked among the Top 5 Departments in PSOM with respect to applicable study registration in Penn CRMS (100%) and for patient research association in those applicable studies (~88% of studies have patient registrations).

Table 2. Subject Enrollment into Penn Orthopaedics Clinical Research Studies by Responsible Org

Participant Enrollment Status	4372-OS-Orthopaedic Surgery	4373-OS-Clinical Research	4374-OS-McKay Laboratories	Grand Total
Declined	14	1,520		1,534
Identified		155		155
Ineligible	17	8,526		8,543
Interested		13		13
Pre-Consent Screening		2		2
Subtotal Disqualified/Pre-Enrolled Subjects	**31**	**10,216**	**0**	**10,247**
Off Study/Withdrawn-Complete Protocol	8	4,939	41	4,988
Off Study/Withdrawn-Disease Progression		3		3
Off Study/Withdrawn-Failed Post-consent Screening	3	98	1	102
Off Study/Withdrawn-Lost to Follow-Up	6	84	5	95
Off Study/Withdrawn-Never Treated	7	92	2	101
Off Study/Withdrawn-PI Decision		28		28
Off Study/Withdrawn-SAE/AE	2	16		18
Off Study/Withdrawn-Subject Decision	4	115	3	122
Off Study/Withdrawn-Subject Relocated		10	2	12
Off Treatment-Failed Post-consent Screening		1		1
Off Treatment-SAE/AE		1		1
Subtotal Inactive Subjects	**30**	**5,387**	**54**	**5,471**
Active Follow-Up	3	289	18	310
Active on Study	12	94	9	115
Consented/Enrolled	3	598	2	603
Long-term Follow-up		73		73
Post-Consent Screening		7		7
Subtotal Active Subjects	**18**	**1,061**	**29**	**1,108**
Grand Total	**79**	**16,664**	**83**	**16,826**

Penn Orthopaedics Update 2024

As shown in Table 3, the Department carries a slightly lower protocol burden from FY22 with 117 open protocols of which 21 are extramurally funded. The funding sources include Industry, Federal, non-Federal, and private.

Adult Reconstruction remains highly productive with 18 open studies, 7 of which are extramurally funded. The myMobility study (NCT03737149) led by Dr. Israelite has completed global enrollment and is proceeding toward closeout. Our site did very well on this project, and we look forward to seeing the results. Dr. Israelite is also pending closure of the Persona Total Knee Arthroplasty Outcomes Study (NCT02255383) which started in 2014. Penn has contributed 55 patients to this study and 37 patients remain in active follow-up.

Dr. Nelson's PCORI funded PEPPER Study (NCT02810704) is in its 8th performance year and has just been renewed. This is a large pragmatic clinical trial to inform patient choice and balance risk tolerances of individuals who face decisions about different drugs and strategies for deep vein thrombosis (DVT) and pulmonary embolism (PE) prevention after total hip (THA) and knee (TKA) replacement. The targeted multi-site enrollment is 24,000 participants. To date we have contributed 193 patients, to this study with 95 completed and 15 remain in active follow up for this study and enrollment is still open. The Rush University Medical Center Consortium Study "Dexamethasone in Total Knee Arthroplasty: What Dose Should We Be Giving Patients Intraoperatively?" (NCT05018091) is designed to determine the most efficacious and safest dexamethasone dose given intraoperatively during TKA that reduces post-operative opioid consumption and pain, improves postoperative nausea and vomiting, and minimizes post-operative complications. Enrollment is now closed, and 19 patients have been enrolled from our site. Dr. Nelson has successfully completed all site activities for the DePuy Ceramic on Ceramic Hip study (NCT02096211) after 11 years (original PI Dr. Hume) with 29 patients completed. Lastly for Dr. Nelson, Congratulations that the "Autogenous Bone Marrow Aspirate Concentrate for the Treatment of Osteonecrosis of the Femoral Head" study (Johns Hopkins, Primary Site, Lynne Jones, PhD PI) has been awarded by NIH! Site setup is in progress.

Dr. Costales has ushered the Smith & Nephew R3 Delta Ceramic Acetabular System PAS U.S. (R3-PAS) protocol (NCT03056534) through closeout after 8 years (Original PI Dr. Lee). Our site contributed 26 patients to this protocol. We thank Dr. Tarity who is completing the Post Approval Study of the Commercially Available U-Motion II+ Acetabular System and UTF Reduced Stem (U-Move) (NCT02761499) (Original PI Dr. Lee). Dr. Sheth continues work on "Analysis of a Tapered Porous Coated Stem and a Cementless Hemispherical Acetabular Component" (NCT03168750) sponsored by Medacta USA.

Foot & Ankle continues to feature Dr. Farber's Treace Medical Concepts, Inc.'s "Early Weight-Bearing After the Lapiplasty Mini-Incision Procedure (Mini3D)" study (NCT05082012). We anticipate that additional updates for the Foot & Ankle Division will be submitted elsewhere in this edition of the UPOJ by colleagues Dr. Josh Baxter and Dr. Casey Humbyrd.

Hand Surgery Dr. Levin's DOD-funded Hand Transplantation Qualitative Research Study (W81XWH1820067) has been successfully completed. A second related study "Assessing the Benefits of Hand Transplant Compared

Table 3. Open vs Funded Protocols by Sub-Specialty Division		
Division	**Total Open Protocols**	**Funded**
Adult Recon	18	7
Foot & Ankle	14	2
Hand	17	2
Oncology	10	0
Shoulder & Elbow	6	3
Spine	7	2
Sports Medicine	19	2
Trauma	18	3
Grand Total	**117**	**21**

with Other Treatments" continues the collaboration among Penn, the University of Delaware, and Walter Reed National Military Medical Center as well as additional sites.

Shoulder & Elbow remains a strong and stable Division in Clinical Research under Dr. Kuntz's leadership. We are in the process of completing closeout activities for the 3 remaining industry-sponsored studies in this Division and look forward to new activities.

Spine Dr. Casper now leads the COMPaSS™ Observational Registry (Clinical Outcome Measures in Personalized aprevo® **Spine Surgery)** funded by Carlsmed Inc. Dr. Smith continues to lead the STRUCTURE study (NCT04294004), a Phase II study enrolling patients undergoing single level transforaminal lumbar interbody fusion.

Sports Medicine Dr. Carey continues in his role as the Local and Global PI on the Vericel sponsored PEAK study (NCT03588975) and the Osteochondritis Dissecans of Knee Prospective Cohort (NCT02771496) under the ROCK Consortium. This registry study is now in its 10th year.

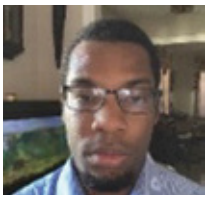
Ortho Trauma Dr. Samir Mehta with Resident Bijan Dehghani, MD received 2 foundation awards this year to investigate whether Next-Gen Sequencing (NGS) will more accurately, and reliably identify potential sources of infection after fracture when compared to standard microbiological cultures. The OREF award ($71,568) focuses on general open fractures and the FOT award ($51,766) concentrates on gunshot related fractures. Also, the study "Novel Topical Antibiotic Therapy to Reduce Infection After Operative Treatment of Fractures at High Risk of Infection: A Multicenter RCT (TOBRA)" funded through the University of Maryland (NCT04597008) has been awarded after 3 years of contract negotiations. The Ortho Trauma team is excited to move forward with the TOBRA study. Additional pre-proposals from the Division of Ortho Trauma for other studies are pending responses from the funders.

Financial Report

Table 4 shows the Total Costs (Direct Costs + Indirect Costs) expended during the periods shown for all categories (Personnel and Non-Personnel Costs). The revenue sources for these expenditures include both current sources and previously earned revenues that remain available from completed projects. Unless projects are grant-funded, revenue supporting Clinical Research is received in a reimbursement method and therefore lags behind the performance period due to the invoicing and payment process.

Table 4. Clinical Research Expenditures FY 21 - FY23				
Division	**FY21**	**FY22**	**FY23**	**Sum FY21 - FY23**
Adult Reconstruction	$120,360	$278,474	$264,879	$663,713
Foot & Ankle	$42,857	$55,406	$10,549	$108,812
Hand	$78,357	$175,873	$88,556	$342,786
Shoulder & Elbow	$131,376	$149,603	$86,586	$367,565
Spine	$21,234	$54,646	$5,958	$81,838
Sports	$44,540	$93,926	$134,812	$273,278
Trauma	$3,007	$106,238	$398	$109,643
Grand Total	**$441,731**	**$914,166**	**$591,738**	**$1,947,635**

Helena Moses
Adult Reconstruction



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