PDA COVID-19 Webinar Series – Remote Regulatory Assessments and Inspections during the COVID-19 Pandemic: Industry Perspectives

July 30, 2020

Sponsored By:

PDA COVID-19 Task Force Webinar Series

- As part of the ongoing work by the COVID-19 Task Force a series of webinars are being created.
- The webinars are focused on the COVID-19 pandemic and its current and future impact on pharmaceutical manufacturing.
- Some of the future webinar topics in the series will cover areas such as:
  - ✓ Remote and virtual internal and third-party audits
  - ✓ Modular manufacturing to speed up available capacity
  - ✓ Keeping manufacturing facilities safe and productive during a pandemic

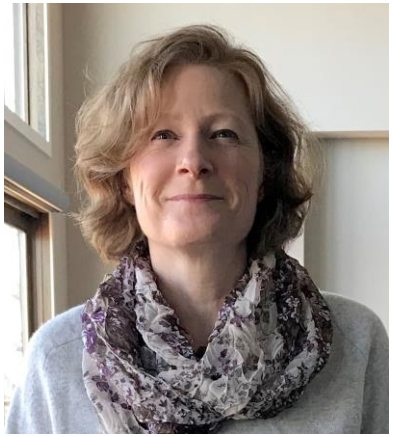
Today's Webinar

- This webinar is intended as a discussion with industry leaders on the topic of remote regulatory assessments and inspections.
- For today's purposes, "remote" includes purely off-site assessments, hybrid inspections with remote and on-site portions and virtual inspections performed using technology.
- You will hear about our panelists' engagement with regulators, including what happened before, during and after the assessment or inspection.
- You will also hear important take-away lessons from their experiences and thoughts about best practices in preparing for and hosting remote assessments and inspections in the future.

Format for Today's Webinar

- We will begin with introductory comments from each panelist.
- We will then transition into a general Q and A discussion.
- The audience can submit questions throughout the webinar.

Mary Oates



VP, Compliance Services, Lachman Consultants

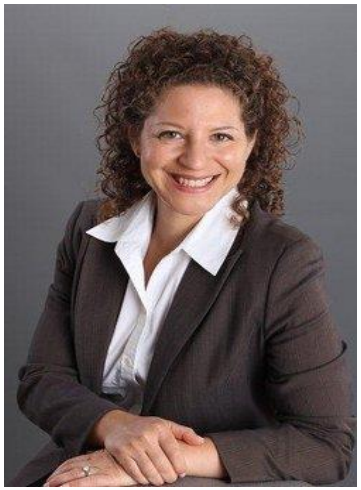
- Mary advises pharmaceutical clients on a range of operational, technical and compliance matters, including organizational and efficiency optimization, preventing and remediating GMP compliance matters and responding to and preparing for health authority inspections.
- Prior to joining Lachman, Mary spent 25 years at Pfizer, where she held senior operational and quality roles, including 8 years as the Global Head of Quality Operations, responsible for quality oversight and serving as the ultimate quality authority for all GMP activities for every product in every market.
- Mary is on the PDA Board of Directors.

Mary Farbman

Executive Director of Global Quality Compliance, Merck

- Mary is responsible for compliance support throughout the network of Merck manufacturing sites and contract manufacturing partners. She is also responsible for supporting inspections at sites, including ensuring sites are permanently inspection ready.
- Mary was a microbiology and facility reviewer for biologics products as well as a compliance officer within FDA's Center for Drug Evaluation and Research (CDER)
- She was also a Peace Corps volunteer in Burkina Faso, West Africa, where she taught high school chemistry and physics for two years

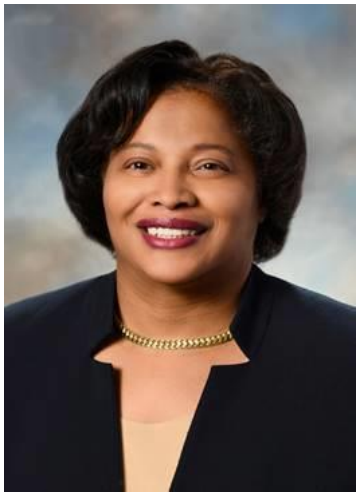
Paula Katz



Special Counsel in the Washington, DC, office of Covington & Burling LLP

- Paula advises clients on pharmaceutical compliance and enforcement across the GxP space. She regularly supports clients in managing and responding to FDA and other regulatory inspections, handling product recalls, and conducting internal investigations.
- She joined the firm after nearly a decade at FDA, where she was Director of Guidance and Policy in CDER's Office of Manufacturing Quality. During her time at FDA, Paula was responsible for developing substantive GMP and compliance policy, and served as a clearing official for warning letters, import alerts, and referrals for judicial actions.

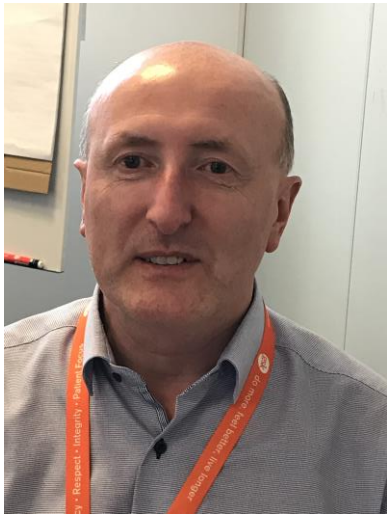
Peggy Speight



VP Enterprise Regulatory Compliance, Johnson & Johnson

- Peggy partners with senior leaders to provide strategy and framework to ensure a strong regulatory compliance profile.
- Peggy also leads the Enterprise Independent Audit and External Manufacturer/Supplier Audit program, Enterprise Standards & Policies, Strategic Compliance Operations, the Office of Special Investigations, and Global Learning and Development.
- She spent ten years as an FDA Field Investigator and member of Team Biologics
- Peggy is a member of the Board of Directors of Rx360

Ian Stewart

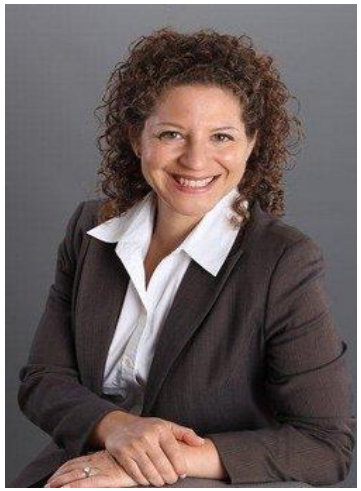


Site Quality Director, GlaxoSmithKline, Montrose, UK

- Ian has been the Site Quality Director at GSK Montrose for the past 7 years.
- He was previously a GMP Inspector for the UK MHRA for 7 years specializing in UK and global inspections of manufacturers of APIs, drug products, importation and virtual businesses, US plasma collection, UK blood services and hospital transfusion laboratories.
- Ian was Head of Quality and Regulatory for the Scottish National Blood Transfusion Service.
- Ian plays the guitar and sometimes Scottish Highland bagpipes.

Legal Framework for Regulatory Inspections

PAULA KATZ



Purpose of Inspections

- Ensure compliance with CGMP requirements
- Follow-up on adverse event reports, complaints, recalls, field alert reports, and biological product deviation reports
- Fulfill statutory mandate to inspect drug establishments on a risk-based schedule

FDA Inspectional Authority

- Legal authority for FDA's administrative inspections is provided by FDCA § 704. There are no regulations applicable to inspections.
- Investigators are permitted to inspect "all records, files, papers, processes, controls and facilities," with some exceptions
- FDA's inspectional authority extends to documents "bearing on whether [] drugs … are adulterated or misbranded … or otherwise bearing on violation of" the FDCA
- FDA inspectional requests are subject to a "reasonableness" requirement, in that FDA can "inspect, at reasonable times and within reasonable limits and in a reasonable manner."

FDA Inspectional Authority

- FDASIA section 706 amended FDCA § 704 to grant FDA authority to seek records in advance or in lieu of inspection ("704(a)(4) Record Request")
- Under FDCA § 501(j), FDA has authority to deem a drug adulterated if "it has been manufactured, processed, packed or held in any factory, warehouse, or establishment and the owner…delays, denies, or limits an inspection, or refuses to permit entry or inspection."

Delaying, Denying, Limiting, or Refusing an Inspection

- **Guidance for Industry: Circumstances that Constitute Delaying, Denying, Limiting, or Refusing a Drug Inspection (Oct. 2014)**
  - Limiting areas of facility available to investigators
  - Delaying production of documents in response to a reasonable request
  - Interfering with investigators taking samples
  - Delaying scheduling of a pre-announced inspection without adequate justification
- **There are serious consequences:**
  - If FDA determines a facility is delaying, denying, limiting and refusing inspection, FDA may deem drugs adulterated.
    - Warning Letters
    - Import Alerts
  - Refusal of inspection is a prohibited act under the FDCA subject to criminal prosecution

FDA Inspections & COVID-19

- **March 2020: most foreign and domestic surveillance facility inspections postponed; mission-critical on a case-by-case basis**
- **Other tools (esp. imported products)**
  - Denying entry of unsafe products into the U.S.
  - Physical examinations and/or product sampling at our borders
  - Reviewing a firm's previous compliance history
  - Using information sharing from foreign governments as part of mutual recognition and confidentiality agreements
  - Requesting records "in advance of or in lieu of" on-site drug inspections.
- **Resumption of "prioritized" domestic inspections beginning July 20, 2020**
  - COVID-19 Advisory Level to assess local area
  - pre-announced, in-person

Issues For Remote Inspections

Record Requests

- **Scope: "The records requested must be records that the Secretary may inspect under § 704(a)." (SMG 9004.1)**
  - APR, batch records, product-specific information, etc.
  - Reasonable timespan
  - Translation
- **"[N]o inspection…shall extend to financial data, sales data…, pricing data, personnel data…, and research data."**
  - Except that FDA can inspect shipping records and information relating to personnel qualifications.
- **Failure to produce: refusal under § 501(j)?**

"Virtual Inspections"

- **If FDA were to conduct them, how would it work?**
- **FDA Policy on Photography (Videography) during inspections:**
  - Investigations Operations Manual (IOM) Chapter 5:
    - FDA asserts a "right" to take photos without asking permission
    - But "photographs should only be taken for evidentiary purposes, e.g., to document violations."
    - Should "be related to…conditions contributing or likely to contribute filth to the finished product, or to practices likely to render it injurious or otherwise violative"
  - Only a policy; legal authority remains unsettled

Merck’s Experiences and Learnings

MARY FARBMAN

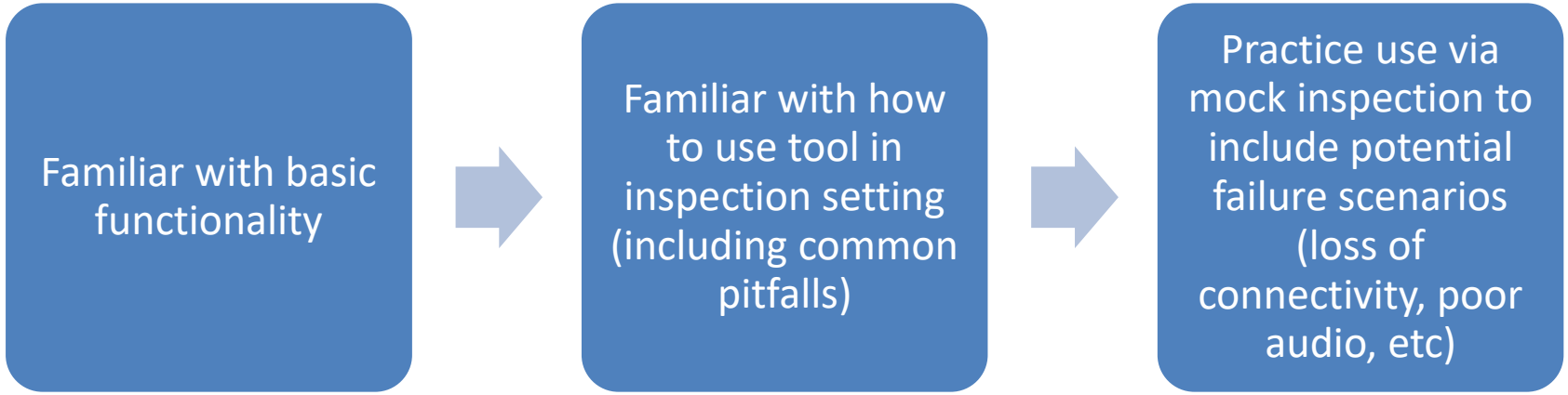
Considerations for Remote Inspections

	Considerations for IT Tools	"Soft Side" Considerations
Sharing Files	• Dropbox with appropriate security controls preferable to email • Hardware for rapid scanning of paper documents • Software for watermark stamping	• Some documents may need introduction or additional explanation. • Be ready to speak to each document uploaded, just as in a traditional inspection.
Virtual Inspection Rooms	• Virtual waiting room to prevent interruptions • Security controls	• SMEs to ensure professional attire, backgrounds, and lighting • Ensure all parties are aligned with policies and laws on recording
Virtual Backrooms	• Seamless interface with request trackers • Embedded scribe, chat functionalities for rapid communication	• Ensure all SMEs (including global SMEs) are well-trained on use of systems • Ensure all SMEs have appropriate access rights to ensure no hidden communication

Considerations for Remote Inspections

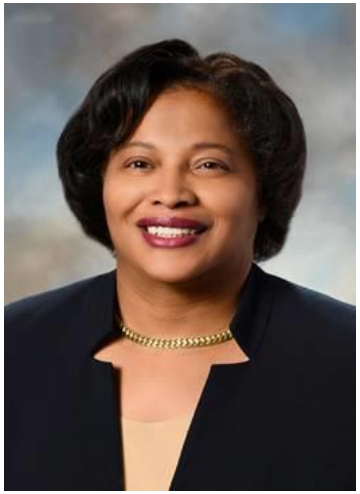
	Considerations for IT Tools	"Soft Side" Considerations
Virtual Tours	• Smart Glasses • Video chat with phone/tablet • Ability to be sanitized for cleanrooms, ability to work in explosion-proof areas • WiFi boosters	• Safety precautions: safe to walk while videoing? • Map out facility wireless Internet connectivity; share findings with inspectors at initiation of inspection • Determine policy on recording of feed

3-Stage Training Paradigm for Inspection IT Tools



Johnson & Johnson's Experiences and Learnings

PEGGY SPEIGHT



Johnson & Johnson (J&J)

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J&J's Experience with Assessments & Remote Inspections

- ✓ FDA Form 4003
- ✓ Rest of World Regulatory Health Authorities
- ✓ Notified Bodies

Take-away Lessons

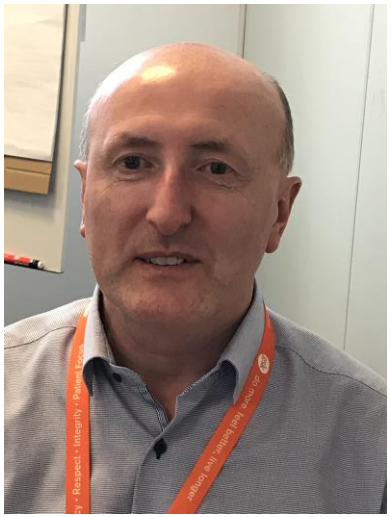
- ❑ **Update your Audit Playbook** to include remote audits, and assessments
- ❑ **Select the right technology** to use during the audit. Try to use technology that both the Auditor and auditee are familiar with
- ❑ **Setup premeeting** with Auditor to determine essential logistics, i.e. if a virtual tour is required (recorded or live), need for document translation
- ❑ Select **secure technology** for document exchange
- ❑ Prepare **backup plans** for **technology** issues that can impede the audit
- ❑ Know how to contact your **IT experts for support**, ideally, have your IT experts included in the audit to provide real time support as needed
- ❑ Setup a **virtual front and backroom**

Take-away Lessons

- Establish **frequent check-in with Auditor** to ensure they understand & are satisfied with the information provided; align on daily opening and wrap-up meetings
- Proactively **prepare storyboards** for applicable topics
- Confirm the **legibility and completeness** of scanned documents
- Be prepared for **additional questions or document request** that may come in **post** conclusion of the **audit**

GSK'S Experiences and Learnings

IAN STEWART



MHRA Remote Inspection – Montrose Site Experience

Montrose site runs inspection readiness sustainability programme throughout the year

Notification 1st April of remote inspection

April

External company shared remote inspection experience

Inspection scope discussion

SMF and compliance report provided

Agreed to use Microsoft Teams for documents and calls

CQA

May

CQA

MHRA indicated request list for early June

CQA supporting versus anticipated scope

SME preparation

June

5th June – MHRA request list (44 items)

CQA

12th June – all info provided to MHRA within Microsoft Teams

IT Systems ready

Social Distanced Room for Virtual Inspection - not used

Positive MHRA inspection outcome

Further RFIs received via Microsoft Teams messaging

July

CQA

Inspection closing meeting – 15th June

2nd July All RFI responses provided within Microsoft Teams

29th June 42 RFI received

Q&A

Please submit your questions!

Questions Submitted by Regulators

- As inspectors, we are required to confirm that the site is operating in compliance to GMP to ensure patient safety: What tools do you have available in-house that could be used to help demonstrate this to an inspector during a remote assessment?
- Is there general industry support for the use of livestreaming both video/audio and records to regulators, and does that support include all inspection types or just some, like for pending applications?
- What challenges has industry experienced when facilitating a remote inspection? How can these challenges be addressed to better enable firms to demonstrate their compliance?

Questions Submitted by Regulators

- Is there anything you think FDA should consider or add in terms of the types of records requested or is there something else (other information) FDA should consider in making this type of regulatory assessment?
- When FDA does a records requests then follows up with an inspection, do you feel better prepared for the inspection?
- With FDA pre-announcing all inspections, do you expect to see an improvement in inspection outcomes and why?

Thank You For Attending Today's Webinar

Our next PDA COVID-19 Task Force Webinar will be:

Utilization of Modular Manufacturing to Enhance/Upscale Capacity During COVID-19

August 20, 2020 at 10:00am EDT

Stay informed of all PDA events at: PDA.org