EXECUTIVE SUMMARY

THE AVOCA GROUP

QUALITY CONSORTIUM SUMMIT 2013

Optimizing Approaches and Establishing Best Practices in Quality Management of Outsourced Clinical Research

May 8-9, 2013
www.theavocagroup.com

The Avoca Quality Consortium Summit, held May 8-9, 2013, in Princeton, NJ, was the Second Annual meeting for The Avoca Group's Quality Consortium, a cooperative effort that brings together quality, outsourcing, and operational professionals from Member pharma, biotech, and CRO organizations to accelerate the development of a best-practices approach to quality management and CRO oversight.

Currently, the Avoca Group's Quality Consortium includes 26 Members: 16 pharma/biotech companies and 10 Contract Research Organizations (CROs). The corporate sponsors of the Quality Consortium are Eli Lilly and Company and Pfizer, Inc. ICON Clinical Research was the corporate sponsor of the May Summit.

Special thanks to our Executive Summary Sponsor, inVentiv Health Clinical.

TABLE OF CONTENTS

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About inVentiv Health Clinical

inVentiv Health Clinical, formerly PharmaNet/i3, is a leading provider of global drug development services to pharmaceutical, biotechnology, generic drug, and medical device companies, offering therapeutically specialized capabilities for Phase I-IV clinical development, bioanalytical services, and strategic resourcing from a single clinical professional to an entire functional team. With 7,000 passionate employees operating in more than 70 countries, inVentiv Health Clinical works to accelerate high quality drug development programs of all sizes around the world. www.inventivhealthclinical.com

THANK YOU TO OUR 2013 AVOCA QUALITY CONSORTIUM SUMMIT SPONSORS

About the Avoca Quality Consortium

THE AVOCA GROUP
QUALITY CONSORTIUM

Founded in December 2011, the Quality Consortium is a membership fee-based consortium designed to help sponsors and CROs optimize their approaches to proactive quality management with an emphasis on bringing them into greater alignment.

The mission of the Consortium is to serve as a catalyst for the acceleration of best practices and industry standards for proactive quality management and risk mitigation.

According to Patricia Leuchten, Avoca's President and CEO, "We know that sponsor companies are striving to become more efficient in the oversight of CROs and are striving to reduce the duplication of effort while focusing on maintaining very high quality. Eliminating the duplication of effort requires collaboration on a higher level. The work of the Quality Consortium is to bridge gaps and serve as a vehicle for developing mutually agreed upon leading practices for quality." Avoca is using its industry and Consortium Member research survey data, consultants, subject matter experts, and partners to set strategic direction and to rapidly develop these industry best practices.

About The Avoca Group

Avoca
THE AVOCA GROUP

Founded in 1999, The Avoca Group Inc. is a consulting and survey research firm based in Princeton, New Jersey. The Avoca Group develops and implements global relationship and alliance management programs for pharmaceutical companies, biotech companies, and pharmaceutical service providers.

Avoca helps clients build, measure, and manage critical business relationships. Avoca's clients include the top five pharmaceutical companies and global contract research organizations as well as small companies seeking aggressive growth within the healthcare industry.

The Avoca Group Inc. conducts industry research on trends in clinical outsourcing each year, presenting the results, *The Avoca Report*, at international conferences and via industry publications. The Avoca team consists of pharmaceutical industry veterans and subject matter experts in the areas of large scale organizational change, relationship management, information technology, and survey research.

2013 MEMBERS OF THE AVOCA QUALITY CONSORTIUM

Dear Colleague,

Pharmaceutical and biotech sponsor companies are striving to become more efficient and effective in the oversight of CROs and to reduce the duplication of effort while focusing on maintaining very high quality. In December 2011, Avoca formed the Quality Consortium to address challenging areas head on and to develop more consistent approaches to the proactive management of the quality of outsourced trials.

While there is no "one-size fits all" formula for quality management that can be applied to all organizations, the Consortium has been able to bridge gaps and develop mutually agreed upon standards of quality that pave the way for improved outcomes.

Now that our Second Annual Quality Summit has concluded, we can appreciate how far we have come since late 2011. In 2012 we:

- Developed a standard quality agreement template for sponsors and CROs to use in outsourced work
- Delivered a prioritized list of quality metrics, which are being further refined in partnership with the Metrics Champion Consortium (MCC)
- Produced a benchmarking report regarding Member practices in quality management
- Provided research around conducting prequalification visits and routine system audits

The result is that these changes are improving operational processes, and enabling more effective long-term strategies and more integrated, intuitive approaches for relationship building and partnering between sponsors and CROs.

Every year, we redefine our goals and initiatives for the Consortium based on Member feedback to reflect the changing business and scientific environment in which we live. This year is particularly important as we have already delivered on a number of exciting initiatives based on your input, and we will continue to deliver more as the year progresses. Notably, we have introduced:

- An initiative to provide definitions, guidelines, and tools for project oversight and proactive quality management
- An assessment of how companies are assessing, managing and sharing risk
- A Setting Expectations Worksheet to strengthen understandings of key principles and practices that will enhance the ability for clinical teams to prepare for project starts and deliver higher quality that meet expectations
- Sessions at the Annual Quality Consortium Summit around change management to help organizations embrace change and a culture of quality

We are proud to have had the participation of the industry's best, brightest and most engaged clinical leaders from sponsors and CROs alike, working in clinical development and quality. We thank all of the Members for their participation in the interactive discussions and in choosing to engage in a forum to find proactive approaches to the fundamental challenges the industry is facing.

We are pleased to present this recap and overview of the 2013 Avoca Quality Consortium Summit. Thank you to everyone who made this year's Summit such a memorable success and we look forward to working with you throughout the year.

Warm regards,

STEVE WHITTAKER
Quality Consortium
Executive Director
The Avoca Group, Inc.

PATRICIA LEUCHTEN
President & CEO
The Avoca Group, Inc.

EVENT HIGHLIGHTS & TESTIMONIALS

"I think changing our mindset in how we think about quality will ultimately enhance quality of the process."

—Jeffrey P. McMullen, Vice Chairman, inVentiv Health, Inc.

"The nice thing about the Quality Consortium is that we are all working on a common purpose. Everybody is on an equal footing. Internally within Grünenthal, there is a massive benefit in the data that the Quality Consortium has put together and seeing where our organization stands."

—Hazel Collie, VP Compound Development and Branding, Head of CDB Quality and Systems, Grünenthal

"We need to refocus our thinking around how to achieve quality objectives and we are doing that already at this summit here today."

—Michael D. Jones, Senior Director Clinical Operations, Eli Lilly and Company

"This Consortium gives us a place where there can be a baseline definition of quality that is agreed upon. It makes the procurement, selection of providers, and operations of clinical trials better."

—Gregg Jewett, Global Procurement Leader - Clinical CRO Services, AstraZeneca

"What I'm really pleased with Avoca and the Quality Consortium group, is that they've actually brought forward tangible improvements and allowed us to implement these and improve the quality in the industry."

—Stephen Cutler, Ph.D., Group President, ICON Clinical Research Services

"This Consortium enables me to listen to the lessons learned and best practices from other companies, both small and large. It has also made me realize that we as an industry have a very inconsistent definition of quality. The value here is to speak and define it, and come to agreement on some key areas around quality."

—Mitchell Katz, Ph.D., Executive Director, Medical Research Operations, Purdue Pharma L.P.

INSIGHTS FROM THE FDA ON EFFECTIVE OVERSIGHT AND RISK MANAGEMENT

ANN MEEKER-O'CONNELL
US-FDA

Ann Meeker-O'Connell, Acting Division Director for Good Clinical Practice Compliance in the Office of Scientific Investigations, CDER, FDA, oversees two branches, one responsible for overseeing marketing application related inspections and providing recommendations on data integrity and subject protections to CDER's review divisions and the other responsible for compliant evaluation, for-cause inspections and development of appropriate administrative and regulatory actions post-inspection. Ann is actively involved in a range of initiatives evaluating innovative models for clinical trial design, conduct, and oversight. Ann is currently serving as a co-lead for a CTTI project seeking to develop models for building quality into the scientific and operational design of trials. Before joining FDA, Ann spent over nine years working in clinical and compliance roles in industry and academia, where she was responsible for designing and implementing a global clinical internal process audit program; serving as the compliance lead for development programs in oncology, immunology, and diabetes; conducting both routine and for-cause audits; drafting and reviewing submissions to the FDA, and developing clinical trial and healthcare compliance policies and procedures.

Ann Meeker-O'Connell joined executives at the Avoca Quality Consortium Summit via Skype, to deliver her insights into effective oversight. She stressed that the industry needs to go back-to-basics, and focus on the needs and activities that are critical, such as determining the right partner for each activity.

She emphasized that effective oversight is a two-way street: There can be activities outlined that a sponsor hasn't carried out or issues that the CRO doesn't take the initiative to speak up about, resulting in activities falling through the cracks. Therefore, the clarity of communication is key.

"All standards emphasize communication as an essential part of risk management," Meeker-O'Connell stated. There should be an opportunity to identify where risks are and to challenge assumptions. However, there should not be an exhaustive list of issues, rather, it should be about planning efficiently, such as the opportunity to focus resources and keep track of things that aren't being addressed.

Meeker-O'Connell cautioned against overcomplicating the risk management process, as it will lead to companies losing faith in the whole process. Avoca data indicated there is a general lack of confidence at (primarily) the operational level within pharmaceutical and biotech companies regarding understanding best practices in risk management.

A question from the audience prompted a discussion about the difference between quality and compliance, drawing the need to make a clear distinction between the two, as it is possible to be compliant without integrating a quality aspect.

"When there is a focus on compliance to the exclusion of quality, that is problematic. There must be conversation on both compliance risks and quality risks. But if the industry has a quality mindset, then the compliance will happen," Meeker-O'Connell commented.

If all else is equal, the simplest solution is the best. Meeker-O'Connell borrowed a statement from Fergus Sweeney from the EMA, saying, "Perfection is achieved not when there is nothing left to add, but when there is nothing left to take away."

CREATING A CULTURE OF QUALITY

MARGARET DAVIS
Founder & President, Margaret Davis Consulting

Margaret Davis is the Founder and President of Margaret Davis Consulting, a culture change and coaching firm based in Princeton, New Jersey. Margaret specializes in culture assessment and analysis, coaching, and services that support these efforts. Margaret Davis received her B. A. from Princeton University in Cultural Anthropology, has been trained in Family Systems Theory at the Georgetown Family Center, and pursues ongoing graduate studies in Psychology and Organizational Development.

Margaret Davis, a culture and organizational anthropologist helps organizations understand how their cultures impact performance. She presented to executives at the Avoca Quality Consortium Summit to provide a framework for how to create a culture of quality. Culture was defined as "the collectively held beliefs and behaviors of a group."

The model that was presented for a high performing culture consisted of four components:

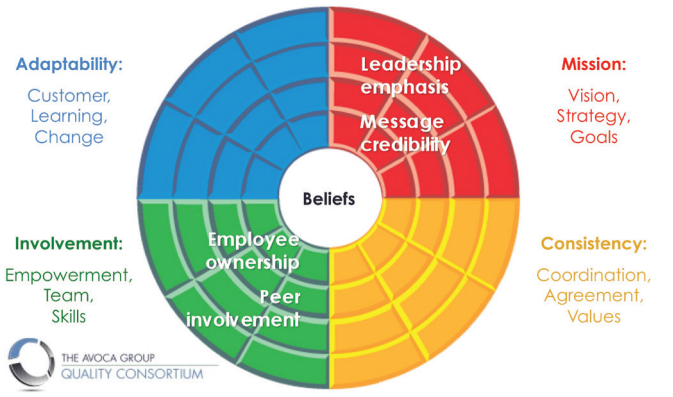
- Mission: Do you know where you are going and is that clear to everybody? Do people understand overall goals and where they fit?
- Adaptability: Does the organization have a realistic connection to the marketplace?
- Involvement: The heart and mind of the workforce; Do people feel engaged?
- Consistency: The infrastructure in place, which includes procedures, metrics, and agreements.

According to Davis, the mission and involvement of people are the real differentiators in creating a culture of quality. "People need to understand where the organization is going and how their roles fit within that. The involvement of the workforce relates to how they feel, and what they see from others' actions, and the ability to speak up when they think an agreement isn't accurate," Davis said.

Frequently mentioned by sponsors and CROs throughout the Summit, some of the barriers to creating a cross-partner culture of quality revolved around issues with trust, transparency, and communication between sponsors and CROs. Particular emphasis was placed on the importance of clarity, accountability, and responsibility and the need for the sponsor to be informed on what is going on within their studies without overcomplicating and over micromanaging their CRO partners.

CREATING A CULTURE OF QUALITY

Culture of Quality



The most important controllable activities, by executives responsible for quality, that differentiate strong from weak cultures of quality include: Employee Ownership, Peer Involvement, Message Credibility, and Leadership Emphasis.

Most importantly, a culture of quality can be defined and measured, can be driven by controllable activities, and affects performance and a company's bottom line. This session provided attendees with a sense of what a "culture of quality" involves, what gaps and opportunities the industry faces, and an overview of the approaches used to establish this culture within organizations.

Key Differentiating Activities

Employee Ownership
- Understand quality fit with job
- Comfortable raising quality concerns & challenging directives
- Empowered to make decisions about quality

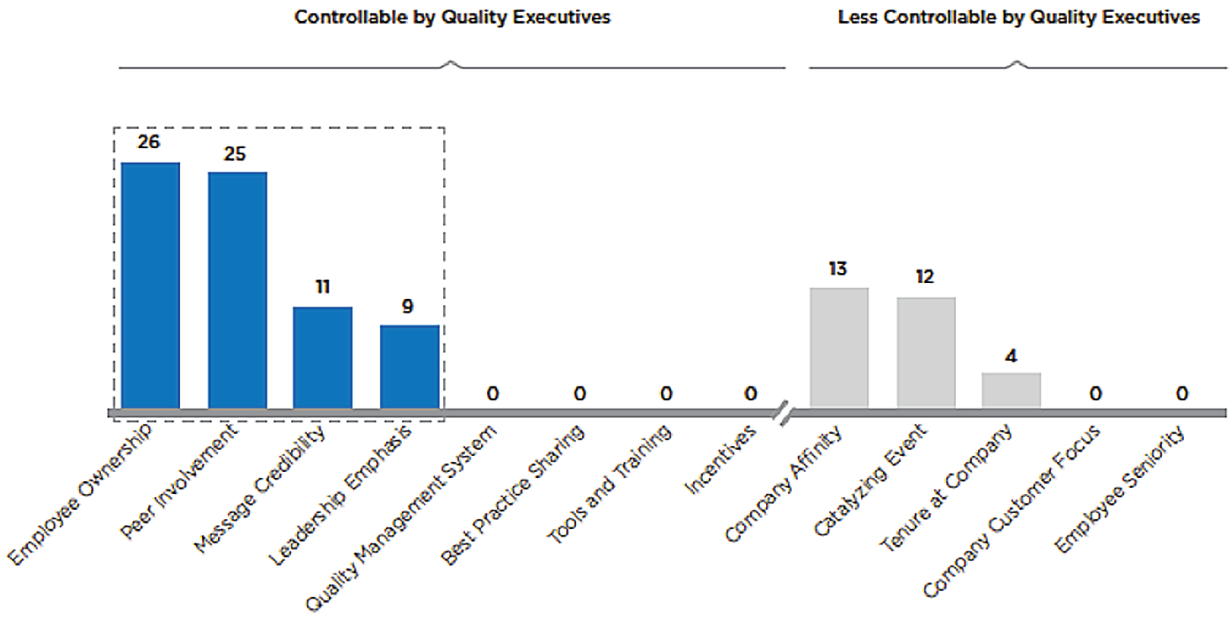
Message Credibility

Messages on quality and priorities are:
- delivered by respected sources
- easy to understand
- appeal to me personally

Peer Involvement
- Have strong network of peers for discussion & guidance
- Peers are involved in and held accountable for quality performance

Leadership Involvement
- Leadership states that quality is a priority
- Manager emphasizes quality's importance, and walks the talk on quality

WHAT ACTIVITIES DIFFERENTIATE STRONG CULTURES OF QUALITY FROM WEAK?



LEADING AND MANAGING ORGANIZATIONAL CHANGE

PETER BREGMAN
CEO, Bregman Partners, Inc.

Peter Bregman is the CEO of Bregman Partners, Inc., a global management consulting firm which advises CEOs and their leadership teams. He is the author, most recently, of 18 minutes: Find your Focus, Master Distraction, and Get the Right Things Done*, named the best business book of the year by NPR, and selected by publishers weekly and the New York Post as a top 10 business book. He is also the author of* Point B: A Short Guide to Leading a Big Change *and co-author of five other books. Featured on PBS, ABC, and CNN, Peter is a regular contributor to Harvard Business Review, Fast Company, Forbes, NPR, Psychology Today, CNN, and Fox Business News. To find out more information on Peter Bregman and to read some of his latest articles, go to peterbregman.com.*

Peter Bregman energized attendees when he launched his presentation on change management with an interactive exercise. His instructions were: 1) "Find a partner" 2) "Get into what appears to be a normal arm wrestling position," and 3) "See who can score the most points." Almost the entire audience proceeded to arm wrestle, as that arm wrestle position put them in a familiar situation where they viewed their partner as an opponent that they were battling against. The few partners who scored many points were ones that worked together and collaborated and helped each other. It was a demonstration of the power of collaboration and a key message was this:

There is an event, followed by a reaction to that event, followed by an outcome. But, when you create a pause and space between the two, you move your thinking from your Amygdala, the emotional part of your brain, to your Neocortex, the part of your brain responsible for logical thinking. This pause allows you to take a moment to assess the goal and react appropriately to create an intended outcome.

Bregman then followed with an additional exercise. Audience members were given five seconds to jot down the number of purple items present in a photograph of a bedroom that was projected onto a large screen. The audience was then asked a series of questions about the details of the picture, and nobody in the audience was able to answer any of the questions successfully. The message: It is easy for you to only see what you are looking for, and miss the "big picture."

*slide from Bregman presentation

Bregman bridged the message of this exercise by inviting audience members to learn about the "big picture" of which change management models work, and how they have proved to be most effective. Bregman presented the ideal change management model as a triangle with three key areas: ownership, capability, and persistence.

"As a leader you don't motivate people, you must create an environment where people are self-motivated," he stressed. The more deeply engaged people are in the change, the more likely that organizational change will be a success. Employees need to be excited about the choices they are making, and they will get excited when they feel like they are making those choices.

"People don't resist change. People resist being changed. And people will change when they feel like they are choosing to change."

Bregman said that the biggest barrier to organizational change is when we try to change people, in effect, against their will, rather than engage them in the change effort themselves. Therefore, the key for companies to effectively implement change requires shifting ownership of the change from the senior leadership who has decided the change has to happen, to the front line, or all of the employees, who need to make the change actually happen. "Those are the people on the ground who need to change their day-to-day actions. And they have to have some ownership; they have to feel and care about the change as much as the people who are telling them that they want the change to happen."

LEADING AND MANAGING ORGANIZATIONAL CHANGE

An audience member asked Bregman how he measures success in a change that may not necessarily be tangible, such as creating a culture of quality.

"We would be successful in creating a culture of quality when the individuals who are doing work in the organization care deeply about quality and are willing to spend extra time, spend extra energy, spend extra focus making sure that the work that they're doing meets the highest quality standards, and also, a step beyond that, are willing to call themselves out when they aren't managing to those standards."

Bregman cautioned against creating a set of metrics that tell you what is accomplished on a given mission because it is easy to achieve metrics without necessarily changing the company culture. Instead, he encouraged changing a company culture through the use of stories.

"If you want to change the culture, you need to change the stories. And the negative stories carry much more weight than the positive ones, so you have got to do something that is noticeable."

Outsourced Pharma@OutsourcedPharm

"**#aqcsummit2013**@RfwrightLSL Peter Bregman: If you're going to change, you have to interrupt your normal, habitual actions."

Outsourced Pharma@OutsourcedPharm

"**#aqcsummit2013** Pfizer's Hilton: When the sponsor and CRO both feel a little uncomfortable, we have hit the sweet spot."

CHANGE MANAGEMENT SPOTLIGHT: **PURDUE PHARMA L.P.**

MITCHELL KATZ, PH.D.

Executive Director of Medical Research Operations, Purdue Pharma L.P.

Dr. Mitchell Katz is Executive Director of Medical Research Operations at Purdue Pharma L.P. In this position he is responsible for leading all operational activities across Purdue's multinational clinical programs. Dr. Katz has 27 years of experience in the pharmaceutical and biotechnology industries, including preclinical research, pharmaceutical operations, and regulatory affairs. Prior to joining Purdue, he served as Vice President of Global Clinical Operations & Data Management at Eisai Medical Research. Dr. Katz has experience working in start-up biotechnology companies, and including Acorda Therapeutics, InterMune, Connetics, and NABI. He also held management positions at Ortho Biotech and Schering-Plough and participated in six successful NDA applications in his professional career. Dr. Katz holds a B.A. in Biology a Ph.D. in Microbiology, and served as a postdoctoral research fellow at Downstate Medical Center in NY.

During the 2013 Avoca Quality Consortium Summit, Dr. Mitchell Katz shared Purdue Pharma L.P.'s use of the Avoca Quality Agreement template. After review by Purdue's legal department, the organization will be implementing the quality agreement with its two strategic CRO partners. With one of the partners, it will implemented on a retroactive basis, and for new partners it is forward going.

"Participating in the Quality Consortium allowed me to understand where we wanted our quality focus. The value of being a Consortium Member for us is receiving and participating in the development of a quality agreement. This is something we didn't have as an organization. By working across the pharmaceutical industry, we are taking best practices and consolidating them in a document that we are now using as a company. In addition, we identified over 200 metrics with emphasis on the top ten that we are going to use to measure quality," Katz shared.

The quality metrics that Avoca provided were not tied to the quality agreement they implemented. Purdue is currently waiting for metrics to get through the Metrics Champion Consortium (MCC) before they finalize their metrics.

Several executives at the Summit questioned Katz about the flexibility around the agreement and what the situation would be if Purdue were to meet with a CRO that has its own quality agreement in place. "We have some flexibility around the agreement, and we haven't really seen too much CRO push back," Katz said.

"Working with the Avoca Group enables us to use them as an organization to help bring the industry together for a best practice approach on how to manage and operate our outsourcing relationships. Although we're coming from different size organizations, companies all are challenged with the same issues. It has been great to have the opportunity to come together and see how all of the organizations are motivated to develop best practices, standards, templates, and tools that we could all use to become more efficient with quality to effectively deliver what we need to within our organizations."

CHANGE MANAGEMENT SPOTLIGHT: **CEREXA, INC.**

JONATHAN LEE

Vice President of Development Operations, Cerexa, Inc.

Jonathan Lee is Vice President of Development Operations at Cerexa, a subsidiary of Forest Laboratories that is developing novel antimicrobials for emergent resistance infections. Jonathan has more than 22 years of drug development experience in biotechnology and pharmaceutical companies, from preclinical through commercial launch at companies such as Genentech Inc., Gilead Sciences, and Inhale Therapeutic Systems/Nektar Therapeutics. He has managed various disciplines of drug development including Clinical Operations, Clinical Supplies, Clinical Outsourcing, Pharmacovigilance, BioMetrics, Project Management, Contract Management, SOPs & Training, Quality Assurance, and Manufacturing. During his career, Jon has participated in successful registration of Pulmozyme for cystic fibrosis, Exubera for type 2 Diabetes, and Teflaro for serious hospitalized infections.

Jonathan Lee shared with Avoca his journey and experience of implementing the Consortium Quality Agreement and quality metrics within Cerexa.

When the Quality Agreement was published to Consortium Members in July 2012, Cerexa first gathered CRO feedback, and then convened a small group of executives that included heads of clinical operations, heads of quality and outsourcing, and the contract management group to review the agreement section by section in order to evaluate potential areas for adjustment based on Cerexa's approach to outsourcing.

Cerexa did not have a Quality Agreement in place, so they adopted and adapted the one provided by Avoca's Quality Consortium. Lee says, "The team realized it is a big document. The document gets at the things that we talk about but don't necessarily write down when it comes to quality expectations with our outsourcing partners. Once everybody on my team reviewed the document, they came back very positive. Although there were some small tweaks, there was a consensus that it was a good agreement."

The changes included incorporating an appendix that lists plans for each individual study. "What we are trying to do is allow the appendix to change to allow for flexibility, but the body of the agreement to stay the same for every study," Lee shared. Most of the changes had to occur with how Cerexa's quality department exchanges information because the department does not outsource quality audits for CROs, so there were areas where language had to be tweaked in order to reflect their needs for large global programs.

Cerexa also revised the quality metrics slightly because they saw duplication with what they measure in their Service Level Agreements. "Cerexa internally has 24 metrics, which is a lot, and the whole idea is that we sit down with each CRO and hone that list down to 6-8 metrics and keep it consistent with each CRO," Lee stated.

In May 2013, Cerexa sent the agreement to three mid-tiered and niche preferred provider CRO partners who they are working with in multiple studies in order to obtain feedback around specific sections of the contract.

Although Cerexa has had discussions with all of their CROs, they are all in different places with different partners at this point in time. With one CRO partner, Cerexa reviewed the conceptual framework of the Quality Agreement template and discussed the key objectives Cerexa has as well as how the organization views this document in relation to other contracts and ongoing projects. That CRO partner is working on providing comments on the document.

"We spoke with the head of operations, quality, and project management to review the framework and concepts outlined in this document. We have an MSA with one of our CRO partners, but they are not under an SLA, so we need to have an SLA to build a Quality Agreement upon because they are complementary pieces. In the SLA we streamlined the entire agreement," Lee commented.

CHANGE MANAGEMENT SPOTLIGHT: **CEREXA, INC.**

Another of Cerexa's CRO partners reviewed the Quality Template document from more of an operational standpoint. They looked to understand the intent behind the document, how the document relates with an MSA or SLA contract, and what elements should be prioritized. They spent a lot of time delving into details of the quality metrics, and provided Cerexa with some "food for thought". Lee shared, "We knew we would need to change some of our internal processes and metrics, and in discussions with our CRO partner, it became clear what some of those areas are."

Lee mentioned the importance of reassuring their CRO partners that the Quality Agreement and metrics were written with a heightened focus on transparency as part of the socialization of the document.

"For example, when our CRO partner has a finding from a regulatory authority in a function that they outsource to us, even if it is not from our outsourced work, we expect to be notified. But it is a two-way street. If we, or our parent company, get audited by a regulatory agency and there are findings in an area that might affect our CRO partner, such as site oversight or contracts management, we would also let them know because it may impact how we are supporting that study," Lee said. "There are also certain things that Cerexa is verifying internally if we can do."

Even with the rounds of CRO feedback, Cerexa is adopting and adapting the Quality Agreement quickly. They have already identified certain sections that need more definition, and the need to provide clarification to their CRO partners on how this document overlays with an MSA. After receiving another set of CRO comments, they plan to issue a second draft to better socialize the Quality Agreement with contracts to their CRO partners.

"My overall goal is to sign this by the end of the summer at the latest."

THE CEREXA 'THREE STEP'

SOCIALIZE QUALITY AGREEMENT

- Cross functional team led effort
  - ClinOps, Legal/Contracts, Quality, Outsourcing
- Tailor standard Avoca Quality Agreement Template
  - Focus on what Cerexa outsources
  - Maintain fairness/transparency
- Revise metrics not to interfere or duplicate with SLA or MSA

INTERNAL

- Senior Management endorsement
- Began discussions at company-wide meetings at least 4 months prior to initial discussion with CROs
- Avoca presented at a company-wide meeting
- Retained Avoca to establish training on Quality Agreement for internal groups

EXTERNAL

- Began telling CROs at least 4 months in advance of generating the Cerexa Quality Agreement Template

CROWDSOURCING SOLUTIONS AND CALL TO ACTION

This year, the Summit introduced an interactive exercise where participants crowd sourced solutions around three key areas: creating a culture of quality, effective outsourcing, and managing risk. The results, provided as brief concepts, were then shared with the group and are included here.

CREATING A CULTURE OF QUALITY

- Create a branding initiative around quality, and an environment that motivates teams within both CROs and sponsors.
- Develop a team "scrapbook" to collect ideas and encourage team building.
- Stop relying on a "quality team" to execute but instead develop individual ownership and empowerment so everyone in the organization takes responsibility.
- Employees should develop an annual quality initiatives plan highlighting their immediate quality objectives for the upcoming year.
- Develop a quality coach role in organizations to help people understand how to incorporate quality into their daily lives.
- Create ambassadors throughout the organization who can drive change and ensure they help to encourage effective communication of the change story—both top down and bottom up approach.
- Identify a central business process owner and give them accountability.
- Acquire best practices from other more mature industries, such as Aerospace and NASA, who have already addressed these types of concerns and developed risk assessment disciplines and techniques.

EFFECTIVE OUTSOURCING

- Establish best practices and scale or model specifics to the Pharmaceutical/CRO industry
- Align expectations; start by agreeing on what the goals of the deliverables, initiatives, and programs should be.
- Develop cross training to gain understanding of other stakeholders' needs and challenges.
- Schedule regular review meetings between CRO & sponsor to share insights and have an open forum dialog between sponsor and CRO.
- Share leading indicators; interpret regulations around what is important.
- Learn from the best of each other's expertise, which can also help build relationships between companies.
- Develop non-monetary incentives for the combined Pharmaceutical/CRO team that encourages competition and unity of objectives and purpose.
- Develop a Sponsor/CRO "exchange program" – where one would work with the other
- Transfer the knowledge learned on the business development side of each project to the project team so that details are addressed.
- Create a "Mascot" that gets passed around and rotate scrapbooks or one-on-one calls.
- Demonstrate value through proven results and metrics
- Ensure root cause analysis
- Establish pilot plans that can be analyzed further

CROWDSOURCING SOLUTIONS AND CALL TO ACTION

MANAGING RISK

- Set expectations around what is quality; survey functional areas to determine how they would define quality and what measure they would use. Use this to check corporate quality definition.
- Agree to and publish definitions of: Clinical Risk Assessment & Project management.
- Develop risk management tools: Utilize the tools and models of other industries.
- Create a list of essential trial level documents and templates that can be shared; risk management plans, communication plans, etc.
- Have the Avoca Quality Consortium identify some KRIs (Key Risk Indicators), similar to what was done with quality metrics.
- Create a FAQ sheet around quality agreement and metrics, and share implementation ideas.
- Study lessons learned before beginning a project, dissect project protocol at the beginning and identify risks upfront in order to mitigate and manage risk.
- Enhance existing processes with quality elements—one example: In study management plan templates, include quality compliance study management plan cycle review time/agreed-upon language.
- Site Involvement: Site relationships are critical to success; ensure sponsor/CRO partnership is always in alignment with site quality expectation and overall site management. Invite and include principle investigators in small group exercise focused on quality and compliance necessities.
- Improve Training
  - Create standard training packages/templates around quality to be used within organizations
  - Train monitors to think like auditors (see the big picture)
  - Schedule joint training sessions between the sponsor and the CRO
  - Training model on yellow light approach with CRO/sponsor working together
  - CRO conducts internal training at sponsor and vice versa
- Become familiar with ICHQ9 guidelines and the draft FDA guidance document associated with risk-based monitoring.
- Create audit portals for the ability to conduct virtual audits of investigative sites or CRO partners.

INTERIM RESULTS FROM 2013 QUALITY CONSORTIUM ASSESSMENT

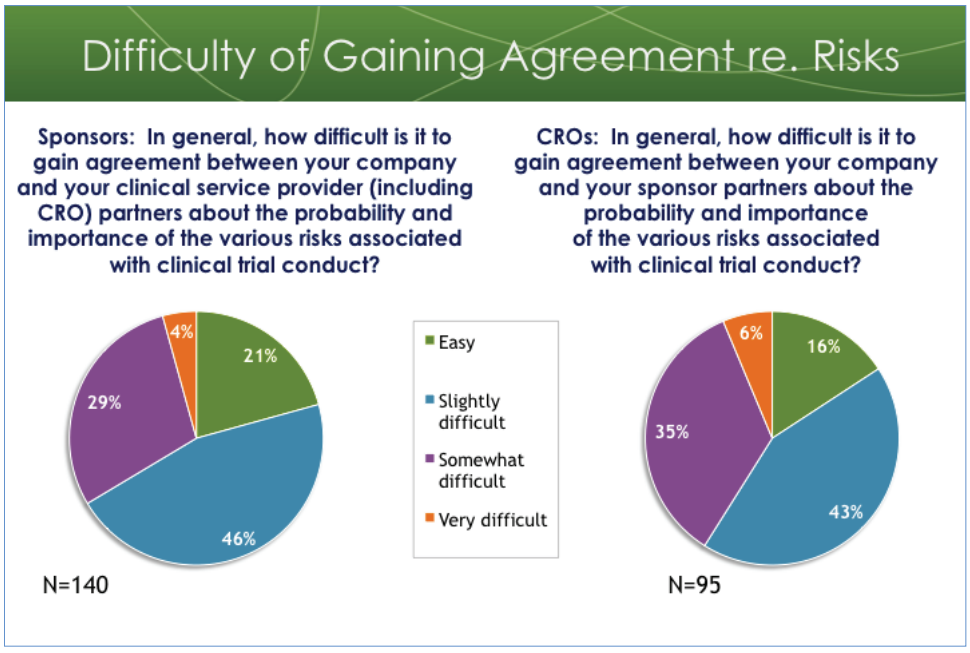
Risk Assessment and Risk Management in Outsourced Clinical Trials

In early 2013, Avoca conducted a comprehensive assessment of the manners in which companies manage risk in the conduct of clinical studies. Avoca investigated the following:

- Risk-sharing models
  - Nature of approaches used
  - Contexts for use
  - Levels of success in increasing efficiency and/or quality
- Risk assessment and management approaches
  - Tasks to which these approaches have been applied
  - Nature of approaches, e.g. qualitative or quantitative
  - Level of success in increasing efficiency and/or quality
  - Regulators' perceptions

Executives at the May Avoca Quality Consortium Summit talked openly about the challenges of embracing risk-based approaches within their organizations. Some noted an overall lack of understanding of such models among their teams, combined with a conservative culture that supports quality in the clinical operations process via the traditional approach of checking everything. In addition, while senior executives may clearly understand risk-based approaches, the operational teams tasked with implementing them often lack the same clarity.

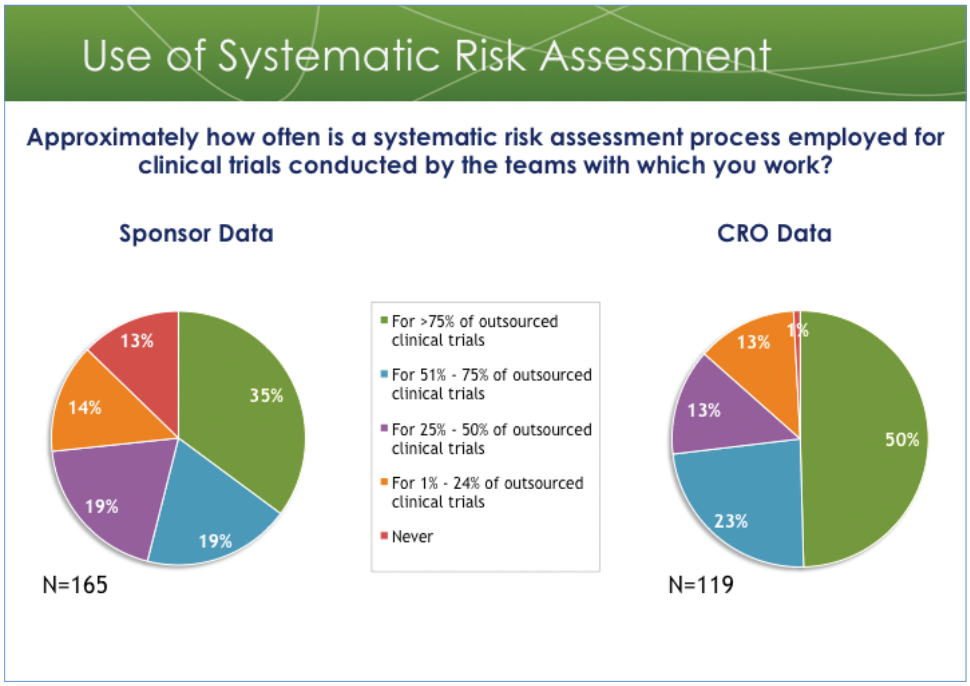
Companies can manage risk only if they are able to effectively assess it—a time-consuming and potentially difficult process involving input and agreement from multiple parties. The figure below illustrates sponsors' and CROs' perceptions of the degree of these difficulties.



INTERIM RESULTS FROM 2013 QUALITY CONSORTIUM ASSESSMENT

Respondents noted that difficulties in gaining agreement are sometimes due to differing views between scientific and operational personnel regarding respective risks. Trouble finding the budget for contingencies is another reason suggested for difficulties gaining agreement. Senior management and clients often won't buy in if proactive mitigations will affect cost and timelines.

Furthermore, merely assessing risk at the beginning of a trial is insufficient; organizations must use these assessments actively throughout a trial. Although many organizations document potential risks at the beginning of a project, they sometimes do not follow through with regular updates of what should be "living documents." Executives at the Quality Summit stressed the need for consistent risk assessment throughout the course of a trial, with constant transparency and communication between sponsors and CROs.

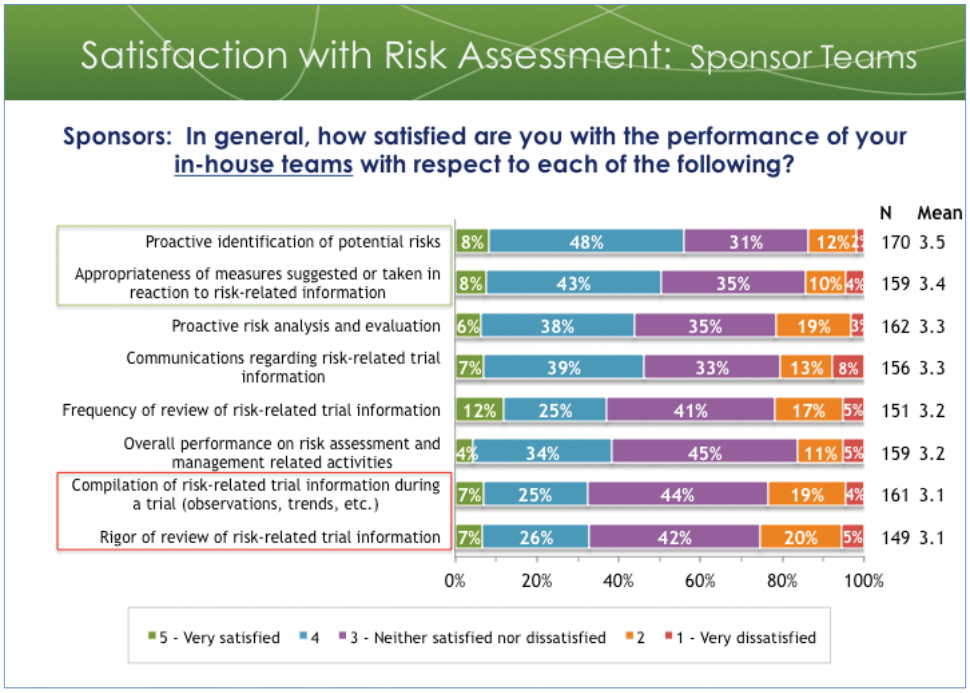


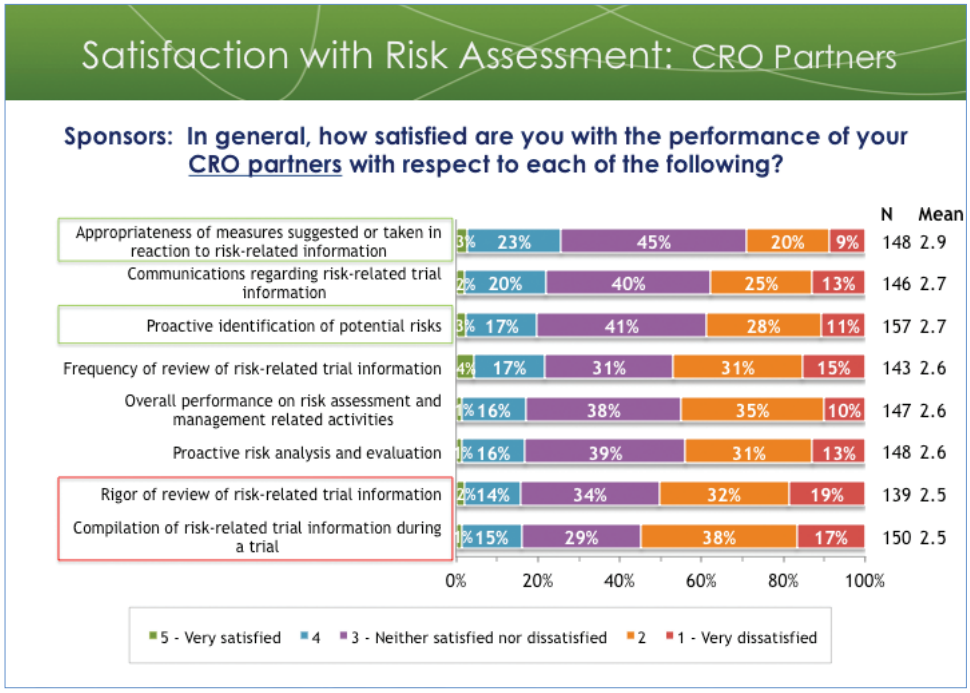
As the charts above show, systematic risk assessment processes for outsourced clinical trials are used to varying degrees among the teams with which respondents work. The approaches themselves also vary a great deal in rigor, and are frequently conducted "in silos." For example, in some cases organizations use "systematic" risk assessments that are recycled from previous studies, with no additional discussion within the team and no adaptation for study-specific nuances.

Conditions under which a systematic risk assessment process is used include:

- During RFP process
- Ad hoc
- At program level, not study level
- For full-service CRO relationships
- For high-risk, complex, or large studies
- For audit strategy
- Upon sponsor request
- For key clients
- When resource limitations are a big concern

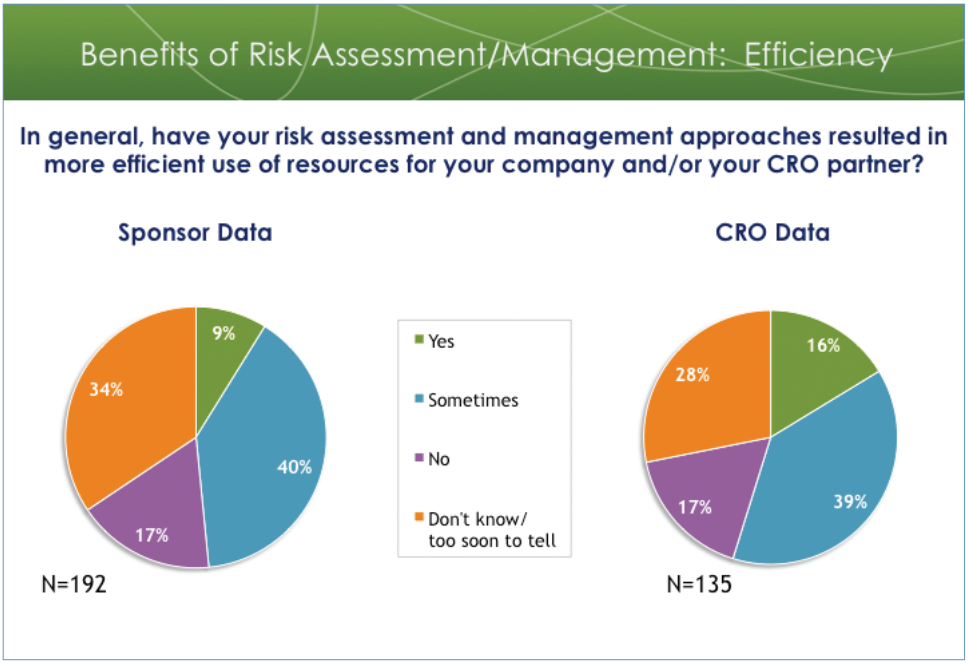
INTERIM RESULTS FROM 2013 QUALITY CONSORTIUM ASSESSMENT





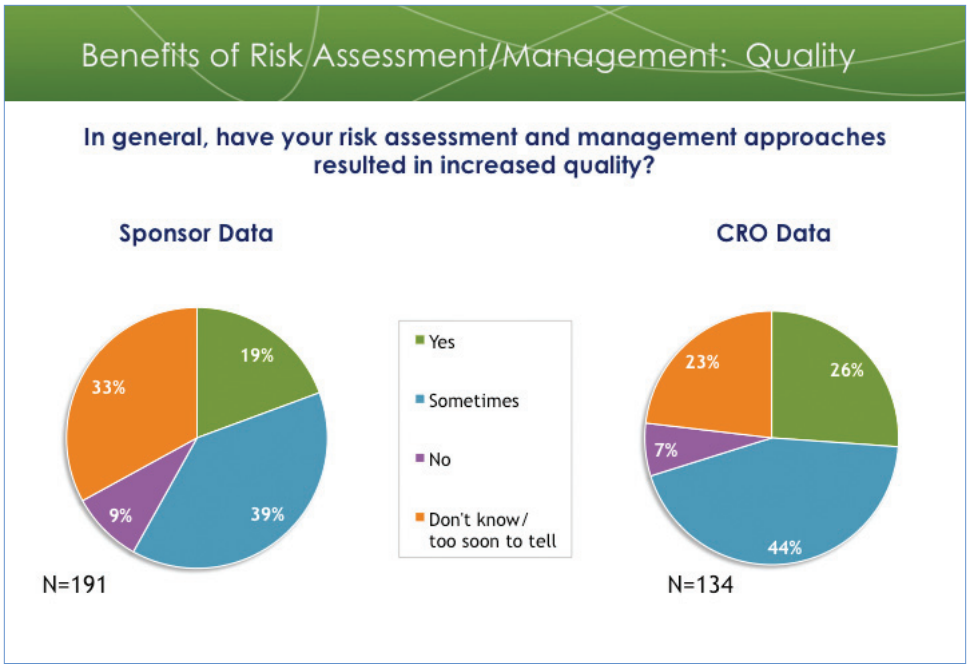
INTERIM RESULTS FROM 2013 QUALITY CONSORTIUM ASSESSMENT

According to the satisfaction ratings obtained from respondents, risk assessment and management are often not strengths of their own organizations or their partners. The ability to accurately assess and manage risks requires deep therapeutic area and operational knowledge, as well as an understanding of the development plan and product strategy, the purpose of the study, and contingencies. It also requires accountability, and a vested interest in success. Support from senior leadership teams is critical, as is an appropriately balanced focus between quality, cost, and timelines. Panelists noted the need for trust and transparency across partners, and for the ability to "put it on the table" without fear or judgment. Risk assessment requires, but does not always attain, a proactive thinking approach rather than a "pure" lessons learned approach that extracts issues from previous studies that may or may not reflect probable important issues for the current study. For CROs, risk assessment may also require a focus on reputation and financial and legal risks, in addition to timelines and compliance.



The figure above illustrates the perceived link between the use of risk assessment/management and efficiency. Some respondents stated that risk assessment and management approaches required that more resources be allocated to the present execution of a trial, while "savings" and efficiencies were measured later in the trial or at regulatory defense. Others raised the point that a lack of proactive risk assessment and management can lead to surprises, resulting in overreactions in analysis and remediation that require more resources than would have been devoted had a proactive approach been used. One respondent stated that it was difficult to see the expected gains from risk assessment approaches, because "we are simply not very good at it yet."

INTERIM RESULTS FROM 2013 QUALITY CONSORTIUM ASSESSMENT



The figure above illustrates the perceived link between risk assessment/management and quality. While not all sponsors are seeing more efficient use of resources through risk assessment and management approaches, most sponsors are seeing increased quality, at least sometimes. Significant proportions of respondents believed that it was too soon in the development of their risk assessment and management approaches to assess the ultimate impact on quality.

Verbatim responses from sponsors and/or CROs regarding challenges and keys to success are summarizedon the following page.

INTERIM RESULTS FROM 2013 QUALITY CONSORTIUM ASSESSMENT

Challenges In Successful Risk Assessment/ Management

- People see it as adding complexity – they know the risks anyway
- Management or partner buy-in for proactive rather than reactive action ("extra cost")
- Getting all stakeholders (departments, partners) to understand (appropriate background), prioritize, and participate
- Timing – needs focus at study start, when other activities are also "burning"
- Not part of the "day job" but a "bolt-on"
- Lack of basic understanding of concepts/process
- Poor facilitation that is list-driven rather than analysis-driven
- Difficult to identify the actual risks correctly, focus on the "wrong risks"
- No visible in-house experts to rely on/mentor
- Poor tools
- "Box checking" risk registers
- Poor (lagging) metrics
- Lack of appropriate data to populate tools
- Unclear accountability, for analysis and triggered actions (including CRO vs. sponsor)
- Inconsistency within sponsors in how this is handled– vendors don't know what to expect
- Process "completely foreign" to vendors beyond CROs
- Fear of "being exposed"

Keys To Succesful Risk Assessment/ Management

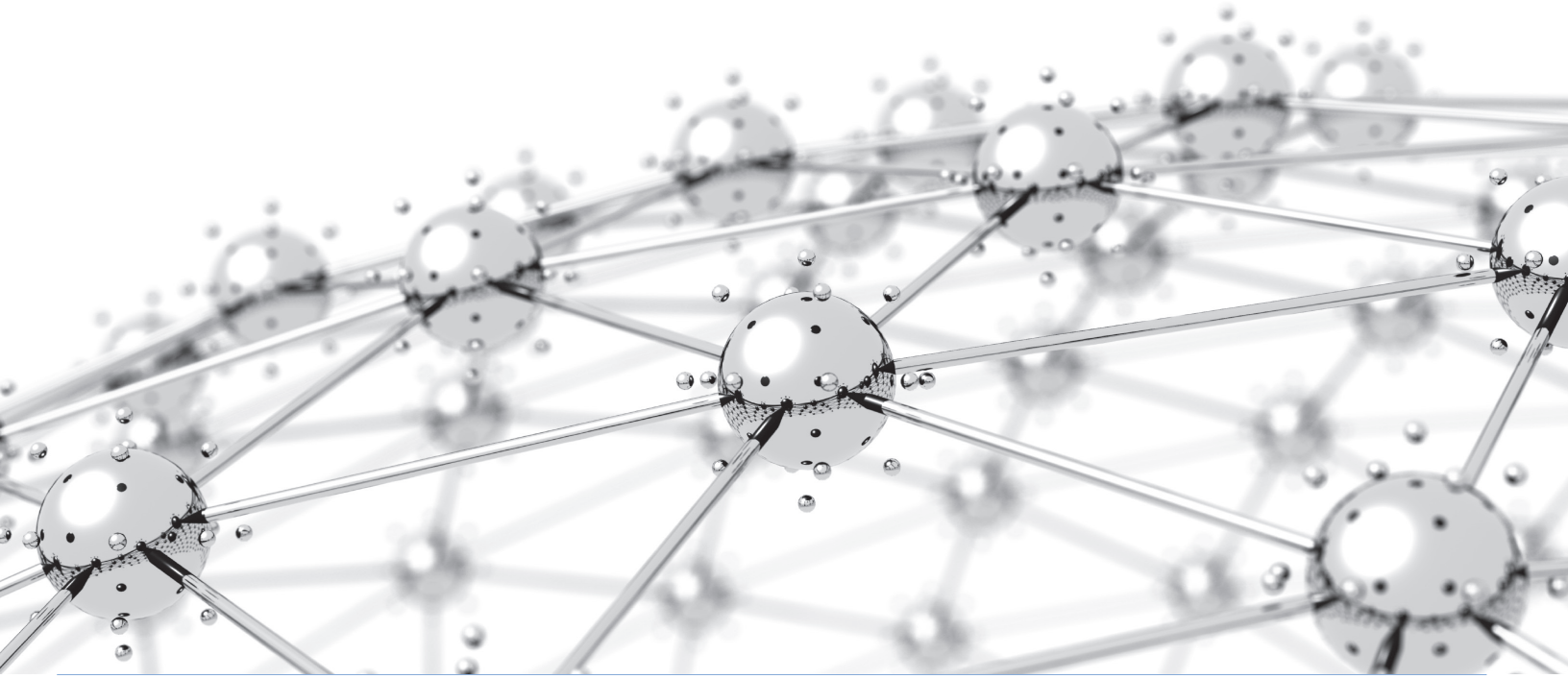
- Vested interest in success
- Trust/transparency between partners
- Budgetary allowance/support from management
- Enforcement of/accountability for process and stipulated actions
- Education on risk assessment and resource allocation according to risk
- Appropriate "mature" experience (therapeutic area, operational, development) and multifunction team to "integrate" risks
- Well-defined roles and responsibilities in assessment and in the action plan
- Right tools/technology/approach to define and monitor risks
- Initial assessment in parallel with protocol writing
- Examples of previous plans to trigger discussion – use of Lessons Learned
- Good metrics
- Beyond recruitment
- Qualitative and quantitative, with scoring
- Update/review throughout a trial - recognized that risks are "dynamic" in that risks may change in probability or level of impact, and the responses, mitigations, or contingencies may need to change as well.

CONCLUSION: CHANGING THE PARADIGM ON QUALITY

In conclusion, the industry is expressing the need for more effective oversight of outsourced trials through effective partnering between sponsors, CROs, and regulators. The importance of a culture of quality was stressed, as culture and quality are closely linked.

The opportunity for the industry to enhance approaches to risk assessment and risk management was a resonating theme at the Avoca Quality Consortium Summit. Risk assessments are often done at the start of a trial, but not actively managed throughout a clinical trial program. There are differences in the risk-tolerance between sponsor companies, which are sometimes related to regulatory warning letters, that impact their risk management approach and level of oversight. Additionally, there are gaps in communicating risk-based approaches from the executive level to the operational teams creating challenges with implementing the approach. This signifies an opportunity for training.

The prevailing thought at the Avoca Quality Consortium Summit was that the industry needs to adopt a more proactive approach to quality management, and think of quality as a key component that is built into the clinical trials process from the beginning, and embedded into the culture of an organization, rather than something that is tacked on or is someone looking over our shoulder. This approach will enable organizations to improve their operational efficiency and strike the right balance between time, cost, and quality.



UPCOMING CONTENT AND ONGOING CONNECTIONS

Although the Quality Summit is over, our work for the Consortium is always in motion. The Avoca Quality Consortium team is committed to keeping its Members up to date on our activities throughout the year.

Stay tuned for our Monthly Newsletter! It features updates on industry news related to quality management.

GET CONNECTED TO THE AVOCA QUALITY CONSORTIUM COMMUNITY TODAY

Twitter: @TheAvocaGroup

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www.theavocagroup.com

SAVE THE DATE!

THE AVOCA GROUP
QUALITY CONSORTIUM
SUMMIT 2014

Avoca Quality Consortium Member Working Session

October 10th, 2013
Princeton, New Jersey

The Westin Princeton at Forrestal Village
201 Village Boulevard
Princeton, New Jersey 08540

The focus of the interactive one-day workshop will be on the implementation and socialization of quality oversight and proactive quality management guidelines and tools within your organization.

2014 Avoca Quality Consortium Summit

May, 2014
Princeton, New Jersey
www.theavocagroup.com

If you are interested in sponsoring Avoca's 2014 Quality Summit, please contact Danya.Burakoff@TheAvocaGroup.com or 619-994-8677.

NEXT STEPS: THE FUTURE OF THE AVOCA QUALITY CONSORTIUM

Avoca welcomes greater involvement in the Quality Consortium from existing Member companies as well as new Consortium Members. Avoca is committed to using the Consortium as a catalyst for change and action, and as a vehicle for bringing together companies interested in positive change within the industry in a short period of time.

Avoca believes that the key to success in developing industry standards for proactive quality management is collaboration and senior executive involvement. We will continue to provide the platform for collaboration and engage the executive leadership of our Members to ensure that standards developed as part of the Consortium and agreed upon by Members are effectively implemented.

Future focus areas to be addressed by the Consortium will be those that the Consortium and its Members feel will have the greatest impact within the shortest period of time, and where high value can be ensured. These will be areas in which there are needs for collaboration to ensure efficiency and cost savings while focusing on high quality.

Over the two days of the Quality Consortium Summit, we heard repeated calls for action. How do we encourage an industry that has been historically slow to change, to move forward in ways that might not be comfortable at first? One executive asked, “How do we go from an idea of what we should be doing in risk management, to something that is being implemented throughout the industry?”

For 2014, The Avoca Quality Consortium will obtain directional input from Member organizations to refine strategies focusing on the area of Risk Mitigation to help the industry move forward with a plan to establish key risk indicators.

THE AVOCA GROUP

QUALITY CONSORTIUM SUMMIT 2013

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