MCRA

CLINICAL RESEARCH ORGANIZATION & STRATEGIC ADVISORY FIRM

SERVICES

Project Management • Study Monitoring • Data Management • Statistics
Regulatory • Reimbursement • Quality Assurance & Manufacturing • Healthcare Compliance

A FULLY INTEGRATED **SPECIALIZED** CRO

MCRA, LLC (MCRA) provides a fully integrated Clinical Research Organization (CRO) that creates value by collecting and presenting evidence for the entire commercialization process, from regulatory approval to reimbursement, for emerging technologies.

MCRA's clients range from medical device startups to the largest publicly traded medical device companies. Our primary focus on cardiovascular and neuro-musculoskeletal devices, biologics, and therapies sets us apart from other CROs.

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CLINICAL STUDY MANAGEMENT & MONITORING

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OVERVIEW

Since MCRA's establishment in 2004, the Clinical Research Organization (CRO) has been involved in designing and/or executing more than 50 clinical studies. MCRA streamlines the clinical trial process by utilizing a unique, integrated approach to achieve faster enrollment and higher FDA approval rates. Our therapeutic specialization and in-house expertise combined with our global network of surgeons make MCRA a valuable clinical research partner that will assist you in getting to market on time and on budget.

MCRA's expertise is unmatched and our cross-services integration is positioned to optimize quality, cost, and time.

MCRA provides comprehensive study support services for Investigational Device Exemption (IDE), post-market and registry studies.

PRE-MARKET STUDIES

An efficiently run IDE clinical trial is essential in limiting both the cost and time for a medical device to receive FDA approval. MCRA provides a fully integrated approach to assist with all phases of the approval process, from study design and Institutional Review Board (IRB) approval to data management and study auditing. In addition, the close collaboration between MCRA's clinical and regulatory departments allows for a smooth transition from trial to submission, thus reducing the amount of time required to submit to the FDA.

POST-MARKET STUDIES

Along with FDA mandated post-approval research, a growing number of medical device companies are proactively implementing post market studies to expand indications, develop white papers, and continue marketing their device. Smart device manufacturers will also plan certain post market activities during the 510(k) or PMA research and submission process to help better understand reimbursement concerns, procedure outcomes and user acceptance in a changing health and economic environment.

REGISTRY STUDIES

Clinical registries are important tools for collecting data on the safety and efficacy of a technology or procedure, the natural progression of a disease, the cost effectiveness of the overall treatment, and/or patient satisfaction.

The design and implementation of a registry can vary substantially based on the purpose and objectives. MCRA customizes clients' registries with the appropriate design, execution, analysis and quality assurance measures to be accepted by the target scientific community and regulatory bodies.

PROJECT MANAGEMENT

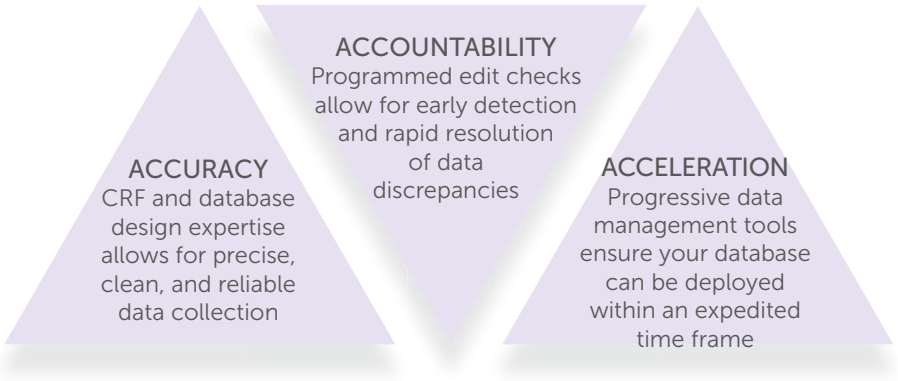
MCRA's CRO offers a beginning-to-end approach to conducting clinical research. We manage all aspects of study implementation, from feasibility and site selection to clinical monitoring and data management, on through PMA/510(k) submission and post-approval studies.

MCRA's project management services include:

- Development of protocol & informed consent forms
- Clinical Trial Agreement (CTA) development & negotiation
- Management of IRB submission process
- Development of monitoring plan
- Creation of patient binders
- Creation of regulatory binders
- Development of case report forms (CRF), and source documents
- Investigator & site selection
- Coordination of study vendors (imaging, core lab, etc)
- Site qualification visits & reports
- Management of site payments
- Site initiation visits & reports
- Interim monitoring visits & reports
- Close out visits & reports
- Remote based monitoring
- Site training & support
- Project status updates & reports
- Clinical Events Committee (CEC) coordination
- Data Safety Monitoring Board (DSMB) coordination
- FDA audit training & preparation

DATA MANAGEMENT

MCRA understands that reliable, cost-effective data management is key to the success of a clinical study. Clients have the flexibility of selecting from paper, electronic or hybrid data capture systems, including tablet PCs for web-based capture of Patient Reported Outcomes (ePRO). Our clinical data management system (CDMS) is equipped with 24/7 monitoring to ensure security and performance, and has the flexibility to interface with other clinical trial management systems. Built using Clinical Data Interchange Standards Consortium (CDISC) standards, it has controlled user access and robust audit logs for Health Insurance Portability and Accountability Act (HIPAA) and 21 Code of Federal Regulations (CFR) Part 11 compliance. Being 100% web-based, it offers real-time data management capabilities to clinical sites and sponsors.



MCRA's Data Management services include:

- Data Management Plan development
- CRF / eCRF design & review
- Database build & testing
- Edit checks programming and testing
- Remote data review
- Ongoing query generation and discrepancy management
- Interim/annual report listings
- Adverse Event & Serious Adverse Event (AE/SAE) tracking and reconciliation
- Customized status reports/trackers
- Electronic Patent Reported Outcome (ePro) technology for Android and Apple mobile devices

MEDICAL, SCIENTIFIC & TECHNICAL WRITING

MCRA's medical writers work closely with our statisticians, data managers, and clinical and regulatory staff to prepare documents to meet regulatory and marketing requirements on an ongoing basis throughout the product life cycle.

MCRA's medical writing services include:

- Clinical & pre-clinical study protocols
- Investigator brochures
- Literature reviews
- Clinical evidence reports
- Abstracts, manuscripts and poster presentations
- Annual, interim, and final clinical study reports
- White papers

AUDITS & COMPLIANCE

Audits identify areas for improvement through an independent assessment. Site and sponsor audits can be very helpful prior to an FDA inspection to identify areas of non-compliance. Independent clinical audits are also useful if there is a suspected clinical issue as they eliminate any perceived bias on the part of the sponsor. MCRA conducts audits of the sponsor and study site operations to evaluate compliance with the protocol, Standard Operating Procedures (SOPs), International Conference on Harmonization (ICH), Good Clinical Practice (GCP) principles, and applicable regulatory requirements.

MCRA's audit and compliance capabilities include:

- Sponsor audits
- Study site audits
- Subcontractor or vendor audits
- Facility audits
- Documentation audits
- FDA Inspection preparedness training

MONITORING

Study monitoring is essential to ensure that the research is conducted in accordance with the protocol, FDA guidance and GCPs. Regular communication between the sponsor, CRO, and sites is essential to ensure the trial is conducted, closed out and reported within the client's time frame and budget expectations. Site initiation visits are undertaken at each participating site once they have IRB approval and essential documents are in place. Interim monitoring visits are scheduled ensuring excellent monitoring coverage without the need for constant change orders to the contract.

At routine monitoring visits, MCRA will ensure:

- Written informed consent is obtained prior to each subject's participation in the trial
- Investigators comply with the protocol & regulatory obligations
- Source records are accurate, complete, up to date & available for review & inspection
- Data entry is current and accurate and discrepancies are resolved in a timely manner
- Required reports, records and regulatory or essential documents are filed on site and with the Sponsor
- Clinical facilities, staff and materials remain adequate throughout the trial
- Effective corrective & preventative action (CAPA) plans are established when non-compliance is observed
- Devices are stored properly, provided only to eligible subjects, and their receipt, use and return is documented appropriately
- New information is provided to the sites and patients in a timely manner
- Sponsor receives timely information regarding enrollment, compliance concerns & safety events

STATISTICS

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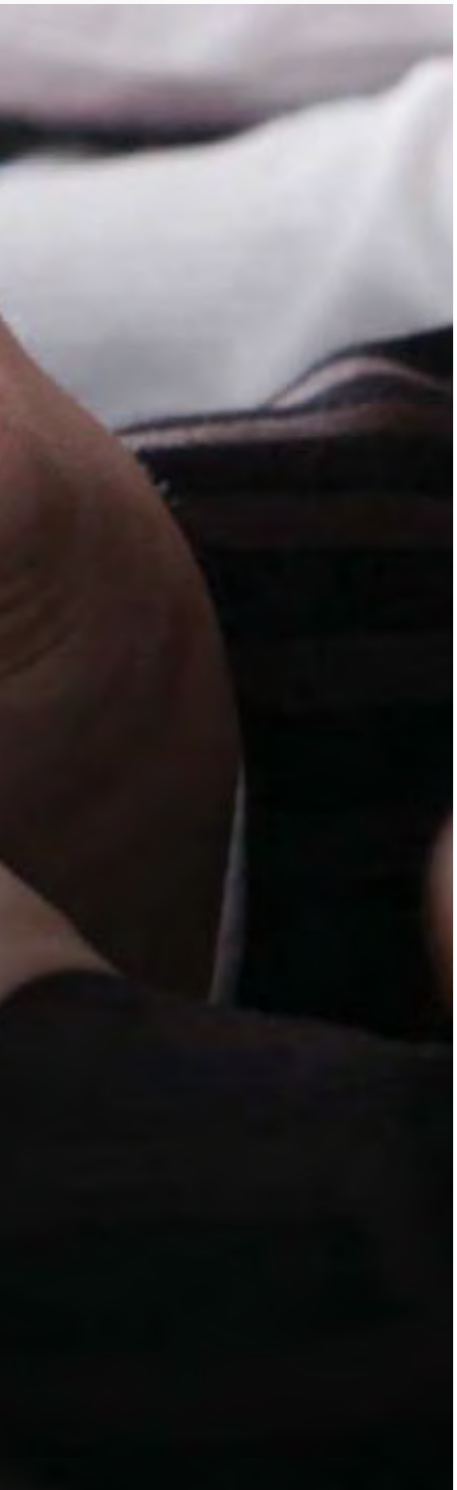

OVERVIEW

MCRA's clinical and regulatory success is made possible with the help of our exceptional biostatistics team. Our goal is to provide the best statistical support and strategy for our clients. Our main services are centered on protocol design, calculation of sample sizes, power calculations, and/or the production of a study randomization scheme. MCRA also offers full tables and listing generation for regulatory submissions and data analysis in support of research manuscripts. MCRA specializes in both Frequentist and Bayesian design and analysis.

MCRA's biostatisticians can help you:

- Determine the optimal statistical strategy to meet your study's regulatory objectives
- Provide statistical support for pre-clinical, clinical & post-market studies
- Specify statistical hypotheses, develop optimal clinical endpoints & justify sample size
- Utilize Frequentist and Bayesian adaptive designs to decrease time to market & overall study costs
- Utilize propensity score (PS) approaches in the principled design of non-randomized comparisons
- Write the Statistical Analysis Plan (SAP) text including comprehensive mock tables, figures & listings
- Negotiate with FDA & other regulatory agencies regarding the proposed statistical design & analysis methods
- Prepare documentation & coordinate with clinical events and safety committees
- Improve efficiency through automated tables generation for annual, interim & final clinical reports
- Write statistical reports, scientific manuscripts & abstracts
- Defend trial results to regulatory agencies

REGULATORY

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OVERVIEW

MCRA's regulatory team includes former senior FDA experts with engineering and scientific backgrounds that enable them to have an in-depth understanding regulatory pathways for orthopedic devices, regenerative therapies, and orthobiologics as well as cardiovascular technologies.

STRATEGIC ADVISORY SERVICES

MCRA's regulatory department has substantial experience guiding musculoskeletal and cardiovascular technologies through FDA approval at all points of the medical device life cycle: from strategy and pre-clinical testing to 510(k)/PMA submission and post commercialization activities. MCRA's competitive advantage lies in its cross-disciplinary approach, pool of spinal and orthopedic specialists, and broad network of contacts within U.S. government agencies. These factors enable our clients to have the best representation when demonstrating the science, safety, and efficacy of their technologies to regulatory agencies.

MCRA's Strategic Regulatory Advisory Services include:

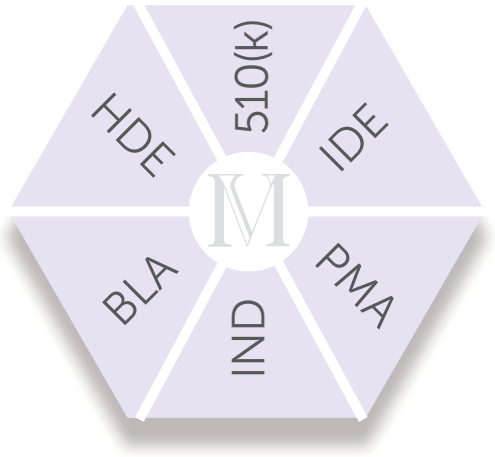
- Interpreting FDA regulations, policies, & guidances
- Researching landscape & device design
- Balancing indications, costs & claims
- Incorporating the regulatory & clinical testing requirements into the product development process
- Developing clinical study & pre-clinical protocols in support of regulatory submissions, marketing & reimbursement activities
- Leveraging regulations, competition, & new opportunities to drive market approval
- Providing technical, clinical and management oversight during clinical studies
- Conducting meetings with the FDA & other regulatory agencies
- Preparing for FDA Advisory Committee meetings
- Evaluating the regulatory impact on marketing campaigns

MCRA advises medical device companies with varying FDA labeling requirements

FDA SUBMISSIONS & OTHER REGULATORY SERVICES

MCRA provides an array of regulatory services, including but not limited to international regulatory approvals, new product acquisitions and transfer of ownership, adverse event reporting, site registrations, device listing, and acting as the U.S. agent for foreign companies.

MCRA's FDA submission and annual update experience includes:



MARKETING & LABELING COMPLIANCE

MCRA is familiar with regulatory requirements, trade association standards and industry best practices relating to the marketing and promotion of medical devices, as well as payments to Medicare and private insurers. MCRA advises medical device companies on FDA's labeling, advertising, and promotional policies to ensure all promotional materials and statements meet FDA and FTC requirements for truthfulness, fair balance, and full disclosure.

QUALITY ASSURANCE & MANUFACTURING

Medical device companies must adhere to strict FDA quality assurance (QA) requirements to ensure product consistency and safety. Failing to meet QA standards costs small and large device firms invaluable time and money. Our QA team, many of whom have worked for regulatory bodies, combines in-depth knowledge of the nuances of this complex arena, with strong relationships with regulatory agencies to guide you through the processes for product review, approval, and regulatory compliance. We reduce your compliance stress by first helping you to bring your device to market, and later by helping you maintain adherence to QA standards.

Our Quality Assurance services include, but are not limited to:

- Quality system regulation (QSR) implementation
- Technical files & risk management
- Design controls
- Audits & audit preparedness training
- Problem resolution
- Supplier management
- Manufacturing
- Employee training
- Due diligence

REIMBURSEMENT & HEALTH ECONOMICS

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OVERVIEW

Today, reimbursement is the most complex and significantly changing factor in healthcare technology commercialization. New government healthcare laws, fee schedules, coding changes, and the need for clinical utilities are placing financial pressures on patients, providers, and payors. Both small and large medical technology companies are highly affected by these dynamics. MCRA believes that a successful reimbursement program, based on an evidence-based clinical approach, is required to continue the commercialization and coverage of innovative technologies.

MCRA's coding, reimbursement, and compliance experts have over 50 years of combined healthcare policy and finance services experience, and a proven track record, servicing over 250 clients nationwide.

PARALLEL DATA COLLECTION FOR REIMBURSEMENT & REGULATORY APPROVAL

You are working under financial, time, competitive, and regulatory constraints. Therefore, the rapid commercialization of your company's technology is imperative. Simultaneously, the medical reimbursement landscape is changing drastically, faster than regulatory or intellectual property law. MCRA believes the real question is not whether your technology will be approved by the FDA, but whether the U.S. commercial market will ultimately cover and reimburse for your technology.

Clinical evidence needed for a successful regulatory approval does not necessarily encompass the clinical data required for successful reimbursement of a technology. We believe that these disparate needs can be solved with a well-planned, integrated regulatory and reimbursement strategy. The solution lies in collecting clinical data that incorporate both regulatory and reimbursement considerations.

MCRA's Clinical Trial Reimbursement Solutions (CTRS) services are designed to optimize parallel clinical trial data collection for reimbursement and regulatory initiatives. Whether your trial is in development or currently in enrollment, MCRA can offer our full suite of services or select services to cater to your needs.

CLINICAL TRIAL SUPPORT

By integrating reimbursement considerations early in the trial design, MCRA's Clinical Trial Reimbursement Solutions (CTRS) are able to advise company management, sites, and payors and offer strategic and administrative support to remove the burden from clinical sites and expedite the clinical trial.

Key services include:

- Assess & negotiate Clinical Trial Agreements
- Provide coding, coverage & payment information to sites for routine care & investigational devices
- Recommend protocol design elements that will facilitate coverage and reimbursement in the future

COVERAGE DURING THE TRIAL

Efficient and accurate handling of claims and payment information drives successful reimbursement during clinical trials. Where possible, MCRA facilitates study site interaction with payors to obtain appropriate coverage and reimbursement. MCRA can assist sites in identifying which treatment costs may be covered pursuant to health plan medical policies.

Benefits of using MCRA's services include:

- Education and assistance with pre-study submission and review requirements for Medicare and commercial health plans
- Ability to offset clinical trial costs where coverage for routine care & investigational devices is available
- Gathering of market intelligence regarding what payors are willing to cover during the study
- Establishment of precedent-setting coverage pre-commercialization

COLLECTION OF PAYMENT & CLAIMS INFORMATION

Insurance payments made for professional services and facility costs during the clinical trial offer tremendous market intelligence. MCRA has developed its own proprietary data collection systems that provide detailed on-demand reporting. Claims and payment data collected are entered into MCRA systems and provide intelligence about codes used by providers at the study sites, place of service, billed charges, allowed amounts, full or partial coverage, etc.

Benefits of using MCRA's services include:

- Ability to identify early payor adopters of the subject technology
- Ability to get added to payor systems from which future payment values will be established
- Collection of data to support future coding and payment requirements of the physician and/or facility

POST-APPROVAL COMMERCIALIZATION SUPPORT

The data being collected during a clinical trial provide market intelligence and, more importantly, build the case for future payor coverage decisions.

Key services include:

- Working closely with Professional Societies for coding applications and adjustments, as well as coverage support & position statements
- Facilitating payor adoption of technology
- Enabling integration of the technology, within local treatment protocols, for the indicated disease/condition

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