

Medical Device Clinical Trials: A Small Company Perspective

By Dawn N. Norman, MS, RAC, Willette Jones-Dabney and Peter A. Takes, PhD, RAC

New device clinical trials can be daunting, particularly for a small company on a limited budget. Most commonly thought of for new drugs, many devices also require clinical studies. This article describes the basic process and many of the issues involved when a small company has a device that requires clinical trials that are conducted under an Investigational Device Exemption (IDE). An IDE is required for devices or indications that pose a significant risk to the patients in the study. Human clinical trials are usually quite costly. Factors affecting cost include different patient and reimbursement concerns, as well as considerations such as trials that are more procedural than treatment in nature (e.g., investigation of an efficiency versus an enabling device).

Besides budget, the obstacles faced by start-up companies include trial monitoring and general experience issues. Small device companies may not have the monitoring and study administration capabilities or expertise to address involved clinical trials. There are multiple consultants and contract research organizations (CROs) available, but these can be costly. In addition, clinical/regulatory staff is often one of the last elements of an organization to be “filled out,” so the requisite regulatory background may not be present within the company’s existing structure.

These factors become increasingly complex with the introduction of newer, state-of-the-art technology. For small, start-up companies, these challenges are quite imposing.

The First Step

The first step to initiating clinical trials is to draft an Investigational Device Exemption (IDE) application to FDA, in order to secure approval to proceed. This must include the nature and design of the device, risk analysis, patient safety, manufacturing, monitoring, clinical protocol and consent forms, institutions and investigators, etc. A “pre-IDE” meeting with FDA, before submission of the application, can be of substantial benefit in understanding the device-specific requirements and successfully obtaining IDE approval.¹ FDA has 30 days to review and comment or approve the application. Further, FDA approval depends on prior approval of the Institutional Review Board(s) of the planned clinical site(s).

Reimbursement to Defray Cost

Clinical trials are costly. Charges for patient procedures, payment to institutions for potentially nonreimbursable protocols and fee-for-service compensation for investigators and associated medical staff all must be considered. In addition, there is the added expense of device placement should the investigation involve a larger surgical or diagnos-

tic device (e.g., an imaging system or computer-assisted technology), which can be prohibitive and could quickly drain a company’s resources. Here, the financial differences between small and large companies are most evident. Particularly for device trials, boundaries also may exist regarding the extent of reimbursement guarantees provided, which may minimize the number of institutions that can be added to a given study.

IDE approval is key to the trial moving forward and also can be critical to the clinical institution’s involvement in relation to the budget effect on the company. Institutional reimbursement for the procedures involving medical devices can save a company considerable expense of the trial. Insurance will not reimburse the cost of the investigational devices, but often will cover the cost of the actual procedure(s) involved, based on the Centers for Medicare and Medicaid Services’ (CMS) categorization granted.

Upon IDE approval, devices are assigned a reimbursement category based on their anticipated risk during the clinical trial. “Category A” devices are considered “experimental,” i.e., “innovative,” for which the “absolute risk” type has not been established. “Category B” devices are considered “investigational,” i.e., those for which “underlying questions of safety and effectiveness ... have been resolved,” or it is known that the device type can be safe and effective.² This cate-

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gorization, done through an understanding between FDA and CMS (formerly Health Care Financing Administration [HCFA]), traditionally defines whether the associated procedures are reimbursable to the institution under Medicare. Category A devices are not reimbursable; Category B devices generally have been. This enables CMS to continue to “reimburse for medical services deemed ‘reasonable and necessary’ for the diagnosis and treatment of an illness or injury, or to improve the functioning of a malformed body member.”³

Important to this element of clinical trials, in September 2000, HCFA mandated full coverage of routine costs for approved clinical trials under a Final National Coverage Decision (NCD),⁴ in order to afford greater patient access to these types of procedures. The policy bound all Medicare and medical plan providers to cover the routine costs of “qualifying clinical trials ... as well as reasonable and necessary items and services needed to diagnose and treat complications arising from participation in all clinical trials.”

Routine costs of the clinical trial are defined as conventional care that is provided whether or not the patient is participating in a clinical trial. Items or services required for the clinical management of the patient while participating in a clinical trial (e.g., monitoring of the effects of the item or service, prevention of complications, etc.) or those required for the diagnosis or treatment of complications also are considered routine costs. The items or services not covered under this policy are self-evident:

- The investigational device(s);
- Items and services provided only for the purposes of data collection and analysis that are not used in the clinical management of the patient (e.g., a CT scan required by the investigational protocol not usually otherwise performed); and ...

- Items and services customarily provided by the research sponsors free of charge to any trial enrollee.

To qualify for Medicare reimbursement, a clinical trial must meet three basic requirements:

1. The purpose of the trial must be to evaluate an item or service that falls within a Medicare benefit category and is not statutorily excluded from coverage;
2. All trials must have a therapeutic intent and not be designed exclusively to study toxicity or disease pathophysiology; and



3. Healthy volunteers may only be enrolled in diagnostic intervention trials. Trials funded or supported by government agencies (e.g., NIH, CDC, DOD, VA, HCFA, AHRQ) automatically qualify.

Mandating that medical providers cover these routine costs will help development companies significantly by not requiring the research sponsor to pay for all medical costs associated with the investigational study. However, it will take time for some providers to adjust to payment if any portion of a procedure is investigational, as it is still a new concept for many. In December 2001 CMS announced the rule on coverage for clinical trials would carry over into calendar year 2002.⁵ To date, the US insurance industry generally has been in concert with reim-

bursement for approved clinical trials on drugs and medical devices.^{6,7}

Sources of Funding

More than \$40 billion in venture capital has been invested in the medical device and biotechnology industries in the past 10 years.⁸ The investment community’s willingness to support a study is dependent on the eventual marketability of the product and how long it will take to get to the market. The regulatory process is key to this. Venture capital firms will want to see that the company has its regulatory processes well planned in advance, avoiding elements that may increase investment risk.⁹

Grants also provide opportunities for clinical trial funding. The National Institute of Health (NIH) annually funds about 900 Small Business Innovation Research (SBIR) and 100 Small Business Technology Transfer Research (STTR) grants to businesses with and without research institution partners. Funding ranges from \$75,000 to \$500,000 for six months to two years.

Trial Logistic Issues

Two other areas potentially consuming significant company resources are costs associated with monitoring clinical studies and compensation for investigators.

Monitoring personnel can be hired and trained as company employees, which can generate significant (and continuing) expense prior to actually beginning the monitoring process. However, many companies prefer this approach, as there is perceived a greater control of the monitoring process.

Small companies must weigh the option of using contract monitors versus hiring personnel or a CRO. Using third-party staffing firms to provide contract personnel on a nonpermanent basis is an option, but it could become expensive depending on staffing needs and the firm’s fees for such services. Hiring a CRO that can do all or any part of a trial can be convenient but usually is costly. Full-time employees often assume vari-



ous nontrial responsibilities within a start-up company, and the right persons in this function could have a hidden long-term financial benefit. Small sponsoring companies must be mindful of these staffing options and must make the proper choice according to specific needs of timing and budget.

Associated with this decision, it is important to consider eventual associated travel that could consume resources rapidly, depending on the sponsor's location and number of trial sites. A good initial strategy is to base the company in a city with one or more major medical centers, with appropriate patient flow to keep enrollment steady and the stature of hospital and investigators to enhance credibility of the study. Proper use of current communication technology (e.g., video conferencing, Web-based conferencing and training) can help minimize travel-associated costs. However, there is no substitute for required on-site institutional monitoring.

Training is essential for educating monitors and trial investigation staff. Schedules and procedures also must be developed to assure consistency among personnel. New technologies present a complicated training challenge. Investigators often need detailed, documented training and practice before study implementation, and this creates a need for in-service training and written training materials. Training and training materials

are the responsibility of sponsor personnel and may require the participation of engineers and scientists involved in device development. Further, monitors need to be trained and totally familiar with the technology, because during visits they will no doubt be prompted with questions by the investigation staff.

Investigator Compensation

It is tempting for start-up companies to provide investigators with "stock options" as a means of compensation. This helps to keep costs down, by indirect compensation to the physicians. However, as attractive as it may seem, it is not the path of choice. First, institutions involved may have both business and ethical restrictions on this form of payment. Second, it can affect the ability to publish the results, if desired. Third, at the time of marketing submission FDA requires investigators to disclose all financial interests in the sponsor and/or devices. This includes, but is not limited to:

- proprietary interest in the device;
- equity interest in the sponsor; and/or
- significant payments with a cumulative value more than \$25,000.¹⁰

This rule extends to one year after study completion. These elements can, however innocent, leave an appearance of study outcome affecting the value of compensation. This can taint the presentation of even the most meticulous data

and increase scrutiny of the results. Although sponsors are not precluded from various forms of equity compensation, this approach is best avoided. Straight fee-for-service arrangements, even if they exceed \$25,000, present the best impression.

Summary

There are multiple factors involved in conducting clinical trials, especially for "high tech" devices. Many have not even been considered in this article. Costs, logistics and support personnel are among the burdens facing small companies. Yet, successful completion of clinical studies is possible with assistance from FDA, a proper approach to controlling costs, planning, and appropriate clinical and regulatory strategy.

NOTES:

1. *Investigational Device Exemption (IDE) Guidance 99-1*, Office of Device Evaluation, Center for Devices and Radiological Health, FDA, 25 March 1999.
2. *Draft Guidance on IDE Policies*, FDA, 20 January 1998.
3. *IDE Blue Book Memorandum D95-2*, FDA, 15 September 1995.
4. Final National Coverage Decision, Health Care Financing Administration (HCFA), 19 September 2000; www.cms.gov.

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5. Operational Policy Letter 2001.135, Centers for Medicare and Medicaid Services (CMS), 20 December 2001.
6. "Clinical Trials—To Pay or Not to Pay," L. Newcomer, *SoCRA Source* 24, 2000; pgs. 5–6.
7. "Clinical Trials Based Cancer Care: Working With Payors to Make It Mainstream Care," J. Stewart, *SoCRA Source* 24, 2000; pgs. 15–17.
8. Devices & Diagnostics Letter, 7 September 2001; p. 4.
9. *Devices & Diagnostics Letter*, 27 September 2001; p. 3.
10. *Guidance: Financial Disclosure by Clinical Investigators*, FDA, 20 March 2001.

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