Musculoskeletal Clinical
Regulatory Advisers, LLC

Industry Whitepaper Series V

September 2010

CHALLENGES IN IDE CLINICAL TRIALS:

Study Enrollment & Reimbursement

Jeffrey D. Zigler, JD
Reimbursement Manager

Musculoskeletal Clinical Regulatory Advisers, LLC

Table of Contents

CHALLENGES IN IDE CLINICAL TRIALS: Study Enrollment & Reimbursement

Many clinical trial sponsors now require investigators and research institutions to pursue insurance coverage as a condition of study participation. Insurance coverage of routine care costs and the investigational technology may be available during the clinical trial. However, seeking coverage from Medicare and commercial carriers during clinical study has proven complex and confusing. Sponsors and investigators will find this whitepaper to be a useful road map when navigating this constantly changing process.

When a clinical study is necessary to prove the safety or efficacy of a new or existing medical technology, medical device manufacturers should observe time- and money-saving practices, guidance, and regulations available to them during the trial. Two key hurdles facing Investigational Device Exemption (IDE) clinical trial sponsors have historically been: (1) the time it takes to start-up all trial sites, and enroll all study subjects; and (2) the overall cost of sponsoring (and underwriting) the studies. Reimbursement of clinical services performed by investigators and other providers of care represents a financial obstacle for many companies, as does the challenge of a swift enrollment of study subjects, particularly during the "start-up" phase of the study. Adding to this burden is the widespread confusion and disparate impact with regard to Medicare's Contracting Reform with private carriers across the United States.

IDE STUDY CHALLENGES:
TIME
COST
MANAGING COVERAGE AND INSURANCE PAYMENT PROCESSES DURING YOUR TRIAL WILL ADDRESS BOTH.

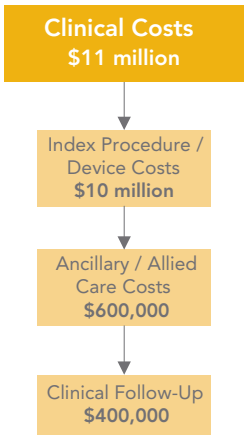
Such obstacles may easily be overcome with appropriate and effective management of study objectives, as well as by heeding laws and regulations affecting the timely completion of sponsors' study goals. This whitepaper will present the rationale and mechanisms for those time- and money-saving opportunities, as well as demonstrate by example how effective management of reimbursement activities during the trial will lead to budget savings, and at the same time may hasten the completion of IDE study.

IDE COST SAVINGS EXAMPLE MCRA's Reimbursement Management of a U.S. Spine IDE Study

IDE Study Profile
Clinical Study Facts

Study Type:	Prospective RCT
Patient Mix	60% Medicare/ 40% Pvt Insurance
# Sites/Subjects:	25/300
Enrollment Period:	12–24 mos
Study Follow-Up:	24 mos
# Follow-Up Visits:	10 visits
Outcome Measures:	ODI/NDI, VAS, SF-36 Radiographic

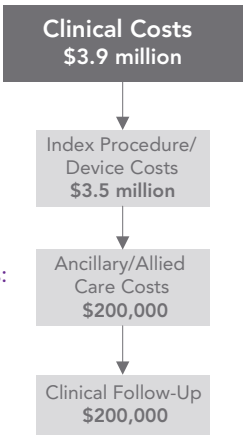
Spine IDE Study Usual Costs



Potential Clinical Cost Savings:
$6.9 million*

* Administrative costs may impact final savings.

Spine IDE Study Costs with MCRA Intervention



MEDICARE'S POLICY OF COVERAGE FOR ROUTINE CLINICAL TRIAL COSTS

Since President Clinton issued his 2000 Executive Memorandum directing the Department of Health and Human Services (HHS) to take action on the issue of reimbursement during a clinical study, the Medicare program has operated under a spirit of encouraging beneficiaries' involvement in clinical trials of technologies which may benefit their health, as long as there is some assurance of safety.[1] By September 2000, Medicare's policy of coverage for clinical trials was binding on all its then-contracted fiscal intermediaries and carriers that processed and paid Medicare claims.[2] Coverage of routine care costs is available from Medicare, as long as the study is approved by the Food and Drug Administration (FDA), and coverage applications are acceptable to the local Medicare contractor(s). Items covered include "routine clinical costs," defined by the Centers for Medicare and Medicaid Services (CMS) in the Medicare Claims Processing Manual as "all items and services that are otherwise generally available to Medicare beneficiaries…that are provided in either the experimental or the control arms of a clinical trial."[3] Contrast the above-defined term with "non-routine" or "administrative" study costs, which typically fall on IDE study sponsors to cover, and are not billed to Medicare.

ROUTINE CARE & TECHNOLOGY REIMBURSEMENT MAY BE AVAILABLE FROM MEDICARE AND COMMERCIAL CARRIERS

Device Coverage Is Based on the FDA's "Category" Designation

Emerging technologies undergoing IDE clinical study may also be deemed reasonable and necessary for Medicare-eligible populations by providers of care. In certain cases, an investigational device or medical service itself may also be covered by Medicare.[4] To define the parameters within which these investigational products or services may be covered, in addition to the routine costs of care normally covered as reasonable and necessary, CMS and FDA entered into a 1995 Interagency Agreement still in effect,[5] whereby Medicare will pay for routine care costs and a certain category of investigational device or service ("Category B") implanted or performed during FDA-approved IDE clinical trials.

Medicare Payment for Category B Devices

For those Category B devices under investigation during the study, Medicare may also cover the device itself.[6] Such devices represent "Non-experimental/Investigational" technology. Payment for a

Category B IDE device or an IRB-approved device (provided to a nonhospital patient) and the related services may not exceed what Medicare would have paid for a comparable approved device and related services.[7]

There are six different levels of Category B designation which the FDA may grant, as follows:

B(1) Devices, regardless of the classification, under investigation to establish substantial equivalence to a predicate device, i.e., to establish substantial equivalence to a previously/currently legally marketed device

- Category B(1) devices are typically those Class II devices seeking marketing clearance with FDA via the 510(k) pathway, and are undergoing a clinical trial in support of that application.[8]

B(2) Class III devices whose technological characteristics and indications for use are comparable to a PMA-approved device

- A Category B(2) designation is typically granted to devices which seek PMA approval to enter the market after another, similar product has already been granted a PMA approval from the FDA. Examples would include joint replacement devices that perform similar to devices already approved via the PMA process.

B(3) Class III devices with technological advances compared to a PMA-approved device, i.e., a device with technological changes that represent advances to a device that has already received pre-market approval (generational changes)

- Category B(3)-designated devices are those which represent the evolution of an already PMA-approved device. An example would be a material design change to the device, which would require additional clinical study to support its use in similar patient populations, for the same indications.

B(4) Class III devices that are comparable to a PMA-approved device but are under investigation for a new indication for use. For purposes of studying the new indication, no significant modifications to the device were required

- Sponsors of clinical trials whose target technology has received a Category B(4) designation are seeking a new or updated indication for use for the device, as clinicians who have experience with the technology or procedure may have noted opportunities for improvement in their usage of similar devices (or of the same device now being investigated – a sponsor may wish to merely "update" its labeling with FDA following approval of the new indication for use). An example of this would be a device PMA-approved to treat stenosis, now undergoing an IDE study for degenerative disc disease indications.

B(5) Pre-amendments[9] Class III devices that become the subject of an IDE after FDA requires premarket approval, i.e., no PMA was submitted or the PMA was denied

- The 1976 Medical Device Amendments to the Food, Drug and Cosmetic Act[10] provide regulations for medical devices, including their classification and reclassification. A Category B(5) designation would be appropriate if the FDA were to decide that an IDE study was necessary to support a PMA submission following a reclassification of the sponsor's device. Such was the subject of an April 2009[11] directive to manufacturers to substantiate whether clinical evidence existed to sufficiently allow their devices' reclassification to Class III, without the need for undertaking a new IDE study with Category B(5) designation.

B(6) Non-significant risk device investigations for which FDA required the submission of an IDE

The above Category B(1-6) designations carry with them an implied offer of coverage by Medicare, as long as certain conditions are met. These varying conditions, and the mechanisms for coverage by Medicare, are discussed in further detail below. Commercial carriers may also follow similar decision pathways, and allow for coverage during the clinical trial.

MANAGING PRE-DETERMINATION & PRE-AUTHORIZATION PROCESSES DURING THE TRIAL LOWERS OVERALL STUDY COSTS WHILE MAXIMIZING REIMBURSEMENT OPPORTUNITIES AND FUTURE COMMERCIALIZATION

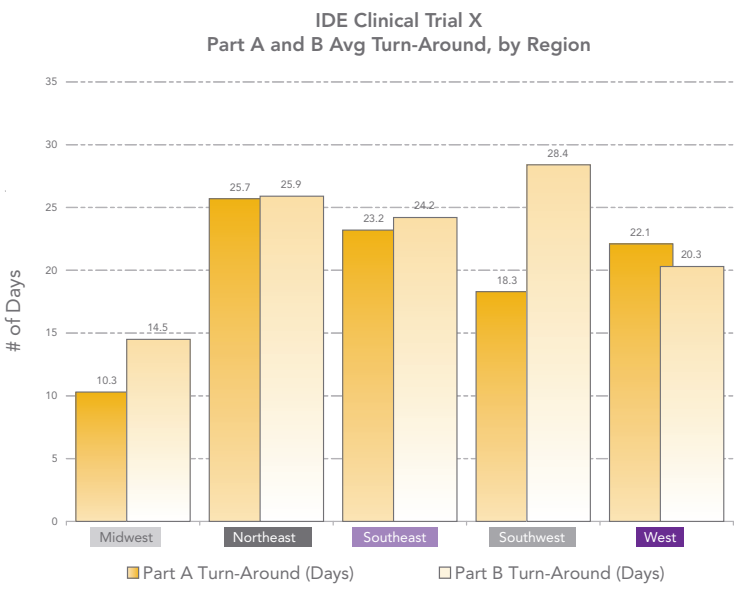
CASE STUDY MCRA's Medicare Pre-Determination Process Management Results in Study Financing & Faster Enrollment Opportunities

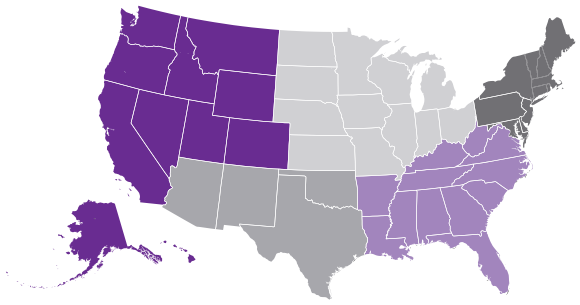
In 2009, MCRA consultants were engaged by a multinational medical device corporation to assist its IDE study by providing reimbursement counsel, support and MAC pre-determination process management. Approximately 200 study sites were initiated, and 2,000 patients enrolled. MCRA secured 100% coverage by Medicare for all treated beneficiaries, following successful up-front communications and managing sites' pre-determination applications.

MCRA consultants challenged Medicare contractors' stated turn-around times for pre-determination approvals, improving upon the averages based on communications made prior to study start-up time periods. Average time-to-approval improved by 44%, even up to 70% for some MACs, as a result of MCRA consultants' interventions. Improving this timeline allowed the study sponsor to save approximately 30 to 40 days of enrollment time at many key sites, during the crucial study start-up phase of the trial.

At all times during the study start-up phase, MCRA consultants provided dynamic reporting of study metrics, including region- and MAC-specific considerations of CMS approval speed, difficulty, and contractor requirement levels; as well as site-specific speed and site personnel sophistication levels. This real-time reporting assisted the sponsor in successfully implementing its study start-up strategies, and even allowed for the "grading" of identified clinical trial sites' CMS capabilities for future study considerations. Below is a graphic report, by U.S. region, of Part A and Part B CMS approval turn-around experience, as reported by MCRA consultants in an executive dashboard update document:

EXAMPLE OF MCRA WEEKLY DASHBOARD REPORTING:
Pre-Determination Process Management





In fact, certain private payors have developed coverage policies and guidelines for clinical trials.[12] Although there is no pre-determination process for private payors, the pre-authorization process followed by many commercial carriers allows for the submitting providers to explain the study and nature of the investigational device to private health insurers. In doing so, sponsors will best position their study providers to obtain coverage of the routine, study-related care costs incurred, but also the investigational products or services rendered during the study. Such study-related communications with private payors also have the ancillary benefit of educating them about the disease state and treatment alternatives, without running afoul of any pre-approval promotional activities prohibited by FDA under 21 CFR § 812.7(a).

Category A Device Considerations

Although CMS agrees to cover Category B devices, there are coverage limitations for Category A technologies as experimental devices for which safety and efficacy remain in question. Under § 68.1 of the Medicare Claims Processing Manual, "Category A IDE devices are considered experimental and, therefore, are not eligible for payment."[13] There are minor exceptions to this non-payment environment for Category A devices, specifically in the case of a Medicare contractor's determination that the device "is intended for the diagnosis, monitoring, or treatment of an immediately life-threatening disease/condition." Other individual exceptions may apply.

MECHANISMS OF COVERAGE BY MEDICARE: MAC PRE-DETERMINATION OF COVERAGE

Following FDA's approval of the IDE, but prior to a site's treatment of Medicare beneficiaries, pre-determinations of coverage by Medicare Administrative Contractors (MACs) are required under the Interagency Agreement in order for Medicare to process and pay claims for services provided under the IDE's protocol, or in the normal course of care during the study.

Defining the Role of "MACs"

MACs are the Centers for Medicare and Medicaid Services' contracting entities responsible for the receipt, processing and payment of Medicare fee-for-service claims, for both Part A (inpatient hospital) and Part B (outpatient hospital, physician and DME) claims processing, appeals, and coverage pre-determination requests.[14] "Pre-Determination" is the process by which CMS, through its MACs, determines coverage of routine and investigational services or products during an IDE. The pre-determination process for each IDE clinical study site begins with a submission by the sites' Part A and Part B Medicare providers, making an affirmative request for approval from the MAC. In some cases, a clinical trial sponsor's submission of confidential or other study-wide materials is appropriate prior to an individual site's submission. Such documents may include the study's protocol, FDA correspondence, as well as relevant clinical articles in satisfaction of MAC requirements.

Conditional FDA Approval

CMS has granted authority to the various MACs to consider granting pre-determination of coverage even when the sponsor has only been granted conditional approval by the FDA to proceed with the study. The FDA's conditions may speak to the safety of the device, or may deal with manufacturing, study design, statistical analysis or other more administrative features of the study. Depending upon the nature of the conditions, MAC medical directors may nevertheless grant full or conditional pre-determination of coverage to submitting study sites, independent of FDA's unconditional study approval.

Special Clinical Trial Coding Requirements[15]

As a further condition to providers' payment for services performed during the study, Medicare requires that physicians and institutions follow strict billing requirements. Institutional providers must bill the Category B IDE number on a "0624" revenue code line, with charges in the covered charges field. Hospital inpatient providers should not bill for the Category B IDE device if receiving the device free of charge.

For hospital outpatient services, the facility will use revenue code "0624" and an appropriate HCPCS code modifier (i.e. "-Q0"). The Category B IDE number must appear on the claim form. Within Medicare's hospital outpatient payment system, if the device is donated by the sponsor, the facility must bill the device using a token charge (e.g. $1.00) along with modifier "-FB", appended to the procedure code that reports the service to furnish the device.

Practitioners must always use ICD-9 diagnosis code "V70.7" as the secondary diagnosis for subjects participating in a qualified clinical trial. The IDE number assigned to the IDE Category B trial must be used (Box 23, "Prior Authorization"), or the claim will likely be denied by Medicare. Modifier "-Q1" should be affixed to the investigational service.

For the control population of patients, the care provider must use ICD-9 diagnosis coding most appropriate to the primary diagnosis. According to CMS, if the control patient is otherwise a healthy subject, "V70.7" should be noted as the primary diagnosis. If not an otherwise healthy control subject, the "V70.7" code should be utilized as secondary to the primary diagnosis. Effective for claims processed after September 28, 2009, with dates of service on or after January 1, 2008, claims submitted with the modifier "-Q1" shall be returned as unprocessable if the diagnosis code "V70.7" is not submitted on the claim.[16]

UNIQUE MEDICARE CONTRACTOR PROCESSES & VARIATIONS

There are 15 MACs responsible for the administration of coverage and claims associated with clinical trials.[17] CMS has delegated clinical trial coverage authority to these MACs, and require applications submitted and approved before any claims will be covered by the individual MAC. Depending upon the penetration of the sponsor's IDE study sites across the United States, the number of MAC "jurisdictions" and regional considerations must be considered carefully at the beginning of a clinical trial. Tactical site selection may be based, in part, upon coverage availability and historical MAC coverage performance.

MACs' Requirements for Pre-Determination Requests Vary

The requirements for submission of a request for pre-determination to MACs vary. Generally, submissions are required to include all applicable Medicare National Provider Identifier (NPI) numbers, or provider numbers of participating facilities and group practices. Typically, MACs require the following information:

1. IDE device information (name, common name)
2. Devices comparable to target technology
3. Up-to-date FDA correspondence (may be confidential to sponsor)
4. IRB approval letter referencing the IDE
5. IRB-approved informed consent form
6. Likely coding to apply to the study
7. Special controls taken to conform with FDA approval
8. Expected volume of Medicare beneficiaries to be treated

An example of additional, required information is Noridian Administrative Services' stated requirements for pre-determination requests[18]. Particular to Noridian Administrative Services are the following requirements:

- Delineate Medicare-billed services in the protocol
- Description of the Provider's protocol for obtaining informed patient consent
- A sample of the patient consent form, which must clearly describe the patient's financial responsibility and financial disclosures for PI, facility and sponsor
- Copies of all agreements between the sponsor and the provider

FREQUENT CHANGES IN MAC AUTHORITY HAS PRESENTED UNIQUE CHALLENGES FOR STUDY SPONSORS & INVESTIGATORS

Medicare's authority to contract with the private Administrative Contractors noted above falls under § 911 of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003. The process by which Medicare awards its contracts occurs every five years, or upon determination that the contractor is not upholding its obligations. Recent reform has attempted to consolidate old fiscal intermediaries and carriers into Part A/B MACs. This process has been significantly slowed over the past several years by older contractors exercising their right to contest new awards which would effectively shut down their operations as a Medicare contractor.

PRESENTLY, THERE ARE SIX (6) MAC JURISDICTIONS WHOSE AWARDS ARE BEING PROTESTED, AFFECTING PROVIDERS IN 18 STATES.

Under the regulation, awards may be formally protested with the Government Accountability Office (GAO), which must render a decision within 100 days of filing the protest. Presently, there are six MAC jurisdictions where CMS' awards are being protested, affecting providers in 18 states[19]. As of July 2010, MAC jurisdictions 2, 6, 7, 8, 11, and 15 are in contention[20]. Legacy fiscal intermediaries and carriers are to be utilized during this time. In the most recent update on this fluctuation, the award for the J11 MAC which had been granted to Palmetto GBA was promptly protested by the old

Part B carrier in North Carolina, Cigna Government Services, resulting in a stop-work order on July 16th. Pending the GAO's review of the award protest, Palmetto GBA may resume its capacity as MAC, or responsibilities may revert to Cigna Government Services, the current legacy contractor who will process claims in the interim.

Issues with CMS Transmittal Interpretation, Disparate Impact

Whenever communicating with Medicare providers, MACs are required to follow all applicable CMS manuals and transmittals, including updates to Provider Communications transmittals (ref: Pub 100-09, Medicare Contract Beneficiary and Provider Communications)[21], which may establish or make updates to affirmative duties or requirements upon the MACs. However, with regard to the issue of responsiveness to providers' requests for pre-determination of coverage during IDE clinical trials, there appears to be no direct transmittal by CMS on this issue.

Some contractors have interpreted portions of transmittal 100-09 to apply in this context[22]. This Transmittal provides contractors 45 business days within which to respond to inquiries or otherwise communicate with study sites' Part A and B providers.

PROGRAM VARIABILITY BETWEEN MACS, ALONG WITH UNSETTLED AUTHORITY AND TRANSITIONS, REQUIRES SPONSORS WORK CLOSELY WITH SITES AND MACS TO ENSURE COVERAGE AND COST REDUCTIONS.

Since only certain of the MACs invoke CMS transmittal 100-09 in their electronic and paper communications regarding IDE coverage pre-determination requests, and others do not, there is an apparent disparate impact for any IDE study spanning more than one jurisdiction. In one IDE clinical trial managed by MCRA, consultants reported response rates ranging from 5 to over 70 days before final pre-determinations were granted.

While most contractors communicate via e-mail or web portal for submission and response to IDE requests, some still require hard-copy submissions from providers, and only respond to IDE requests via traditional mail methods. This approach results in delayed responses (e.g. IDE pre-determination request approval letters) taking more time to reach providers, which delays are unnecessary in light of modern technical infrastructures supporting total electronic conversion by this time. Site selection which includes Medicare and commercial insurance coverage considerations is strongly encouraged

Study Site Confusion About the MACs' Requirements, Transitioning

An investigator who may belong to health systems whose claims are administered outside the territory has led to confusion by some MACs. For instance, an Oregon hospital that is part of a health system based out of Ohio would map to the MAC for the state of Ohio (not Oregon). This confusion is compounded by the fact that various MACs maintain different timelines for review, and have differing requirements for submissions of claims and requests for pre-determination of coverage of routine costs of care provided during participation in IDE clinical trials. A "split" submission may be required in certain jurisdictions, as the physician provider may submit to one MAC, but the hospital must submit to another (as in the example above), which may have the effect of extending review timelines the providers had not previously anticipated.

Even where the given MAC jurisdiction would allow for a joint (as opposed to a split) submission for an IDE pre-determination of coverage request for both Part A and B providers, some hospitals belong to health systems which do not allow for the facility's joint submission with the physician provider(s). This effectively creates a split-submission situation, with all of the drawbacks noted above, as well as coverage problems for many physician providers. If Part B providers are not well-informed of the fact that the facility (Part A) will not be submitting on their behalf, they run the risk of not receiving critical pre-determination of coverage from their MAC for routine costs of care they provided under an IDE study protocol. Wise sponsors seek opportunities to manage these processes, and use management support systems designed to expedite the approval process.

Strategic Timing Considerations in Filing Pre-Determination Requests

Although a conservative approach to assuring coverage would no doubt involve seeking pre-determination prior to any Medicare beneficiary's treatment during the study, many regional and academic institutions deem CMS' approval a pre-requisite to beginning clinical trial agreement negotiation and IRB submission. This may delay even those commercially-insured patients' enrollment into the study, a typical practice of motivated study sites awaiting their MAC's approval.

Such a bar to study start-up activities may impact enrollment of the study. MCRA consultants commonly engage in prospective communications and negotiations with these sites, reaching agreement that will lead to the more timely completion of the CMS pre-determination process possible. Just as individual MACs maintain policies of coverage that must be carefully managed, so too must study sponsors tailor messaging to each individual site's administration.

Although submissions for pre-determination of coverage remain the sole responsibility of the Part A and Part B providers intending to eventually bill Medicare for such products or services, study sponsors may provide assistance by way of instructions and materials pertaining to the specific requirements of the MAC(s); and in some cases, by exercising close follow-up directly with the MAC(s), where allowable. Managing this process closely will ensure that:

(1) The time it takes to start-up all trial sites, and enroll all study subjects is hastened; and
(2) The overall clinical cost of sponsoring the studies is reduced.

CONCLUSIONS & CONSIDERATIONS

Coverage is available by Medicare and private insurance carriers for the routine cost of care provided during clinical study. By following specific prior authorization and billing guidelines for each carrier, study sponsors may offset costs, expedite enrollment, as well as allow for early payor experience with the technology, enabling future coverage opportunities.

Start-up of a clinical study involves a concerted effort on the part of sponsor, CRO and other consultants to make those critical up-front site inspection visits and contractual agreements which will establish the protocol and financial arrangements controlling the sites' activities throughout the duration of the study. However, Medicare's coverage of IDE clinical services is hampered by MACs' contracting and jurisdictional confusion, differing submission requirements, and widely disparate review timelines. As Medicare contracts turn over following successful protests, or as seated contractors revise their submission policies and optimize review timelines, MCRA will continue to analyze and report upon the impact such changes may have on fee-for-service health care professionals and IDE clinical trial stakeholders alike.

Insurance coverage during the trial currently affords the wise sponsor opportunity to take advantage of these valuable benefits. Contact MCRA at (202) 552-5800 to discuss clinical trial reimbursement management, and how best to expedite enrollment while reducing the overall cost of the clinical trial.

ABOUT THE AUTHOR

Jeff Zigler has been an orthopedic and cardiovascular medical device consultant with MCRA since September 2007, advising clients on reimbursement and regulatory matters. He is a non-practicing attorney licensed in the State of Texas and the District of Columbia. He has assisted mid- and large-cap medical device manufacturers in drafting and negotiating IDE clinical trial agreements, as well as drafted sponsors' IDE reimbursement policies and procedures that limit financial exposure while expediting study start-up objectives. If you have any additional questions or comments on this whitepaper or a related matter, you may contact him at jzigler@mcra.com or (202) 552-5800.

ENDNOTES

1. Source: http://www.hhs.gov/news/press/2000pres/20000607.html

2. Source:
http://www.cms.gov/ClinicalTrialPolicies/Downloads/finalnationalcoverage.pdf

3. Ref Medicare National Coverage Determinations Manual Chapter 1, Part 4 § 310.1
Source : http://www.cms.gov/manuals/downloads/ncd103c1_Part4.pdf

4. In some cases, Category A devices may also be covered by Medicare, but this would be determined following individual review by MACs' pre-determination processes.
Ref Medicare Claims Processing Manual, Chapter 32, § 68 et seq, "Investigational Device Exemption (IDE)
Source: http://www.cms.hhs.gov/manuals/downloads/clm104c32.pdf

5. Ref Implementation of the FDA/HCFA Interagency Agreement Regarding Reimbursement Categorization of Investigational Devices, September 15, 1995 (D95-2). Per this agreement, the process of CMS' pre-determination and coverage will:
   - assure Medicare beneficiaries greater access to advances in proven medical technology;
   - encourage clinical researchers to conduct high quality studies; and,
   - clarify Medicare coverage of reasonable and necessary medical services during clinical trials for investigational devices.

   Source: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080302.htm

6. Ref Medicare Claims Processing Manual, Chapter 32, § 68 et seq, "Investigational Device Exemption (IDE)
Source: http://www.cms.hhs.gov/manuals/downloads/clm104c32.pdf

7. Medicare Benefit Policy Manual, Chapter 14.

8. Class II devices are subject to General Controls and a variety of Special Controls that FDA may implement from time to time. Examples of Special Controls include guidance documents, performance standards and labeling. When General and Special Controls do not provide the FDA assurance that is sufficient to ensure safety and effectiveness of a device, FDA classifies the device as Class III. Class III devices are subject to premarket approval (PMA).

9. A "preamendments" device is one that was in commercial distribution in the United States before May 28, 1976, the day the Medical Device Amendments became law. "Preamendments" devices are classified after FDA has received the recommendation from FDA's advisory committee, published the panel's recommendation for comment with a proposed regulation classifying the device and published a final regulation. Preamendments Class III devices may be marketed by means of a cleared premarket notification or 510(k) without submission of a premarket approval application until FDA issues a final regulation requiring premarket approval. Unclassified devices are those that were not classified at the time of the Amendments' promulgation, and which are regulated as unclassified devices via premarket notification.

10. Ref Medical Device Amendments to FDCA, P.L. 94-295 (May 28, 1976).

11. A January 2009 GAO report noted deficiencies in the FDA's clearance of certain "preamendments" devices, as well as those post-"amendments" products claiming substantial equivalence to them. These devices, although classified as Class III, were never formally reclassified or reviewed through the PMA process.

12. Ref Aetna Clinical Policy Bulletin on Clinical Trials (CPB 0466).

13. Ref Medicare Claims Processing Manual, Chapter 32, § 68 et seq, "Investigational Device Exemption (IDE)
Source: http://www.cms.hhs.gov/manuals/downloads/clm104c32.pdf

14. Source : http://www.cahealthadvocates.org/news/basics/2008/23new.html

15. Coding is subject to change and should be reviewed on a recurring basis. Please see Medicare's billing instructions for clinical trial coding within Medicare's Billing Manual, Chapter 32, Section 69.6 for additional information.

16. For additional information about clinical trial coding, please reference MLM Matters Number MM6776 found at
https://www.cms.gov/MLNMattersArticles/downloads/MM6776.pdf.

17. There are 15 regional MAC jurisdictions across the United States and its territories, and 11 private contractors which serve them: Cahaba Government Benefit Administrators (GBA); Cigna Government Services; First Coast Service Options; Highmark Medicare Services; National Government Services; National Heritage Insurance Corporation; Noridian Administrative Services; Palmetto Government Benefits Administrators (GBA); Pinnacle Business Solutions; TrailBlazer Health Enterprises; and Wisconsin Physicians Service.

18. Ref Noridian's FDA Approved Investigational Device Exemption (IDE) Contractor Required Information
Source: www.noridian.com

19. States affected by the ongoing Medicare Contracting Reform, as of July 2010: Alaska, Arkansas, Idaho, Illinois, Indiana, Kentucky, Louisiana, Michigan, Mississippi, Minnesota, North Carolina, Ohio, Oregon, South Carolina, Virginia, Washington, West Virginia, and Wisconsin.

20. Ref CMS Spotlight: Medicare Contracting Reform
Source: https://www.cms.gov/MedicareContractingReform/02_Spotlight.asp

21. Ref CMS Transmittals 25 and 26
Sources: 1) http://www.cms.hhs.gov/Transmittals/downloads/R25COM.pdf;
2) http://www.cms.hhs.gov/manuals/downloads/com109c06.pdf

22. Based on MCRA consultants' 2010 communications with MAC administrative offices on this topic.

REGULATORY • CLINICAL • INTELLECTUAL PROPERTY • REIMBURSEMENT

Musculoskeletal Clinical Regulatory Advisers, LLC is the leading neuro-musculoskeletal/orthopaedic consulting firm assisting established and emerging companies in the development and commercialization of their technologies. MCRA's consultants are industry leaders who support Clinical, Regulatory, Quality Assurance, Reimbursement, Manufacturing, Healthcare Compliance, and Intellectual Property initiatives. MCRA's integration of these key value creating initiatives, as well as its focused specialization, creates unparalleled expertise to its clientele.

Musculoskeletal Clinical Regulatory Advisers, LLC

Washington, DC
1331 H Street, NW 12th floor
Washington, DC 20005
Phone: 202.552.5800
Fax: 202.552.5798

New York, NY
505 Park Avenue, 14th floor
New York, NY 10022
Phone: 212.583.0250
Fax: 212.750.2112

Hartford, CT
63 East Center Street, 3rd Floor
West Manchester, CT 06040
Phone: 212.583.0250
Fax: 212.750.2112

info@mcra.com ***www.mcra.com***