



Medicines & Healthcare products  
Regulatory Agency



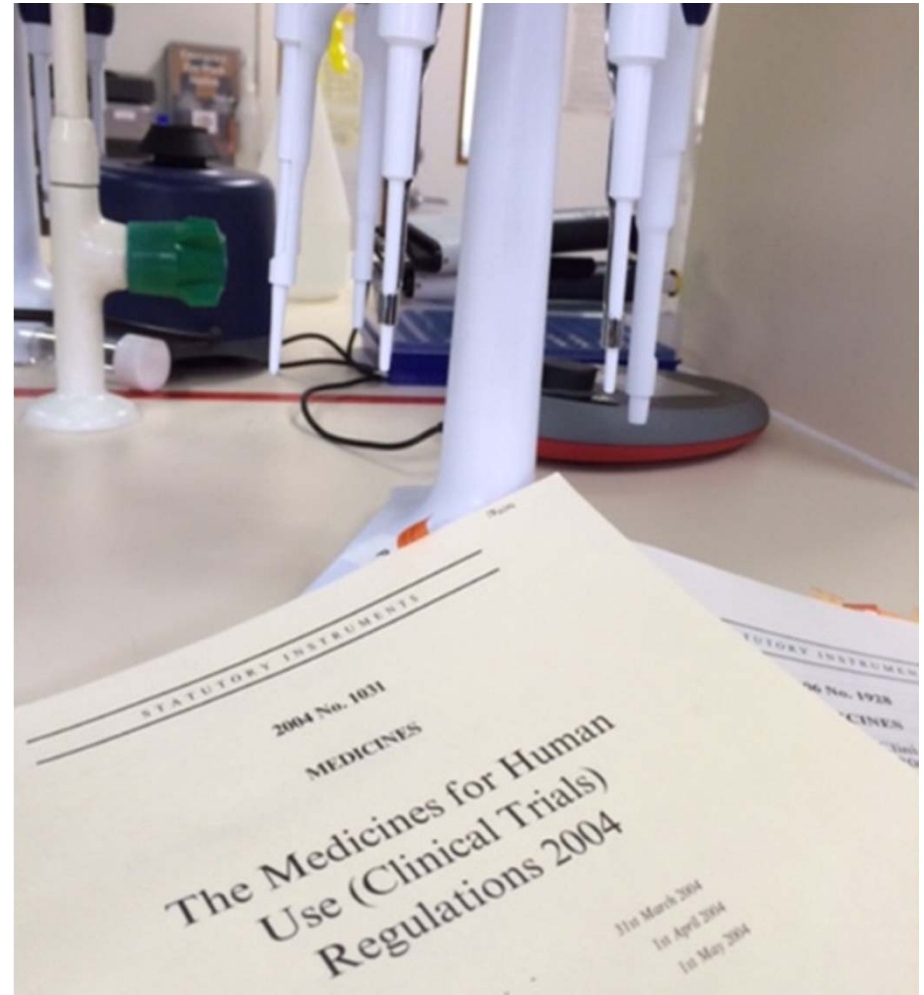
# GCP Labs Stakeholder Engagement Meeting

Tuesday 7<sup>th</sup> May 2019



# Agenda

- Introduction to the stakeholder group – participants, purpose and terms of reference
- Inspectorate sources of information and communication channels
- Introduction to the GCP labs inspection programme
- Safety labs
- Clinical trial sample analysis and BS EN ISO 15189:2012
- Multi-track analysers
- GCP training for laboratory staff
- Further discussion and questions
- Feedback - what do you want from this stakeholder group?



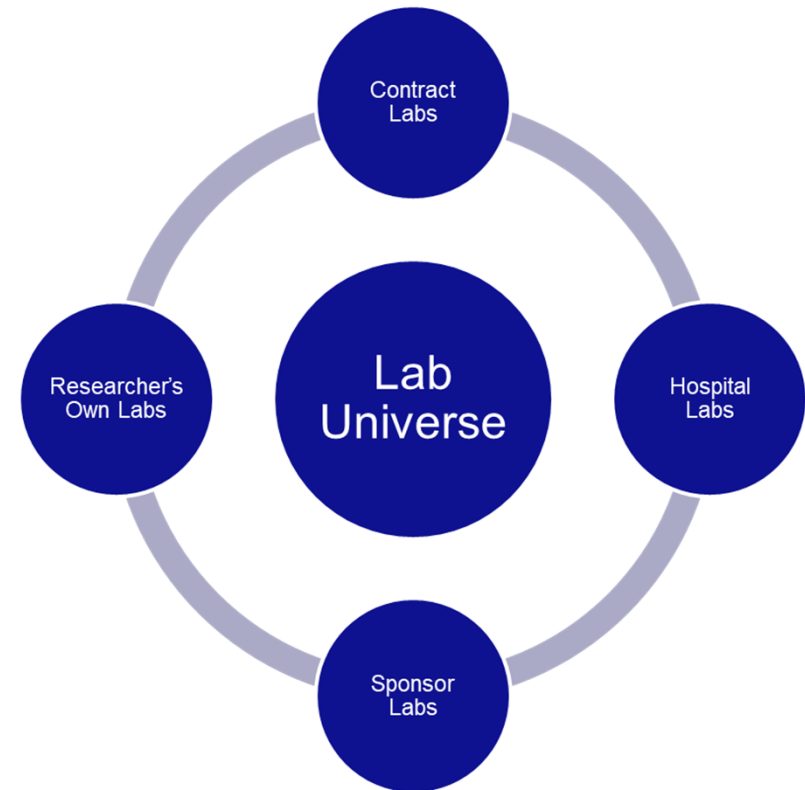
# Regulatory Background

“The verification of compliance with the standards of good clinical practice and the need to subject data, information and documents to inspection in order to confirm that they have been properly generated, recorded and reported are essential in order to justify the involvement of human subjects in clinical trials.” (2001/20/EC (15))

“To verify compliance with the provisions on good clinical and manufacturing practice, Member States shall appoint inspectors to inspect the sites concerned by any clinical trial conducted, particularly the trial site or sites, the manufacturing site of the investigational medicinal product, any laboratory used for analyses in the clinical trial and/or the sponsor’s premises” (2001/20/EC Article 15)

# Inspection Programme Introduction

- Increased use of laboratory data
- EMA Data collection exercise (data from 2012 – 2018)
- Questionnaires to facilities (September 2016 onwards)
- Started with GLP/GCP joint labs
  
- 209 UK sites currently identified (multiple labs at some locations)



# Risk-Based Inspection Programme



- 'Stand-alone' inspections
- Joint inspections (GCP/GLP)
- Phase I labs
- Investigator sites
- Triggered inspections
  - Licensing
  - Serious breaches / issues

UK only at present but likely to expand in the future

# Common Issues

## Dossier / information submission

- What trials are we involved with? Cross-checks
- CT vs routine practice (common with eligibility assessment tests and safety bloods)

## Trial Selection

- Retrieval of data
- Electronic data



# Common Issues (2)



## Data Integrity

- Controls
- Permissions / shared log-ins
- Audit trails
- 'Touch-points' between systems

Use of kits / adapted kits

Method validation



# Common Issues (3)

- Sample analysis
- Equipment & facilities
- Data acceptance criteria
  
- Due diligence – approvals / consent
  
- Reporting
- QA activities





# Safety Labs

- Focus of inspection programme is labs generating data to support primary and secondary objectives or where used for key decision making (dose escalation, eligibility)
- Legislation and guidance does not differentiate between these labs / tests and those performing routine safety bloods or those generating data not directly linked to the trial (same applies to exploratory endpoints)
- Required that all labs implement appropriate measures to assure the quality and integrity of the data whilst ensuring subject rights are not compromised

## Safety Labs (2)

- Focus is on trial specific analysis
- May look at some aspects of safety / routine lab analysis but not generally the focus
- Don't tend to review sample processing for external analysis if this is all that is done for a particular trial
- Control of blinded information reviewed

# Discussion and Questions



# GCP vs ISO EN 15189

- Demonstrates existing, externally reviewed, quality system
- ISO 15189 does not include GCP specifics
- Common to spend less time on QMS, training etc when accredited lab and focus on GCP aspects and trial data but some review still required for trial specific activities
- Have previously worked with UKAS/CPA to look at common topics and audit/inspection approaches

# Discussion and Questions



# Multi-track Analysers

- Only analyse what you have permission for
- No additional tests
- Protocol input and study set-up important

Ethical dilemma –  
What to do if you analyse additional parameters that you don't have consent for and it comes back with a significant result?



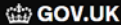
# Discussion and Questions



# GCP training for Laboratory Staff

General GCP training expectations:

- Appropriate knowledge, experience & training
- Awareness of roles and responsibilities (organisation's set-up & trial conduct)
- Training appropriate & proportionate for the role
- Documented training, experience & competence

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**Making GCP Training Relevant and Applicable: It's Not Just for Clinical Staff**

Jason Wakelin-Smith, 5 November 2018 - Compliance matters, Good clinical practice, Good laboratory practice



# Relevant and Proportionate...

Clinically significant deviations:

- What is a clinically significant deviation?
- Mechanism for notifying the PI & escalation
- Protection of trial blinding

Informed consent:

- Need to know that can only perform the tests described in the protocol and informed consent form
- Don't need to know about the process of consent

# Wider Awareness

Lots of guidance out there!

Think broadly...

The image displays four overlapping document covers, each representing a different regulatory guidance document:

- Top Left:** European Medicines Agency (EMA) cover for "Guideline on bioanalytical method validation". It includes a table with key dates: Draft agreed by the Efficacy Working Party (September 2009), Adoption by CPMP for release for consultation (28 November 2009), End of consultation (deadline for comments) (31 May 2010), Agreed to Pharmacovigilance Working Party (PWP) (June 2011), Adoption by CPMP (21 July 2011), and Date for coming into effect (3 February 2012).
- Top Right:** Medicines & Healthcare products Regulatory Agency (MHRA) cover for "'GXP' Data Integrity Guidance and Definitions".
- Bottom Left:** International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) cover for "ICH HARMONISED GUIDELINE BIOANALYTICAL METHOD VALIDATION M10". It notes a Draft revision ended on 26 February 2019 and is currently under public consultation.
- Bottom Right:** European Medicines Agency (EMA) cover for "Guideline on the content, management and archiving of the clinical trial master file (paper and/or electronic)". It includes a table with key dates: Draft adopted by GCP Inspectors Working Group (GCP IWG) (30 January 2017), Start of public consultation (12 April 2017), End of consultation (deadline for comments) (11 July 2017), Final revised document after comments received from public consultation adopted by GCP Inspectors Working Group (GCP IWG) (06 December 2018), and Date of coming into effect (6 months after publication). It also lists keywords: Trial master file, FMP, eFMP, essential documents, GCP inspection, archiving, scanning, retention, destruction.

# Discussion and Questions



# Engagement – What Do You Want?

Hope that you will bring topics and questions for discussion

Submit in advance if possible

