

Covance, Kendle and i3 Research Are Top CROs in Europe

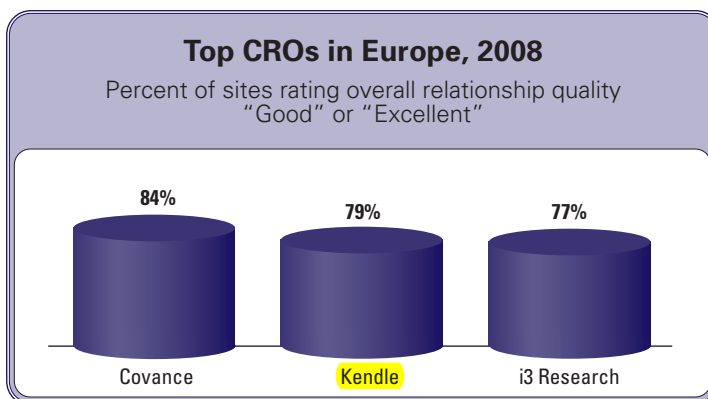
Results of the CenterWatch 2008 Survey of Investigative Sites in Europe found Covance the top rated contract research organization to work with. Also rated highly were Kendle and i3 Research.

Responses to CenterWatch's 2008 Survey came from 36 countries across Europe, as well as Canada. This is an increase from 2006, when sites from 26 European countries participated. Nearly one-third of the responses came from Central and Eastern Europe this year.

Covance dominated the results for contract research organizations (CROs) in the CenterWatch 2008 Survey of Investigative Sites in Europe. While Covance has made top three appearances in both the U.S. and European site surveys conducted by CenterWatch before, it is the first time that either Kendle or i3 Research has ranked as one of the top three CROs in CenterWatch's survey of European investigative sites.

The average score for CROs was 70%, unchanged from 2006, but the top score went from 79% (MDS Pharma) in 2006 to 84% for Covance this year.

In addition to the top overall score, with 84% of sites rating



Source: CenterWatch 2008 Survey of European and Canadian Investigative Sites, (n=653).

Covance "Good" or "Excellent," Covance earned the top three "Excellent" scores for 27 of the 29 attributes that ratings are based on, and best in 14 of them. Only Covance and Parexel improved their scores in each of the six categories of attributes.

"Covance is honored to be named the number one CRO in the 2008 CenterWatch European Site Survey...Covance values the CenterWatch European Site Survey for its objective and independent position, and for measuring an absolutely key driver of success: the level of comfort and satisfaction found at the front lines of clinical trials, the investigative sites. We see this survey as a bellwether capturing both individual CRO performance and feedback on best practices in general. The results of this survey help pinpoint both areas of good performance and areas in need of improvement, naturally com-

binated with our own recurring site and client satisfaction surveys," said Robert J. Davie, Ph.D., vice president and general manager, Europe, Covance.

Kendle, which received the highest score in CenterWatch's survey of U.S. sites in 2007, had the second highest score in this year's survey, with 79% rating the company "Good" or "Excellent." Kendle was rated in the top three of "Excellent" scores 19 of 29 times.

"We are thrilled to have received this recognition in Europe. It is particularly gratifying, having had such a strong finish in the U.S. survey in 2007, and it suggests that our unique approach to site relationships is working on a global scale. To be recognized in this fashion in such a high-profile publication is equally important to us. I am proud of our associates and the way that they are working with these very important relationships. So often

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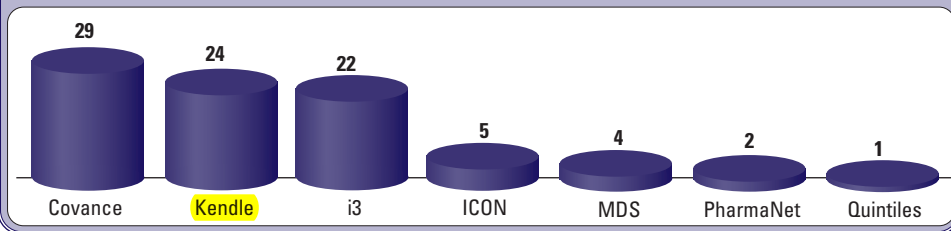
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Highest Frequency as a Top 3 Rated CRO Across 29 Relationship Attributes

Frequency of top 3 rating "Good" or "Excellent"



Source: CenterWatch 2008 Survey of European and Canadian Investigative Sites, (n=653).

when we talk about the development of strategic relationships people assume that it means relationships with our customer, but obviously investigative sites are of primary concern to us in being able to deliver the business, so it is very satisfying when we get such prestigious feedback that we are doing a good job, particularly in Europe...It's great that we have been able to achieve this. We take great store in CenterWatch," said Simon Higginbotham, president of Kende.

i3 Research was in the top three a total of 22 times, a remarkable feat. Consistency across all aspects of the clinical trial operation marks all three leaders in the survey, and suggests that thoroughness is critical to site satisfaction, and ultimately to project success. Considering the evolving nature of clinical regulation around the world, clear understanding among sites, CROs and sponsors is more crucial than ever.

"We would acknowledge that CenterWatch itself is respected and valued in the provision of information and thus, [i3 Research's ranking] really counts. I do think that this additionally represents a vindication of our plans, the approaches, really the focus on quality and customer service, that has been a hallmark of our operation, the founding principles around the customer service and quality pieces that we must have been able to sustain despite a period of what was very considerable growth and expansion for us. I think this speaks to how well-embedded those values in the organization are and the quality of the management in place and the delivery of training to those in the field. [i3 Research's ranking in the CenterWatch survey] also means to me that the efforts that we've been taking to reinforce what I would describe as

the inclusiveness of the delivery environment—by that I mean this holistic view of CRAs, sites and internal support structures—that's been working. We're delighted. I feel it's a very nice reflection or feedback that proves the things we've been trying to do have indeed worked," said Nigel Page, president of i3 Research.

Being organized and prepared for a study was the attribute rated most important in CRO performance, with more than 85% listing it as of the highest importance. With only 39% of sites finding CROs "Excellent" in this regard, it remains a critical area of improvement for CROs. "Has professional, well-trained monitors/CRAs" was the other attribute rated important by more than four sites out of five (83%). "Maintains open communications" (76%), "Provides good overall protocol design" and "Has professional medical staff" (74% each) are the rest of the five most important attributes, those that are essential to study success.

Survey Methodology

CenterWatch conducted the survey of investigative sites in Europe and Canada between January and April 2008. A 10-page survey was

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emailed to 17,000 sites conducting trials in Europe and Canada. The survey instrument, which has been used since 1997 in both North America and in Europe, was developed with input from clinical research professionals at sponsor companies, CROs and investigative sites. A total of 653 investigative sites have completed the survey, representing a 4% response rate.

Approximately 80% of the sample are principal or sub-investigators, with the remaining 20% describing themselves as study coordinators or administrators. Investigators had an average of 12 years of experience with clinical research. More sites are engaged in research full time, 30%, while four years ago, the number was 12%.

Investigators were asked to rate the CROs that they have worked with during the past two years on a wide range of attributes and responsibilities. Investigators were also asked to provide ratings for the three companies that they have worked with most frequently and to rate these companies on 29 relationship attributes involving project management, personnel, workstyle, study initiation and ongoing study conduct activities. Sites were also asked to rate the importance of all the attributes to the success of their clinical studies.

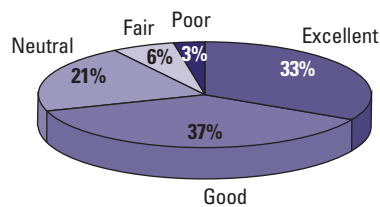
Responses came from 36 countries across Europe, as well as Canada. This is an increase from 2006, when sites from 26 European

Countries that Provided Responses

Austria	Finland	Latvia	Serbia
Belarus	France	Lithuania	Slovakia
Belgium	Germany	Montenegro	Slovenia
Bulgaria	Greece	Netherlands	Spain
Canada	Hungary	Norway	Sweden
Croatia	Iceland	Poland	Switzerland
Czech Republic	Ireland	Portugal	Turkey
Denmark	Israel	Romania	Ukraine
Estonia	Italy	Russian Federation	United Kingdom

Source: CenterWatch 2008 Survey of European and Canadian Investigative Sites, (n=653).

Average Rating for the Typical CRO in 2008



Source: CenterWatch 2008 Survey of European and Canadian Investigative Sites, (n=653).

countries participated. Nearly one-third of the responses came from Central and Eastern Europe. Canada was not surveyed in 2006.

Detailed Highlights

The aggregate score earned by CROs in the CenterWatch survey this year was 70%, somewhat lower than the 75% sponsors received. On the other hand, the 84% score by Covance was higher than the 80% of Eli Lilly, the top sponsor in that portion of our survey (see the May issue of *The CenterWatch Monthly*). Traditionally, the highest-scoring CRO has not earned a higher score than the highest scoring sponsor in CenterWatch's site surveys.

In addition to assessing companies by 29 different attributes, the CenterWatch survey also asks sites to assess the importance of those attributes in both CROs and sponsors. Some comparison between the two gives a bit more insight on the tasks sites rely on CROs for more than sponsors, and vice versa. Almost half show little or no difference between CRO and sponsor in terms of how important an attribute is.

The items more important for sponsors tend toward laying the overall framework of

the study—the alignment of the protocol to scientific and clinical realities, timeliness of drug availability, protocol design and informative nature of investigator meetings. These can be described as the base upon which study success rests.

On the other hand, sites rely on CROs for more day-to-day activities. Minimal amendments to protocols, the efficiency of query handling and responsiveness to inquiries, low staff turnover, and technological efficiency are what sites prize CROs for. Most of all, being organized and prepared was rated essential to both groups, but even more so for CROs (85% vs. 80%)

Attributes that sites value sponsors and CROs equally for tend toward financial, professionalism and communication skills. The promptness of grant payments, their fairness and scheduling, as well as funding for recruitment efforts all relate to the financing of trials, and of equal importance in all cases is to keep these activities predictable and sufficient. Professionalism of all staff groups as well as their knowledge levels are important no matter if a sponsor or CRO sends them. Communications issues also have equal weight. Openness of communications, ongoing help in running the studies, being organized and prepared, flexible and realistic all must be considered “Excellent” on all sides for studies to succeed.

General Project Management

The attributes making up this category explore whether sponsors are organized and prepared, how realistic their project timelines are, sponsor responsiveness to inquiries, how realistic patient enrollment goals are, whether CROs work effectively with sponsors and how well open communication is maintained.

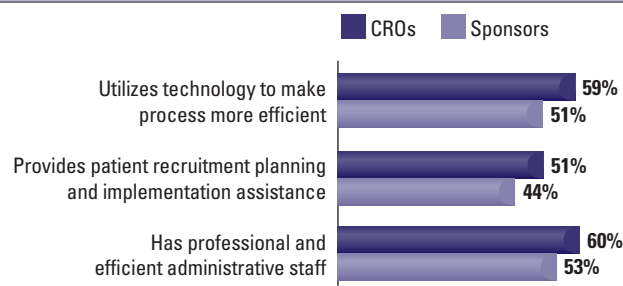
“Is organized and prepared” was rated very important by 85% of sites, the attribute to receive the highest rating of importance. Covance, with 57% of sites rating it “Excellent,” led in this category. This was the highest single score for any attribute by any company, and in the top essential area. Covance showed further leadership in the areas of “Is responsive to inquiries” (55%), and “Effectively works with sponsors” (52%).

“A detailed review of our own extensive experience servicing clinical trials revealed that in the current day drug development paradigm, an increasing proportion of overall costs is being devoted to data verification and remediation—trying to address performance consistency challenges as they invariably crop up during the trial process. The after-the-fact remediative approach evidently erodes timelines, preparedness, communication and satisfaction on all fronts, including staff retention...The review led us to recast our own internal teams and processes based on a proactive planning paradigm. Specifically, we have developed processes to build quality into the initial selection, initiation and training of investigator sites, and developed ongoing processes and tools for tracking and optimizing the program throughout its lifecycle,” said Covance’s Davie.

“Our experience with this site-centric operational platform indicates that an approach favoring risk prevention, rather than remediation of investigator errors, delivers improved productivity, lower operational risk, and improved scientific robustness, not to mention increased staff and investigator satisfaction.

Attributes Rated More Important for CROs than for Sponsors

Top 3 Attributes where sites rated CRO performance “Very Important” higher than the same rating for a sponsor



Source: CenterWatch 2008 Survey of European and Canadian Investigative Sites, (n=653).

General Project Management Attributes Evaluated

Percent of Sites Rating a Typical CRO "Excellent"

General project management	2004	2006	2008
Is organized and prepared	35%	41%	39%
Sets realistic project timelines	28%	35%	32%
Is responsive to inquiries	32%	36%	38%
Sets realistic patient enrollment goals	*	33%	35%
Effectively works with sponsors	35%	41%	38%
Maintains open communication	34%	42%	43%

* Question not asked in this year

Source: CenterWatch 2008 Survey of European and Canadian Investigative Sites, (n=653).

This paradigm, which we call the Predictive, Proactive, Preventative (P3) operational platform, features: Predictive feasibility and modeling—analyzing and leveraging similar study experiences to optimize study design and site selection to best meet the requirements of a specific study; Proactive project planning—anticipating sources of poor performance and shifting study budget allocations away from error detection and repair activities towards study center performance prediction and risk mitigation; and Prevention of errors—emphasizing new approaches to investigator grants that encourage improved pre-activation preparation efforts, and promoting and rewarding primary data quality at the sites,” Davie said.

Maintaining open communications was another of the essential attributes, with 76% of sites rating it very important. i3 Research was rated “Excellent” by 54% of sites in this critical area.

“I do think it’s the underlying behaviors and philosophies that will actually be driving [i3 Research’s rating]. Firstly, you may be aware that the values of i3, the three i’s, are intelligence, innovation and integrity. It’s that integrity piece that we really interpret as having very straightforward dealings. We like it when people ask us what we think and we tell them. We’ve never sought to be just the arms and legs of an operation. And because we hire the individuals we do, the caliber of individuals we do, that dialogue is one that they are incredibly happy to enter into with all manner of site personnel. I point to this rather inclusive approach that we’ve tried to always build, a combination of both philosophy or value, plus the quality of the individuals we hire. In Europe, and particularly across many of the Central and Eastern European countries, we

have a high proportion of individuals who came out of the state systems where they may indeed have been investigators themselves. I think all of that really facilitates very straightforward, very open, very honest communication and provides a kind of continual assistance that goes beyond the ‘box-ticking brigade,’ as I call them,” said i3 Research’s Page.

Study Initiation

Attributes making up this category include good protocol design, good CRF design, informative investigator meetings, and scientific rationale aligned with good clinical practices realities. Of all these attributes, “Provides good protocol design” was one of the essentials, with 74% of sites rating it important. Covance was rated “Excellent” by 48%.

“Our systematic, quantitative operations-driven trial management platform is coupled with, and driven by, our site-centric project management approach which places the investigator at the heart of the study. We specifically organize project teams around the individual investigative site to maximize patient accrual and improve data quality. This approach has led to operationally smoother studies and, subsequently, to higher investigator satisfaction, which translates into satisfaction with the sponsor and drug. Another element in this approach is fast study site activation services: study start-up is labor-intensive, detracting staff from other project activities, and potentially causing delays that will affect all subsequent deliverables. However, we have had decades to operationalize and optimize logistics to efficiently handle the administrative, repetitive and time-consuming tasks surrounding site activation, and avoid any potential pitfalls. From a site-centric point

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of view, investigators and site personnel are freed up to focus on their core, value-added functions,” said Covance’s Davie.

Kendle was strong in the area of protocol’s science being aligned with clinical realities, (54%).

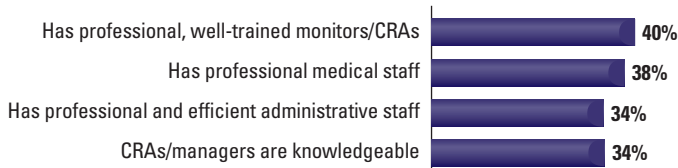
“We have significantly strengthened our global medical affairs group who work with the customer to look at the protocol and walk through it from the perspective of the patient from start to finish. That is a very important step, as it blends scientific expertise with the practicality of the patient experience. I think one thing we have learned, particularly with our patient access and retention programs and working with sites, is that the patient is at the heart of the experience and we need to be sure we are taking into account how the patient will work through that process when we’re looking at the protocol,” said Kendle’s Higginbotham.

i3 Research was the best rated at “Ability to carry out protocol” (45%) and “Provides uncomplicated case report form” (38%).

“In terms of the ability to carry out the protocol, there are two things. The first is, the most overt manifestation of specialization in i3 Research is the therapeutic specialization. What that translates to is having customers that are frequently asking us to help them design the protocol in the first place. And clearly when you are in a position of being able to help shape a protocol with knowledge beforehand, if you will, because of your own experiences of working in that country with those sites with that apparatus, if you will, what naturally tends to result from that is something which sites themselves can readily sign up to, feel good about, and get going. I think where people talk about ability to carry out the protocol, that is undoubtedly one piece of it because, again, there’s been a high level of interaction and dialogue based upon a) our knowledge of the therapeutic area and b) our knowledge of the environment in which that

Quality of Staff Professionalism

Percent of sites rating CRO "Excellent"



Source: CenterWatch 2008 Survey of European and Canadian Investigative Sites, (n=653).

protocol will be conducted that we are uniquely positioned to bring together," said i3 Research's Page.

"The other piece, which is where we have not had the opportunity to directly either write or provide input to protocol design and do become the executors of that, I come back to having people who have the therapeutic expertise and depth of experience to be able to not just look at it as some kind of cookbook or recipe but rather have an understanding of truly what that means when it comes to the operational execution of that protocol and the nuances that may be associated with clinical developmental research in that particular country. Whether we've shaped it, written it entirely or not, the common thread is the therapeutic expertise," said Page.

Ongoing Study Conduct

The attributes of good drug availability, good support of patient recruitment, good funding for patient recruitment, the use of technology to improve efficiency, ongoing support, low monitor turnover and an efficient query handling process comprise the category of ongoing study conduct. Kendle was given top marks for timeliness of study drug availability (56%), i3 Research edged Covance in "Provides ongoing help in running the study" (45%) and got a 33% score for "Efficient contract and budget negotiations when responsible for overseeing," an area of weakness for all CROs.

"We implemented originally a few years back now—but we do refreshers from time-to-time—the Ritz-Carlton customer service training. One of the things it seeks to do is really speak to the ownership of problems and issues, even if you are not the person who would actually be solving them. This ownership, accountability, follow-through-to-completion is something that we've really tried to

instill in the organization. What that means is for the CRA and site, maybe the issue or problem they pick up has absolutely nothing to do with monitoring *per se* but nonetheless they are the face of the organization. They are the people that prevent a site from having to potentially navigate through our structures, which may be either difficult or impossible for them to do, and really means that there is a mechanism of having that human touch point that sees something through even if they're not the person solving it from start to finish," said i3's Page.

The importance of attributes was rated by sites both in relation to CROs and to sponsors in the CenterWatch 2008 Survey of Investigative Sites in Europe. Two attributes in the Ongoing Study Conduct category were rated more important to CRO performance than for sponsors. "Utilizes technology to make processes more efficient" (8%) and "Provides patient recruitment planning and assistance" (7%) are areas where sites look to CROs as the key performer. Covance had the best scores of "Excellent" in these areas.

Staff Professionalism

The two final attributes rated essential by sites relate to the professionalism of study staff.

"Has professional, well-trained monitors/CRAs" and "Has professional medical staff" were rated important by 83% and 74% of sites, respectively. Kendle had the best rat-

ings of "Excellent" in both of these areas; professionalism of monitors/CRAs was 56% and medical staff quality 52%.

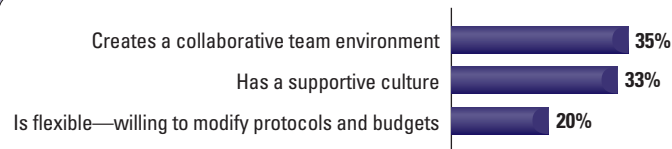
"Kendle places the project leader [PL] at the center of the project to ensure there is a single point of oversight across the delivery of a program, particularly if it is a global program. I think we have done a good job of making sure that the PLs really understand the importance of the sites in terms of delivery, and this has been the key to our success. Another imperative, particularly in relation to Europe, is the importance of the CRA being able to build a relationship with a site. In Europe, perhaps more than anywhere else, sites are much more relationship-driven. That good relationship means that we're better able to deliver for our customers. So we focus on the CRAs really being site managers as opposed to just site monitors," said Higginbotham.

Workstyle

The attributes in this category are sponsor flexibility, supportive culture and the ability to create a collaborative team environment. This is an area to focus on for improvements. Only one in five investigative sites gave CROs a top rating in terms of their flexibility—or willingness to modify protocols and budgets. Of the 29 attributes on which CROs are ranked, this was the lowest score. While this may seem to be an area where CROs would have limited impact relative to the contribution of sponsors, the ratings of importance were equal to both groups, 55%. i3 Research was the only company found "Excellent" by even

Quality of Workstyle

Percent of sites rating CRO "Excellent"



Source: CenterWatch 2008 Survey of European and Canadian Investigative Sites, (n=653).

a quarter of sites (27%) in this area. Kendle was rated best at creating a collaborative team environment (46%).

“One of the things that differentiates Kendle is that we see ourselves as a people-based business, and we realize that it is the people that deliver the results. Collaboration is very important, so comprehensive communication is critical. Without establishing strong lines of communication, a collaborative effort is much more difficult to maintain. In fact, we see strong communication as a corporate priority—and not just as it relates to the way we interact with sites. We see it as a priority in developing strategic relationships with customers, sites and with all stakeholders necessary to ensure delivery of program goals on time and at the highest quality,” said Kendle’s Higginbotham.

Grant Payment Process

The grant payment process is made up of several attributes including fair grant payment amounts, realistic grant payment schedules and promptness of grant payments.

Sites have not traditionally been generous when assessing the grant payment process. Fortunately for CROs, this is an area where the contributions of sponsors are rated more important. Parexel had the best rating for “Offers realistic grant payments” with 32% of sites finding them “Excellent.” ICON Clinical Research was tops for “Provides prompt payment of grants” (32%).

Conclusions

All three top CROs in the CenterWatch 2008 Survey of Investigative Sites in Europe emphasized that their ranking resulted from listening to sites’ needs and to being able to determine what sites could offer. Both Kendle and i3 Research mentioned the need to work with “the right sites” from the beginning, which may be key to their success.

“Our feasibility group takes a lot of care to try and match the right sites with the right studies. It is essential to assign realistic and achievable recruitment goals and then to make sure that you can support those recruitment efforts through the sites. I think we do a great job with that. We have continued to strengthen our dedicated global patient access and retention organization who actually work very closely with our sponsors and the sites. Depending on the study, they can provide specific patient-branded approaches, which support and enhance patient access and retention,” said Kendle’s Higginbotham.

i3 Research’s Page described an initiative his company has undertaken as “investment in how we structure around, perform, then record information arising through feasibility work. What that’s done is led to earlier and better identification of the right sites. Obviously ‘right sites’ perform better by comparison to the ‘wrong sites.’ You get into a virtuous circle because if you’ve aligned that bit right, sites are able to perform, they feel better about it, they in turn work better with you. It’s a positive feedback loop.”

Ultimately, what all three top CROs hold in common is the drive to continuously improve their site relationships.

Covance’s Davie concluded, “We have consistently received a top ranking in the CenterWatch investigator site surveys since their inception, and to see a strong run now capped with the lead position is special cause for celebration. At the same time, we also see this top ranking as a challenge and indeed an obligation to not fall victim to complacency, but continue to listen to our clinical trial partners and put in place specific, carefully tracked initiatives to ensure our relationships continually improve and strengthen.

“We acknowledge that once current accomplishments have been celebrated, it is imperative to reinforce best practice, pinpoint and address areas of improvement and put in place frameworks to promote improvement also going forward.”

—Paul Dewberry and Sara Gambrill

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