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Mock Inspections: A Critical Tool To Ensure Inspection Readiness

WEBINAR PRESENTED BY:

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HOSTED BY:

eXL events

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Meet Your Presenter

Kristen Jonathan Bennett

Associate Director, Client Delivery

The Avoca Group

A member of the Avoca Group's integrated consulting and Avoca Quality Consortium® workstreams, Kristen Bennett provides consulting services to top pharmaceutical, biotech, and contract research organizations, and oversees client deliverables, systems, and processes across The Avoca Group.

Kristen has expertise in clinical trial execution, process development, and strategic management. Her previous professional roles include project, data, and site management.

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Webinar Objectives

- Demonstrate how periodic screenings are an important part of inspection readiness
- Discuss where hidden challenges lurk and how periodic screenings can bring these items to light
- Formulate appropriate remediation plans that are organizationally focused and not study specific

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Agenda

- Polling Question – Getting to know you
- The evolving and complex GCP landscape
- The importance of periodic health checks/screening
- Considerations for your Inspection Readiness/Wellness Plan
- Check Ups/Screenings – What should be in your toolbox
- Q&As

The Avoca Group

A life sciences consulting firm dedicated to improving **quality** and **compliance** in the clinical trial execution process.

Our mission is **to have a positive impact on all clinical trials** by helping clinical research companies increase quality, ensure compliance, and improve efficiency so that medicines can reach patients faster.

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Avoca Quality Consortium® (AQC)

100+ Member Companies: Sponsors, CROs, Clinical Service Providers, and other organizations engaged in clinical trial execution.

Avoca Research: Quantitative and qualitative data from across the industry on key topic areas.

Leading Practices: Access to 450+ guidelines, tools, approaches, standards, and templates focused on proactive quality and risk management.

Collaboration: Leadership Advisory Boards, Annual Quality Summit, Working Sessions, Regional Networking Events, Educational Webinars, and Online Community, *Aha!*

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Current AQC® Members

as of 6/26/2019

Polling Question

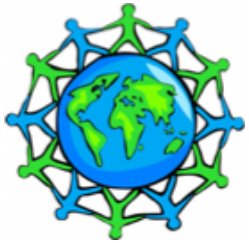
Has your company established any good measurements or indicators of “inspection readiness”?

a) YES – We have a fully established process to measure inspection readiness

b) SOMEWHAT – We are in the process of establishing ways to measure inspection readiness and/or a mock inspection process

c) NO – We have no formal mock inspections or ways of measuring inspection readiness

The Evolving GCP Landscape



- Number of inspections is on the increase worldwide
- ICH E6 (R2) implementation is expanding
- Sharing of information and approaches between regulators (e.g., EMA/FDA joint inspection experience)
- Increasing use of global data in newer markets (e.g., China)
- Emerging market regulators starting foreign inspections
- Focus on data integrity, particularly with e-Systems (eCOA, eTMF)
- Challenges of applying quality principles to new technologies (e.g., artificial intelligence, wearable devices)
- Trial design- more complex, innovative

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ICH E6 (R2) – What Has Happened and Why?

Sets a More Modern Standard for Clinical Study Processes

- GCP Inspection findings have surfaced topics/expectations that needed further guidance/clarification
- Imperatives in the pharmaceutical industry
  - Conduct trials more efficiently
  - Drive cost reductions and help deal with increasing complexity
  - Improve patient safety, rights, and data integrity in addition to data reliability
- Technology offers important tools and opportunities
  - Utilize new and better technological solutions
  - Expand capabilities to use trial information in real time to make informed decisions
- ICH E6 (R2) takes this evolution and technology into consideration and encourages sponsors to pursue innovative approaches

ICH E6 (R2) Directly Affects Operations

Proactive Quality Management - Incorporates QbD

- Minimize risk through planning; early signaling and mitigation of problems
- Use data and pre-established tolerance limits for decision making
- Execute routine risk reviews
- Investigate root causes of emergent problems as part of corrective action process

Risk-based Strategies

- Provide oversight commensurate with risks that matter
- Document rationale for chosen strategy; reconcile roles/responsibilities and monitoring/oversight reports with chosen strategy
- Responsive/dynamic vs static system of oversight
- Risk-based Monitoring Plan, Risk-based Oversight, Risk-based Inspection Preparedness and Risk-based Quality Management must be documented as appropriate QMS

Oversight

- Sponsor and Investigator retain accountability for quality

Important ICH E6 (R2) Changes

Electronic Systems

- Validation and quality control through qualified users and SOPs covering system setup, installation and use
- Implicitly advises to move away from paper-based CRFs/tracking systems

Serious Breaches

- Inform regulators, where warranted by local authorities, when non-compliance is a serious breach of protocol or GCP

Essential Records

- ALCOA+C; location of source/essential documents
- Some process documents become essential documents
  - Risk review requires traceability of decision making
- Must document how risk management oversight is exercised (Monitoring Plan/Integrated Quality Management Plan) – Quality Management Plan; outcome of any centralized/statistical monitoring with actions taken
- Monitoring activities should be traceable and documented
- End of trial report on effectiveness of risk management

ICH E6 (R2)

ICH E6 (R2) expects a more comprehensive, holistic oversight program that reflects:

- **Risk-based thinking** incorporating **risk management into supplier selection** at the organizational, operational and trial levels

- **Prescribed risk management steps**
  - **Critical process/data** ID, risk ID, evaluation, control, communication, review, reporting and **root cause analyses** for excursions outside of tolerance limits/emerging risks

- Data-based, repeatable, and **objective risk assessments**

- **Proactive and proportional management** of risks/opportunities
  - Determine risk measures, tolerance limits, treatment actions/controls
  - Continuously improve through application of emergent CAPAs; review of risk management choices to ensure they remain effective and relevant

- **Auditable documentation**
  - All risk management and continuous improvement **activities and decisions**
  - Presents and **justifies control and optimization choices**/strategies

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Inspection Readiness

Proactive and Risk-based

- ICH E6 (R2) encourages sponsors to pursue innovative approaches
- Inspection Readiness needs to keep pace with this philosophy:
  - Proactive
  - Risk-based
  - Flexible/Agile

The Importance of Periodic Health Checks & Screenings

Benefits of
Inspection Readiness
Screenings/Wellness Plan

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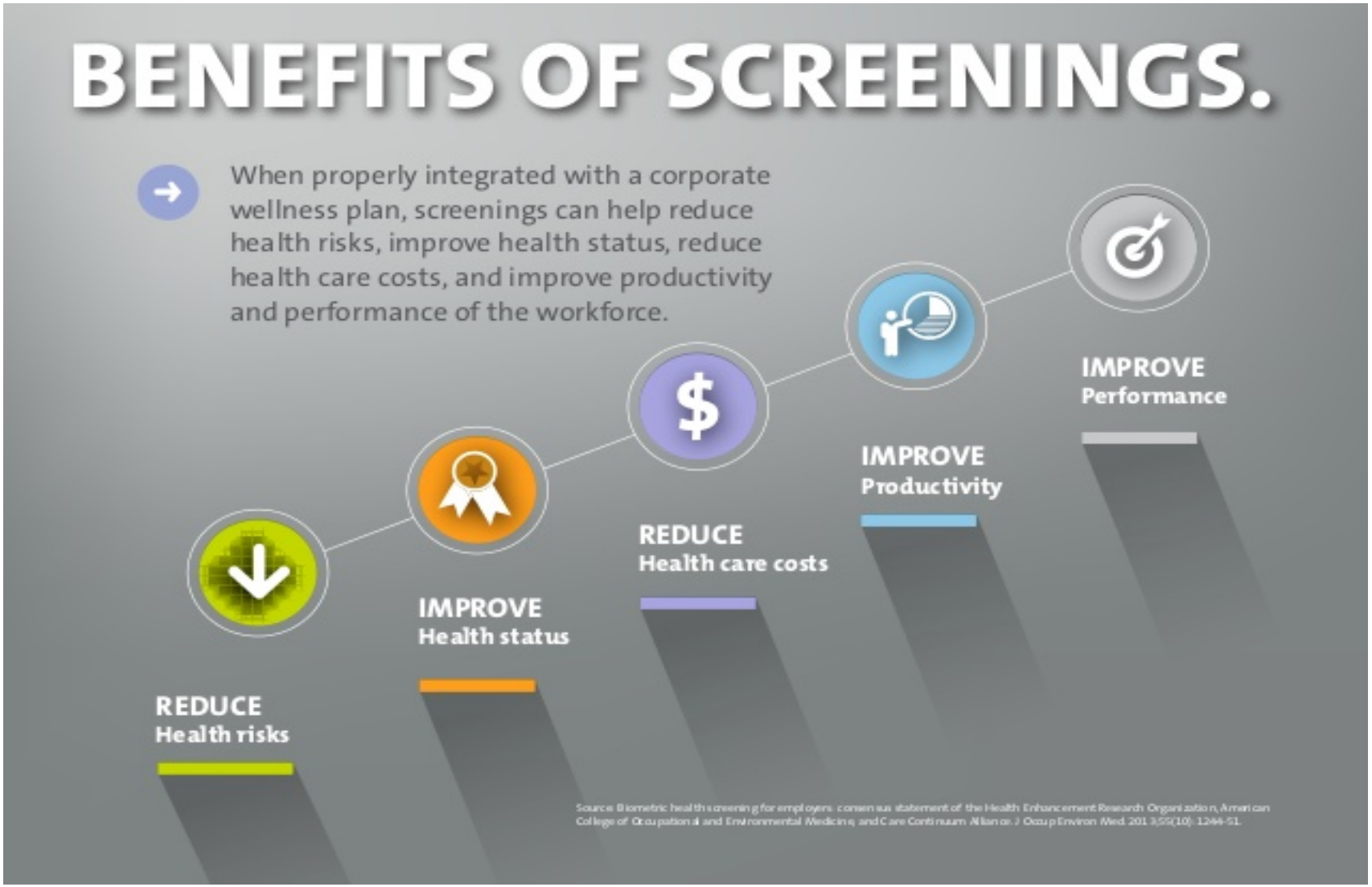
Benefits of Health Screenings/Wellness



Biometric health screening for employers: Consensus Statement of the Health Enhancement Research Organization, American College of Occupational and Environmental Medicine, and Care Continuum Alliance. J Occup Environ Med. 2013; 55(10):1244-51.

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Polling Question

How important is it to your company to be better prepared for upcoming inspections (with less stress at the last minute!)?

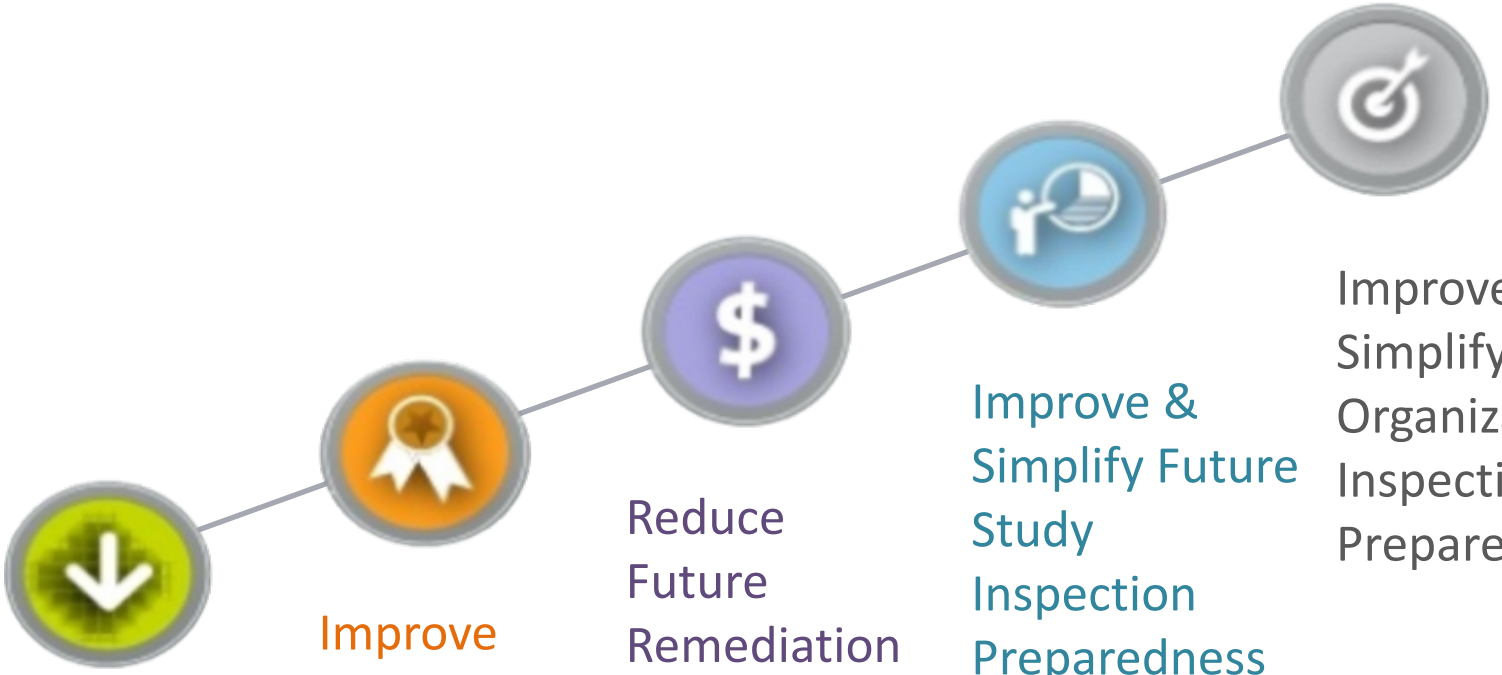
a) This is one of our top priorities

b) This is important, but not our top priority

c) Somewhat important

d) Not important at all

Benefits of Inspection Readiness Screenings/Wellness Plan



Baseline Survey Results – Overall Understanding

Surveys were distributed to core and extended study team members prior to the Study Health Check Kick-Off Meeting

FSI Milestone Studies

Please select who you feel is accountable for inspection readiness?

More Details

Global Study Leader (GSL)	12
Director of Clinical Developme...	1
Core Study Team	6
Core Study Team + Extended ...	29

Please rate your level of understanding with regards to what is required for a study to be inspection ready.

More Details

Clearly understood	14
Moderately understood	26
Somewhat aware	6
Unaware	2

Baseline Survey Results – Overall Understanding

Maintenance Studies

Please select who you feel is accountable for inspection readiness?

More Details

Global Study Leader (GSL)	5
Director of Clinical Developme...	0
Core Study Team	2
Core Study Team + Extended ...	16

Please rate your level of understanding with regards to what is required for a study to be inspection ready.

More Details

Clearly understood	9
Moderately understood	12
Somewhat aware	2
Unaware	0

Baseline Survey Results – Overall Understanding

DBL Milestone Studies

Please select who you feel is accountable for inspection readiness?

More Details

Global Study Leader (GSL)	4
Director of Clinical Developme...	1
Core Study Team	2
Core Study Team + Extended ...	11

Please rate your level of understanding with regards to what is required for a study to be inspection ready.

More Details

Clearly understood	5
Moderately understood	9
Somewhat aware	4
Unaware	0

Baseline Survey Results – Study Specific

FSI Milestone Studies

Questions 16-19 relate to inspection readiness specifically for your current study. If your study was inspected today, how confident are you with your functional area's (SMO, Stats, programing, DM, medical oversight, etc.) level of inspection readiness?

More Details

Extremely confident	2
Very confident	10
Somewhat confident	36
Not so confident	1
Not at all confident	0

Baseline Survey Results – Study Specific

Maintenance Studies

Questions 16-18 relate to inspection readiness specifically for your current study. If your study was inspected today, how confident are you with your functional area's (SMO, Stats, programing, DM, medical oversight, etc.) level of inspection readiness?

More Details

Extremely confident	0
Very confident	6
Somewhat confident	14
Not so confident	3
Not at all confident	0

Baseline Survey Results – Study Specific

DBL Milestone Studies

Questions 16-18 relate to inspection readiness specifically for your current study. If your study was inspected today, how confident are you with your functional area's (SMO, Stats, programing, DM, medical oversight, etc.) level of inspection readiness?

More Details

Extremely confident	0
Very confident	0
Somewhat confident	15
Not so confident	3
Not at all confident	0

Inspection Readiness/Wellness Plan

It Starts with an Inspection Readiness/Wellness Plan

- Proactive: Forward thinking, active approach
- Risk-based: Focused activities on areas of greatest risk
- Flexible/Agile: Adaptable to changing timelines, resources, risks

Polling Question

At your company, when do you prepare for an inspection?

a) At the time we file a new application

b) On a continual basis

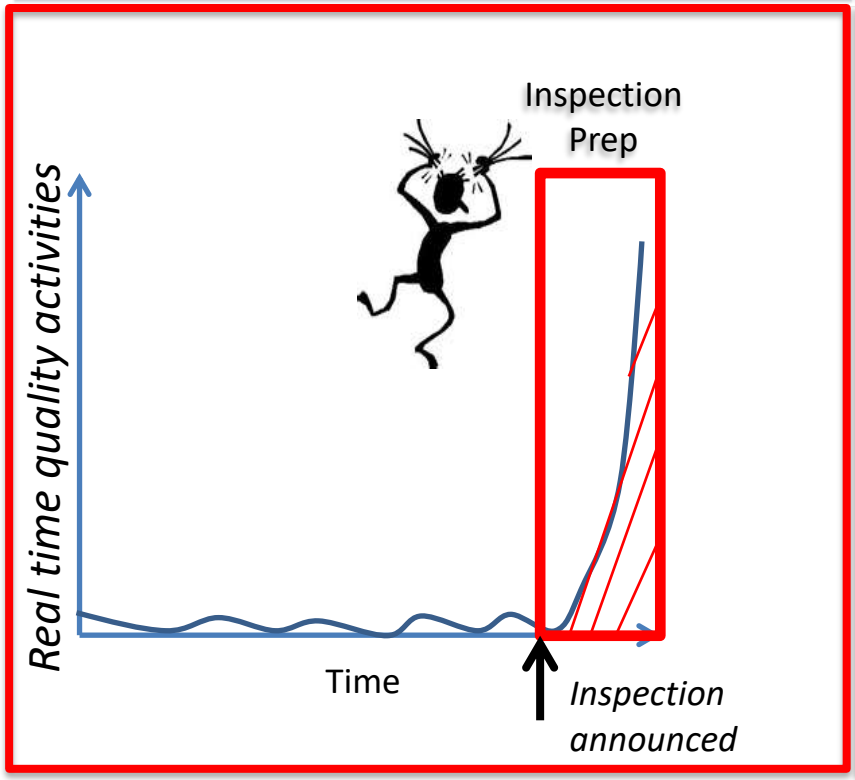
c) When we anticipate an inspection for reasons other than filing

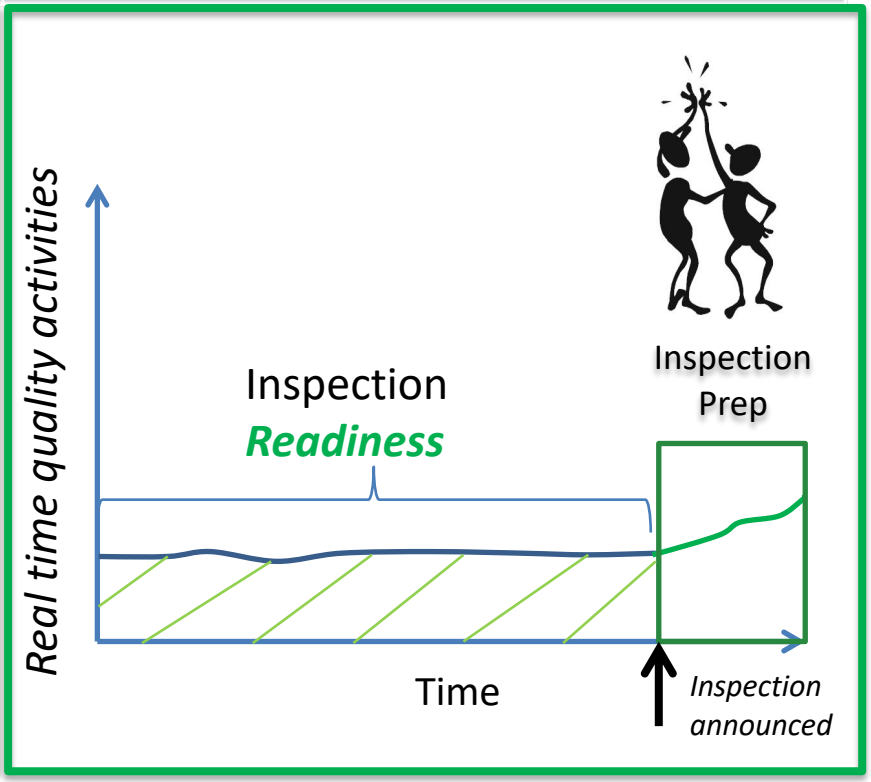
d) We don't prepare for inspections

Proactive Approach: Preparedness vs. Inspection Readiness

The aim to move the current state from variable reactive processes to a comprehensive system which yields a proactive state of Inspection Readiness.

Inspection Preparedness	Inspection Readiness
Effort to prepare documentation, people, systems and processes for inspections	State of being; not a preparation activity; it is more than a "one time" event





Inspection Readiness/Wellness Plan Considerations

- Standard Inspection Readiness Plan/Road Map
- Tailored for each trial in tandem with Risk Assessment
- Revisited when new risks/timelines are identified
- Identifies the appropriate Inspection Readiness action(s)/checks and timing based on the risk
- Outlines process for tracking and communicating and new resulting risks
- Includes the feedback loop for organizational improvement
- Describes expectations for lessons learned activities

Mock Inspection

Things to consider…

- What areas need to be considered when planning a mock inspection?
- Who needs to be involved?
- What is the appropriate timing for a mock inspection?

IR Plan: Common Risk Areas to Consider

(Based on Common Inspection Observations)

EMA

- Essential documents
- Source documentation
- Protocol compliance (safety reporting and selection criteria)
- Investigator site

MHRA

- Record keeping/Essential documents
- Pharmacovigilance
- Data integrity
- Monitoring
- Quality systems

FDA

- Inadequate monitoring
- Inadequate accountability for the investigational product
- Failure to obtain FDA and/or IRB approval prior to study initiation
- Failure to bring Investigators into compliance:
  - Protocol deviations
  - Inadequate investigational product accountability
  - Inadequate subject protections

2014 → 2017

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IR Plan: Common Risk Areas to Consider

- Trial documentation (TMF)
- Critical trial processes
  - Informed Consent
  - Protocol deviations
  - Monitoring
- Investigator site trial execution
- Critical trial data and analysis (data integrity)
- Team knowledge and preparation

Periodic Check Ups and Screenings

What is in Your Toolbox?

Periodic Screening/Health Check Activities

Planned throughout the conduct of the trial:

- Document quality control checks/review
- Co-monitoring/on-site visits
- Sponsor oversight visits
- Metrics & performance reviews
- Investigator site risk review
- Periodic self and/or independent assessments
- Regular risk assessments & reviews
- Issue management (with proactive storyboarding)
- Audits
- Scorecard
- Mock inspection

Results

Periodic Inspection Readiness Screenings/Health Checks can often uncover hidden challenges. A few examples:

- Project teams that are not trained in Regulatory Inspection Interviews
- Study documentation is incomplete, missing, and/or inadequate
- Study activities are not executed according to process/procedure and/or protocol, unclear processes, or process gaps
- Study oversight and risk management activities are not effectively identifying and mitigating risks and issues
- Inadequate documentation of transitions, handovers

Remediation Plans

Effect an Organization

The goal is not just to correct the impacted study, but ensure the rest of the organization is learning:

- Create a library of lessons that future teams can access as they plan for a new project or a new phase of a project
- Reduce the likelihood that teams experience the same or similar issues over and over again; openly share experiences and update clinical tools
- Share and replicate new practices or ideas that allowed a prior project to run more smoothly; define feedback loop into continual improvement and operational excellence initiatives
- Improve conformance to budget and timeline and improve the quality of future project execution
- Reduce the number of “negative surprises” and repeat inspection observations on future projects

Summary

Confident Risk-based Inspection Readiness in three key steps:

*Remember: Proactive Quality Management is **the key** to Inspection Readiness!*

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Questions?

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Upcoming Webinars & Conferences

T3: Tech, Trials and Transformation

August 8-9, 2019 | Philadelphia, PA | Join Avoca for these sessions…

- *The Future Evolution of Partnerships and Collaborations — Accelerate Timelines, Reduce Costs and Increase Engagement and Success in Your Clinical Trials*
- *State of the Industry Report — Analysis of The Avoca Group's Survey of Emerging Technology and Data Sources in Clinical Trials*

[WEBINAR] AQC Knowledge Center Monthly Demo

August 13, 2019 | 11:00am – 12:00pm EDT

- *Held the second Tuesday of every month and open to the industry, this Webinar offers a live demonstration of the AQC Knowledge Center.*

ExL's 8th Clinical Trials Inspection Readiness Summit

August 14-15, 2019 | Philadelphia, PA | Join Avoca for this session…

- *Mock Inspections: A Critical Tool To Ensure Inspection Readiness*

ExL's 10th Clinical Quality Oversight Forum

October 16-18, 2019 | Philadelphia, PA | Join Avoca for this session…

- *KEY FINDINGS FROM THE TUFTS CSDD-AVOCA VENDOR QUALIFICATION BENCHMARKING STUDY: Quantify Vendor Qualification Practices and Experiences and Identify Improvement Opportunities*

8th Annual AQC Fall Member Meeting

November 7, 2019 | Seattle, WA

- *Attendance at the Fall Member Meeting is one of many benefits of Membership of the Avoca Quality Consortium. Participants gain practical knowledge and experience in a casual, interactive learning environment.*

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THANK YOU FOR PARTICIPATING!

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