

Hints and tips on surviving an inspection

David Pottinger
Director Global Compliance and
Training, Quality

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Wyeth
Research

Introduction

- **My background**
- **MHRA Inspections**
- **Starting with the end in mind..**
- **Inspection preparation**
- **Pre-inspection information**
- **Inspection activities**
 - ▶ Awareness and information sharing
 - ▶ People
 - ▶ Technology
 - ▶ Information
 - ▶ Facilities
 - ▶ Inspection
 - ▶ Post inspection debrief
 - ▶ Final report responses

My background

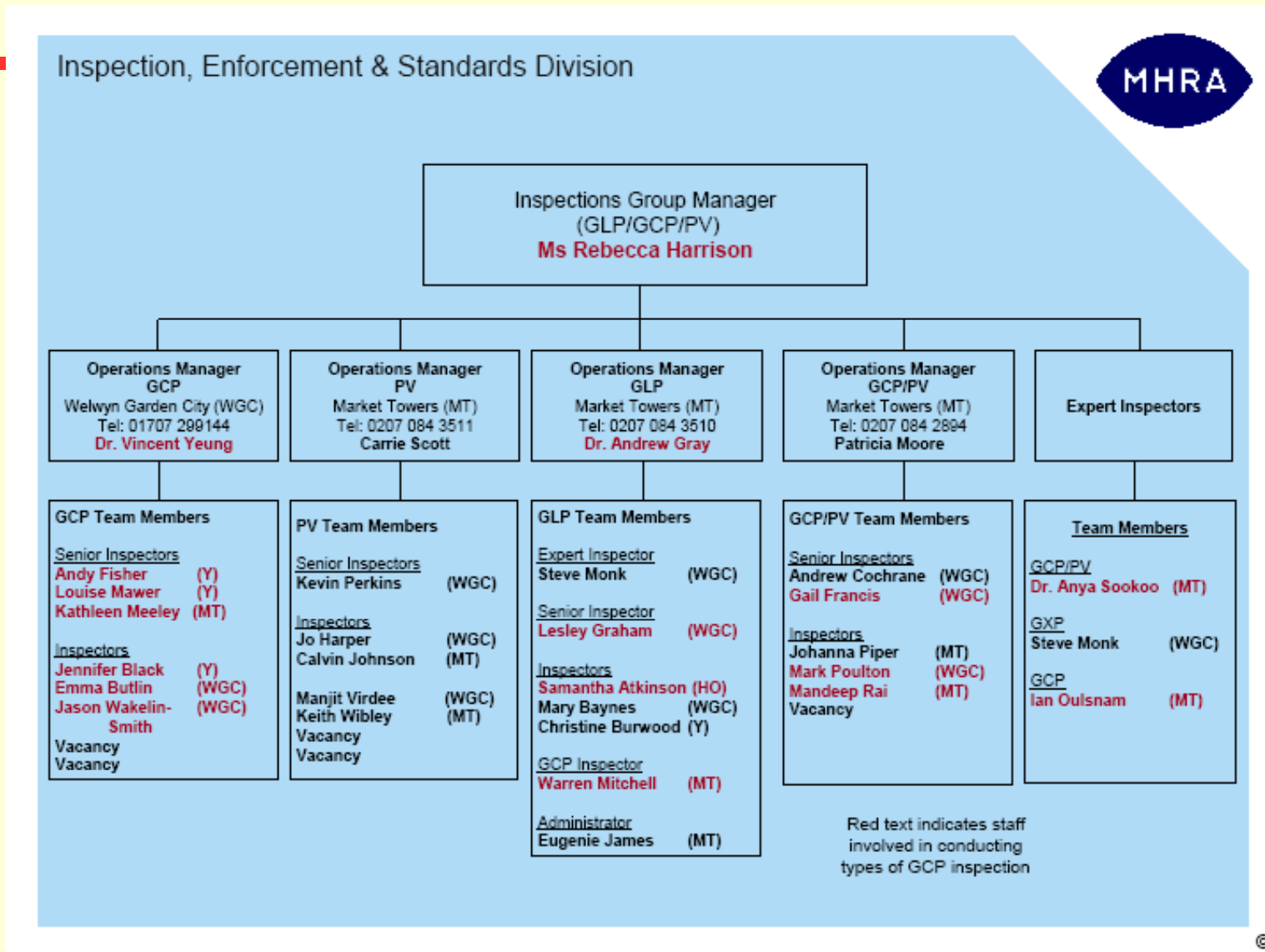
- **25 years in the defence environment**
 - ▶ Developing quality systems – Def and BS/ISO standards
 - ▶ Interface for ISO certification inspections
 - ▶ Managing production, testing facilities, internal audit and vendor assessments
- **Last 12 in clinical research**
 - ▶ Contract Research Organisation – 4 years
 - ▶ Pharmaceutical companies – 8 years
 - ▶ Participated in 4 MHRA inspections, 1 IMB, 1 FDA, 1 EMEA
- **Wyeth – Global Compliance and Training Group**
 - ▶ Quality system
 - ▶ Training development and delivery
 - ▶ Compliance advice
 - ▶ Support in preparing for inspections and managing outcomes

MHRA Inspections

Inspections by MHRA

- Good Clinical Practice (GCP)
- Good Manufacturing and Distribution Practice (GMP/GDP)
- Good Laboratory Practice (GLP)
- Good Pharmacovigilance Practice (GPvP)

MHRA Inspections



MHRA Inspections

GCP Inspectors assess compliance with the requirements of legislation and guidelines* relating to conduct of clinical trials involving investigational medicinal product.

CPMP/ICH/135/95

* Statutory Instrument 2004/1031 and subsequent amendment 2006/1928

EU Directive 2001/20/EC

EU Directive 2005/28/EC

Include pharmaceutical companies, CROs, non-commercial organisations, e.g. universities, NHS Trusts and charities, investigational trial sites, clinical laboratories, GCP archives and other facilities involved in clinical trial research.

MHRA Inspections

There are three types of GCP Inspections:

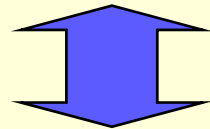
- **Routine inspections**
- **Triggered inspections:** MHRA licensing requests or reports received on suspected breaches of legislation relating to the conduct of clinical trials.
- **CHMP requested inspections resulting from central MA submissions:** in relation to marketing applications via EU centralised procedure, as coordinated by EMEA. (cf FDA)

Starting with the end in mind....

- **The new employee**

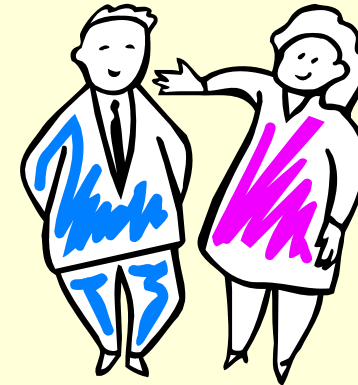
- ▶ Welcome

- General HR topics
- Company policies



- ▶ Departmental induction including....

- Quality system... filing and archiving for retrieval...process improvement
- Learning management system
- Audits and Inspections
 - **Effective and timely resolution of issues**



Inspection preparation – charter & team(s)..

- **Charter..**

- ▶ Scope the activity
- ▶ Team details
- ▶ Methods of communication – eRoom, Meetings..

- **Steering Committee**

- ▶ Cross functional senior management
 - Guidance
 - Smooth the way
 - Resolve issues

- **Project Team (Core plus study*)**

- ▶ Functional managers and subject matter experts
 - Do / manage the activity
 - *Modified when studies to be inspected are known



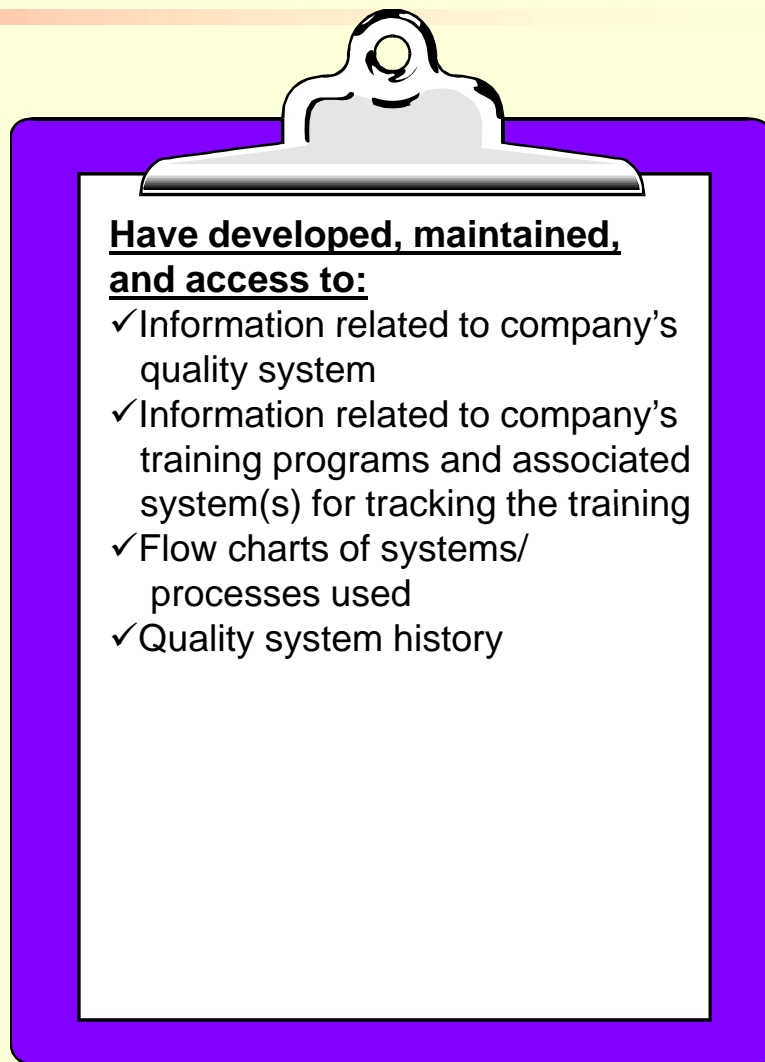
The coordinator
Meetings
Communication
Progressing
activities

Defining Roles and Responsibilities

Core Team

- **Quality system / Training Member(s):**
 - ▶ **Preparation (Prior to Inspection):**
 - Ensure overall quality system and training documentation are up to date and readily available

Core Inspection
Prep Team



Roles and Responsibilities

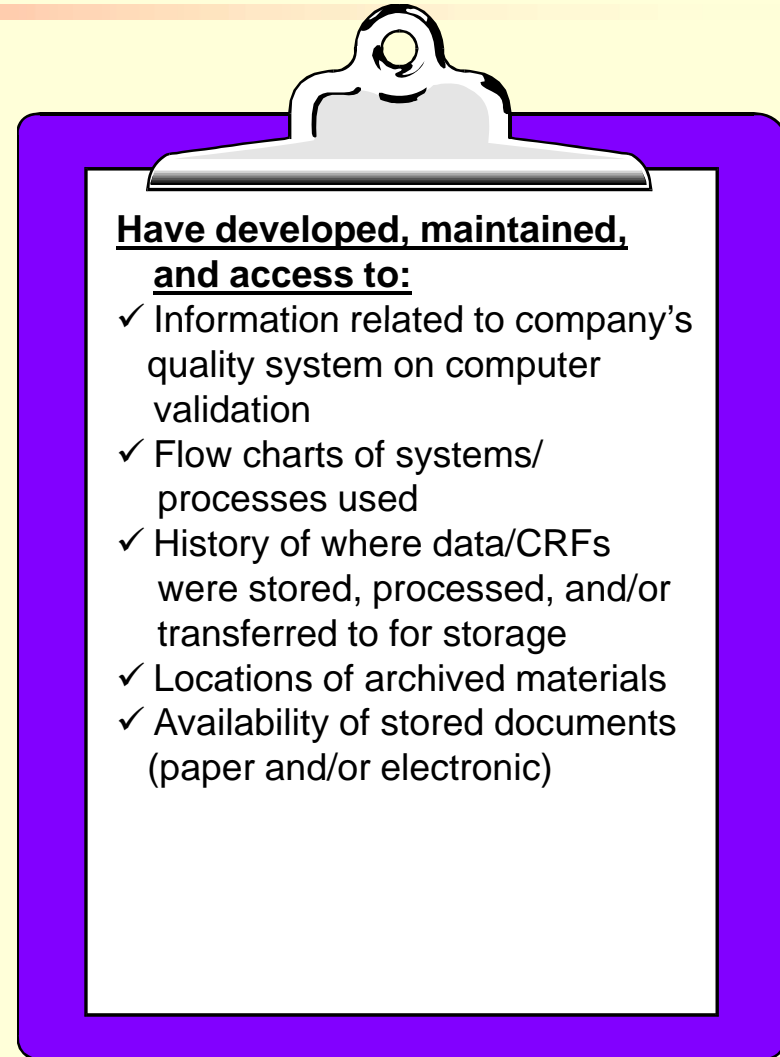
Core Team

- **Data Management Member(s):**

- ▶ **Preparation (Prior to Inspection):**

- Ensure data management and computer validation materials are updated and readily available

Core Inspection
Prep Team

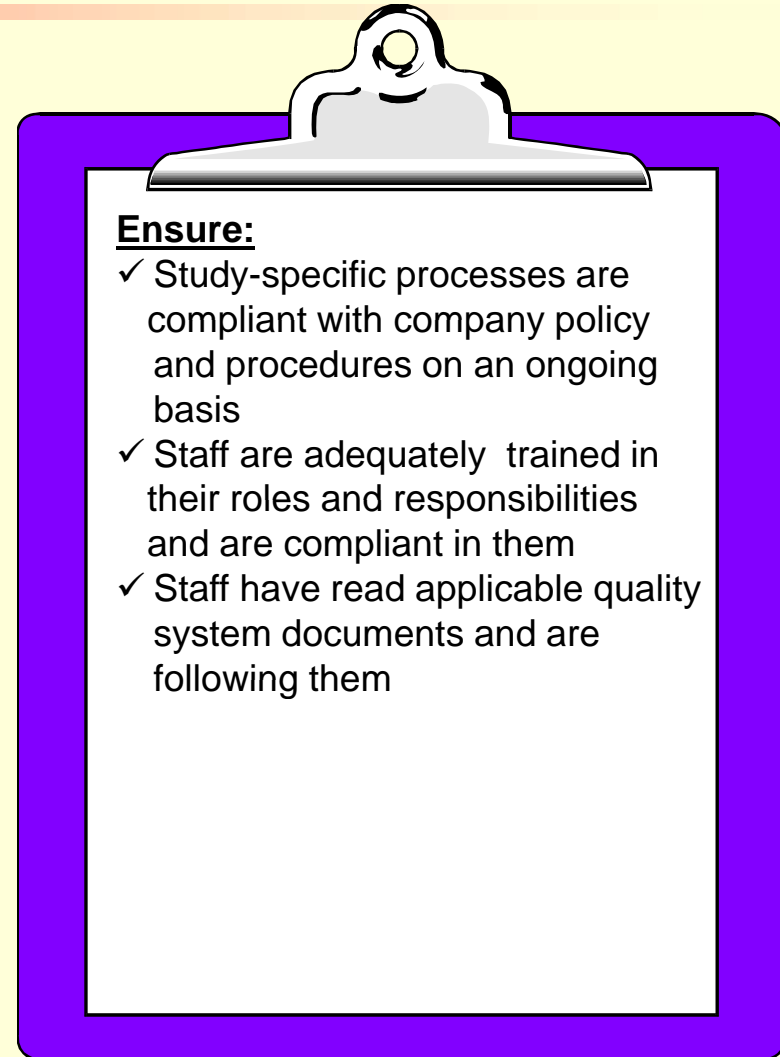


Roles and Responsibilities

Study Team

- **Leader(s):**
 - ▶ **Preparation (Ongoing):**
 - Oversee the study team and ensure they are compliant with applicable quality system requirements and GCP-related regulations

Study Team



Pre-inspection information

- **Dossier**

- ▶ Organisation charts* and organisation details
- ▶ Lists of procedures
- ▶ Safety reporting procedures
- ▶ Computer systems and validation status
- ▶ List of clinical trials – 3 years
- ▶ Outsourced activities
- ▶ Summary of key processes/departments

- **Inspection Plan**

- ▶ Modified by inspection history
- ▶ Dates
- ▶ Department/activity to be inspected with timeframe
- ▶ Individuals to be interviewed*



*link

Inspection history..

- **Findings and related corrective and preventive actions (CAPAs)**
 - ▶ Documented
 - ▶ Assigned
 - ▶ Progressed to completion against agreed timeframe
 - ▶ Assessed for effectiveness
 - ▶ Objective evidence readily available



MHRA Inspection Agenda

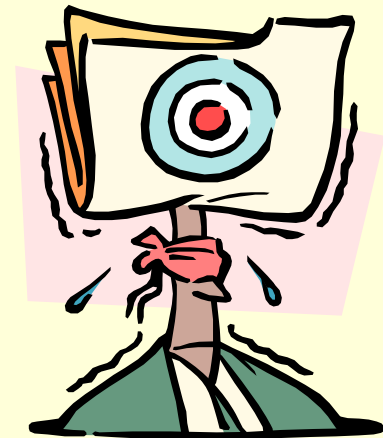
Day One:		Approximate Time
Inspectors Arrival		10.30 – 11.00
Opening Meeting Introduction to Inspectors, overview of inspection plan and procedures by Inspectors. (to include 10 minute overview of company)		11.00 – 11.30
Parallel Session	Follow-up of CAPA from previous inspection Changes since last inspection and planned future changes	11.30 – 12.30
	Contracts, Agreements and Insurance Provisions for contracting with CROs, subcontractors and Investigators. (We will require copies of your standard agreement(s) templates, indemnity and insurance)	11.30 - 12.30
TMF and Document Review (to include lunch) <ul style="list-style-type: none"> • Study a • Study b • Study c Appropriate CRA/Project Manager to be available during inspection to answer any queries on these studies during the inspection		12.30 – 17.30

MHRA Inspection Agenda

Day Two:		Approximate Time
QA, Document Control & Training		09.00 – 10.00
TMF & Document Review (to include lunch)		10.00- 15.30
Parallel Session	Pharmacovigilance & Medical Expertise Procedures for capture, assessment and onward reporting of clinical trials cases and safety monitoring (phase I-IV) Medical input into the clinical trial process.	15.30 – 17.00
	Monitoring & Site Management All monitoring activities in the UK to include training of CRAs, interactions with Project Management and Investigator Sites (IMP release to site etc)	15.30 – 17.00
Day Three:		Approximate Time
TMF & Archiving		09.00 – 10.00
TMF & Document Review (to include lunch)		10.00 – 14.00
Inspectors closed session (14.00 deadline for document requests)		14.00 – 15.00
Closing Meeting		15.00 – 16.00

Inspection awareness

- **Provide an overview of any previous inspections**
- **Discuss the inspection process**
- **Method of questioning**
 - Inspector dependent, some closed questions
 - Process oriented
 - Interested in **current** processes
 - Documentation required to support answers
- **Provide details of the rooms being used**



How to share information

- **Know ‘your’ policies, procedures and detailed instructions**
- **Make sure you understand the question, ask for clarification if not**
- **Answer one item at a time – concise and accurate**
- **Restrict to answering a specific question**
- **Clarify any acronyms that you may use**

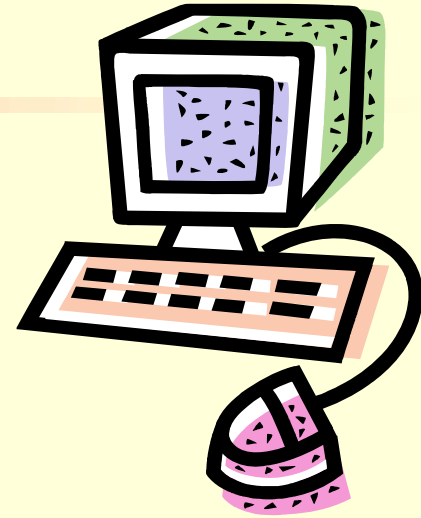
People related

- **Organisation charts**
- **Curriculum Vitae**
- **Job Descriptions**
- **Training**
 - ▶ **Role**
 - Curriculum – relevant training
 - Learning management system
 - Paper records
 - ▶ **Inspection awareness**
 - What to expect
 - How to share information – role play



Technology

- **Electronic systems list**
 - ▶ Dossier requirement
- **Validation**
 - ▶ Documentation available
- **Access**
 - ▶ 'On the job' vs demonstrations
 - TMF
 - Training
 - Safety database
 - Quality System
 - ▶ Key users



Information

- **Quality system – Global and Local**

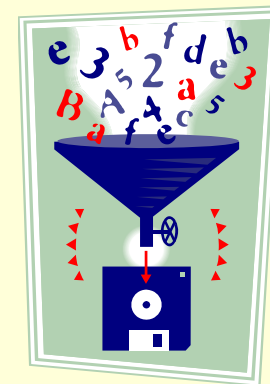
- ▶ Policy
- ▶ Cross functional processes
- ▶ Local instruction
- ▶ Access

- **Trial Master Files**

- ▶ Available
- ▶ Maintained
- ▶ Accessible

- **Study Information**

- ▶ Maintained
- ▶ Available
- ▶ Standard vs specific reports



Facilities for the days...

- **Rooms**

- ▶ Available
- ▶ Securable - storage of information
- ▶ Suitable

- **Equipment tested**

- **Process evaluated**

- ▶ Review of finding and provision of compliant responses
- ▶ Effective tracking of requests and their completion

- **Staff to manage the process**

- ▶ Regulatory
- ▶ Audit group
- ▶ Compliance
- ▶ SMEs
- ▶ Study team

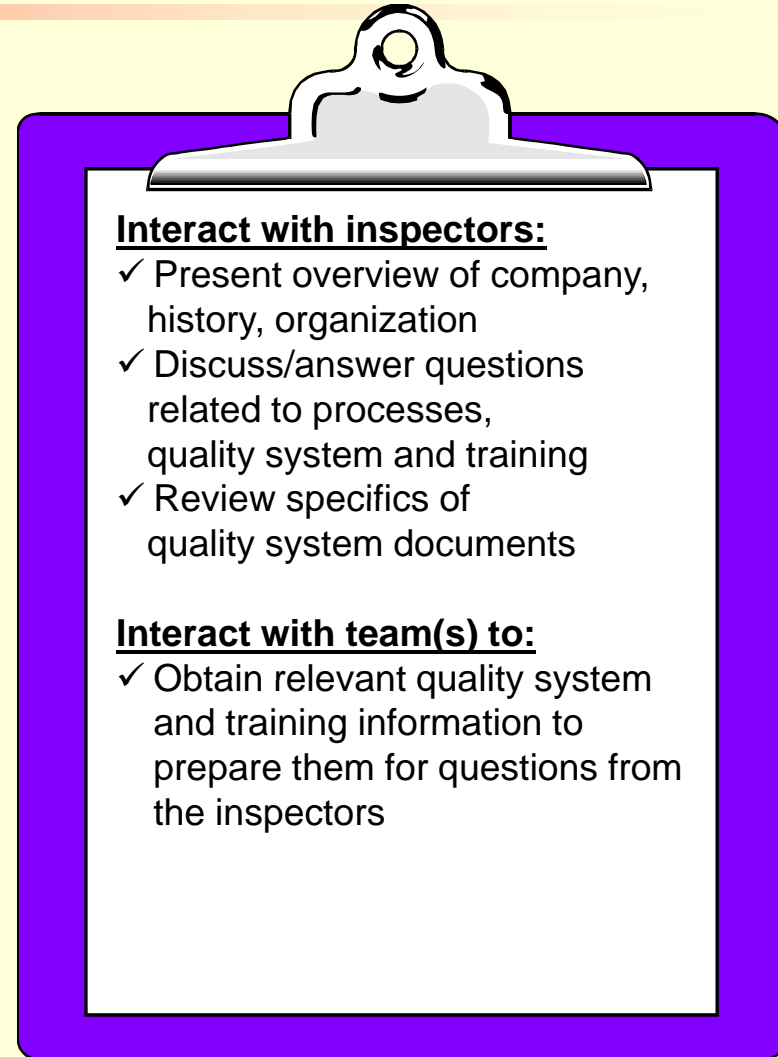


Roles and Responsibilities

Core Team

- **Quality System / Training Member(s):**
 - ▶ **During the Inspection:**
 - Serve as spokesperson for processes, procedures, and training

Core Inspection
Prep Team



Roles and Responsibilities

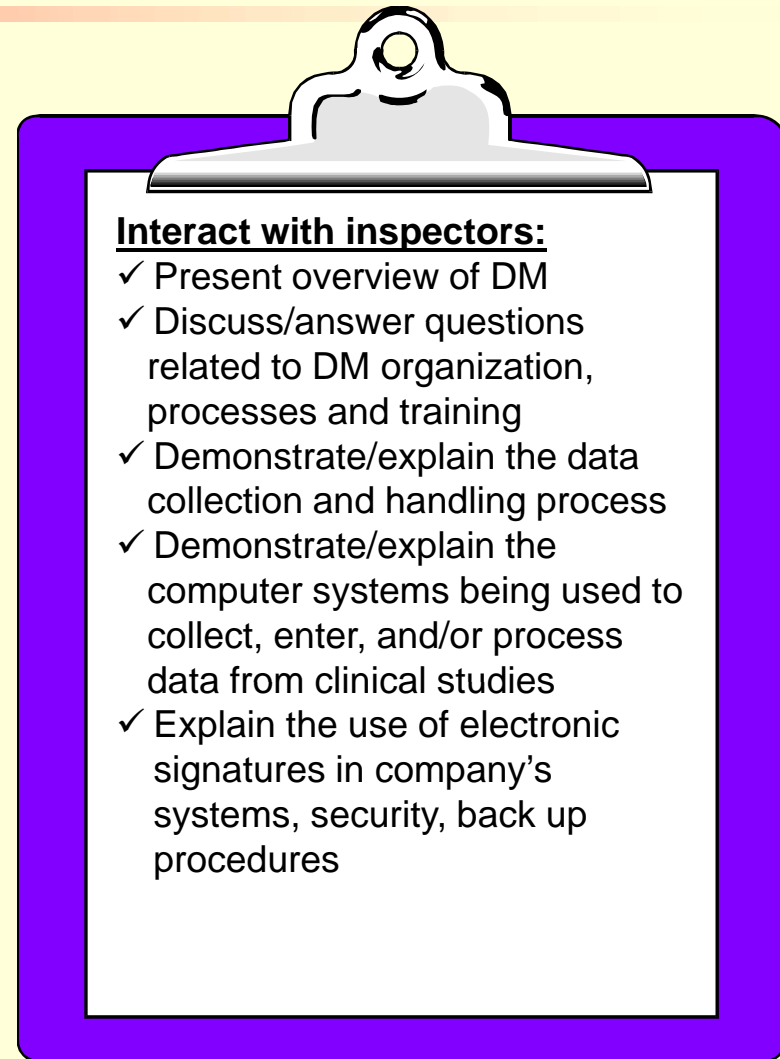
Core Team

- **Data Management (DM) Member(s):**

- ▶ **During the Inspection:**

- Serve as spokesperson for data management and computer validation regulations

Core Inspection
Prep Team



Roles and Responsibilities

Project Team

- **Team Spokesperson:**

- ▶ **During the Inspection:**

- Provide project-specific information/ materials to the inspectors

Project Team

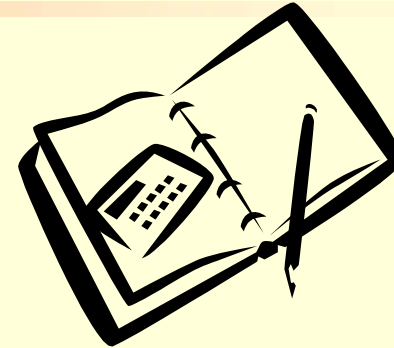


Interact with inspectors:

- ✓ Provide overview of project(s) being inspected
- ✓ Explain purpose, scope, and history of selected study(ies)
- ✓ Provide overview of process as conducted by company and associated procedures for studies under inspection
- ✓ Provide an overview of the TMFs
- ✓ Describe organizations (internal and external) involved and what their roles and obligations to company were/are
- ✓ Answer any study-specific questions
- ✓ Describe protocol development process

Post inspection debrief...

- **Understand the findings**
- **Document accurately**
- **Assign to suitably qualified staff**
- **Prepare draft responses ahead of receiving the final report...**



Final report responses....

- Provide achievable CAPAs
- Assign, monitor, progress..
- Implement the changes
- Assess the changes for effectiveness
- Be prepared for the return visit...



Discuss with the MHRA if the target date is not going to be met