Managing

INVESTIGATOR INITIATED TRIALS

RITA E. NUMEROF, PH.D., PRESIDENT, AND MARK T. MORGAN, M.S., SENIOR BUSINESS ANALYST, AT NUMEROF & ASSOCIATES INC. (NAI), ST. LOUIS, DISCUSS THE PROS AND CONS OF INVESTIGATOR INITIATED TRIALS. NAI PROVIDES STRATEGIC CONSULTATION IN THREE BROAD AREAS: STRATEGY DEVELOPMENT AND EXECUTION, OPERATIONAL EXCELLENCE, AND ORGANIZATIONAL INFRASTRUCTURE. FOR MORE INFORMATION, VISIT NAI-CONSULTING.COM.


Dr. Rita Numerof


Mark Morgan

Investigator initiated trials (IITs) can be a valuable part of a pharmaceutical or medical-device manufacturer's marketing claims arsenal, according to Rita Numerof, Ph.D., president, and Mark Morgan, M.S., senior business analyst, at Numerof & Associates Inc.

The two contend that IITs are relatively low cost because much of the up-front work is performed by the investigator, and the investigator normally "donates" facilities and staff to the conduct of the trial. In addition, ideas received from independent researchers can be a source of valuable new claims concepts and the perception of the independence of the research is stronger than it is for company directed trials.

"These trial formats have the added benefit of cementing relationships with investigators with clinical and research expertise, providing valuable insights into unmet patient and physician needs, and potentially contributing to the future success of the organization," Dr. Numerof says. "On the other hand, companies that support IITs face a number of potentially serious risks — legal, ethical, and financial — that need to be managed up front."

Making rational decisions regarding the support for IITs requires knowing the reason for conducting the trials in the first place.

This might seem obvious but it isn't always made clear to the often technically oriented people who make IIT funding decisions.

LEGAL CONCERNS

Mr. Morgan says at the practical end of the scale is the need to manage the flow of incoming proposal ideas.

"Once an organization has decided to entertain IIT proposals, it will need staff to evaluate them, negotiate the details of contracts to supply materials needed for the study, and track the status of individual proposals," he says. "After a reputation for entertaining IITs has been established, the flow will increase, and this increase needs to be planned for as well."

The tracking of individual proposals also has another legal purpose. The inability to systematically organize previously submitted proposals leaves an organization open to charges of intellectual property (IP) theft, because study concepts are a form of IP.

"Over time, the number of previously submitted study concepts becomes enormous, and the risk that an internally conceived study or a new external study will substantially duplicate one of these becomes significant," Mr. Morgan says. "The solution is a good tracking system that ensures the ability to rapidly and accurately cross-check newly proposed trials against older proposals to identify potential overlap."

The design of such a tracking system is complex. Studies can differ along a number of dimensions, and the overlap needn't be perfect to represent a potential infringement. Engaging legal counsel familiar with IP law is advisable. As a rule of thumb, however, proposals looking at the effectiveness of a product for different indications are unlikely to raise concerns, nor are proposals to conduct studies in different populations — unless aspects of the study design itself, for example a method of locating suitable participants, are novel. A good tracking system should allow easy access to prior proposals along at least those dimensions.

ETHICAL CONCERNS

Dr. Numerof offers that the primary concern, from an ethical perspective, is presenting the appearance that research performed and the conclusions drawn from it are independent of the pharmaceutical or medical-device company, when in fact they were not.

"Independence can be compromised in a number of ways," she says. "At the extreme end of the scale is dictation of study design and methods in line with the desires of the manufacturer, with any deviation resulting in

The positives associated with investigator initiated trials (IITs) are many. At the same time, companies face a number of potentially serious risks — **legal, ethical, and financial** — that need to be managed at the outset.

the withdrawal of support. If such a study were published indicating that the manufacturer merely 'supported' it, that would clearly misrepresent the independence of the investigator."

Dr. Numerof poses the challenges regarding more mundane interactions, such as discussions between a manufacturer's biostatistician and an investigator about ways to improve the proposed analysis, or suggesting ways a study might be redesigned to increase the potential payoff, or reduce the risk, to the manufacturer. The question is whether these are also ethically troublesome.

"As is the case with many ethical issues, there is a large gray area since any given individual might reasonably draw a firm line," she says. "Organizations will need to balance their commitment to high ethical standards — and the potential risk to their reputations that could result from violating them — against the need to be responsive to investigators and the desire to maximize the value of their investment in IITs. We believe one caution is in order, however. Manufacturers should act under the presumption that the details of their engagement with independent investigators will become known. It's the old leadership advice: always act as if someone is watching, because they usually are — in a different context."

FINANCIAL CONCERNS

The two consultants remind companies that with every study, there is a risk that something unexpected — and unwanted — will happen.

"If an IIT examines the effectiveness of a drug in a new population and has to be terminated because of a high rate of adverse effects, it will almost certainly impact sales of the drug both within and outside that population," Mr. Morgan says. "Burying the data is not a viable legal or ethical option, so the risk to the bottom line is inherent in conducting the study."

Dr. Numerof says if risk is inherent in IITs, and it is balanced by potential benefits, then the goal should be to choose to support clinical studies that maximize the benefits and minimize the risk. This requires more than a quick "once over" of the study design; a glance at the name of the researcher submitting the proposal and his or her institutional affiliation, if any; and a glimpse at the amount of support being requested.

"It requires looking at the study in the context of the organization's strategy, and assessing the potential risks and rewards in that context," she says. "In some cases the manufacturer's goal is to identify potential new markets, or justify new market positioning, which often implies a focus on a few trials with highly favorable short-term financial risk-benefit profiles. In other cases, the goal is to establish a reputation as a leader in a particular field, which may justify supporting a much broader range of trials, still seeking to minimize risk, of course, but viewing the benefits as cumulative and the cost of support as a long-term investment."

The point is that making rational decisions regarding the support for IITs requires knowing the reason for conducting the studies in the first place.

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"Despite the risks, IITs have become a valuable part of many manufacturers' efforts to promote their products and their reputations," Mr. Morgan says. "Clear definition of the desired benefits, effective management of the risks, and careful selection of trials to support will maximize this positive impact."✦

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