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SPECIAL REPORT

Clinical Research Investment

Assessing the Factors Driving Nutrition Industry Firms to Support Scientific Trials

With regulatory agencies, consumer watchdog groups and an increasingly competitive industry landscape raising the bar, companies must take a proactive approach to developing clinical research. **INSIDER** fielded an online questionnaire on clinical research investment to our readers in January 2012, asking about their level of investment in clinical research, how they handle clinical trials related to their ingredients/products and some of the lessons learned from unsuccessful research investments.

by Heather Granato

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Table of Contents

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ROI, regulatory concerns drive firms to support clinical trials

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While clinical trials were originally defined by FDA as voluntary research studies in human subjects designed to substantiate the safety and efficacy of medical therapies and drugs, regulatory agencies now are looking for this level of research and investigation in evaluating claims for nutritional and nutraceutical ingredients, as well as finished goods containing these sometimes novel offerings. In addition, a more educated populace and an increasingly competitive industry are mandating companies make an investment to ensure their products are safe and efficacious when used as directed.

In most cases, the randomized controlled trial (RCT) is considered the "gold standard" for efficacy studies, regardless of the product under investigation. While companies are bringing qualified, experienced personnel in-house to help in research oversight, many are still learning the intricacies involved in designing and executing a clinical trial that will yield appropriate results. For example, substantiating the efficacy of a nutraceutical ingredient for addressing a specific disease state may be a fascinating trial; however, claims related to a disease state are limited to drugs, making the return on investment (ROI) questionable in such a situation. Further, clinical studies are highly regulated, and obtaining regulatory approvals for the study protocol, recruiting an appropriate study population and following good clinical practices can be challenging and costly.

INSIDER fielded an online questionnaire to our readers in January 2012, asking about their level of investment in clinical research, how they handle clinical trials related to their ingredients/products and some of the lessons learned from unsuccessful research investments; percentages are accurate within +/- 9 percent. The majority of respondents (n=138) were supplement manufacturers/marketers (40 percent), followed by ingredient suppliers (24 percent); a number of personal care manufacturers/marketers (13 percent) and food manufacturers/marketers (10 percent) also responded. More than 20 percent of respondents were CEOs, with corporate management and C-level execs making up another one-quarter of respondents. This report summarizes some of the findings as well as how executives are learning from past failings in clinical research investments.

> "We need to be certain trial design reflects statements that marketing customers desire to make on the ingredient."

Dietary supplement industry execs are investing in clinical research and science, with 80 percent stating their investment is either "significant" or "some;" only 12 percent of respondents said they have little or no investment in clinical research and science. The investment has yielded positive results, with 59 percent of respondents noting they have supported between one and five clinical trials on their ingredients and/or products. Eighteen respondents (13 percent) have supported more than 20 clinical trials. Even so, the majority of companies plan to increase their investment in clinical research and science during the

next three years. Forty-three percent of respondents (n=60) see their investment increasing significantly, with another 36 percent expecting some increase.

At the same time, the amount of money it takes to deliver workable results poses a major challenge for some companies. A corporate manager at one ingredient supplier noted, "In today's regulatory environment, the requirement is for large, full-scale studies of more than 100 patients. These are very expensive to run and to manage, and the lead times from start to finish are also very long. This puts a huge financial strain on new startup companies wanting to contribute and compete in the industry." Another cost consideration relates to the inclusion levels of ingredients in finished goods. "The majority of research studies are performed in an attempt to initially obtain a dose response, and then additional research studies are performed to demonstrate an efficacy at lower doses," said the CEO of an ingredient supplier. "The challenge is to hopefully discover a dose response that translates to a cost-effective dose for a manufacturer—which will hopefully include our ingredient as a 'keynote' ingredient in their new/revised product formulation."

As far as where the research dollars are going, more than half of respondents (56 percent) said they are using a mixture of in-house and outside support, whether utilizing a contract research organization (CRO) or teaming with an academic institution. More than one-quarter of respondents outsource most aspects of clinical trial development and oversight, with 17 percent stating they exclusively outsource clinical trials on their ingredients and/or finished products. Using independent researchers or third-party organizations such as CROs to conduct clinical trials and review the relevancy of their claims to the research can increase the integrity and enhance the statistical significance of trial results. Such outside oversight can also help avoid trial failures. The owner of one ingredient supplier said in past studies, the biggest failing was, "relying too much on inadequate internal expertise to design, implement and measure. Future trials will use more outside input and expertise." Similarly, the president of a dietary supplement manufacturing firm said one of the biggest failings his company experienced was due to "sloppy oversight by the principal investigator. Moving forward, we have hired a professional CRO to oversee all aspects of our clinical trial."

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Of course, part of finding success means evaluating CROs to make the right match. A dietary supplement manufacturing firm's director said his company's biggest "failing" was finding the right research partner; "That is, finding a partner that can not only deliver a well-researched and thought-out proposal, but also can deliver on the study on time and on budget. Our team has gotten better at knowing which questions to ask up front and checking references of the labs."

The decision to get outside support, whether in part or total, often stems from concerns related to managing the different aspects of a clinical trial. Myriad factors can influence study

design and timing, including target population; primary endpoints; mode of delivery; and intended use of the active, accepted biomarkers.

When examining different aspects of implementing a clinical trial, 70 percent of respondents said they are extremely concerned with deciding the right methodology and clinical endpoint. This was closely followed by 60 percent of respondents who cited both cost and ROI as aspects they are extremely concerned about; in fact, only five respondents indicated they were not at all concerned with either cost or ROI. The aspect that had the most even distribution of levels of concern was the possibility of publication, with 18 percent of respondents ranking it at the unconcerned side of the scale, and only one-third stating it was a major concern.

ROI also played into the rationale behind investing in clinical research, as 79 percent of respondents said claims substantiation is one of the primary reasons they invest in clinical research on their ingredients and/or finished products. Further, it is critical to ensure the claims match the study results. A corporate manager at an ingredient supplier said the company struggles with "some of the oversight required in planning the study protocol and parameters in order to justify or create specific marketing claims." And the vice president of a supplement manufacturer said, "We need to be certain trial design reflects statements that marketing customers desire to make on the ingredient."

Another 58 percent of respondents stated regulatory compliance is driving their investment approach. Given the fact that regulatory authorities are increasingly seeking RCTs to substantiate health claims, companies making structure/function claims for dietary supplements and foods should consider following a similar standard to avoid scrutiny down the road. Further, the New Dietary Ingredient (NDI) Draft Guidance issued in July 2011 made clear FDA believes a high level of evidence of safety is required for any NDI being introduced into commerce.

Companies are also thinking proactively about their investments, with 68 percent of respondents stating they invest in clinical research for strategic market positioning; in contrast, only 19 percent said they invest to address a competitor's claims or marketing. Advance planning is also seen in the decision of 48 percent of respondents to invest in clinical research to discover new health effects or applications for their ingredients, and the same number stating a primary reason for investment is to develop new ingredients, new products or new technologies. That proactive approach can help guide the entire process. The manager at a supplement manufacturing company shared the lesson his firm learned: "We invested in good clinical trials that generated interesting results, but the ingredients were impossible to market in the format used in the study because of cost and taste issues. We now always evaluate the potential final product(s) and the manufacturing cost before initiating a clinical."

With regulatory agencies, consumer watchdog groups and an increasingly competitive industry landscape raising the bar, companies must take a proactive approach to developing the clinical research that substantiates the safety and efficacy of their ingredients and finished products if they wish to find long-term success in the broader consumer market. ❑

Heather Granato is an 19-year veteran of the natural products industry, currently serving as the group editorial director in VIRGO's Health & Nutrition Network for the Natural Products INSIDER, Food Product Design, inside cosmeceuticals and SupplySide brands. She has been a presenter at industry events including SupplySide, Natural Products Expo, the Natural Gourmet Show and MarketPlace. Her additional publishing experience includes Country Living's Healthy Living, Natural Foods Merchandiser, Delicious Magazine and WomenOf.com. She graduated magna cum laude from the University of Richmond, VA, in 1992 with a bachelor's degree in journalism.

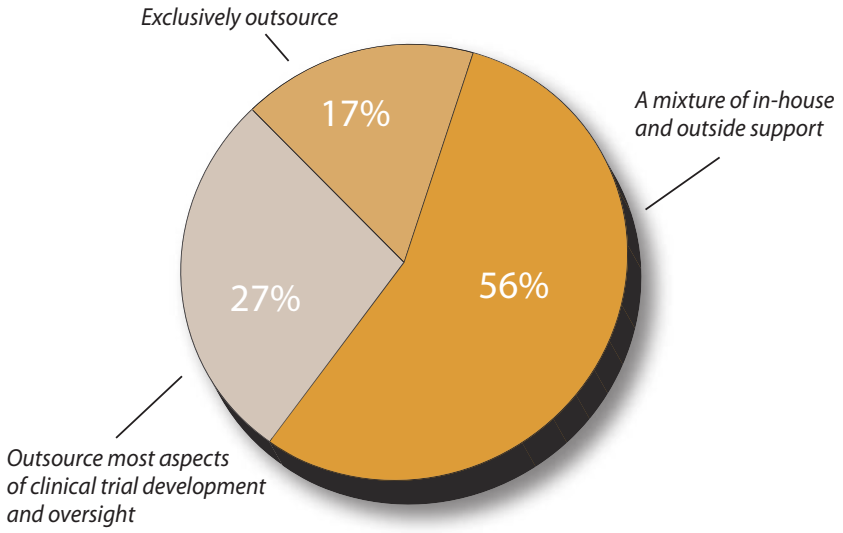
Implementing a Clinical Trial

"How concerned are you with the following aspects of implementing a clinical trial?"
(Ranked 1 to 5 with 1 being "not at all concerned" and 5 being "extremely concerned.")

	1	2	3	4	5
Deciding the right methodology and clinical endpoint	4%	3%	8%	15%	70%
Obtaining the appropriate size and population sample	7%	4%	16%	20%	53%
Cost	1%	3%	20%	16%	60%
Possibility of publication	9%	9%	20%	28%	34%
Oversight/management	7%	6%	20%	30%	37%
Return on investment	2%	6%	13%	20%	59%

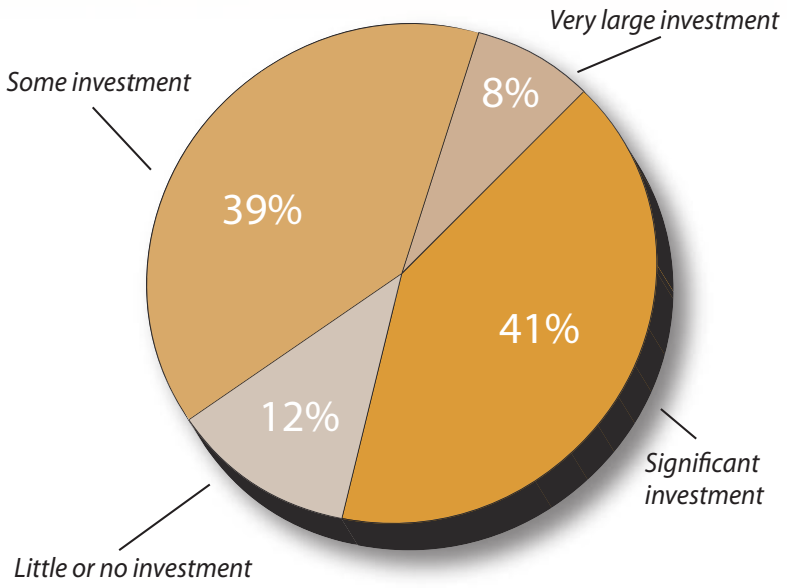
Management of Trials

"How do you handle clinical trials related to your ingredients and/or finished products?" (Reported by %)



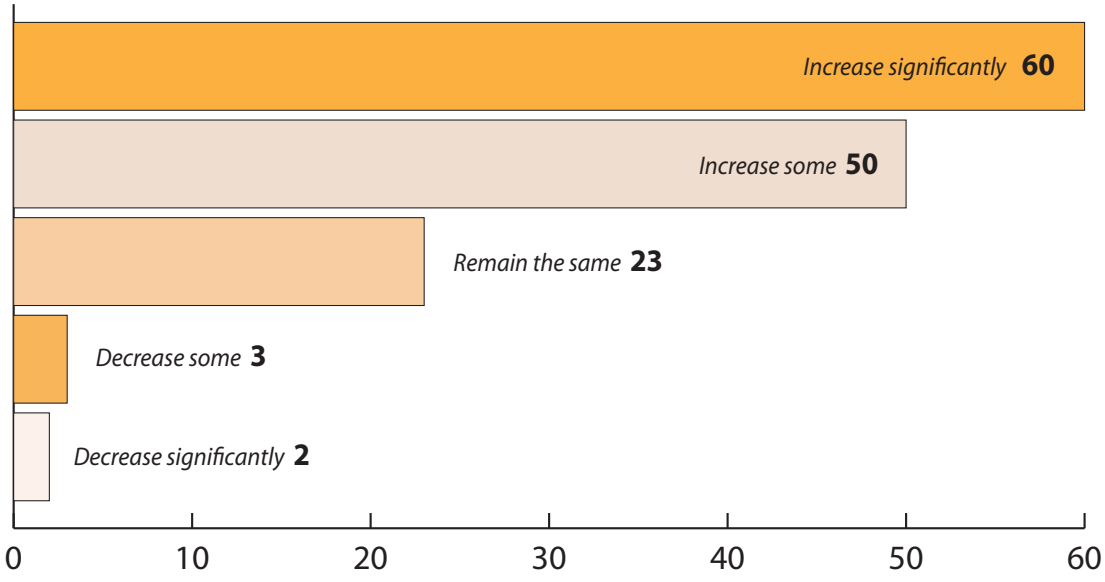
Current Investment in Clinical Research

"How would you rank your current investment in clinical research and science?" (Reported by %)



Future Investment in Clinical Research

"Over the next three years, our investment in clinical research and science will:" (Reported by #)



Investment Rationale

"What are the primary reasons you invest in clinical research on your ingredients and/or finished products?"
(Respondents could select more than one answer; reported by %)