MHRA Stakeholder Engagement Meeting
(StEM)
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GCP Inspection Feedback and Discussion

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Disclaimer

- I am an employee of Daiichi Sankyo UK and have received support from my employer to attend this meeting.
- The data and information contained in this presentation have been obtained from a number of Pharmaceutical companies and CROs for the specific purposes of this meeting.
- The views expressed in this presentation are a collation of the comments volunteered from the above companies; they are neither my own personal views nor do they represent the position of my employer.

Introduction

- The great majority of GCP regulatory inspections by MHRA and other EU regulatory authorities are conducted within scope, concentrating on focus areas most relevant to subject safety and data integrity, with on-time communications and reports.
- The members of our stakeholder groups fully recognize the value of regulatory inspections, not only to protect subject safety and data integrity, but also in promoting best practices in clinical research.
- We recognize that MHRA has always held a tradition of implementation of regulation by consensus and our comments are intended to assist greater understanding and collaboration.

Introduction (cont.)

- This presentation will review some perceived exceptions, to raise areas of potential inconsistency for discussion.
- Data has been gathered from a representative number of pharmaceutical companies and will be presented in the form of summary metrics, comparisons between MHRA and other EU inspections, and anonymised feedback to illustrate specific points.
- Not all companies answered all questions, but all data provided has been presented without pre-selection in order to avoid bias.

Data Collection and Analysis

- Data and information from inspections by MHRA, EMA and non-UK EU national authorities were collected from 11 Pharma companies and CROs.
- Data collection period = last 2 years (i.e. since the last StEM meeting in March-2016).
- The 3 areas of feedback cover the following:
  1. Inspection performance metrics (e.g. timelines from notification to inspection date; inspection report turnaround timelines).
  2. Access requests (e.g. audit report access; remote access to documents/systems)
  3. Inspection focus (e.g. inspector approaches to non-significant quality or compliance issues)

Feedback area 1: Inspection performance metrics

# MHRA Inspections	# MHRA Inspections outside timelines	# EMA or non-UK EU Inspections	# EMA or non-UK EU Inspections outside timelines
24	9* (37%)	195	38** (19%)

* MHRA: 9 inspection reports issued 3 or more months after inspection (range 3-7m)

* MHRA: 2 outliers related to delay between first submitting dossier and inspection (16m), or between initial notification and inspection (>24m)

** Non-UK: 38 inspection reports issued late (range 3 to 14 months), after "substantial delays," or not received at all.

Feedback area 2a: Requests for audit reports

# MHRA Inspections	# MHRA Inspections where audit reports requested (Adequate vs. Inadequate justification)	# EMA or non-UK EU Inspections	# EMA or non-UK EU Inspections where audit reports requested (Adequate vs. Inadequate justification)
24	3 vs. 0*	195	5 vs. 5**

* MHRA have not requested to see internal audit reports without reasonable justification (e.g. to investigate significant non-compliance or quality issues).

** EMA have requested to see and obtained internal audit reports without reasonable justification on 2 occasions. On 3 further occasions, EMA suggested they may ask for audit reports, but did not after review of MVRs and follow-up letters showed evidence of CAPA implementation.

Feedback area 2b: Requests for remote access

# MHRA Inspections	# MHRA Inspections where remote access to eCRF and/or eTMF has been requested pre/post-inspection	# EMA or non-UK EU Inspections	# EMA or non-UK EU Inspections where remote access to eCRF and/or eTMF has been requested pre/post-inspection
24	4* (16%)	195	18** (9%)

* MHRA requested remote access to eCRF and/or eTMF pre-inspection, or post-inspection up to the time the report was issued.

** Non-UK: remote access to eCRF and/or eTMF was requested pre-inspection, or for several months post-inspection. (In at least 2 inspections, MHRA was part of an EMA inspection team.)

Feedback area 3: Inspection focus

# MHRA Inspections	# MHRA Inspections where focus included "low risk" areas*	# EMA or non-UK EU Inspections	# EMA or non-UK EU Inspections where focus included "low risk" areas*
21	5 (24%)	179	30 (17%)

*These represent inspections where, in the opinion of the inspected companies, disproportionate focus was placed on areas of low risk.

For example, valid issues were observed but they did not impact data integrity or subject safety or welfare in a meaningful way.

Frequent areas include minor issues with the TMF, audit trails, validation, source data identity, monitoring oversight. Detailed examples are provided in the next few slides.

Examples of low risk inspection focus: MHRA

- MHRA's focus on eTMF system functionality was considered excessive. Expectations for the system appeared to be for ease of MHRA inspection, at expense of company needs. Inspectors appeared negative when offered advice on how to use the system during the inspection.
- Inspection sample included a completed study for an indication where the development programme had been discontinued.
- MHRA emphasis on eTMF was driven by their own inspection expectations, and not directly related to subject safety, study outcomes or data integrity.
- MHRA duplicated a finding (regarding RSI) from a PV inspection that occurred approx. 6 months previously, although the CAPA previously provided for the PV inspection had been accepted.