The 2019 Avoca State of the Industry Report:

Quality Oversight in Clinical Outsourcing

July 2020

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Introduction

Each year, The Avoca Group surveys industry professionals to understand trends in clinical development, with a particular focus on outsourcing dynamics and relationships between research Sponsors and Providers. This report summarizes key findings with respect to outsourcing trends and key relationship indicators, including analysis of the influence of specific performance attributes on levels of satisfaction.

In this year's industry review, Avoca examined how Sponsors and Providers think about and manage quality in clinical trials. This topic is a continuation of research first conducted in 2011, titled *Clinical Quality Management & Provider Oversight*. This report includes longitudinal comparisons of key variables, where applicable.

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Background

In the past decade, the clinical trials industry has undergone transformative changes to its operating model. The sophistication of medicines being developed, the scientific and operational complexity of study designs, the use and influence of technologies, and the diversity of its value chain have all grown in breadth and depth.

Concurrently, regulatory expectations for quality oversight have become more explicit with each revision to guidance and in recent direct communications from regulatory bodies.

In the report that follows, we summarize the current state of quality oversight in clinical trials, including the usage and perceived effectiveness of incumbent and emerging quality oversight practices.

We anticipate the insights contained within this research will inform a path to maintaining high quality and compliance as we navigate the rapid transformation instigated by COVID-19.

Methodology

- All fieldwork was conducted between October and December of 2019.

- A total of 98 completed surveys were received from respondents representing Sponsor organizations.

- A total of 99 completed surveys were collected from respondents representing Provider organizations.

- Classification information about respondents and companies they represent can be found in the appendix of this report.

Perceptions of Quality in Outsourcing Today

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Quality Oversight

Perceptions of quality have shown a gap between Sponsors and Providers over time, which has continued to widen.

## Trend in Overall Assessment of Quality

Mean Ratings on 5-Point Scale
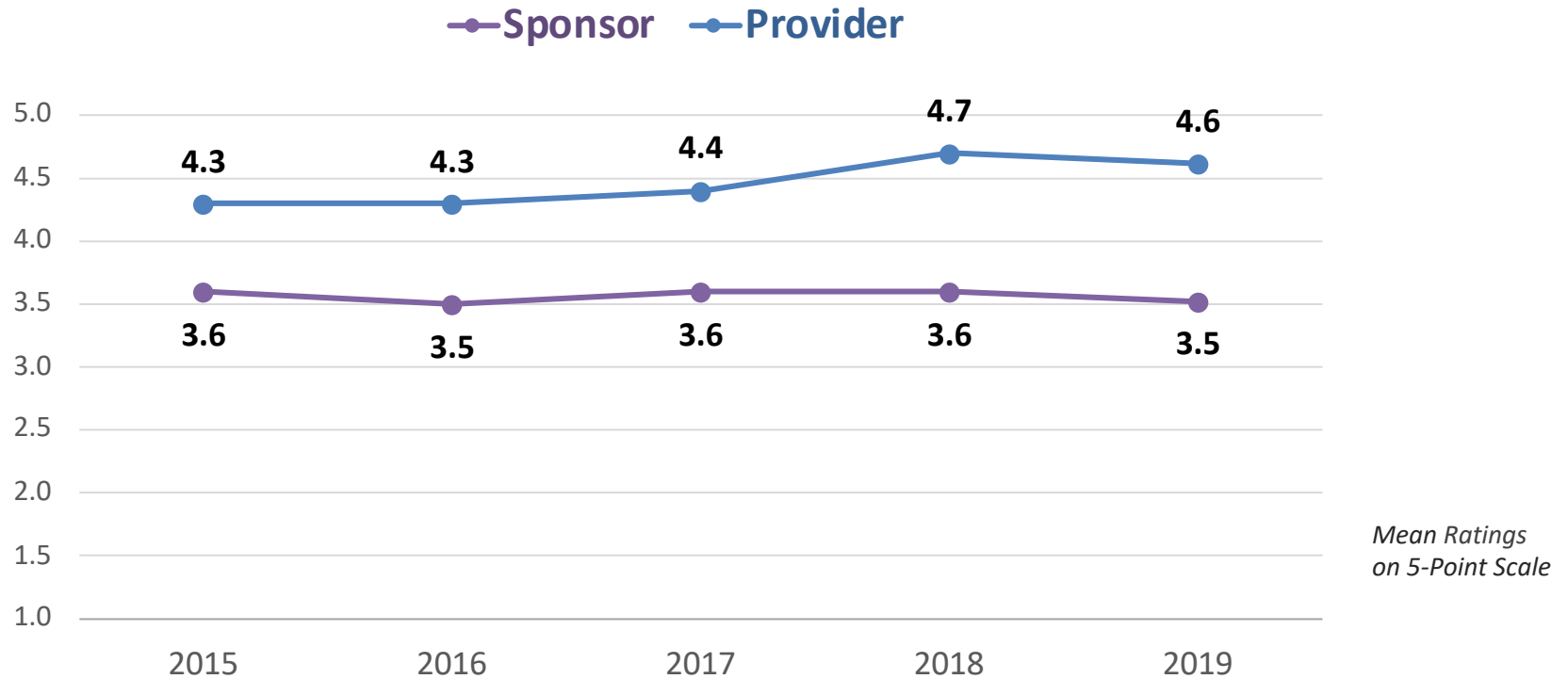
Q. Thinking about your experiences in [YEAR], how satisfied are you with… (1=Very dissatisfied, 5=Very satisfied)

Quality Oversight

Looking at reasons for quality ratings, adherence to timelines, communication, deliverables, and commitment are key drivers of satisfaction. Turnover, change orders, too much oversight, and issues with deliverables result in weaker satisfaction.

Sponsor: Reasons for Quality Ratings

Very dissatisfied | 4% | 23% | 14% | 37% | 23% | *Very satisfied*
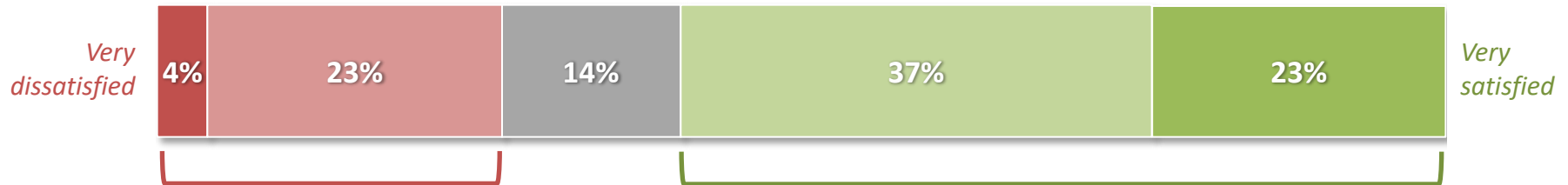
Themes: Turnover, change orders, requires too much oversight, inability to meet agreed upon deliverables/timelines

- *"Multiple change orders, inability to deliver on what they stated they would, constantly shifting timelines."*

- *"Especially with large CROs: rigid processes, little flexibility, even standard or routine practices lead to change orders. Staff turnover at CROs, staff quality at CROs."*

Themes: Adherence to timelines, communication, quality of deliverables, established relationship/commitment to success

- *"They align their science and client delivery team for long-term understanding of our business."*

- *"Timely and efficient communication and workflow; high quality work product."*

- *"The niche Providers are able to supply a team with low turnover of key functions, thus leading to a high and consistent study conduct."*

- *"Continuity in relationship management and responsiveness to requests."*

- *"Worked with us to manage and keep the timelines and quality of the work."*

N: Sponsors=57
Q: You indicated that you were not satisfied with the quality delivered by your Clinical Service Providers in 2018. Why is that?
Q: You indicated that you were satisfied with the quality delivered by your Clinical Service Providers. What, specifically, led you to provide this rating?

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Quality Oversight

Among Sponsors, similar issues are raised as top challenges to providing effective oversight.

Sponsor: Volunteered Challenges in Providing Oversight

Turnover, involvement of senior staff, not fully dedicated to one project

"Staff turnover and many employees not experienced enough to provide requested services."

"Junior staff making major decisions and no oversight or thought of checking with the Sponsor."

STAFFING

Metrics, proper measurement

"Defined metrics & systems to track/manage/control."

PROCESS

METRICS

Alignment on SOPs, avoiding redundancy

"Too many hand-offs between functional groups between both the Provider and organization. Messages get diluted or miss the appropriate audience completely. A lack of flexibility toward processes both from the Provider and the organization which usually leads to gaps in delivering on expectations."

COMMUNICATION

TRANSPARENCY

Openness

"Working on the relationship to facilitate transparency; and ensuring that as a Sponsor we are aware of all relevant issues – this takes time and very often there are resource constraints that make it extremely challenging to find the time needed."

Communicating effectively, clearly, responsiveness

"Ensuring we are speaking the same language. Terminology can mean different things to different companies."

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Q: What do you feel is the biggest challenge you face when providing oversight to your Clinical Service Providers?
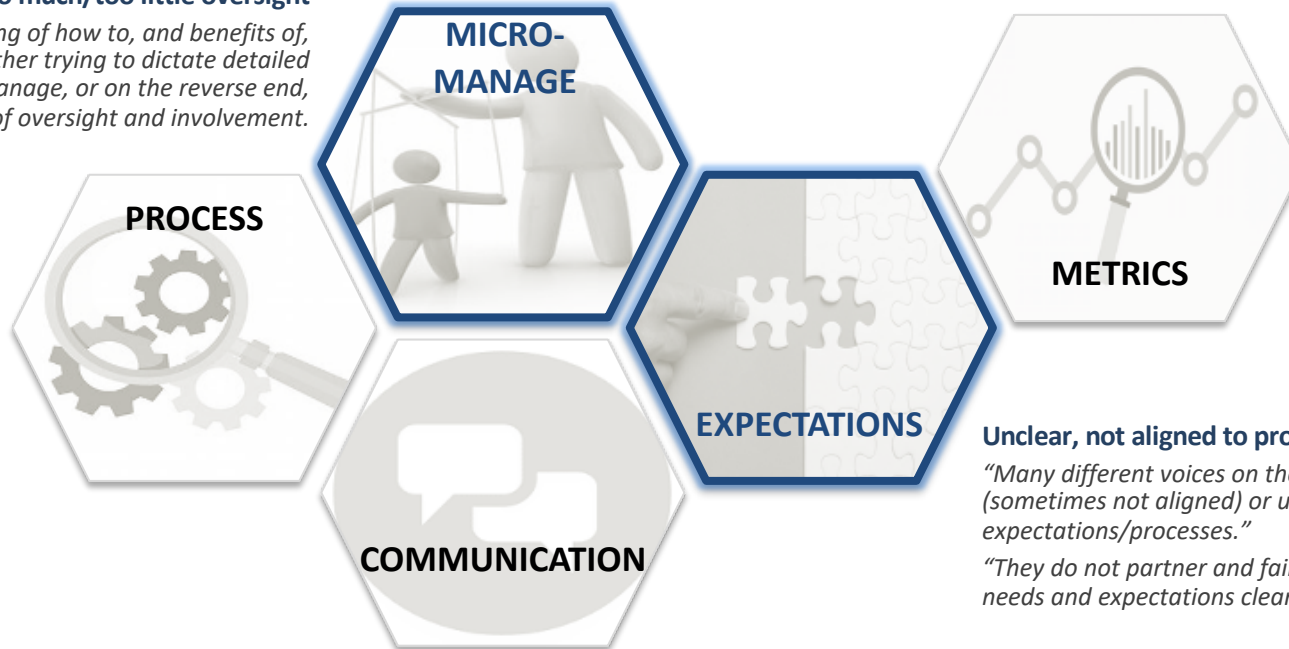
Quality Oversight

Providers echo many of the same challenges as Sponsors, but specifically call out misaligned expectations and micromanagement as key challenges that are faced from their perspective.

Provider: Volunteered Challenges in Providing Oversight

Too much/too little oversight

"Lack of understanding of how to, and benefits of, outsourcing. Either trying to dictate detailed process and micromanage, or on the reverse end, having complete lack of oversight and involvement."

PROCESS

MICRO-MANAGE

METRICS

COMMUNICATION

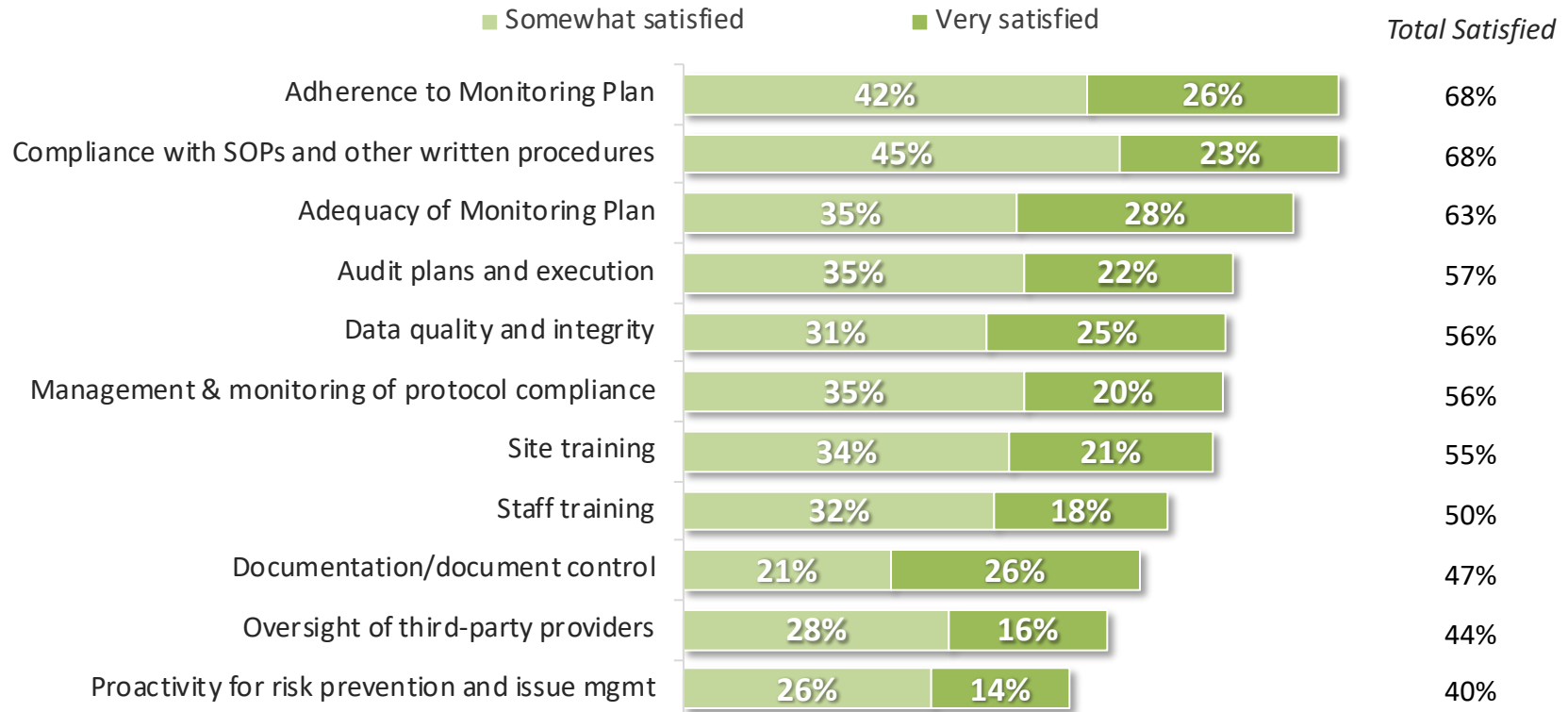**EXPECTATIONS**

Unclear, not aligned to process/SOPs

"Many different voices on the Sponsor side (sometimes not aligned) or unclear expectations/processes."

"They do not partner and fail to communicate needs and expectations clearly."

Q: What do you feel is the biggest challenge you face with how Sponsors oversee your activities as a Clinical Service Provider?

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Quality Oversight

Regarding Sponsor ratings of Provider performance on quality dimensions, higher ratings are given for adhering to established plans and SOPs, but lower satisfaction is expressed for documentation, oversight of third-party vendors, and proactivity in terms of risk prevention.
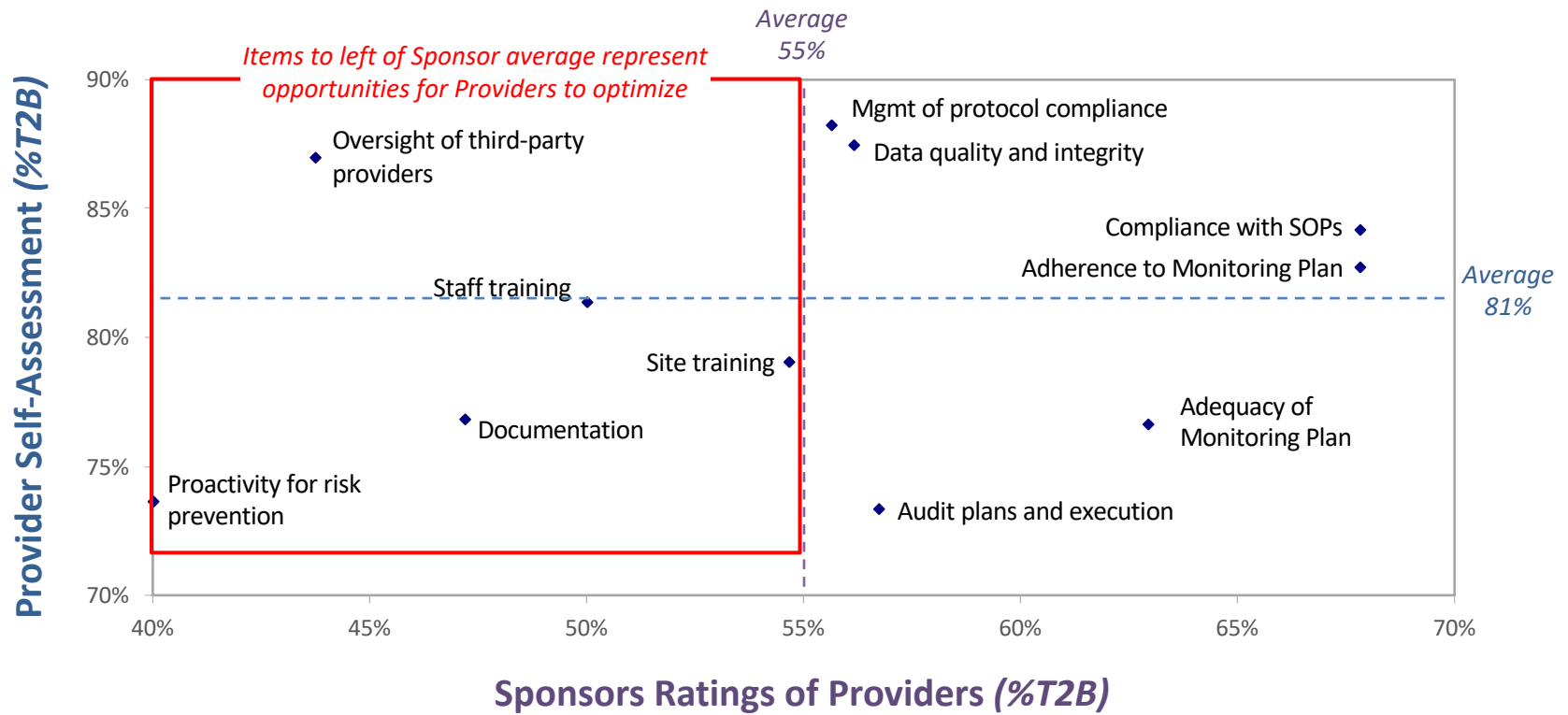
Sponsor: Satisfaction with Quality Dimensions

■ Somewhat satisfied   ■ Very satisfied

Quality Dimension	Somewhat satisfied	Very satisfied	Total Satisfied
Adherence to Monitoring Plan	42%	26%	68%
Compliance with SOPs and other written procedures	45%	23%	68%
Adequacy of Monitoring Plan	35%	28%	63%
Audit plans and execution	35%	22%	57%
Data quality and integrity	31%	25%	56%
Management & monitoring of protocol compliance	35%	20%	56%
Site training	34%	21%	55%
Staff training	32%	18%	50%
Documentation/document control	21%	26%	47%
Oversight of third-party providers	28%	16%	44%
Proactivity for risk prevention and issue mgmt	26%	14%	40%

N: Sponsors=74-90
Q: Thinking specifically about the CROs you have worked with in the past 12 months, please rate your satisfaction with the quality oversight your CROs have demonstrated.

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Quality Oversight

Providers' self assessments on these same measures are stronger than Sponsor evaluations. In particular, there appears to be misalignment on third-party oversight and proactivity for risk prevention, where the largest gaps are observed between Sponsor and Provider ratings.

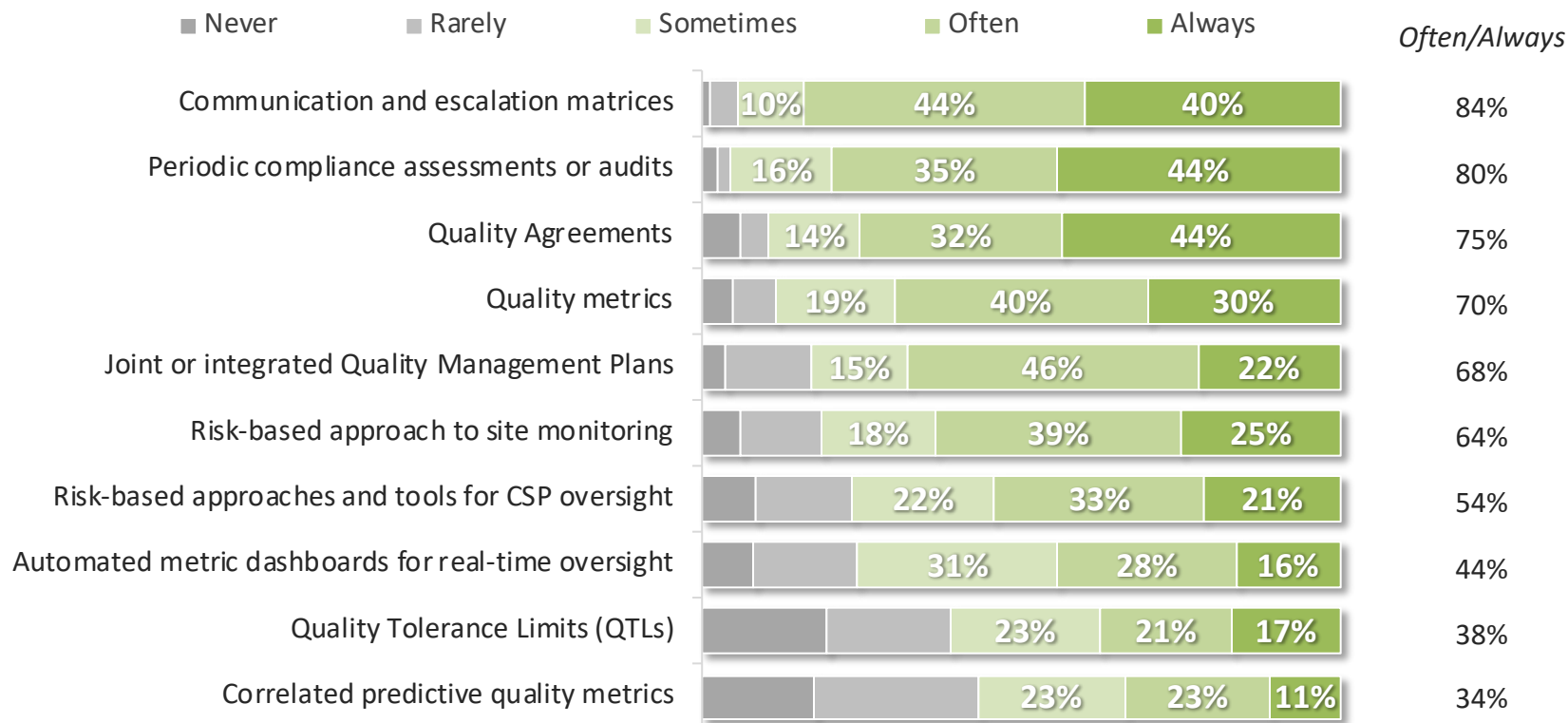## Quadrant Analysis: Sponsor vs. Provider Ratings on Quality Dimensions

Items to left of Sponsor average represent opportunities for Providers to optimize

Average 55%

Average 81%

Y-axis: Provider Self-Assessment (%T2B) — 70%, 75%, 80%, 85%, 90%

X-axis: Sponsors Ratings of Providers (%T2B) — 40%, 45%, 50%, 55%, 60%, 65%, 70%

Data points:
- Oversight of third-party providers
- Mgmt of protocol compliance
- Data quality and integrity
- Compliance with SOPs
- Adherence to Monitoring Plan
- Staff training
- Site training
- Documentation
- Adequacy of Monitoring Plan
- Proactivity for risk prevention
- Audit plans and execution

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Quality Oversight

Today, Sponsors indicate greater usage of the more "foundational" aspects of quality oversight – communication matrices, compliance audits, quality agreements, and metrics.

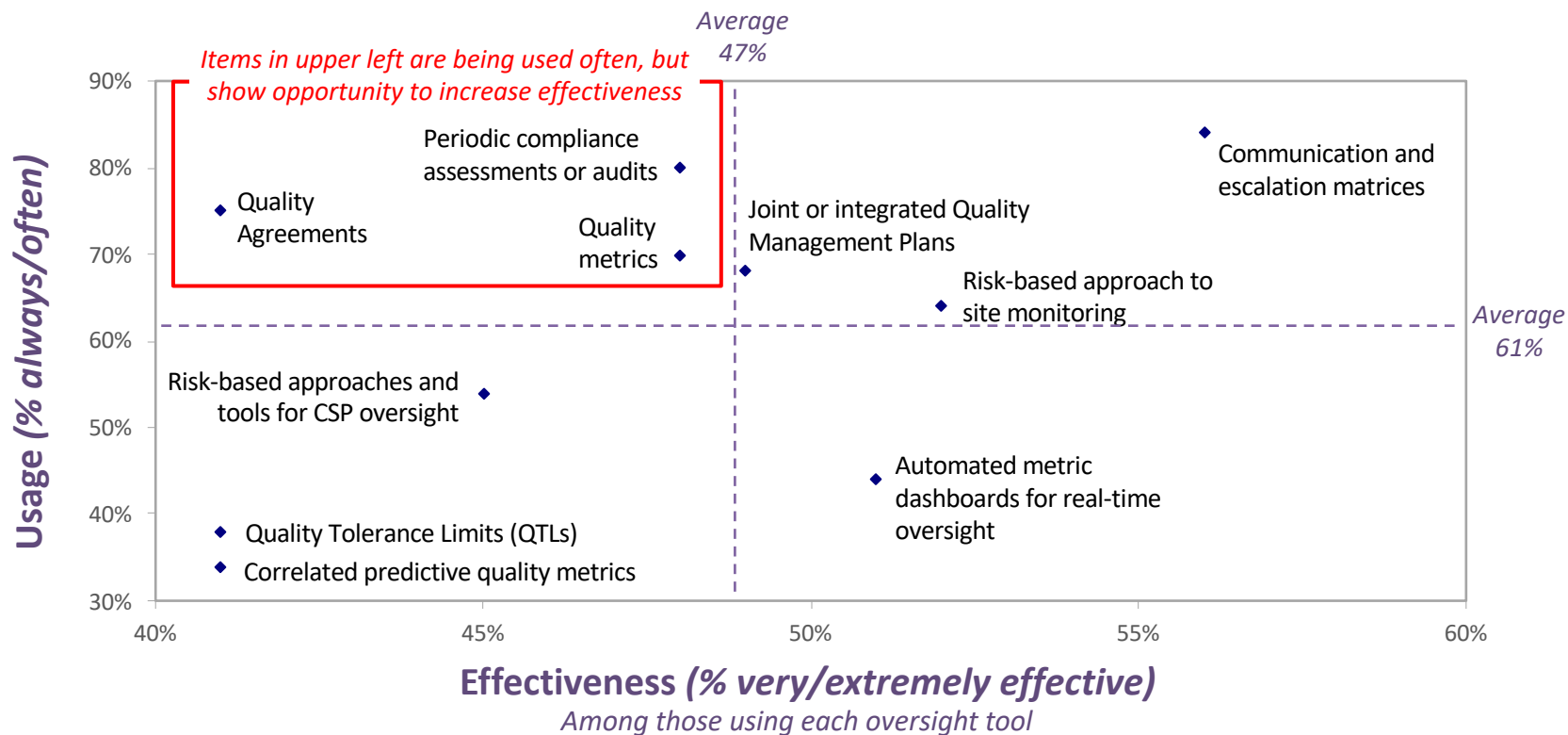## Sponsor: Usage of Oversight Practices/Tools

Legend: ■ Never ■ Rarely ■ Sometimes ■ Often ■ Always

Practice/Tool	Sometimes	Often	Always	Often/Always
Communication and escalation matrices	10%	44%	40%	84%
Periodic compliance assessments or audits	16%	35%	44%	80%
Quality Agreements	14%	32%	44%	75%
Quality metrics	19%	40%	30%	70%
Joint or integrated Quality Management Plans	15%	46%	22%	68%
Risk-based approach to site monitoring	18%	39%	25%	64%
Risk-based approaches and tools for CSP oversight	22%	33%	21%	54%
Automated metric dashboards for real-time oversight	31%	28%	16%	44%
Quality Tolerance Limits (QTLs)	23%	21%	17%	38%
Correlated predictive quality metrics	23%	23%	11%	34%

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Quality Oversight

Communication and escalation matrices are most used and are also thought to be most effective. Compliance assessments, quality metrics, and agreements are being used but are perceived as less effective in ensuring quality in trials.

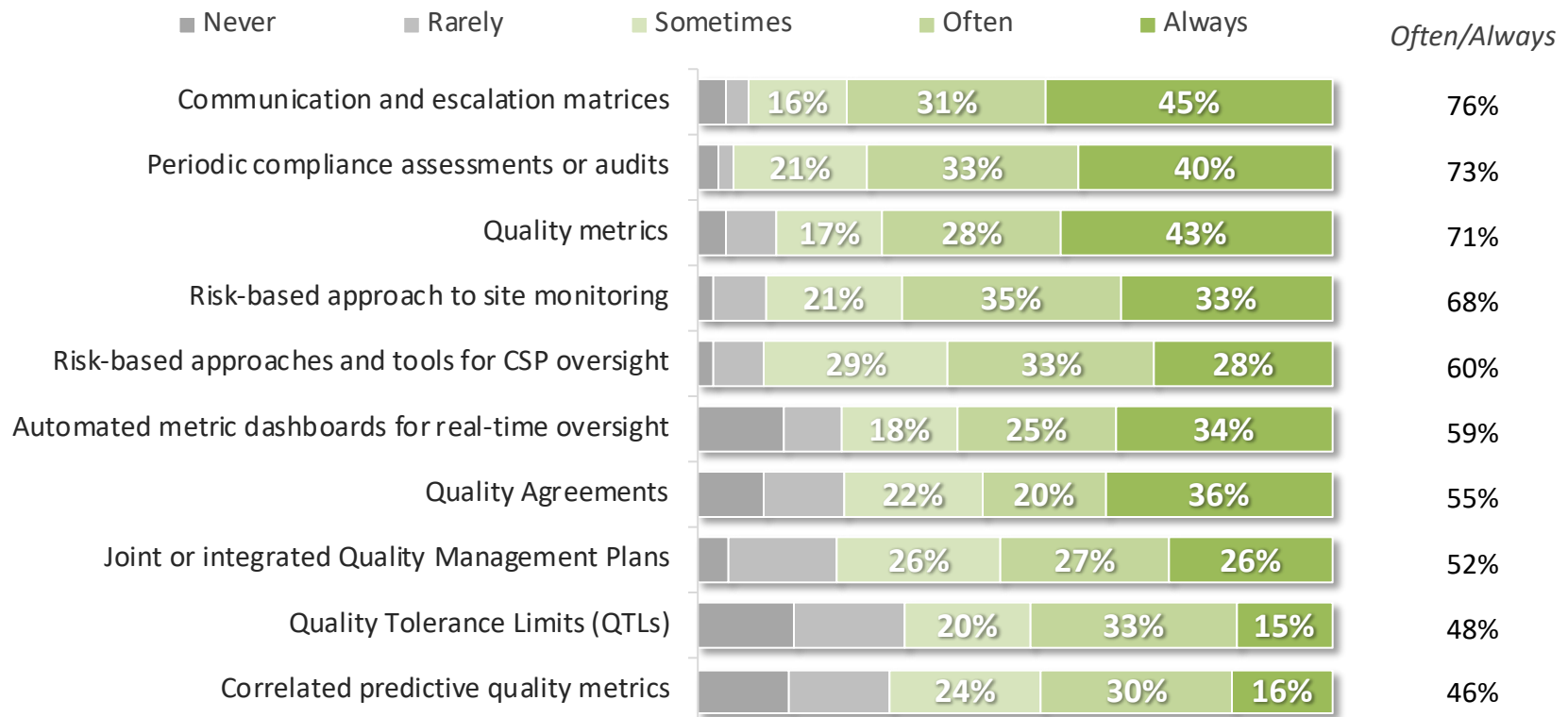## Sponsor: Usage of Oversight Tools vs. Perceived Effectiveness

Items in upper left are being used often, but show opportunity to increase effectiveness

Average 47%

Average 61%

Usage (% always/often)

- Periodic compliance assessments or audits
- Quality Agreements
- Quality metrics
- Joint or integrated Quality Management Plans
- Communication and escalation matrices
- Risk-based approach to site monitoring
- Risk-based approaches and tools for CSP oversight
- Automated metric dashboards for real-time oversight
- Quality Tolerance Limits (QTLs)
- Correlated predictive quality metrics

Effectiveness (% very/extremely effective)
Among those using each oversight tool

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Quality Oversight

Providers share three of the same top four most used oversight tools as Sponsors – communication matrices, compliance assessments, and quality metrics.
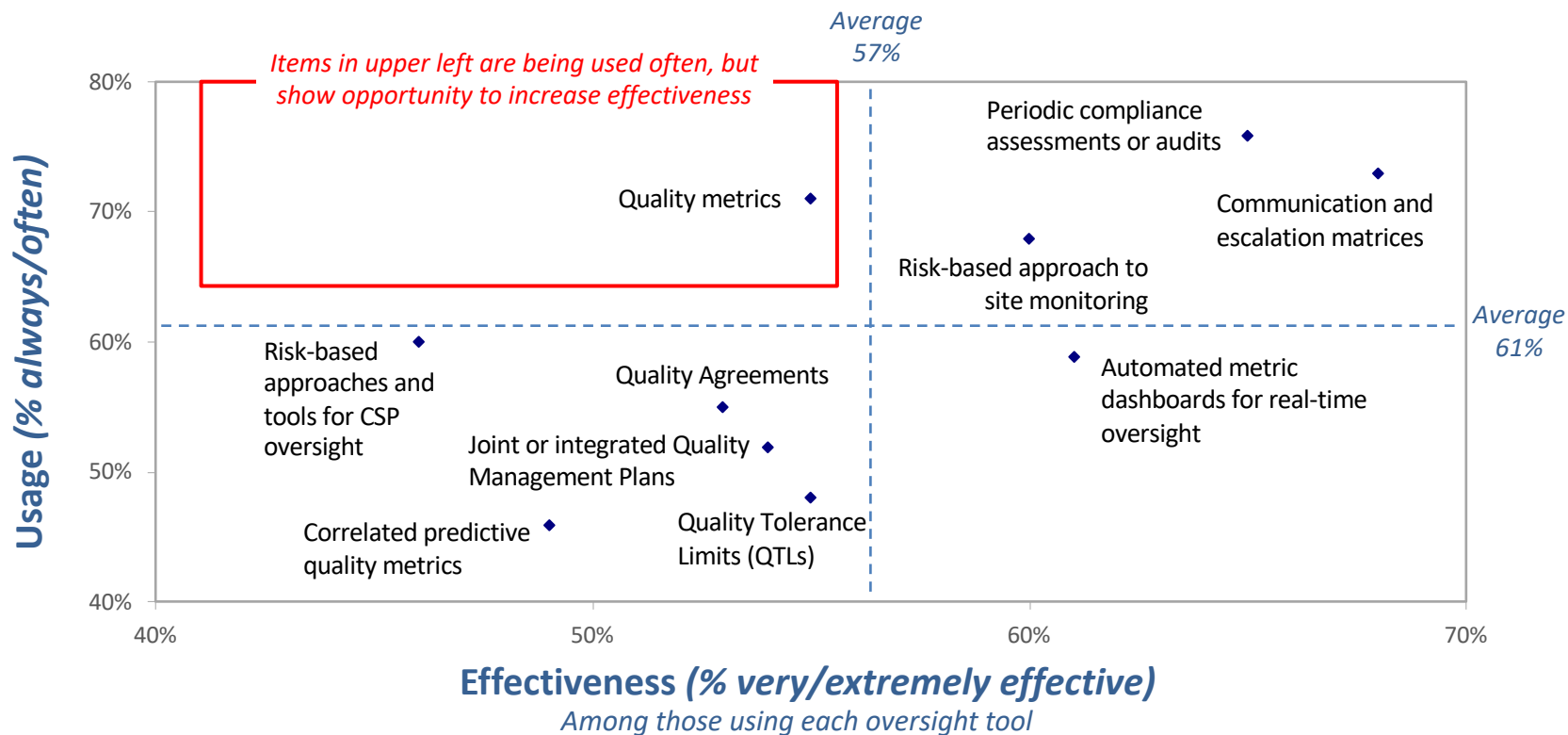
Provider: Usage of Oversight Practices/Tools

Legend: ■ Never   ■ Rarely   ■ Sometimes   ■ Often   ■ Always

Practice/Tool	Sometimes	Often	Always	Often/Always
Communication and escalation matrices	16%	31%	45%	76%
Periodic compliance assessments or audits	21%	33%	40%	73%
Quality metrics	17%	28%	43%	71%
Risk-based approach to site monitoring	21%	35%	33%	68%
Risk-based approaches and tools for CSP oversight	29%	33%	28%	60%
Automated metric dashboards for real-time oversight	18%	25%	34%	59%
Quality Agreements	22%	20%	36%	55%
Joint or integrated Quality Management Plans	26%	27%	26%	52%
Quality Tolerance Limits (QTLs)	20%	33%	15%	48%
Correlated predictive quality metrics	24%	30%	16%	46%

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Among the Provider audience, compliance audits enter into the top right quadrant as a tool being used often and is perceived to be efficacious. Joint Quality Management Plans are not being used often by Providers, though Sponsors indicated finding these both highly used and effective.

Provider: Usage of Oversight Tools vs. Perceived Effectiveness

Average 57%

Items in upper left are being used often, but show opportunity to increase effectiveness

Quality metrics

Periodic compliance assessments or audits

Communication and escalation matrices

Risk-based approach to site monitoring

Average 61%

Risk-based approaches and tools for CSP oversight

Quality Agreements

Automated metric dashboards for real-time oversight

Joint or integrated Quality Management Plans

Correlated predictive quality metrics

Quality Tolerance Limits (QTLs)

Usage (% always/often)

80%
70%
60%
50%
40%

40%   50%   60%   70%

Effectiveness (% very/extremely effective)
Among those using each oversight tool

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Quality Oversight

Looking across audiences, there are some consistencies. Automated metric dashboards are rated as being relatively effective by those using them but are used less often – financial resources required for start-up appears to be a key barrier.

More Use/Lower Effectiveness

- Quality metrics

More Use/Higher Effectiveness

- Communication and escalation matrices
- Risked-based approach to site monitoring

Less Use/Lower Effectiveness

- Risk-based approaches and tools for CSP oversight
- Quality Tolerance Limits (QTLs)
- Correlated predictive quality metrics

Less Use/Higher Effectiveness

- Automated metric dashboards for real-time oversight

"Not sufficient resources available for the upfront work." [Sponsor]

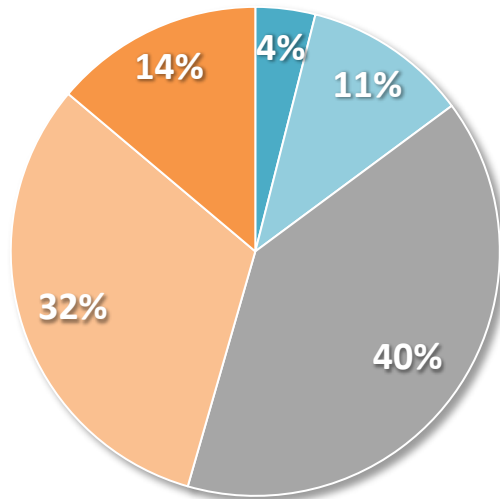*"Technology platform too expensive."* [Provider]

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How does *outsourcing model* impact perceptions of quality?
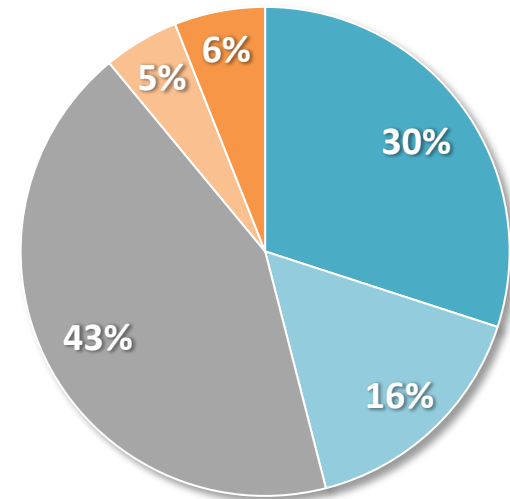
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Quality Oversight

Sponsors and Providers have opposing viewpoints on which outsourcing model delivers better on quality – Sponsors favor FSP, while Providers favor full service.

Perceptions of Quality Delivery by Outsourcing Model

Sponsor

- 4% (Full service much better)
- 11% (Full service somewhat better)
- 40% (Equal)
- 32% (FSP somewhat better)
- 14% (FSP much better)

Provider

- 30% (Full service much better)
- 16% (Full service somewhat better)
- 43% (Equal)
- 5% (FSP somewhat better)
- 6% (FSP much better)

Legend:
- ■ Full service much better
- ■ Full service somewhat better
- ■ Equal
- ■ FSP somewhat better
- ■ FSP much better

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Quality Oversight

Sponsors voice that FSPs provide for stronger communication/collaboration, more expertise, flexibility, and control.

Sponsor: Ratings of <u>Quality</u> Perception by Outsourcing Model

FSP
Delivers Better Quality

Full Service
Delivers Better Quality

| 46% | **14%** Much | **32%** Somewhat | **40%** Same | **11%** Somewhat | **4%** Much | 15% |

FSP Themes: Stronger relationship/better collaboration, more expertise/ can select best in class, greater flexibility, Sponsor retains control

- *"FSP tends to foster greater collaboration than the traditional CRO-Sponsor relationship."*

- *"Not all CROs are good in all things or trial designs. therefore, FSP model allows for flexibility to choose the best fit."*

- *"You generally are able to operate under your own company's SOPs and staffing tends to be more stable - less turnover - ability to have input into training of personnel."*

- *"More flexibility with FSP to make changes if needed to improve quality."*

- *"You can control the staff allocated to your project better. Better relationships with allocated staff. In the full outsourcing model, many players are 'hidden' and for sure not dedicated to your study(ies)."*

Full-Service Themes: Familiarity with this model; "all in one" approach provides better outcomes/relationship

- *"The people on the study get to truly know the study inside and out."*

- *"Full-service model is usually more organized and consistent."*

- *"All in one service, better communication."*

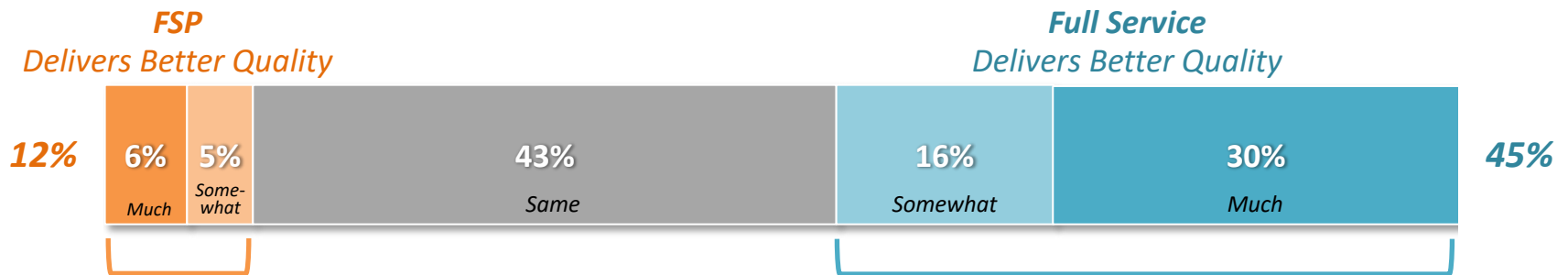- *"Negotiated rates, familiarity, governance model in place."*

N: Sponsor=81

Q: Regardless of what models you may employ/provide today and based on your experience working with varied sourcing models, please select the statement that best reflects your perspective in terms of the quality that is delivered.

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Quality Oversight

Providers, who feel that full-service engagements deliver better, cite the strength of the relationship, ability to integrate, and efficiencies gained.

Provider: Ratings of Quality Perception by Outsourcing Model

FSP
Delivers Better Quality

Full Service
Delivers Better Quality

12%

6% Much	5% Some-what	43% Same	16% Somewhat	30% Much

45%

- *"FSP is more specialized to deliver on specific requirements."*

- *"The more familiar you are with a client the better able you are to predict their needs and how to serve them best."*

- *"The difficulty in accurately defining Sponsors' strategic needs and goals."*

Full-Service Themes: Stronger relationships/ collaboration/integration, allows for big picture/strategic thinking, greater efficiency

- *"A deeper team integration seems to allow for better collaboration and improved efforts on both sides."*

- *"Better integration with the whole clinical trial life cycle requirements, deliverables and expectations from Sponsor to CRO."*

- *"Less issues due to fewer reconciliation of issues and miscommunications."*

- *"We tend to have closer/tighter oversight when it's full service."*

- *"Because you're not as silo'd and working with the other groups in your same company allows for more knowledge transfer."*

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Implications

Perceptions

- Persistent, widening gaps in perceptions of quality between Sponsors and Providers are heavily influenced by the 'softer' elements of quality oversight – effective, open communication regarding expectations, risk, and issues.

- Pragmatic challenges working together within key components of an effective Quality Management System – specifically alignment around SOPs/processes, metrics, and oversight practices – also influence perceptions of quality.

- These factors appear to have influence on perceptions of outsourcing model performance – and potentially on model selection – with Sponsors viewing the flexibility, control, and expertise/quality of staff as key differentiators for FSP.

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Implications

Practices

- More progressive, proactive quality management tools and practices are less frequently used and perceived to be less effective despite encouraged use in recent regulatory guidance.

- Quality tolerance limits and predictive quality metrics are less frequently utilized by Sponsors and Providers alike – and may represent common challenge areas in aggregating and analyzing data to support risk-based decision making.

- As the regulatory landscape continues to evolve concurrently with greater focus on virtualization and clinical trial continuity in the post-COVID reality, quality oversight practices must continue to evolve to address the new risks and opportunities that lie ahead.

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How Avoca Can Help

For more information and case studies describing how The Avoca Group supports Sponsors and Providers, please contact Dawn.Auerbach@theavocagroup.com

- QMS Gap Assessment and Implementation Support

- Vendor Oversight and Management Framework Design and Improvement

- ICH E6(R2) Compliance

- Mock Inspection and Inspection Preparation Support

- Quality Tolerance Limits and Quality Metrics

- Risk Management and Risk-Based Approaches to Quality

- Sponsor-CRO Bi-directional Relationship Assessments

- Site Feedback Surveys

- Market Perception Assessments

- Client Satisfaction Surveys

- Virtual and Instructor-led Training and Workshops

- Vendor Qualification Assessments

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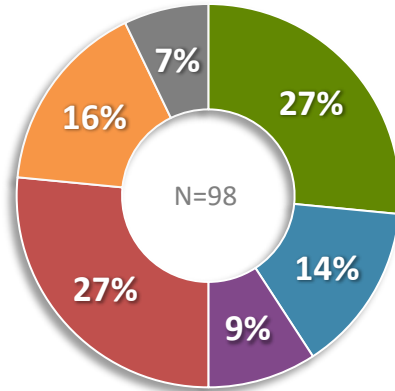**info@theavocagroup.com**

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Appendix

Company Characteristics

Sponsor: Company Size

- Top 20 Biopharma ($10+ billion sales)
- Top 50 / Mid-sized Biopharma ($2.0 - $9.9 billion sales)
- Other Mid-sized Biopharma ($500 million - $1.9 billion sales)
- Small / Specialty Biopharma (<$500 million sales)
- Pre-Revenue Biopharma ($0 sales)
- Other

N=98

27% · 14% · 9% · 27% · 16% · 7%

Provider: Company Type

- Large CRO ($500+ million sales)
- Mid-sized CRO ($50 - $500 million sales)
- Small/Specialty CRO (<$50 million sales)
- Non-CRO Clinical Service Provider
- Academic Research Organization (ARO)
- Consulting Company
- Other

N=99

24% · 21% · 20% · 4% · 15% · 7% · 8%

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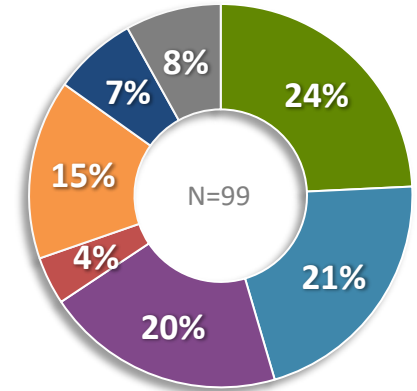
Respondent Characteristics

Sponsor: Tenure in/at…

N=98

	Mean Years
Pharmaceutical industry	18.5
Current company	6.6
Current role	4.8

Provider: Tenure in/at…

N=99

	Mean Years
Pharmaceutical industry	15.9
Current company	6.5
Current role	5.5

Sponsor: Primary Functional Area

N=98

Functional Area	Percent
Clinical Development/Ops	46%
QA/QC & Compliance	22%
Executive Management	8%
Procurement/OS/Vendor Mgmt	7%
Medical Affairs/Scientific	6%
Clinical Data Management	4%
Regulatory Affairs	3%
Biostats/Stat Programming	2%
Other	1%
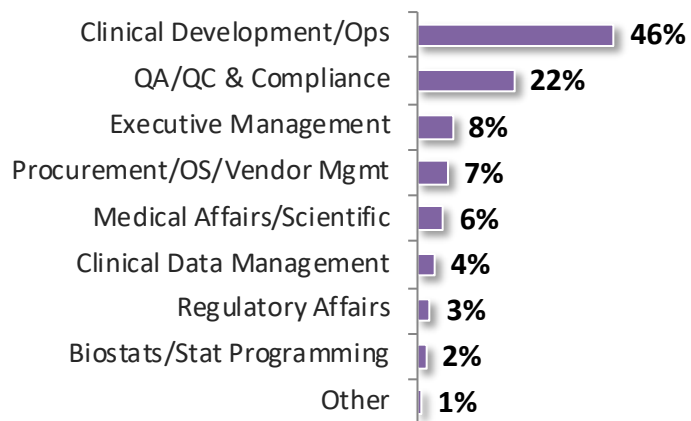
Provider: Primary Functional Area

N=99

Functional Area	Percent
Clinical Development/Ops	36%
QA/QC	19%
Executive Management	12%
Regulatory Affairs	10%
Business Development	7%
Medical/Scientific	6%
Data Management	3%
Other	6%

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