GCP Regulatory Inspection Readiness

March 29, 2018

MassBio
MASSACHUSETTS BIOTECHNOLOGY COUNCIL

GCP Regulatory Inspection Readiness

Panelists:

- **Kathy Goldstein**, PharmD, Sr. Director, R&D Quality and Compliance, Alexion Pharmaceuticals, Inc.
- **David Ives**, Head, Trial Master File, Vertex Pharmaceuticals
- **Jorge Rodriguez-Larrain**, MD, FACC, Executive Director, Clinical Operations, Alexion Pharmaceuticals

Moderator:

- **Christine Sahagian**, Head of Clinical and Medical QA and Compliance in the R&D QA & Compliance Group, Shire

GCP Regulatory Inspection Readiness Massachusetts Biotechnology Council

Christine Sahagian

March 29, 2018

Shire

Audience Poll

- What function do you represent?
  - Quality Assurance/Compliance
  - Clinical Development/Operations
  - Other

- Have you participated in a GCP inspection?

- Have you been involved with inspection readiness activities?

Most Frequent Inspection Findings: Sponsor/CRO

X = critical inspection finding specified in report; FDA report does not provide differentiation

Finding (Inadequate)	FDA	MHRA	EMA
Essential Documents / TMF / Archiving	X	X	X
Sponsor Oversight / Monitoring	X	X	X
Data Integrity / Data Management	X	X	X
Quality System / SOP Adherence		X	X
Regulatory / IRB Authorization to Initiate Study	X	X	
Contracts / Agreements			X
Pharmacovigilance		X	
Inadequate IP Accountability	X		

European Medicines Agency. Annual report of the Good Clinical Practice Inspectors Working Group 2016, Adopted by the GCP IWG on 2 June 2017

Food and Drug Administration. Bioresearch Monitoring (BIMO) Metrics – FY'16

Medicines & Healthcare products Regulatory Agency. GCP Inspectorate. GCP Inspections Metrics Report. Date of Issue: 21st July 2017

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Examples of Sponsor/CRO CRITICAL Findings

- Essential Documents / TMF / Archiving:
  - TMF was not readily available, directly accessible, and complete
  - TMF was not defined. No way to confirm that all TMF systems/repositories were controlled, linked, and available
  - Records in the TMF were not filed/located per the TMF table of contents
- Data Integrity / Data Management:
  - Insufficient source data to support changes made to electronic patient diaries
  - Audit trail from the Interactive Response Technology (IRT) system was not made available during inspection
  - Process for defining/classifying protocol deviations was not documented, which led to the inclusion of ineligible subjects in the per protocol analysis
  - Inconsistencies between the site's source data and the clinical database; unclear data entry guidelines

Examples of Sponsor/CRO CRITICAL Findings

- Sponsor Oversight /Monitoring
  - IMP dosing calculation errors were not detected during routine monitoring or the data cleaning process
  - Failure to bring Investigator sites into compliance
- Quality System / Adherence to SOPs
  - CAPA commitments from the previous inspection were not fulfilled; Preventive measures taken were not sufficient in addressing the fundamental cause(s) of the problem(s)
  - Lack of a quality system to cover the requirements of sponsorship and to cover key sponsor responsibilities
- Pharmacovigilance
  - Reference Safety Information (RSI) was updated without an amendment being sent to the MHRA or any assessment of new expected terms carried out
  - No process to ensure Investigator Brochures that contain RSI were reviewed on an annual basis
  - Multiple errors in the SAE listings; No QC checks on the data provided; Discrepancies between the SAE report forms and the clinical database

Shire

Let’s Meet the Panel

Kathy Goldstein, PharmD

Sr. Director, R&D Quality and Compliance

Alexion Pharmaceuticals

David Ives

Head, Trial Master File

Vertex Pharmaceuticals

Jorge Rodriguez-Larrain, MD, FACC

Executive Director, Clinical Operations

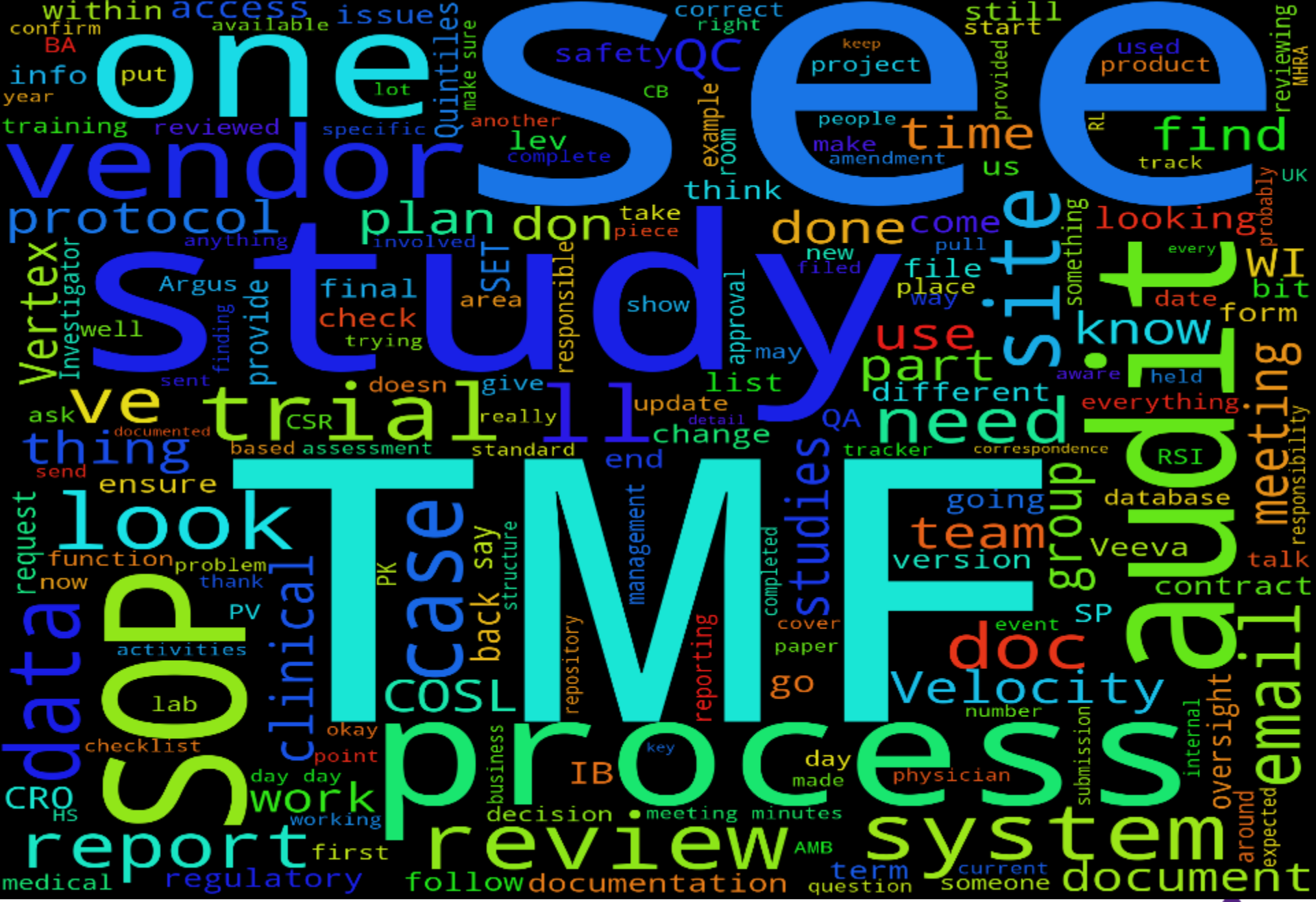
Alexion Pharmaceuticals

KATHY GOLDSTEIN, PHARMD

- **Sr Director, R&D Quality and Compliance at Alexion Pharmaceuticals**
- **Prior experience:**
  - PK/DM lab associate
  - CRA
  - Clinical project manager / clinical operations
  - Hospital pharmacist

KATHY GOLDSTEIN, PHARMD

- **Current role:**
  - Quality Operations supporting Clinical Operations, Biometrics, Medical Sciences
  - Day-to-day quality support of clinical trials
  - Inspection readiness / preparation / management
  - Inspections
    - PMDA (sponsor and site)
    - FDA (sponsor and site)
    - MHRA preparation



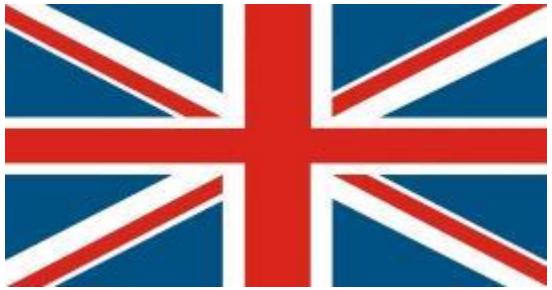
David Ives, Head TMF Compliance and Oversight, Vertex Pharmaceuticals

VERTEX

Background and Health Authority Inspection Experience

- 10+ years of GxP regulated information management experience across a wide variety of systems and management of paper archive.
- Currently inspection point person for Trial Master File (TMF) and GCP Archiving leading function responsible for end to end TMF management in multiple models with a variety of partners.

4 FDA: 3 GCP
1 GLP



2 MHRA: 2 GCP

1 HC: 1 GCP

MASSACHUSETTS'S BIOTECHNOLOGY COUNCIL:

GCP REGULATORY INSPECTION READINESS

JORGE M. RODRIGUEZ-LARRAIN, MD, FACC

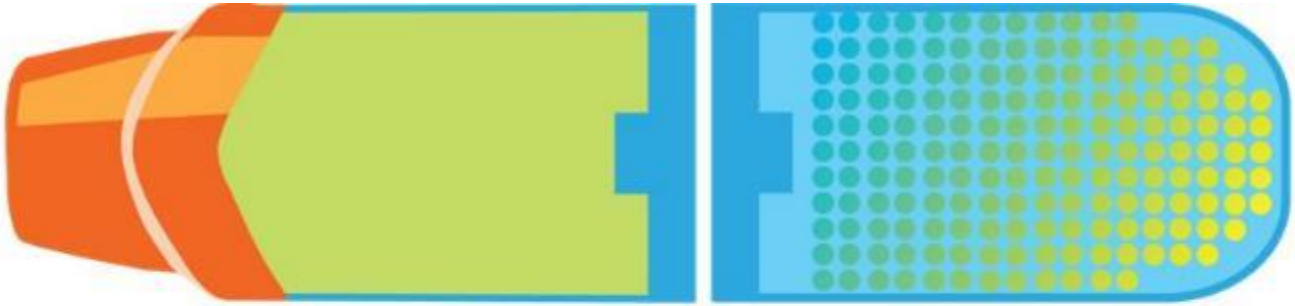
- **More than 25 years of experience in global clinical operations, including:**
  - Alexion Pharmaceutical: Head Clinical Operations - Complement Franchise
  - Alcon Pharmaceutical (A Novartis Company): Head of Global Clinical Trial Management
  - Merck & Co.: Regional Operations Director LATAM
- **Experience with the following agencies (among others):**
  - FDA (US): sponsor and site level
  - BfAr (Germany): sponsor and site level
  - MHRA (U.K.): sponsor and site level
  - EMA (EU): sponsor and site level
  - CanadaFDA (Canada): sponsor and site level
  - ANMAT: sponsor and site level
  - ANVISA / CONEP (Brazil): sponsor and site level
  - INVIMA (Argentina): sponsor and site level
  - COFREPIS (Mexico): sponsor and site level

ALEXION

Questions??

Upcoming Forums

- **March 29, 11:30-1:30 - National Fire Protection Association (NFPA) Code, Hazardous Materials - SEF**
- **April 10, 8-10am - How Current Immigration Policies Affect the Massachusetts Biotech Industry – HR**
- **April 12, 8-10am - Sustainability & Climate Change: From the Boiler Room to the Board Room – SEF**



THE CONVERGENCE OF MEDICAL DEVICES & DRUGS:

Advances in Drug Delivery

May 3, 2018; 12:00pm – 5:00pm

The Westin - Waltham, MA

Registration is now open