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White Paper:

Abridged Situational Market Analysis™ (SMA™) Report -

"Contract Research Organizations: Market Perspectives from Clinical Trial Sponsors and Sites"

CONFIDENTIAL REPORT

Date: **Final Report – 4 December 2001**

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EXECUTIVE SUMMARY

Clinical trial sponsors are constantly searching for ways to lower the costs of clinical research and accelerate the clinical research element of the drug or device development process. These two forces continue to drive increases in clinical research outsource spending. The worldwide market for clinical outsourcing services is now estimated at $4 to $5 billion dollars annually.

Trends and Developments

While sponsor companies increase their clinical outsourcing, they are also seeking to take control of those clinical research dollars. Sponsors are outsourcing a wider range of clinical research activities to a variety of clinical research service providers. More importantly, sponsor companies are selecting these contractors based on their ability to fulfill specific project requirements.

General dissatisfaction with large Contract Research Organization (CRO) service providers has caused many of these dollars to flow to small and medium-sized CROs who are often more responsive to sponsor needs. Speaking with several clinical research managers, TNP found that sponsor companies are primarily concerned with:

1. Quality of services
2. Flexibility
3. Responsiveness

In this environment, small and mid-sized CROs have gained substantial market share from the large service providers.

Sponsors' and Clinical Sites' Impressions of CROs

TNP recognizes that sponsor companies are not the only constituents that provide valuable information about CRO performance. Investigative clinical sites also have first-hand perspective on CRO's capabilities. A July 2001 CenterWatch Monthly Newsletter analysis surveyed 405 investigative sites to evaluate the performance of CROs. TNP offers a side-by-side comparison of CRO rankings by sponsors and investigative sites in the table below. In the left column are CROs identified by TNP's interviews with sponsors. In the right column are CenterWatch results from a published survey of investigative sites. Highlighted in gray, are three CROs identified as performance leaders by the CenterWatch survey and by TNP's primary market research. They are:

1. Covance, Inc.
2. Quintiles International Corp.
3. Parexel International

These three CROs are often mentioned because they are well recognized as the industry leaders based on their large size and length of time established.

Sponsors' and Clinical Sites' ratings of the Top CROs

#	Sponsor Ratings of Top CROs*	#	Research Sits Ratings of Top CROs**
1	Quintiles Transnational Corp.	1	Ingenix
2	Covance, Inc.	2	Covance, Inc.
3	Stat-Trade Inc.	3	PPD
4	Eminent Research Systems, Inc.	4	MDS Pharma
5	Paragon Biomedical, Inc.	5	Omnicare
6	Synteract, Inc.	6	Parexel
7	Parexel International	7	Quintiles Transnational Corp.

* Source: The Next Phase Consultancy, Inc. - survey of selected sponsors
**Source: CenterWatch 2001 Survey of 405 Investigative Sites

Another interesting parallel between the investigative site evaluations and TNP's research is the perceived advantage of working with a smaller CRO. Small CROs were attributed with better responsiveness to both sponsor and investigative site needs.

Probable CRO Strategies

To address these issues, large CROs will need to become more responsive to their clients specific project demands. A few large CROs may even reorganize to improve quality across service categories and exploit therapeutic areas of expertise. Small and mid-sized CROs, must also manage their growth in a way that does not adversely affect their quality of service. These companies will likely remain organizationally flat in order to keep their clients in close contact with their service staff.

Sponsors will likely pursue a strategy of "preferred provider" agreements with CROs that meet their needs in the areas of responsiveness, consistent quality and therapeutic expertise. Preferred provider agreements will be a leading indicator for future CRO market leaders.

CRO MARKET ANALYSIS

I. CRO MARKET ANALYSIS

CRO Market Summary

The U.S. medical industry spent an estimated $3.3 Billion on Contract Research Organization (CRO) services in 2000. According to CenterWatch, a leading publisher on the subject in the industry, $2.6 billion or roughly 80% was spent on contract clinical research. The remaining 20% was spent on preclinical research services. Worldwide sponsors spent an estimated $5.2 Billion on CRO services.[1]

The Next Phase Consultancy, Inc. (TNP), interviewed several clinical research managers at pharmaceutical, biotechnology and medical device companies in North America. In general, the information gathered from these interviews was corroborated by TNP's secondary market research.

In general clinical research managers told TNP they are looking for CRO's with the capability to provide:

- Highly specified types of knowledge, experience and know-how
- Flexible and customized services based on project requirements
- Consistent quality and staff capability across all services offered

The above criteria unanimously took precedence over the issue of pricing among clinical research managers. Accordingly, there has been a shift in clinical research outsourcing practices whereby sponsors are looking to small and mid-sized CROs to meet their project specific needs.

In recent years, large full-service CRO's have encountered financial hardships due to increasing competition in the CRO market from small to mid-size CROs and recent pharmaceutical company mergers resulting in fewer clinical projects per sponsor company. One recent CenterWatch article showed that on average pharmaceutical mergers have reduced the number of clinical projects in those companies' pipelines by 10% over a three-year period.[2] Furthermore, large CROs are feeling competitive pressures from small to mid-size CROs who are gaining market share by catering to niche markets.

These changes are demonstrated by the shifting outsourcing practices of sponsor companies reported in the January 2001 CenterWatch survey. CenterWatch reported that 41% of sponsor companies said they plan to use small CROs more often in the coming years. Comparatively, 18% said they plan to use large CROs more often in the coming years. CenterWatch surveyed 17 leading pharmaceutical and biotechnology companies. On average, these sponsors reported using five different CRO's at any given time.

[1] CenterWatch, January 2001; A CenterWatch Publication Volume 8, Issue 1.
[2] CenterWatch, June 2000; A CenterWatch Publication. Volume 7, Issue 6.

This new multi-vendor strategy has thus far favored the small niche players in the CRO industry who often have expertise in a specific function or therapeutic indication. Small boutique CROs are also perceived by sponsors to be more responsive according to the January 2001 CenterWatch survey.[3] In response to competition from the smaller CROs, full-service CROs will need to position their businesses based on quality of service, responsiveness and timely turnaround rather than on price, full service selection and global coverage.

A dynamic that favors full-service CROs is sponsor preference for long-term relationships with their research partners. The January 2001 CenterWatch survey showed 71% of sponsors reported having "preferred provider" agreements.[4] This indicates that sponsors are interested in establishing long-term relationships with full-service CROs that offer a complete array of services needed to bring a product from early development through commercialization.

Overall, the market for CRO services will likely continue to grow. The same CenterWatch survey reported that pharmaceutical and biotechnology companies use CROs in 61% of their clinical development projects. In addition, 60% of sponsors interviewed expect their CRO use to increase, while only 10% expect their use of CROs to decrease.[5]

CRO Definition

CROs serve the healthcare industry by assisting pharmaceutical, medical device, and biotechnology companies to bring new medical products to market. The primary objective of a CRO is to carry out, on behalf of multiple clients, medical and scientific studies on a contractual basis. CROs provide part or all of the process of clinical research including clinical trial management.

Over a thousand-contract research organizations participate in this $4-5 billion global market. Services include Phase I through Phase IV clinical trial management, planning, protocol design, clinical data management, statistical analysis, electronic data capture, medical writing, regulatory consultation and more.

Some of the larger CROs seek to cover the entire spectrum of drug discovery and development from the chemical synthesis of new molecules, through preclinical and clinical development and regulatory submission, and even marketing of an approved product. Other companies focus on specific aspects of drug and device development.

[3] CenterWatch, January 2001; A CenterWatch Publication Volume 8, Issue 1.
[4] Ibid.
[5] Ibid.

II. RESULTS OF PRIMARY MARKET RESEARCH

Sponsor-Side Perspectives

TNP conducted interviews with several clinical research managers at pharmaceutical, medical device and biotechnology companies in North America. The intent of these interviews was to gain a client-side or sponsor-side perspective of CROs and to better understand:

- What sponsor companies look for in a CRO.
- Which CROs have the best and worst reputations.
- Industry trends and how sponsor companies use CROs.
- What sponsor companies expect of CROs in the future.

With the answers to these questions TNP identified differences and commonalities in CRO usage among pharmaceutical, medical device and biotechnology sponsors.

Summary of Results from CRO Client Interviews

What Sponsors Look for In a CRO

Clinical research professionals were specifically asked about the criteria they use when evaluating CROs. Several common themes were listed. They are prioritized below:

1) Quality of services
2) Flexibility
3) Responsiveness
4) Project management capabilities
5) Pricing

Most notably, pricing was secondary concern among clinical research managers. Their primary concern when evaluating CRO project proposals is the ability of CROs to provide quality services.

The intent of clinical research outsourcing is to lower costs, by lowering the overhead costs that a sponsor organization would incur if it would manage the project itself, and speed up the clinical drug or device development process. Therefore, sponsors are asking CROs to provide services based on their ability to satisfy highly specific project requirements. This pick-and-choose approach by sponsors requires CROs to be more flexible by customizing their service sets on a project-by-project basis.
The clinical research managers TNP spoke with also placed great emphasis on the CRO's ability to be responsive in the case changes arise. One clinical research manager placed great importance on her ability to quickly contact and effectively communicate with the service staff of the CRO. This also relates to the CRO's project management capabilities.

There are increasing requests from sponsors to jointly manage and co-monitor their clinical trials in an effort to control costs and improve quality.

CROs with the Best and Worst Reputations

Understandably, many clinical research professionals interviewed were reluctant to identify CROs they are currently working with or have worked with in the past. More so, they did not want to discredit the reputations of CROs with which their experiences were not optimal. However, some managers were willing to provide endorsements and criticism under the pretense of anonymity. The CRO firms and corresponding comments are as follows:

<u>Positive Responses</u>

- **Quintiles Transnational Corp.** – a widely recognized industry leader with name recognition and a huge market presence. Quintiles has been in business for nearly 15 years.
- **Covance, Inc.** –strong reputation and name recognition. Covance has been in business for well over 10 years.

<u>Moderately Positive Responses</u>

- **Stat-Trade Inc.** – strong reputation within the industry.
- **Eminent Research Systems, Inc.** – strong reputation within the industry.
- **Paragon Biomedical, Inc.** –strong reputation within the industry.
- **Synteract, Inc.** – strong data management services.

<u>Specific Issues Sited with Large, Full-Service CROs</u>

- **Parexel International** – less responsive than was desirable.
- **Quintiles Transnational Corp.** – less responsive than was desirable and inconsistent quality.
- **Covance, Inc.** – heavy on management costs.

Since the clinical research professionals TNP interviewed for the most part declined to identify CROs with which they had poor experiences, TNP asked the interviewees to discuss those experiences. Several comments were forthcoming.

Several clinical research professionals recognized that there has been a recent reluctance to contract larger CROs. No names were given, but in general they thought large CROs were becoming less responsive and top-heavy with their management fees. Nevertheless, sponsor company experiences with large CROs reportedly varied from group to group. One clinical research manager reported inconsistent quality when working with a large CRO that she described as a market leader. As the situation was explained, after a positive first project with the CRO, the sponsor company decided to contract another set of services and was disappointed. Inconsistent quality within the same CRO, between project teams and services, was a common theme reflected in the responses of other clinical research professionals as well.

Most respondents considered reputation and name recognition important. However, greater emphasis is typically placed on a CRO's capabilities and their relevant experience with similar projects. In the case of medical device trial sponsors, previous experience in medical device trials and within a specific therapeutic indication is very important. Medical device companies told TNP they often turn to small CROs and niche market players to meet these needs.

Trends and Future CRO Usage

Sponsor companies will continue to search for ways to lower costs and accelerate the clinical research process. The CROs that can best serve this need will prevail. Currently, large CROs have a distinct edge over small CROs in two areas:

- ✓ First, large CROs are better equipped to conduct clinical trials that require global reach, particularly large Phase III clinical trials.
- ✓ Second, their data management capabilities tend to be better than their small niche counterparts.

However, small CROs have equally as valuable strengths since they can:

- ✓ Serve the specific needs of their clients
- ✓ Adapt more quickly when those needs change.

Several clinical research managers told us that small CROs are also easier to communicate with and are more responsive.

Large CROs are trying to be more flexible in the services they provide. However, they are currently struggling to balance their quality of work with their flexibility of services. Look for large CROs to continue make efforts at customizing their services to their clients needs.

Finally, communication between the sponsor and the CRO firm is extremely important to clinical research managers. Wherever possible, sponsors prefer to develop a long-term relationship with CROs. Flatter organizations allow sponsor companies to work more closely with the CRO service staff rather than management.

Differences in CRO Usage Between Biotechnology, Medical Device and Pharmaceutical Sponsors

TNP was able to identify some differences in CRO usage practices. TNP's findings indicate that:

- ➢ Biotechnology and medical device companies in general have much smaller product development budgets than large pharmaceutical companies. A pharmaceutical company can spend nearly $500 million to develop one drug through commercialization. However, medical device companies typically have product development budgets that are one to five and at most ten percent of a large pharmaceutical company's budget; a biotech company could have a budget that is somewhere in between.

- Many of the clinical research managers at small medical device and biotech firms told TNP they contract most of their services from small niche CROs.

One reason for this may be the lack of products in Phase III clinical trials. Products in early clinical development require smaller clinical trials many times one-tenth to one-twentieth the patient population size of large Phase III trails with hundreds to thousands of patients. Small niche CROs are better equipped to serve these markets as they can often provide specialized services specific to location and regulatory environment. Niche player CROs often provide expertise relating to a specific therapeutic indication.

In contrast, two situations where biotech and medical device sponsor companies look to large full-service CROs is when they need:

1) Global reach for a large clinical trial
2) Advanced data management services.

All clinical research managers TNP spoke with described a multiple vendor strategy when outsourcing clinical research projects. The goal of this strategy is to best match a CRO's capabilities with project requirements; hopefully, resulting in better project execution. Some sponsors even juggle multiple vendors on the same clinical development project. Consequently, sponsor companies must take an active project management role, both monitoring and coordinating the research process. In these situations, it is important that CROs precisely match their procedures with the sponsor company's requirements.

III. RESULTS OF SECONDARY MARKET RESEARCH

TNP's secondary market research supports what was determined from interviewing clinical research managers. Most clinical trial sponsors considered their impressions and opinions of CROs to be a part of their companies' competitive strategies and were unwilling to reveal with which CROs they are working. Sponsors are therefore reluctant to endorse or criticize CROs by name due to reasons of legality, confidentiality and competitive intelligence.

Sponsor-Side Research

TNP obtained market perspectives from additional sources. The CenterWatch Monthly Newsletter's survey issued in January 2001 was on chosen that assessed the change in CRO usage rates (Please see Appendix I). The CenterWatch survey found that clinical trial sponsors are increasingly using a multi-vendor approach to outsourcing. This represented a major shift in outsourcing practices.[6]

According to the CenterWatch survey, there was a notable change in the "Top CRO Selection Criteria" from their previous study the company sponsored in 1998. In the January 2001 survey, sponsors reported the following as "essential" criteria:

- The Ability to Deliver Patients = 59%
- Therapeutic Area Expertise = 59%
- Strong Reputation = 41%

In the 1998 survey, "Cost of Services" and "Reputation of the CRO" topped this list. Although, "Cost" was ranked as an "important" factor by nearly 88% of sponsor companies in the January 2001 survey, it was no longer considered essential. Sponsor companies are now putting a premium on a CRO's ability to successfully execute their projects.

Sponsors in the pharmaceutical and biotechnology industries use niche CRO services to address specific project needs. CenterWatch reported that, "8 of 10 sponsors indicate that they expect to increase their use of smaller and more focused service providers over the next several years." This positive trend is credited to the small CRO's ability to provide a focused and quality service. In general, trial sponsors thought smaller CROs were more responsive.

Added to this analysis was speculation that **Quintiles** and **Covance** (and possibly other large, full-service CROs) may be letting their recent financial hardships adversely affect their service quality. However, large CROs have an advantage in providing site management, electronic data capture, and data management services. In the future large CROs are expected to try and reinvent themselves to function more like small CROs.

[6] CenterWatch, January 2001; A CenterWatch Publication Volume 8, Issue 1.

Clinical Site-Side Research

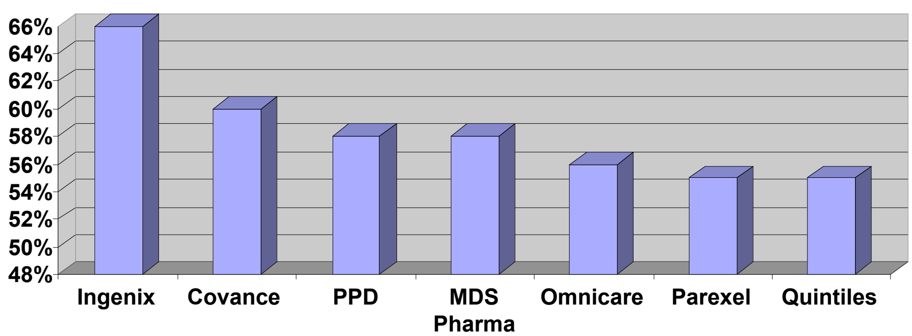
Since the CenterWatch research noted above does not include information specific to sponsor ranking of CROs and sponsor respondents to TNP's primary market research were unwilling to discuss specific CROs, other sources and constituents were consulted. Clearly sponsor companies are not the only constituents that can provide evaluations of CRO performance. Clinical research sites are one source for this information. A July 2001 CenterWatch analysis surveyed 405 investigative sites to evaluate the performance of CROs. This information from interviews with investigative sites was also used to rank CRO performance.

An unidentified senior executive at a major CRO is quoted as saying, "Maintaining the best possible site relationships yields strong returns for everyone. Our performance has improved in terms of getting studies started faster and in getting cleaner data. And we have sites recommending us to sponsors. By building better relationships the site becomes our advocate and advantage." Since research sites are essential to the success of CROs, there evaluations should carry great import in any CRO analysis.

Results of the July 2001 CenterWatch analysis of CROs resulted in the following rankings for clinical research management:

The Top 7 CROs to Work With

Percent of sites rating "Very Good" to "Excellent"



CRO	Ingenix	Covance	PPD	MDS Pharma	Omnicare	Parexel	Quintiles
% "Very Good" to "Excellent"	66%	60%	58%	58%	56%	55%	55%
*Sample Size	126	297	105	272	118	246	298

Source: CenterWatch July 2001 Survey of 405 Investigative Sites[7]

[7] CenterWatch, July 2001; A CenterWatch Publication Volume 8, Issue 7.

As with sponsors, CRO size matters to investigative sites. According to investigative sites in the CenterWatch survey, small to mid-sized CROs are "typically more responsive, more accessible, and less bureaucratic with higher staff retention rates." The percent of total investigative sites that perceived an advantage of working with smaller CROs for each to the attributes noted below were:

- Better Communication = 59%
- More Responsive = 32%
- Fewer People = 16%
- Less Staff Turnover = 14%

While there are clearly advantages to scale, both sponsors and research sites place great emphasis on their relationships with CROs. Personalized service and the ability to communicate effectively with constituents are lost when organizations build additional levels of management, as is the case for many large CROs.

IV. CONCLUSIONS AND RECOMMENDATIONS

Collective findings from TNP's research have lead to the following insights and conclusions:

- Sponsor companies consider the identity of and the specific services provided by the CROs they work with to be confidential. Picking the optimal CRO or combination of CROs for a specific project tasks gives sponsors significant competitive advantage. Therefore, sponsors will preferentially continue to work with CRO partners who can provide consistent service quality and technical expertise.

- Future "preferred provider" service agreements will likely surface in the next year or so with the purpose of establishing long-term strategic relationships between sponsors and the CROs that best meet sponsor's needs.

- Sponsors are commonly interested in highly specified types of knowledge, expertise, experience, know-how, and, therefore, service.

- Optimally most sponsors wish to selectively pick from menus of services within several CROs who are capable of working together or at least that can be coordinated by a sponsor's management.

- In general, sponsors look for CROs with global perspective no matter if a given CRO is chosen for the whole project or just portions of that project as doled-out by the sponsor's clinical management team.

- Sponsors often want services offered by the CRO to be consistent in both professional presentation, depth of coverage and the CRO's staff's expertise and capability. They prefer quality across all services to be evenly balanced between these attributes so there are no surprises for the sponsor.

- Future trends will likely reveal full service CROs that are reorganized for their multiple service groups or by their depth of experience with specific indications, or modalities for therapy or diagnosis to fulfill changing demands from sponsors

- Small and medium-sized CROs will continue to grow. However, to remain competitive they will have to maintain flat organizational structures to better serve their clients. They will also need to manage their growth so it does not affect the quality of their services and products provided to both sponsors and clinical sites.

For a brief overall summary of this report's findings please refer to the Executive Summary located at the beginning of this report.

APPENDIX

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