

i3 Research, PPD, Kendle, Covance Rated Top CROs in Europe in 2010

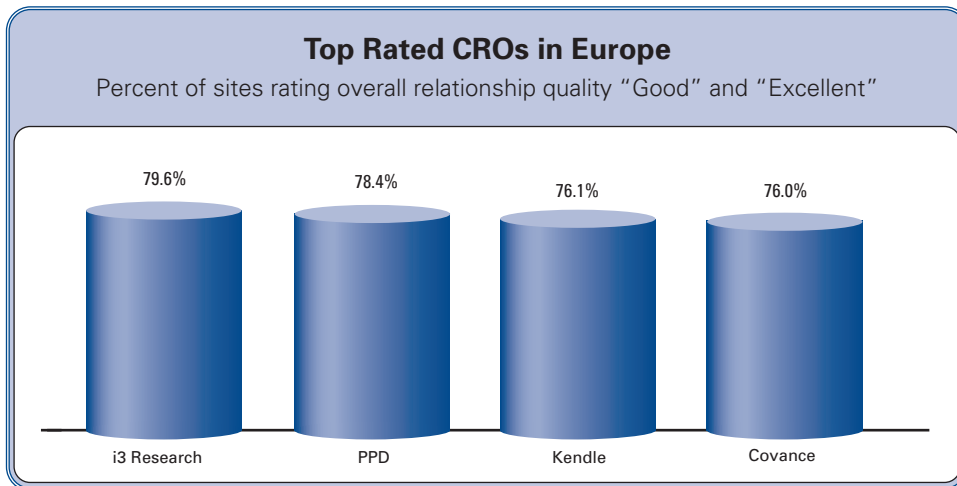
► i3 Research, Kendle and Covance remain top-rated CROs in the 2010 CenterWatch European Site Survey. i3 Research outpaced other CROs this year to achieve a top CRO rating in overall relationship quality with investigative sites.

► PPD made a significant improvement compared with the 2008 survey and earned a second-place distinction in the 2010 survey, exhibiting strengths in organization/preparation, responsiveness to inquiries and demonstrating a supportive culture.

Last month, the relationship between European investigative sites and sponsors was explored. CenterWatch now shifts its focus to the relationship between sites and contract research organizations. Undoubtedly, an effective relationship between sites and contract research organizations (CROs) is also essential to the success of a clinical study.

Investigative sites across Europe evaluated their relationships with CROs in the 2010 CenterWatch European Investigative Site Survey. Feedback was obtained from 924 investigative sites across 30 countries. Sites rated CROs across 29 relationship attributes ranging from general project management to grant payment processes.

While European investigative sites have consistently regarded Covance highly in past CenterWatch surveys, the 2010 CenterWatch European Site Survey is the first time i3 Research, PPD and Kendle have surpassed Covance with regard to the percentage of sites that rated these CROs as



Source: CenterWatch 2010 Survey of European Investigative Sites (n=924)

“Good” or “Excellent” for overall relationship quality. i3 Research was consistently rated a top CRO across general project management attributes, in personnel and work-style areas and across specific project-related characteristics.

“It’s a great honor and we’re very pleased to have this recognition,” said Tracy Tsuetaki, president of i3 Research. “We say that because, within the investigator sites, this is really where the value that we provide in some ways gets implemented. In other words, the services we provide ultimately will serve the needs of the same sites and those investigators that we work with. Having that insight and the ability to be recognized by these sites to make their jobs easier, in the end of the day, is as important to our sponsors as it is to us. They are, in fact, a very important piece of how we can serve the development and clinical trials side of our business well.”

Sites rated PPD among the top three CROs in 26 of the 29 total attributes. In

particular, PPD was rated the highest by sites for organization and preparedness—an attribute deemed to be extremely important to the success of a study across both sponsors and CROs.

“We have done a lot in the last two years in general just looking at the way we interact with sites and the way our staff interacts with sites,” said Sebastian Pacios, PPD’s senior vice president, clinical development, for Europe, Middle East and Africa. “One of the things that we have done is to have more specialized teams for different phases of a project, so the sites can count on specifically trained people to help them with specific tasks. In terms of project management, sites have counted on specific resources depending on the need that they have.”

Kendle was rated highly in both Europe and the U.S.—sites rated the company a top CRO in the 2009 U.S. site survey. In 2010, Kendle achieved scores in the top 3 tier of CROs on 21 of the 29 attributes that were

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evaluated by European sites. In particular, Kendle was rated highly for protocol design quality and for having protocols where scientific rationale is aligned with clinical practice realities.

"This is a tough business," said Kendle senior vice president and chief operating officer Stephen Cutler, Ph.D. "Doing clinical research within a clinical practice situation is always challenging. If you want to succeed in that business—if you want to encourage sites to recruit patients—you need to build a good two-way relationship with them. They need to be heard, and they need to have their voice heard with the sponsors.

"There are some sites, I've heard in the past, that prefer to work with the sponsors directly, but I hear that less now because I think the industry has taken on the need to represent the sponsors but also to represent the sites—to be the go-between, if you will. I think there's a lot of really good information that comes back from sites, and not just about their particular trial. To have that feedback come back to us and to the sponsors, I think is important, and to respect that relationship and to respect that opportunity, is something we take very seriously."

Survey highlights include:

- ▶ The total percentage of sites that rated i3 Research "Good" or "Excellent" for overall relationship quality was 79.6%—up from 77% in the 2008 survey.
- ▶ 78.4% of sites rated PPD "Good" or "Excellent" for overall relationship quality. PPD managed to increase its score by an impressive 16 percentage points from its rating in 2008.
- ▶ Both Kendle and Covance achieved lower total "Good" or "Excellent" scores in the 2010 survey compared with the 2008 survey, but both CROs are still top CROs this year.

- ▶ The "Good" and "Excellent" score for the average CRO was 73%, a slight increase from the 70% achieved in the 2008 survey. This compares to an average sponsor rating of 76.6% in 2010.

The most important attributes to clinical study success have remained consistent among CROs over the years. In 2010, 63% of sites identified the quality of monitors/CRAs as "Very Important." Organization and preparation was also perceived as "Very Important" to 62% of sites. Finally, 58% of sites identified good overall protocol design as a critical aspect of study success.

According to investigative sites, some project areas were clearly more important for CROs than for sponsors when the importance of attributes was contrasted between the two. Specifically, sites placed more of an emphasis on protocols that required minimal amendments for CROs than for sponsors. A collaborative team environment and the use of technology to make processes more efficient were also perceived to be more important for CROs. In contrast, sites placed more value on study initiation issues for sponsors than for CROs—such as good overall protocol design and a protocol aligned with clinical practice realities.

Attributes sites viewed as equally important for both sponsors and CROs were general characteristics of excellence for any organization. These attributes included open communication, supportiveness, proper organization/preparation, staff professionalism and financial responsibilities.

Areas for improvement trended similarly to the survey findings among sponsors. A gap between the percentage of sites that rated the quality of monitors/CRAs "Excellent" (46%) and the percentage of sites that rated this same attribute among CROs very important (63%) was apparent. However, survey results over the

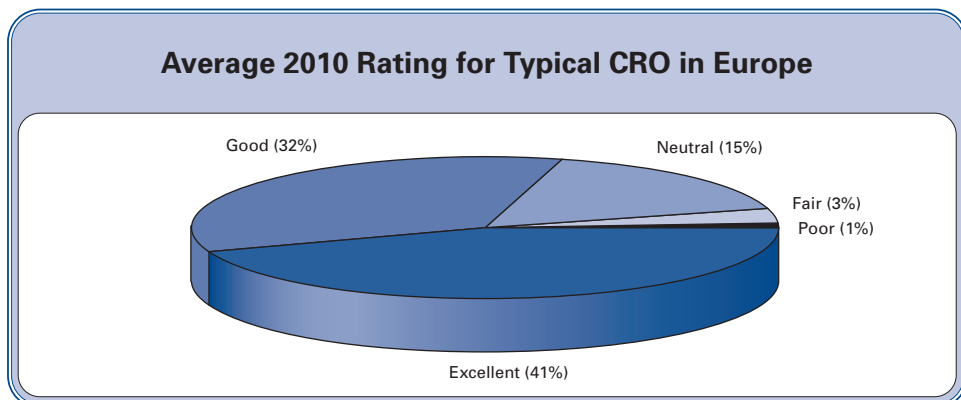
past years indicate a steady increase in the percentage of sites rating monitoring staff “Excellent,” which indicates progress in this area.

Similar gaps were evident in the areas of protocol design and organization/preparation. Specifically, 58% of sites found protocol design to be “Very Important” and 43% of sites rated the average CRO “Excellent.” For organization and preparation, 62% of sites rated this attribute “Very Important” and 48% of sites rated the average CRO “Excellent.”

Survey Methodology

CenterWatch conducted its survey of investigative sites in Europe between January 2010 and March 2010. The survey was conducted online and emailed to a broad sample of investigative sites located throughout Europe. The survey instrument, used since 1997 in North America and Europe, was developed with the help of clinical research professionals at sponsor companies, CROs and investigative sites. A total of 924 responses were collected and analyzed.

Similar to the 2008 survey, 77% of respondents were principal investigators and 13% of respondents were sub-investigators. The remaining sample comprises study coordinators/nurses. The average number of years of experience in



Source: CenterWatch 2010 Survey of European Investigative Sites (n=924)

clinical research was 13 (compared to 12 in the 2008 survey) and three-quarters of the survey sample practiced clinical research on a part-time basis. Survey respondents practiced clinical research in a broad range of therapeutic areas, and 77% of those surveyed have received formal training in clinical research.

In the survey, sites were requested to rate the CROs they worked with in the past two years on a range of attributes relating to general project management, personnel and work-style and project-specific areas—such as protocol design, grant payment issues and drug availability. In addition, sites also provided feedback on the importance of these attributes when conducting their clinical trials.

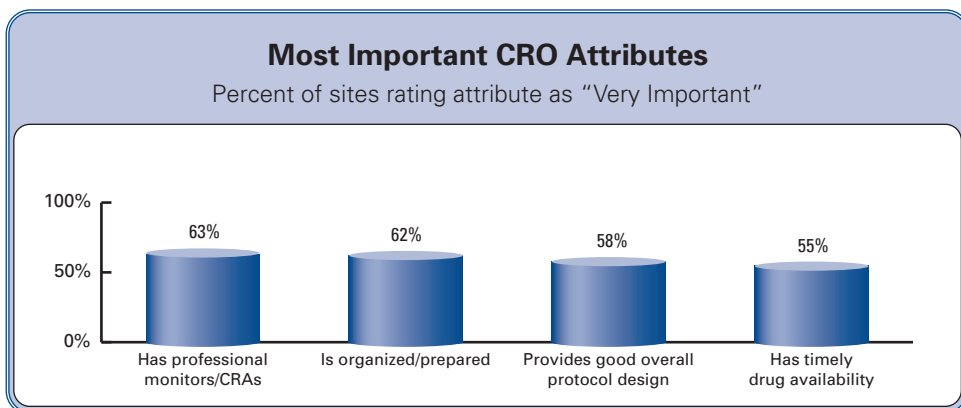
Responses originated from 30 countries across Europe—with 42% of responses from Eastern and Central Europe.

General Project Management

This category included the following attributes: organization/preparedness, project timeline and patient enrollment goal feasibility, responsiveness to inquiries, communication effectiveness with sponsors and the ability to maintain open communication. Organization/preparation was identified as the most important attribute in this category with 62% of sites rating this attribute as “Very Important.”

CROs that received the highest percentage of “Excellent” in this category included i3 Research (54.4%), PPD (50%) and Covance (47.2%). Sites provided i3 Research the highest percentage of “Excellent” ratings for five out of the six attributes in this category.

“I think what you will hear throughout the success that we have—whether that’s in general project management, study initiation, ongoing study conduct, etc.—is really a commitment to our focus around quality, service and value,” said i3’s Tsuetaki. “We are very committed to a process whereby what we say, we do. We work very closely with our sites, and our monitors are extremely supportive. They work with sites in all levels of details from patient recruitment strategies to query resolutions, and they are extremely knowledgeable, responsive and accessible



Source: CenterWatch 2010 Survey of European Investigative Sites (n=924)

General Project Management Evaluated

Percent of sites rating a typical CRO "Excellent"

	2004	2006	2008	2010
Is organized and prepared	35%	41%	39%	48%
Sets realistic project timelines	28%	35%	32%	43%
Is responsive to inquiries	32%	36%	38%	45%
Sets realistic patient enrollment goals	*	33%	35%	41%
Effectively works with sponsors	35%	41%	38%	43%
Maintains open communication	34%	42%	43%	50%

*Question not asked this year

Source: CenterWatch Survey of European Investigative Sites - 2004, 2006, 2008, 2010

to the sites to answer questions in a very timely manner.”

PPD was rated the highest for being organized/prepared, with 54.8% of sites rating PPD “Excellent” for this attribute.

“The sites and the people who interact with the sites have the support of not only one person but three,” said PPD’s Pacios. “They have a clinical team manager who basically supports the day-to-day operation from a protocol perspective and everything related to site management, patient recruitment and specific protocol compliance. At the same time, they are supported by a specific project manager who helps and supports the CRA, the rest of the staff and the site for everything related to a protocol. The third thing is that not only the CRAs but also the sites are supported by line managers. Line managers can’t give specific support about the protocol. But they give specific support about national legislation, national regulations, compliance in general, functional support, and if there are things that need to be escalated at the national level—because you know that Europe is a big community but every single nation is different—they have someone on the ground at a higher-level who can interact and help solve issues with investigators.”

Study Initiation

This category comprises the following attributes: good protocol design, good case report form design, informative investigator meetings, protocols that require minimal amendments, efficient contract and budget negotiations and protocols that are aligned with clinical practice realities. Among CROs in this category, sites placed the most value on good protocol design and protocols where scientific rationale is aligned with clinical practice realities—with 58% and 54% of sites, respectively, rating these two attributes as “Very Important.”

Sites perceived that i3 Research, Kendle and PPD excelled in the study initiation aspects of a clinical trial. The percentage of sites that rated these CROs “Excellent” in this category was 53.5%, 45.2% and 42.5%, respectively. Kendle received the highest percentage of “Excellent” ratings for its protocol design (48.5%) and for protocols where scientific rationale is aligned with clinical practice realities (50%).

“Like most CROs, when we write the protocol, we do it very much in line with our sponsors and our sponsors’ medical folks,” said Kendle’s Cutler. “In many cases, we are given a protocol and we get asked to comment on it—the feasibility of the protocol, the suitability with respect to medical

and clinical practice. From that point of view, for protocol development, we have a strong medical group that understands clinical practice and clinical research very well. Our medics are able to take a protocol that a customer has drafted and provide some very useful input into that protocol to ensure it can be implemented in a practical sense at a site. There’s nothing more frustrating for a site than to have a lot of patients for a particular indication that they’re not able to enter into a protocol because of some esoteric inclusion or exclusion criteria. Our medics are very much involved.

“We also have our regulatory people take a look at the protocols fairly early, and we encourage them to be fairly forthright in their feedback to customers. To their credit really, our customers take that feedback very well and, in many cases, make changes to enhance the protocol. They’re not always able to, but they take that feedback on board, and I think that makes the whole protocol much more valid for the population that they’re treating—and easier to run—while still being in compliance with the regulatory requirements to get the drug to market.”

Sites rated i3 Research the highest on four out of the six attributes in the study initiation group.

“When it comes down to study initiation, preparation is the key,” Tsuetaki said. “Part of our innovation and uniqueness here around the study initiation that we have been doing a great deal of work on is what we would call ‘rapid-study startup.’ There is a great majority of studies that often miss their timelines due to poor study startup or initiation. We’ve actually shown through our rapid-study startup program that we’ve been able to shorten the startup and enrollment phase to meet or exceed the timelines for our drug development

programs—a vast improvement from the industry average. By developing an electronic site evaluation form, we’ve been able to reach agreement with sponsors on identifying at least key sites and specifications to be able to startup these sites and initiate these sites quickly.”

Ongoing Study Conduct

Timely drug availability, adequate funding for patient recruitment, patient recruitment assistance, low monitor turnover, ongoing support in running the study, the utilization of technology to make processes more efficient, and an efficient query handling process are the attributes included in this area. Among CROs, sites perceived providing ongoing help during the study (51.4%) and an efficient query handling process (47.3%) as the most important attributes in this category.

i3 Research, Kendle and PPD led the way once again in the ongoing study category. Sites provided these CROs with the highest percentage of “Excellent” ratings. Sites identified i3 Research as the top CRO for providing ongoing help during studies and for having the most efficient query handling process—with the percentage of sites rating i3 Research “Excellent” in these two areas at 59.5% and 57.5%, respectively.

“Our staff begins the work in a study with a well-laid out plan and agenda, including putting together the expectations that are provided in advance so that sites will understand and know what’s going to happen in an upcoming visit,” said i3’s Tsuetaki. “The monitors that we have are known to be extremely supportive. They work with sites in all levels of details from patient recruitment strategies to query resolution. Our team tends to be very proactive. They tend to seek out issues early on and own them and take accountability to get them addressed. I think the ability to

train staff not just in the therapeutic specialization but to train staff in terms of how to address these problems really helps the sites have great confidence in i3.”

Staff Professionalism

The attributes included in this category were professional and knowledgeable medical, monitoring and administrative staff. Sites placed the most value on professional, well-trained monitoring/CRA staff—with 62.7% of sites rating this attribute as “Very Important.” This was the most important attribute overall for both sponsors and CROs. Professional medical staff was also deemed very important—with 54% of sites rating this attribute as “Very Important.”

At Kendle, staff professionalism and training is part of what has led to sites’ satisfaction with protocol design.

“You’ve often got to sort of sell a protocol to a site,” Kendle’s Cutler said. “We take pride with our CRAs in terms of their training and making sure they know the protocol-specific and the indication aspects of the trial. We want to make sure that they understand the disease area they’re working in. We will, in many cases, take time out specifically to train them prior to the study.

We train them in the protocol so they’re able to explain the protocol to the sites, and, importantly, they remain a strong resource to the site throughout the trial. A site can call a CRA or one of our medical experts and ask a question or get a clarification on a specific question within the protocol pretty much in real-time. We take a lot of pride in making it as easy as possible for sites to enroll patients in trials. The easier we can make it, the better it is for us and for them.”

Sites viewed i3 Research, PPD and Covance as having the most professional staff. These CROs achieved the highest percentage of “Excellent” ratings in this category. i3 Research received particularly high ratings for its knowledgeable and well-trained monitoring/CRA staff—with 70.5% of sites rating i3 Research “Excellent” for this attribute.

“We do have what we believe is lower than industry staff churn within our teams,” i3’s Tsuetaki said. “I think that allows for continuity certainly within the projects and certainly within the sites that monitors work with. We leverage quality councils internally as a way to make sure that individuals are well-trained, and we



Source: CenterWatch Survey of European Investigative Sites - 2008, 2010

also have our own internal training group that makes sure CRAs and others are very knowledgeable not only in the areas related to their functional activities but with regard to the therapeutic areas as well. Our monitors are very well trained and versed in the current standards of the care not just in terms of understanding the protocol but specific to the countries that they are monitoring within.”

Kendle also emphasized the importance of continuity when it comes to working with sites. Cutler estimated that the average turnover rate for monitors across the industry is approximately 25% to 30%, but, at Kendle, turnover averages 12% to 15%.

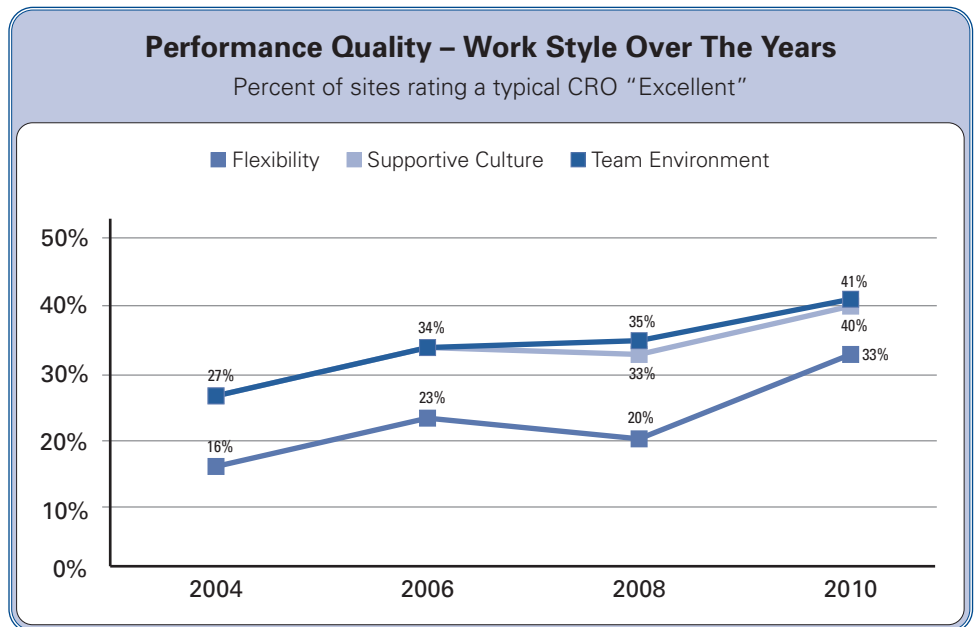
“We try to link our CRAs with sites and have them develop long-term relationships with those sites,” he said. “Whenever possible we assign the same CRAs to sites for subsequent studies to target their therapeutic expertise and continue to build the relationship. We also focus on retaining our monitors and on keeping monitors involved in the therapeutic area. They are a critically important aspect of the clinical development process.”

Work Style

A flexible, supportive culture and collaborative team environment were the attributes included in this category. Sites placed the most value on a collaborative team environment—with 48.1% of sites rating this attribute “Very Important.”

i3 Research and PPD were the highest-rated CROs, achieving 51.3% and 44.9% “Excellent” ratings in this category. This was compared to a rating of 38.2% for the average sponsor. Sites perceived PPD to have the most supportive culture—with half of sites rating PPD “Excellent” on this attribute.

“We have made a conscious effort in the last two years in providing our CRAs, our staff and anyone who’s really interact-



Source: CenterWatch Survey of European Investigative Sites - 2004, 2006, 2008, 2010

ing with sites with training that goes beyond the specific function and protocol training,” said PPD’s Pacios. “We have implemented soft skills training—training that helps people dealing with conflicts, more complicated situations. It goes beyond just what is required for the job. It talks about conflict situations, helping understand the other party.”

Sites regarded i3 Research highly for demonstrating a collaborative team environment and exercising flexibility with regard to modifying protocols and budgets.

“When we initiate sites, we do spend a lot of time in terms of listening to sites and creating country-specific and legally-compliant contracts to make things easy for them,” said i3’s Tsuetaki. “Some organizations may have a standard template to work within. We try to customize those for the countries and really provide our sponsors with specific needs that will allow for contracting to flow much easier and are specifically customized to the regulatory environments that we work within.

“I don’t want to say that we are an organization that unilaterally changes a

protocol. We are an organization, however, that customizes needs and provides a high level of detail to sponsors and really tries to be very flexible when it comes down to contracting with sites to make sure that they recognize that we understand the regulatory environment as well as recognize some of their needs that may be different than other sites.”

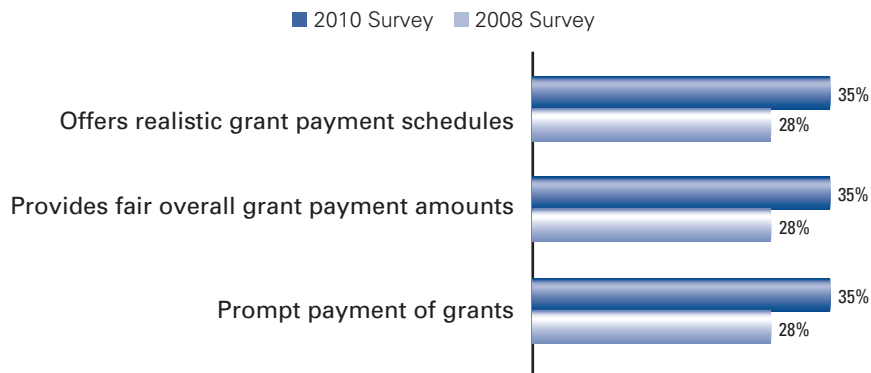
Grant Payment Process

This category comprises the fairness and promptness of grant payment amounts, as well as providing realistic grant payment schedules. Consistent with findings among sponsors, sites perceived the fairness of grant amounts to be the most important (41.3%) financial aspect of a study.

The grant payment process attributes were some of the lowest-rated attributes overall in terms of excellence. The “Excellent” rating for the average CRO in this category was 35.1%, similar to the rating for the average sponsor. CROs that surpassed this rating include i3 Research (47.7%), Kendle (35.6%) and PPD (35.4%).

Quality of Grant Payment Process

Percent of sites rating a typical CRO "Excellent"



Source: CenterWatch Survey of European Investigative Sites - 2008, 2010

“We have worked on grant payment processing quite a lot lately,” said PPD’s Pacios. “We have developed a good system of first making sure that the payments that we initiate with the sites are fair and not overrated or underrated, but just at the right level. We have acquired different systems, including databases that help us have the right information about the level of payment in every country for specific indications. We use that tool in combination with our investigator database and our clinical trial management system database so we can compare with similar protocols, similar indications and similar levels of work. In terms of timeliness, this really leads to project management. They go together. We have a trial management system that links procedures with payments.”

i3 Research was rated the highest for providing fair overall grant payments—with 48.8% of sites rating i3 Research “Excellent” on this attribute.

“Part of the basis of this has to do with communication,” Tsuetaki said. “I think it comes down to the fact that as an

organization, we do treat our sites as customers, and, therefore, when we look at the payment itself, we’re looking at the timeliness of that. The way we do that in Europe is a centralized process for payments. In other words, we do not only work directly with country-level management and monitoring, but we also coordinate this in a centralized way with a finance function that explicitly is attuned to making sure that sites get paid in a timely fashion.”

Conclusion

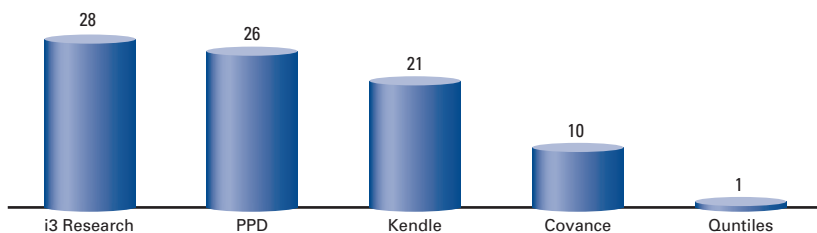
i3 Research and PPD have truly emerged as leaders this year as evidenced by the quality

of their relationships with European investigative sites. Kendle and Covance have stayed true to their words of continuous improvement from previous years—actively listening to the needs of investigative sites, implementing change when needed—and generally adopting a proactive strategy to strengthen their relationships with sites.

“We’re now more able and more assertive in being able to put forth our thoughts and ideas to customers and sponsors in terms of what will work and what won’t work,” Kendle’s Cutler said. “To their credit, our sponsors are much more open to our experience and our expertise in these areas. Some of our sponsors will come to us halfway through a protocol and ask, ‘What do you think of this? Can you do some feasibility? Can you test this for us? Can you give us some feedback in terms of what will work,’ whereas perhaps five to 10 years ago, they’d throw the protocol over the wall, and you’d be asked to run with it. It was much more difficult to make changes or to suggest changes. These days—really over the last five years or so—it has been a much more collaborative approach. I think it’s good for the sites, I think it’s good for the sponsors, and I think it’s good for us as well.”

—Annick Anderson and Molly Row

Highest Frequency as Top 3 Rated CRO Across 29 Relationship Attributes



Source: CenterWatch 2010 Survey of European Investigative Sites (n=924)