Musculoskeletal Clinical Regulatory Advisers, LLC

CRO Services

MCRA's unique Clinical Research Organization (CRO) enables international and US-based orthopedic companies of all sizes to successfully execute a clinical study. Our philosophy is to streamline the clinical trial process by utilizing our integrated approach to guide you through the medical device lifecycle. MCRA's expertise in the orthopedic industry is unmatched to our competition, while our cross-services integration is positioned to optimize quality, cost, and time.

MCRA's CRO uses dedicated and experienced staff to actively manage our statisticians, investigators and IRB's, leading to faster enrollment and ultimate success. Our orthopedic expertise, coupled with our global surgeon relationships, makes MCRA a valuable musculoskeletal clinical research organization that will get your product to market on time and on budget. MCRA's professional clinical staff has 35 + years combined experience dedicated exclusively to the clinical study arena.

MCRA Clinical – More Than Your Average CRO

Clinical • Regulatory • Quality Assurance • Reimbursement • Intellectual Property • Healthcare Compliance

- Clinical Project Management
- Site Management and Study Monitoring
- Data Management
- Auxiliary Services
- Medical Writing
- BioStatistical Services

1331 H Street, NW 12th floor • Washington, DC 20005 • Phone: 202.552.5800 • Fax: 202.552.5798 • www.mcracro.com

Musculoskeletal Clinical Regulatory Advisers, LLC

Clinical Project Management

MCRA assigns one Project Manager for each study. The Project Manager's main focus is to keep the project moving in a manner that both meets and exceeds the client's expectations while staying within budget. Within this scope of work, the Project Manager acts as the liaison between the sponsor and the study team, executes the monitoring plan, resolves concerns and issues raised by sites and/or vendors.

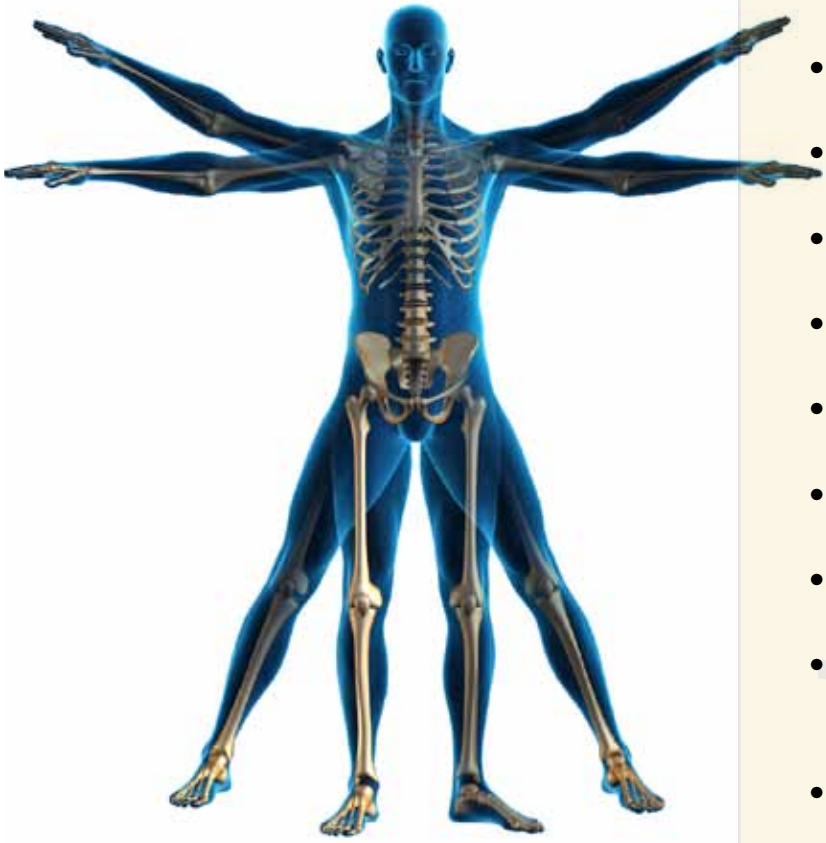
Services:

- **Clinical Study Planning**: Development to submission and publication, based on client need
- **Clinical Study Design**: Design a clinical study strategy that meets the Clients expectations
- **Clinical Study Strategy**: Oversee all phases and associated activities of the clinical trial, create milestones and timelines with the client
- **Clinical Study Communication Plan**: Select the project team members and create the Communication Plan
- **Budget and Payment Tracking**: Provide cost-effective budget and payment tracking
- **Investigator/Coordinator Meetings**: Coordinate Investigator/coordinator meetings and training
- **Key Service Integration**: Institute seamless integration between Regulatory Affairs and Reimbursement Support Services
- **Safety Review**: Manage IRB process of central or local IRBs, Clinical Event Committees (CEC) and Data Safety Monitoring Boards (DSMB).

Musculoskeletal Clinical
Regulatory Advisers, LLC

Site Management and Study Monitoring

MCRA provides first-in-class site management and clinical study monitoring. MCRA's team of highly trained Clinical Trial Managers and Clinical Research Associates manage the day-to-day activities of the study. MCRA's team of monitors are regionally based across the United States providing the Sponsor a more cost-effective solution for monitoring.



Services:

- Site Management
- Site and Surgeon Identification
- Site Qualification and Initiation
- Site and Staff Training
- Interim Site Monitoring
- Monitoring Enrollment
- Monitoring Data Capture
- Monitoring Query Resolution
- Monitoring Regulatory Document Preparation and Collection
- Institute seamless integration with Reimbursement Services
- Investigator Meeting Planning and Presentation
- Clinical Study Material Accountability
- Site Close Out Visit

Musculoskeletal Clinical
Regulatory Advisers, LLC

Data Management

MCRA has established strategic partnerships with several leading data management companies, each with over 15 years of clinical trials experience. Each company offers proven solutions in electronic data capture (EDC), clinical data management (CDM), and adverse event reporting (AER). Each software platform provides an integrated clinical data management solution that leverages the power of the Internet to accelerate the clinical trial process and helps to ensure rapid database lock and facilitate FDA approval. Additionally, each web-based solution reduces the cost of delivering medical devices to market and transforms the current time-consuming paper based process. At MCRA, we believe that by providing our clients with data management options we can customize the data management program to suit the exact needs of each of our clients.

Services:

- Streamlined data collection and data cleaning
- Electronic case report forms with a complete audit trail of all data entered and modified
- Online patient enrollment and randomization
- Integrated Central Coding solution
- Online automated and manual query creation, resolution and tracking
- Complete study monitoring tools
- Integrated online protocol and eCRF completion guidelines

Musculoskeletal Clinical Regulatory Advisers, LLC

Auxiliary Services

In addition to providing full CRO services for clinical trials, the clinical department may also provide smaller scale projects to meet client's need. The following services are provided to help meet our client's need and to better position them in the market.

Services:

- Clinical Evidence Landscapes
- Retrospective Data Collection and Evaluations
- Mock FDA Clinical Inspections
- Clinical Study 'Rescue' Services:
  - Data Discrepancies
  - Site Re-training
  - Supplying Monitoring Resources, Etc.
- Extensive Literature Searches and Analysis Reviews to Support:
  - CE Mark Technical Dossiers (MDD)
  - 510K Submission Packet

Medical Writing

MCRA's medical writing staff comes from a broad range of experiences, not limited to orthopedics. All of MCRA's experienced medical writing staff are associated with numerous scientific peer-reviewed journals (JAMA, Spine, J of Biol. Chem, Am J Epidemiol, etc.).

BioStatistical Services

MCRA's statistical services specialize in the design, implementation, and presentation of regulatory clinical trials with special focus on trials involving orthopedic devices. Statistical Plans are carefully developed to meet the specific goals of the clinical study .

Clinical Trial Continuum Chart

I

PHASE I – IDE APPROVAL AND CLINICAL STUDY START-UP

- FDA Negotiations and Responses
- Clinical Site Qualification and Selection
- Reimbursement Review and Analysis
- Plan Investigator / Coordinator meetings
- CTA & LoA Development and Approval

II

PHASE IIA – CLINICAL PHASE (INITIATION)

- Ongoing Communication with FDA
- Clinical Site Qualification and Selection
- CTA Negotiation
- Coverage Support for IDE Category B Devices
- DSMB / CEC Charter

PHASE IIB – CLINICAL PHASE (INTERIM)

- Patient Enrollment
- Data Collection
- Interim Monitoring Visits
- Data Management
- Interim Study Statistical Analysis
- DSMB / CEC Meetings

PHASE IIC – CLINICAL PHASE (COMPLETION)

- Resolution of Outstanding Queries
- Site Close-Out Visits
- Database Lock
- PMA Development and Submission
- DSMB / CEC Final Adjudication

III

PHASE III – REGULATORY SUBMISSION

- Summary of Safety and Effectiveness Data/Labeling
- Statistical Analysis for Post-Approval Study Planning
- PMA Submission
- Pre-Approval Payor Messaging

IV

1331 H Street, NW 12th floor • Washington, DC 20005 • Phone: 202.552.5800 • Fax: 202.552.5798 • www.mcracro.com

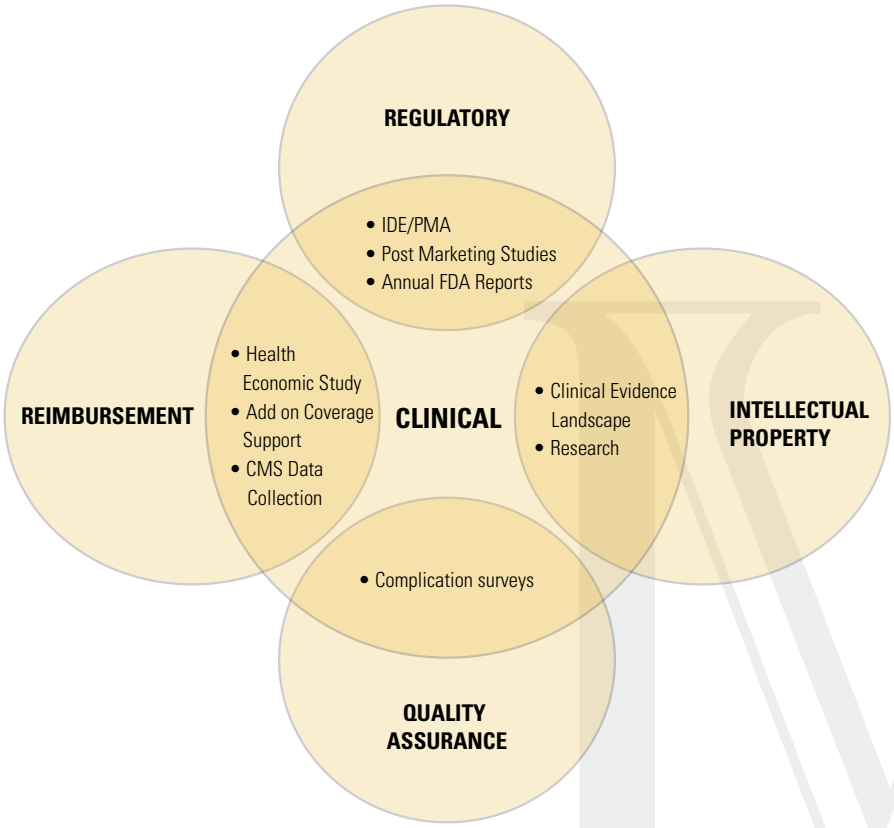
Musculoskeletal Clinical
Regulatory Advisers, LLC

The MCRA Advantage

- Full service experienced CRO team
- Orthopedic specific device industry experience
- Cost efficient services and increased path to market
- Integrated services approach
- Variety of services to meet your specific study goals
- Cutting edge electronic data management services
- Complimentary service capabilities calls
- Friendly and knowledgeable staff

Integrated Services

MCRA's Regulatory, Reimbursement and Clinical Teams Work Closely Together to Guide Companies Through the Medical Device Lifecycle.



1331 H Street, NW 12th floor • Washington, DC 20005 • Phone: 202.552.5800 • Fax: 202.552.5798 • www.mcracro.com