Remote Compliance Auditing During the Covid-19 Pandemic

Julie Barnhill, PhD

Meridian BioGroup LLC

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PDA Parenteral Drug Association Capital Area Chapter

MERIDIAN BioGroup

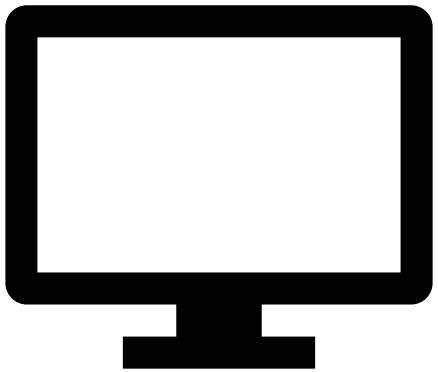
4539 Metropolitan Court
Frederick, MD 21704

301.360.9771
www.meridianbiogroup.com

Agenda

- Why remote auditing?
- Advantages and disadvantages of remote audits
- Conducting and optimizing remote audits
  - Planning/Scheduling
  - Design of effective agenda
  - Audit Execution
  - Close out and reporting
- Challenges to consider
- Questions and Answers

Poll Question #1



"I can't remember—do I work at home or do I live at work?"

Why perform audits?

Compliance audits are necessary for critical GXP* suppliers to ensure that they meet compliance and quality standards. Further, the FDA views suppliers as an extension of the sponsor:

200.10 Contract facilities (including consulting laboratories) utilized as extramural facilities by pharmaceutical manufacturers.

(b) The Food and Drug Administration is aware that many manufacturers of pharmaceutical products utilize extramural independent contract facilities, such as testing laboratories, contract packers or labelers, and custom grinders, and ***regards extramural facilities as an extension of the manufacturer's own facility.***

***GXP = cGMP, GLP, GCLP, GCP**

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Why remote audits?

Few might have anticipated how our lives would change with the Covid-19 pandemic this year,

BUT

The work of qualifying and monitoring GXP vendors (cGMP, GLP, GCP and GCLP) must continue to ensure contracted work is performed in a compliant manner as these essential companies contribute towards drug development and/or provide much-needed clinical and commercial drugs to patients.

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Why remote audits?

- Social distancing guidelines, travel restrictions, and efforts to eliminate non-essential personnel on sites force us to be creative and perform effective remote audits now and for the foreseeable future.
- Companies must perform risk assessments of its suppliers to determine which remote audits should be performed as a priority. If possible, audits of critical suppliers should not be postponed.

Qualification and monitoring audits must stay on track!

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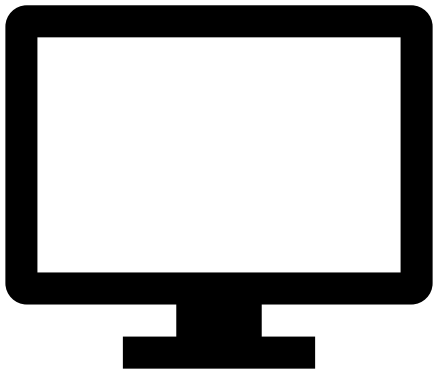
Poll Question #2

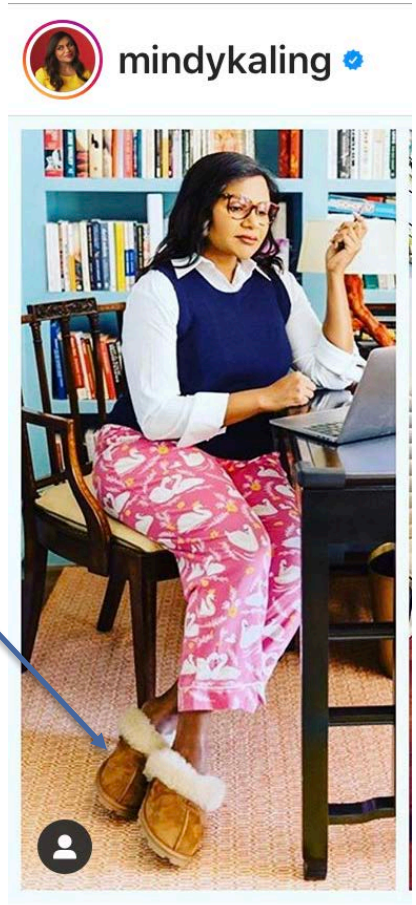


Advantages and Disadvantages of Remote Audits

ADVANTAGES	DISADVANTAGES
Safe and effective	Limited or no ability to visualize facility and equipment, culture of the organization, and the body language of the auditees
More flexible with scheduling	Time zone issues (more on this later!)
No travel time and travel costs	Lag in speaking with Subject Matter Experts (SMEs)
Requires the auditor to be more prepared than while on site (no tour to drive document requests and discussions)	Auditor burn out--there are no tours or lunches with the auditees to break up the day
You can assess the compliance status of an organization from your home office while wearing slippers	No time for spontaneity with regards to document and SME requests

Working from home according to Mindy Kaling

Slippers are a must along with good lighting!



Remote Audit Conduct

- **Good planning is the key to an effective audit!**
  - Is the supplier willing, able and ready to host a remote audit? Do they have the IT infrastructure/capability to share a large number of documents electronically in a secure manner?
  - A detailed audit letter with an agenda must include the scope of the audit and what will be covered specifically and at what times
  - A questionnaire and detailed list of documents that you want to review (including SOPs) should be shared at least 2-3 weeks prior to the audit date(s)
  - Do your homework! You want to find out as much as possible about the company you will be auditing before the audit date
  - If it will be a repeat/surveillance audit, review past reports so you can zero in on previous observations and confirm they have been addressed and fully resolved

Remote Audit Conduct

What should your letter, agenda and document request list look like?

Audit Letter Excerpt

Purpose and Scope of the Audit

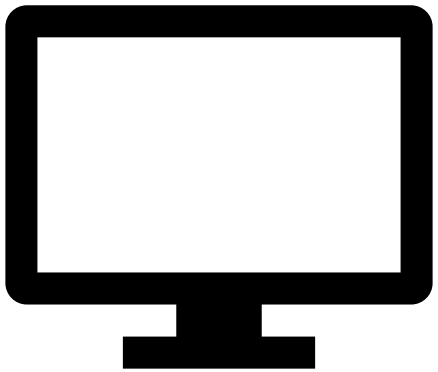
The purpose of this audit is to assess the cGMP compliance (21 CFR 210 and 211) of your quality systems, *production controls, facilities and equipment, organization and personnel, and technical capabilities related to the aseptic filling/manufacturing, visual inspection, packaging, release testing, and stability storage and testing of phase 1 clinical trial material batches of ABC drug product.*

The scope of this audit will include an assessment of the overall compliance with the Current Good Manufacturing Practices and related documentation.

In order to prepare for an efficient audit, please forward any pre-audit preparation package that may exist for the facility. As permitted by your procedures, please provide a copy of the following by 17 August:

1. *Organizational Chart*
2. *Floor Plan*
3. *List of Licenses and Certifications*
4. *Controlled Document Index*
5. *History of Regulatory Inspections (5 years) including a summary of findings*
6. *Quality Manual*

Poll Question #3



Audit Agenda-Overseas Remote Audit Day 1

Time	Schedule
6:00 a.m. EDT, 1:00 p.m. (GMT+3)	Opening meeting ▪ Introductions; review agenda and audit objectives ▪ Organizational overview ▪ Brief Company/Facility Presentation presented by Company ▪ Virtual tour of warehouse, GMP suites and Quality Control and Microbiology Laboratories ▪ Media fill SOP and record review and discussions
6:30-9:30 a.m. EDT, 1:30-4:30 p.m. (GMT+3)	Document review, SMEs discussions on training, quality systems and equipment • Site Master File • Validation Master Plan • Quality Systems SOPs and Quality Metrics • Management Review • Deviations, OOSs, CAPAs • Change Control • Equipment Records and SOPs • Training and qualification of personnel including operators and visual inspection personnel • Environmental Monitoring Trend Reports • Computerized Systems
9:30 a.m. EDT, 4:30 p.m. (GMT+3)	Brief check-in discussion and planning for Day 2
9:45 – 3:30 p.m. EDT	Document review, continued

Audit Agenda-Overseas Remote Audit Day 2

Time	Schedule
6:00 a.m. EDT, 1:00 p.m. (GMT+3)	Brief call to discuss comments and questions from Day 1, audit plan for Day 2
6:15-7:00 a.m. EDT, 1:15-2:00 p.m. (GMT+3)	Quality Agreement Discussion
7:00 – 9:30 a.m. EDT, 2:00– 4:30 p.m. (GMT+3)	Document review, SME discussions • Review of Laboratory Controls • Material and Product Controls • Internal and External Audits and Supplier Controls
9:30 – 9:45 a.m. EDT, 4:30 – 4:45 p.m. (GMT+3)	Auditor review of notes and findings
9:45 – 10:00 a.m. EDT, 4:45 – 5:00 p.m. (GMT+3)	Audit close out meeting

Detailed list of documents to review

- **Tip 1** - Request an SOP index prior to the audit and provide the list of SOPs you want to review during the audit so they are waiting for you when you start!
- **Tip 2** - Be as specific and comprehensive as possible when generating the list of documents you want to review. While you will have some time to request other documents during the audit, it will make for a more efficient and smooth audit if you can anticipate and request all documents for review BEFORE the audit.

Detailed list of documents to review-Part 1

1. Organization Chart
2. Floor Plan
3. Detailed floor plan for manufacturing areas that includes air, personnel, materials, product and waste flow
4. SOP Index
5. Quality Manual
6. Validation Master Plan
7. Site Master File
8. GMP Equipment List
9. Changeover SOP
10. Risk Assessment/Report for introduction of new products into your facility
11. List of Computerized System and each system's function and validation (21 CFR part 11) status
12. Equipment Validation/Qualification SOPs
13. IOPQ, Calibration and Preventive Maintenance Documentation for 4 pieces of equipment (-20 °C and 2-8 °C Controlled Temperature Units, Sterility Incubator, Autoclave)
14. Regulatory Inspection History Summary from 2017-present including inspection reports, observations and responses
15. SOPs for Sterility Testing, Endotoxin and Bioburden
16. Deviation and CAPA SOPs
17. Out of Specification SOP
18. Change Control SOP
19. Supplier Qualification SOP
20. Evidence of Qualification of at least two critical suppliers or contractors (report cover sheet, etc.)
21. Approved Supplier List
22. Data Integrity SOP
23. Disaster Recovery SOP
24. Business Continuity SOPs/Plans for supply chain, personnel, etc.
25. Risk Management SOP

Detailed list of documents to review-Part 2

26. Aseptic Process Validation (Media Fill) SOP
27. Gowning Qualification SOP and qualification documentation for a current technician/operator
28. Media Fill Schedule that contains vials filled, vial, stopper and seal type and results
29. Representative/recent Media Fill Batch Record including all QC results and growth promotion testing
30. Raw Material Inspection SOP(s) and raw material file for the media used in the batch record provided in #29 above
31. Internal Audit SOP and proof of completion for audits performed in 2019-2020
32. Management Review/Quality Metric Reporting SOP and proof of completion of your most recent Management Review Meeting
33. Training SOP, Training Requirements, and Training Files for at least 3 employees including one in QA, QC and Manufacturing
34. Visual Inspection SOP
35. Qualification of Visual Inspectors SOP and representative qualification documentation for a current inspector
36. Environmental Monitoring and WFI Trend Reports for 2019 and any 2020 reports completed to date
37. Complaint SOP
38. Recall SOP
39. Batch Record Review SOPs
40. List of any/all sterility failures in the last 5 years
41. Deviations, CAPAs, OOSs and Change Controls for CLIENT

Virtual Tour

- Nice to have but certainly not all companies are willing and able to provide a virtual tour
- Some companies have uploaded facility walk-throughs on their website and these are readily accessible
- For example, LSNE offers a video library that anyone can access on its website:

https://www.lyophilization.com/resources/video-library/

Before the Audit Commences

- Double check to ensure you have all the Nondisclosure/Confidentiality Documentation executed
- Make sure you can access the document ‘share site’ prior to the audit if possible to ensure it is accessible and functioning properly
- Check with the auditees to determine how long you will have access to the documents
- Make sure you have downloaded whatever cloud platform will be used during the audit: Zoom, WebEx, Microsoft teams
- Have a list of questions that you can discuss if necessary after the opening presentation
- Create a detailed game plan for document review BEFOREHAND

At the beginning of the audit

- Provide some information about yourself during the introductions
- State the purpose and scope of the audit
- Create a communication plan for the audit:
  - Who can you email or call if you have questions?
  - Set up call times to check in (at least twice during one audit day)
  - Set up the audit wrap-up meeting date and time so that the auditees can have all necessary personnel present for the close-out
- Request a copy of their opening presentation for your records

During the audit

- Stick to the agenda but remain flexible to accommodate discussions when SMEs are available
- I recommend you start with regulatory inspections (483s, EIRs, company responses to inspections) to gauge the compliance track record for a company. Go back at least 3-5 years to ensure that there are no repeat 483 observations
- Keep detailed notes and start a table of documents reviewed during the audit that will become an attachment to the audit report (write as much during the audit to save time with the report)
- Be transparent—Don't wait until the close out meeting to share observations. You want to be sure you understand any deficiencies which will require discussions with the auditee, allowing them to correct mis-impressions if needed

Audit Close-Out Meeting

- An audit close-out meeting is a MUST to present:
  - What systems and documents were covered (high-level)
  - What observations you've identified (don't classify them until the report-more on this in the next slide!)
- Thank the auditees for their time and for hosting the audit
- Communicate when the audit report or list of observations will be presented to them (determine who will be the respondent) and request that they respond in writing within 30 calendar days

Audit Reporting

- The deliverable for the audit - the Audit Report - should look the same as if you conducted an onsite audit.
- The audit report or list of observations should be presented as a signed PDF report within 30 calendar days
- Any CRITICAL observations should be communicated immediately.
- Send a thank you email the next day to thank the audit team for hosting the audit.

Challenges to consider

- **Time zone differences.** You need to be on their time zone as much as possible.
- **No in person communication.** Use video sharing as much as possible for check-ins in addition to opening and closing meetings
- **Time**. There never seems to be enough of it during any audit. Your audit review 'game plan' must be generated before the audit. Efficiency and prep work are key.
- **Auditor Burn-out.** There are no lunches or tours to break up the audit day(s). If possible, take frequent short breaks, perform as much of the audit standing and take a walk when you normally would be having lunch at the audit site.
- **Communication**. Use screen-share to review a document with the auditees if needed as opposed to playing email ping pong.

Final Thoughts

- While remote audits cannot replace the on-site, in-person audits, they are an effective means of performing a compliance assessment of a company.
- IT infrastructure of the company being audited is of critical importance in document review.
- Patience and professionalism are important. Take your time while speaking on Zoom calls and allow each participant to speak and be heard.
- I think that the ability to perform remote audits as ‘the new norm’ won’t go away even post-pandemic, as they are quite cost-effective with no travel time or expenses.

Questions?

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Thanks for your attention!

CONTACT INFORMATION

Jbarnhill@meridianbiogroup.com

443.421.0828

Speaker Background

Julie Barnhill, PhD

Senior Technical Specialist at Meridian BioGroup providing QA Compliance expertise to Biopharma companies with products in preclinical, clinical, and commercial stages of drug development along with clients with commercial products. My primary objective is to help clients advance their drugs through the pipelines and regulatory processes.

20 years of experience in the Pharmaceutical/Biotech industry in QC/QA/Compliance, including QC Director at CBL (now Emergent), head of Compliance QA at Alpharma/Actavis; PD manager at Charles River and QA head at Osiris Therapeutics.

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Your Vision, Our Talent, Precisely Aligned.

Meridian BioGroup LLC is a Maryland-based validation, compliance, and regulatory contract service provider to the biotechnology and pharmaceutical industry. Meridian brings qualified specialists from manufacturing, quality control, quality assurance, engineering, and validation to meet its clients' needs in GXP-regulated environments, as well as compliance with ISO and CLIA.