Medicines & Healthcare products Regulatory Agency

MHRA
Regulating Medicines and Medical Devices

GCP INSPECTORATE

GSK CLINICAL UNIT CAMBRIDGE (CUC) INSPECTION REPORT

INSPECTION No: INSP GCP 5866/37356-0010

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Inspection Summary

Inspection & Organisation Information	
Inspection Number	INSP GCP 5866/37356-0010
Purpose of Inspection	Statutory GCP Systems and Phase I Accreditation Inspection
Type of Inspection	Onsite
Organisation Inspected	GSK Clinical Unit Cambridge (CUC)
Organisation Address	Addenbrooke's Centre for Clinical Investigation (ACCI), Addenbrooke's Hospital, Hills Road, Cambridge. CB2 0QQ
Organisation Type	Commercial Sponsor and Phase 1 Clinical Research Unit
Dates of Inspection	05 to 08 July 2021 (Onsite) 16, 23, 27 and 28 July 2021 (1.5 days of remote office based inspection for [redacted] and [redacted])
Lead Inspector	[redacted] Inspector
Accompanying Inspector(s)	[redacted] Inspector [redacted] Inspector
Date of Closing Meeting	08 July 2021 (last document received 28 July 2021)

Clinical Trials Reviewed	
Protocol Reference and Title	[redacted] A randomised double-blind, placebo controlled, single ascending and repeat dose, [redacted] study in [redacted]
EUDRACT Number	[redacted]
REC Reference Number	[redacted]
IMP Details	[redacted]
Protocol Reference and Title	[redacted] A randomized, double-blind, placebo-controlled, [redacted]
EUDRACT Number	[redacted]
REC Ref Number	[redacted]
IMP Details	[redacted]
Protocol Reference and Title	[redacted] a double-blind randomized, placebo-controlled, single and repeated oral dose escalation study [redacted]
EUDRACT Number	[redacted]
REC Reference Number	[redacted]
IMP Details	[redacted]

Inspection Report Version History (For Inspectorate Use Only)

01 - Inspection Report Date	01 September 2021
01 - Response Receipt Date	06 October 2021
01 - MHRA Review Date	22 October 2021
02 - Response Receipt Date	11 November 2021
02 - MHRA Review Date	23 December 2021

Inspection Close Date	21 March 2022

Background Information

Previous Inspection History

GSK CUC were last reaccredited on 17 August 2018. Since then, there have been a number of personnel changes addressed via variations approved on 17 April 2019, 16 September 2019, 01 December 2020 and 19 May 2021.

GSK were last inspected in May 2018, followed by a triggered inspection in July 2019 (due to the identification of a critical finding at the GSK laboratory in Ware by the GCP Laboratories group (inspection reference 5866/27277-0030)) which resulted in the findings identified for GSK as the sponsor of the trials.

Inspection Scope

This routine inspection of GSK CUC was conducted to review GCP systems and also Phase I reaccreditation of the CUC. Trials were selected, including [redacted] (EudraCT Number [redacted], however this trial was not reviewed during the inspection.

Due to the ongoing global pandemic, a full review of facilities was not conducted. Instead a review was performed of facilities that have been refurbished since the last inspection in 2018, including the new screening area and bathrooms and toilets within the clinical space on level [redacted]

Interviews were conducted using [redacted] video calls to reduce in person interaction.

The inspection confirmed that the MHRA Phase 1 accreditation continues to remain in place and a new certificate will be issued on receipt of satisfactory responses to this inspection report.

Definitions of Findings

Critical:

a) Where evidence exists that significant and unjustified departure(s) from applicable legislative requirements has occurred with evidence that:

   i) the rights, safety or well-being of trial subjects either has been or has significant potential to be jeopardised, and/or
   ii) the clinical trial data are unreliable and/or
   iii) there are a number of Major non-compliances (defined in (d) and (e)) across areas of responsibility, indicating a systematic quality assurance failure, and/or

b) Where inappropriate, insufficient or untimely corrective action has taken place regarding previously reported Major non-compliances (defined in (d) and (e))

c) Where provision of the Trial Master File (TMF) does not comply with Regulation 31A 1-3, as the TMF is not readily available or accessible, or the TMF is incomplete to such an extent that it cannot form the basis of inspection and therefore impedes or obstructs inspectors carrying out their duties in verifying compliance with the Regulations

Major:

d) A non-critical finding where evidence exists that a significant and unjustified departure from applicable legislative requirements has occurred that may not have developed into a critical issue, but may have the potential to do so unless addressed, and/or

e) Where evidence exists that a number of departures from applicable legislative requirements and/or established GCP guidelines have occurred within a single area of responsibility, indicating a systematic quality assurance failure.

Other:

f) Where evidence exists that a departure from applicable legislative requirements and/or established GCP guidelines and/or procedural requirement and/or good clinical practice has occurred, but it is neither Critical nor Major.

Reference Texts

- UK Medicines Act 1968.
- The Human Medicines Regulations 2012, SI 1916 and the applicable statutory instruments including 2004/1031 (and subsequent amendments)
- ICH E6 "Note for Guidance on Good Clinical Practice".
- Annex 13 to the EU Guide to Good Manufacturing Practice, 'Manufacture of Investigational Medicinal Products', July 2010.
- ICHE2A "Note for Guidance on Clinical Safety Data Management: Definitions and Standards for Expedited Reporting"
- Communication from the Commission — Detailed guidance on the collection, verification and presentation of adverse event/reaction reports arising from clinical trials on medicinal products for human use ('CT-3') (2011/C 172/01)
- EMEA/CHMP/SWP/28367/07: "Guideline on strategies to identify and mitigate risks for first in human clinical trials with investigational medicinal products"
- MHRA Phase 1 Accreditation Scheme, Version 4 (09 April 2021)

List of Common Abbreviations

AE	Adverse Event
ADR	Adverse Drug Reaction
ASR	Annual Safety Report
ATMP	Advanced Therapy Medicinal Product
CA	Competent Authority
CAPA	Corrective Action Preventive Action
CI	Chief Investigator
CRA	Clinical Research Associate
CRF	Case Report Form
CRO	Contract Research Organisation
CSR	Clinical Study Report
CSV	Computer Systems Validation
CTA	Clinical Trial Authorisation or Clinical Trial Agreement
CTFG	Clinical Trial Facilitation Group
CTIMP	Clinical Trial of an Investigational Medicinal Product
CV	Curriculum Vitae
DE	Dose Escalation
DSMB	Data Safety Monitoring Board
DSUR	Development Safety Update Report
eCRF	Electronic CRF
eCOA	Electronic Clinical Outcome Assessment
ePRO	Electronic Patient Reported Outcome
eTMF	Electronic Trial Master File
FIH	First in Human
FPFV	First Patient First Visit
GCP	Good Clinical Practice

GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
HRA	Health Research Authority
IB	Investigator's Brochure
ICF	Informed Consent Form
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IDMC	Independent Data Monitoring Committee
IMP	Investigational Medicinal Product
IRT	Interactive Response Technology
ISF	Investigator Site File/Investigator TMF
LPLV	Last Patient Last Visit
MAA	Marketing Authorisation Application
MHRA	Medicines and Healthcare products Regulatory Agency
MVR	Monitoring Visit Report
PI	Principal Investigator
PIS	Patient Information Sheet
PV	Pharmacovigilance
QA	Quality Assurance
QC	Quality Control
QMS	Quality Management System
QP	Qualified Person
RA	Regulatory Authority
RAMPCT	Risk Assessment ad Management Plan for Clinical Trials
R&D	Research and Development
REC	Research Ethics Committee
RMP	Risk Management Plan
RSI	Reference Safety Information
SAE	Serious Adverse Event
SAR	Serious Adverse Reaction
SDV	Source Data Verification
SDR	Source Data Review
SmPC / SPC	Summary of Product Characteristics
SI	Sub-investigator
SOP	Standard Operating Procedure
SUSAR	Suspected Unexpected Serious Adverse Reaction
TMF	Trial Master File
TOPS	The Over-volunteering Prevention Scheme
UAT	User Acceptance Testing

Inspection Findings

INSTRUCTIONS TO INSPECTED ORGANISATION

Inspection responses and any subsequent clarifications should be completed in the fields provided for each numbered finding. Please ensure there is a different row for each corrective and preventative action with the planned completion dates. Do not append any additional documentation or insert any file links. Please provide any other referenced documents as separate files.

No responses are required to any observations and recommendations.

1.0 Critical Findings

There were no **Critical findings** identified during this inspection.

2.0 Major Findings

There were no **Major findings** identified during this inspection.

3.0 Other Findings

There were **8 Other findings** identified during this inspection relating to **CRF Data/Source Data, Data Integrity Control Processes, Dose Escalation, Facilities and Equipment, Informed Consent, Protocol Compliance, Quality Assurance** and **Record Keeping/Essential Documents**.

3.1	**CRF Data/Source Data**
3.1.1	Stickers were being used in subject notes that obscured details recorded underneath. Examples were seen in the [redacted] rial for subjects [redacted] and [redacted] including for subject [redacted] screening window 30 days from previous' which was on top of another sticker, covering some writing on the sticker that was underneath.

Inspected Organisation's Response 01	
Evaluation & Root Cause	[redacted]
Corrective Action 1:	
Preventative Action 1:	

	[redacted]
MHRA Review 01	[redacted]

3.2	Data Integrity Control Processes
3.2.1	GCK CUC were transferring from the use of [redacted] to [redacted] Wave 1 had been completed in November 2020 with Wave 2 to occur later in 2021, as per the [redacted] (provided as part of the inspection dossier). Wave 1 concerned the management of the volunteer panel and tracking of clinical samples and Wave 2 would be to implement clinical trial data capture. The [redacted] system writes and retrieves data from a [redacted] server database located at the sponsor's [redacted]. Whilst a number of assessments had been conducted of GXP requirements, including in the [redacted] dated 16 May 2018, controls for access in the [redacted] dated 10 July 2020 and a [redacted] dated 16 October 2020, there was no evidence of an assessment of the segregation of the sponsor and investigator responsibilities under GCP. For example, the granting of access to staff to edit data by the Principal Investigator as the source data should be under the control of the Principal Investigator but the data is held by the sponsor on their servers and whether there is sufficient mitigation to prevent undetectable and unauthorised edits to the data. *The EMA's Reflection Paper on expectations for electronic source data and data transcribed to electronic data collection tools in clinical trials dated 01 August 2010 should be consulted. Additionally, MHRA is due to publish guidance on sponsor remote access to electronic health records and this should also provide additional guidance.*

Inspected Organisation's Response 01	
Evaluation & Root Cause	[redacted]
Corrective Action 1:	

	[redacted]
Preventative Action 1:	

MHRA Review 01	Response acceptable.

3.3	Dose Escalation
3.3.1	The people required to attend the DE meeting as per the [redacted] dated 25 September 2020 for the [redacted] trial was not adhered to. Both the Clinical Ward Manager and Clinical Development Manager were required to attend but were not listed on the meeting minutes for the DE meeting on 29 September 2020 for the decision to escalate to [redacted]. There were also inconsistencies noted between the meeting minutes and the Dose Escalation Decision Memo, which did not include the Medical Monitor as an attendee although the meeting minutes did.

Inspected Organisation's Response – 01	
Evaluation & Root Cause	[redacted]
Corrective Action 1:	
Preventative Action 1:	
Preventative Action 2:	

Preventative Action 3:	[redacted]

MHRA Review 01	[redacted]

3.3.2	It was not possible to reconstruct the data reviewed for Dose Escalation decisions. For example, in the [redacted] trial: • Part [redacted] Cohort [redacted] Treatment Period [redacted] there were three versions of the Safety Report with embedded documentation. Whilst some data was printed, it was not possible to reconstruct which data was included in which report and the associated version. Of the printed data, the protocol, title and page numbers were hand written without provenance or date, the demography listing from [redacted] was over 5 pages and difficult to match-up data to subjects and the Spirometry data did not have columns expanded so was missing data or was only visible as '########'. • Part [redacted] Cohort [redacted] Treatment Period [redacted] had two versions of the Safety Report but [redacted] dated 11 January 2021 was not filed in the Site Investigator File (SIF). Lab results were printed but only contained a header stating [redacted] Other files embedded in the Safety Report [redacted] dated 25 January 2021, including listings of AEs, Spirometry or ECG results were not printed (although this is not an exhaustive list). Examples were also seen in the [redacted] trial where the [redacted] printed paper data listings lacked any version control to link them to the relevant version of the CUC safety report, for example, listings associated with Part [redacted] Cohort [redacted] (periods [redacted] and [redacted] . Whilst the SOP was not explicit in regards to the printing of the data, the [redacted] that was referenced within it (and provided as document request [redacted] required to 'store CUC Safety Report and QC'd source data in SIF'. This was a finding at the previous inspection in July 2019.

Inspected Organisation's Response – 01	
Evaluation & Root Cause	[redacted]
Corrective Action 1:	

	[redacted]
Corrective Action 2:	
Preventative Action 1:	

MHRA Review 01	[redacted]

3.4	**Facilities and Equipment**
3.4.1	A number of errors were identified with the testing of alarm call points. Whilst there was evidence of testing available, it was not sufficiently robust to demonstrate effective checking of all the alarm call points and pagers to ensure they were all checked on a regular monthly basis as required by [redacted] dated 21 October 2020 [redacted] section [redacted]. For example: • There was evidence of what appeared to be weekly testing taking place, but in some cases, i.e. November 2019, testing was appeared ad hoc and was performed on 9th, 10th and 23rd (twice). • The documentation of the monthly testing did not give sufficient information about what the testing procedure involved to confirm compliance with the SOP, for example, it did not reflect that a sample of pagers were tested because all the pagers were listed, so it could not be seen which ones were actually tested. • Some tests were not signed off (for example August 2019 monthly and 20 August 2019 weekly) to confirm the test had been completed. • There was a dating error on the sign-off of weekly test on 21 January 2020 (as the year was entered as 2019). • The system was changed so the process for the weekly testing including re-booting was no longer valid, but this had not been changed in terms of the job instructions for the site engineering department so there were comments about this on the documentation (for example 03 July 2020 and 24 July 2020). The [redacted] SOP's change history did not detail any change to remove weekly testing requirement, but it was not present in the current SOP.

Inspected Organisation's Response – 01	
Evaluation & Root Cause	[redacted]
Corrective Action 1:	
Preventative Action 1:	
Preventative Action 2:	

MHRA Review 01	[redacted]

3.5	Informed Consent

3.5.1	The template informed consent documentation used did not sufficiently differentiate between 'GSK - the sponsor' and 'GSK - the investigator' regarding access/storage/ transfer of subject data. There should be clarity for subjects and compliance with data protection regulations (please also see finding 3.2.1).

Inspected Organisation's Re	
Evaluation & Root Cause	[redacted]
Corrective Action 1:	
Preventative Action 1:	

MHRA Review 01	[redacted]

3.6	**Protocol Compliance**
3.6.1	In the [redacted] trials, deviations relating to inclusion/exclusion criteria were recorded as non-significant (in both paper logs and [redacted] tracking sheets) which was not in compliance with [redacted] dated 25 March 2020 appendix [redacted] which indicated that deviations relating to inclusion/exclusion criteria were examples of significant deviations.

Inspected Organisation's Response - 01	
Evaluation & Root Cause	[redacted]
Corrective Action 1:	
Preventative Action 1:	
Preventative Action 2:	
Preventative Action 3:	

Preventative Action 4:	[redacted]

MHRA Review 01	[redacted]

Inspected Organisation's Response 02

[redacted]

MHRA Review 02	[redacted]

3.6.2	A non-significant deviation was raised incorrectly in the [redacted] trial for subject [redacted] (raised on 13 May 2021) pertaining to the subject not meeting the protocol inclusion criteria for Body Mass Index (BMI). However, the subject met the inclusion criteria for the trial at screening.

Inspected Organisation's Response - 01

Evaluation & Root Cause	[redacted]

	[redacted]
Corrective Action 1:	
Preventative Action 1:	

MHRA Review 01	[redacted]

3.7	Quality Assurance
3.7.1	The CAPA effectiveness checks conducted on the Dose Escalation finding CAPA identified at the MHRA GCP inspection in July 2019 (INSP GCP5866/37356-0009) were insufficient. Although a significant amount of work had been conducted on the end to end process of dose escalation, including creating and/or updating document templates, strengthening processes and conducting gap analyses, these have failed to prevent findings being identified at this inspection (please also see finding 3.3). *It was acknowledged that management monitoring exercises have been performed on four trials (including selected trials [redacted] and [redacted] in January and February 2021 and further CAPAs were implemented. It was also noted that the planned Clinical Quality Assurance (CQA) audit in 2020 for reviewing the process was delayed to accommodate the process revision and to allow a sufficient sample size to have adopted the new ways of working. This was further delayed due to the COVID-19 pandemic as there were few trials being run post the implementation of CAPAs and training. It was acknowledged that an audit is on the schedule for Q3 2021.*

Inspected Organisation's Response - 01	
Evaluation & Root Cause	[redacted]
Corrective Action 1:	
Preventative Action 1:	

MHRA Review 01	[redacted]

3.8	Record Keeping/Essential Documents

3.8.1	There were a number of documents that formed part of the SIF that were not filed and were only available via document request. In the [redacted] trial this included (although is not an exhaustive list): • Correspondence and ordering of rescue medication. • Evidence of the independent review of the starting dose described in the RAMPCT. • Site Signature and Delegation of Responsibilities Log.

Inspected Organisation's Response - 01	
Evaluation & Root Cause	[redacted]
Corrective Action 1:	
Corrective Action 2:	
Preventative Action 1:	

MHRA Review 01	[redacted]

3.8.2	The Study Reference Manual for the [redacted] trial did not list [redacted] on the front cover, only [redacted] dated 16 September 2020, which was after the first subjects were dosed. Therefore it appeared that the manual was not in place in a timely manner.

Inspected Organisation's Response - 01	
Evaluation & Root Cause	[redacted]

	[redacted]
Corrective Action 1:	
Preventative Action 1:	

MHRA Review 01	[redacted]

3.8.3	Inconsistencies were seen between the paper deviation log dates (for example the date the deviation was raised) and what was documented in the non-significant spreadsheet in [redacted] kept in the GSK database for the [redacted] trial.

Inspected Organisation's Response - 01	
Evaluation & Root Cause	[redacted]
Corrective Action 1:	
Preventative Action 1:	

MHRA Review 01	[redacted]

The following are observations and recommendations to which no response is required.

Observations and Recommendations
Dose Escalation • For the [redacted] trial, it was not possible to reconstruct when Pharmacy were made aware of the outcome of the Dose Escalation Meeting. A Dose Confirmation Form (version dated 11 March 2020) was completed but there was no requirement for Pharmacy to confirm receipt. Therefore in trial [redacted] following the Dose Escalation Meeting to decide on the dose for Part [redacted] Cohort [redacted] Treatment Period [redacted] Dose it could not be confirmed when Pharmacy received the details. It was noted that the current version (dated 10 February 2021) did require Pharmacy confirmation of receipt and was appropriately completed for Part [redacted] Cohort [redacted] Treatment Period [redacted] Dose). **IMP Management/Pharmacy**

- It was noted that the QP still was certifying IMP to European Union (EU) 2001/20 EC 13.3. For example, the [redacted] trial subject [redacted] QP certification on 28 April 2021. The recommendation from the MHRA's [redacted] Inspector would be that a Great Britain (GB) based QP no longer operates under the Directive and, as the EU would not recognise the certification, reference to the UK Statutory Instrument should be used. A batch certification done under a Northern Ireland (NI) MIA(IMP) would be recommended to quote the EU Directive and the UK SI to cover use of the IMP in GB and NI/EU.

Project/Trial Management

- GSK staff member [redacted] stopped working for GSK in June 2019 but had not yet had their employment status changed and was therefore still present on the [redacted] report.

Subject Eligibility

- For subject [redacted] in the [redacted] trial, the PI initially confirmed the subject as eligible on 07 September 2020 using a GP Report dated 18 Jul 2019, which was outside of the requirement to use a version from within a year. There was no documentation to require that a more up to date GP Report would be required. It was noted, however, that a later GP Report dated 02 June 2020 was reviewed and eligibility re-confirmed again on 08 September 2020.

Subject Recruitment

- It was recommended that Study Reference Manual templates is reviewed to determine if the TOPs checks and GP Report requirements should be included as they were not contained in the version for the [redacted] trial.
- It was recommended that clarification is provided regarding the exclusion criteria pertaining to 'current enrolment or past participation within the last 30 days before signing consent in any other clinical study intervention of any other type of medical research.' It was not clear if this pertained to 30 days of last dose or the final visit. In trial [redacted] a non-significant deviation for subject [redacted] (raised on 13 May 2021) recorded that the subject met this exclusion criteria but was previously dosed on 10 March 2021 and the subject signed consent for the [redacted] trial on 12 April 2021.

Quality Systems

- It was stated to inspectors at interview that that the deviation investigation report had a completion timeframe of T + 30 days (where T = deviation notification date). However [redacted] dated 25 March 2020 [redacted] that this was T + 25 days.

Report Author and Reviewer

Report Author:

[redacted] Inspector, MHRA

Report Reviewer:

[redacted] Inspector, MHRA

The factual matter contained in the Inspection Report relates only to those things that the inspection team saw and heard during the inspection process. The Inspection Report is not to be taken as implying a satisfactory state of affairs in documentation, premises, equipment, personnel or procedures not examined during the inspection.

Appendix I Summary of Activities

Inspected Organisation				
Clinical Trial	Assessed			Comment
	Yes	Partial	No	
[redacted]		✓		Risk assessment, delegation, dose escalation, subject recruitment
[redacted]		✓		Risk assessment, delegation, protocol compliance, subject recruitment, consent
[redacted]		✓		Risk assessment, dose escalation, subject recruitment, Consent, IMP.
[redacted]			✓	

Inspected Organisation				
Activity	Assessed			Comment
	Yes	Partial	No	
Analytical Laboratory			✓	
Archiving			✓	
BE/ BA activities			✓	
Clinical Pathology Laboratory			✓	
Clinical Trial Reporting			✓	
Computerised Systems			✓	
Contracts & Agreements	✓			
Data Management			✓	
eCRF / Diaries / IVRS			✓	
IMP Management		✓		
Medical Affairs			✓	
Monitoring			✓	
Pharmacovigilance			✓	
Project Management			✓	
Quality Assurance	✓			
Quality Systems	✓			
R&D Unit (Non-commercial only)			✓	
Regulatory Affairs			✓	
Statistical Analysis			✓	
Technical Facility (i.e. x-ray)			✓	
Training	✓			
Trial Master File/Essential Documents		✓		
Other	✓			Dose escalation Emergency trolley Subject recruitment Compliance with Phase I Accreditation Scheme

Appendix II Additional Findings Related to Phase 1 Accreditation Requirements

In order to maintain accreditation in the voluntary Phase I accreditation scheme, the following accreditation specific findings are required to be addressed. ***Evidence will be required to be submitted with the response in order to assess for the continued acceptance into the Phase I accreditation scheme.***

A1	**Risk Assessment** There was no formal procedure that included requirements to check any conditions imposed by MHRA or REC had been considered and addressed, for example as part of the risk management plan.

Inspected Organisation's Response 01	
Evaluation & Root Cause	[redacted]
Corrective Action 1:	
Preventative Action 1:	
Listing of CAPA evidence provided	

MHRA Review 01	[redacted]

[redacted]

A2	**Risk Assessment** The signature for the review of the RAMPCT for the [redacted] trial in relation to the protoco[redacted] dated 21 October 2020 update was of the Clinical Development Manager [the Project Manager], not the PI. Whilst it was stated that the PI had discussed the plan verbally, there was no documentation to support that the no changes assessment was approved by the PI who was responsible for the completion of the RAMPCT.

Inspected Organisation's Response 01	
Evaluation & Root Cause	[redacted]
Corrective Action 1:	
Preventative Action 1:	
Listing of CAPA evidence provided	[redacted]

MHRA Review 01	[redacted]

A3	**Subject Identification & Recruitment** There were issues identified with the registration of subjects in TOPS. Subjects were not registered in TOPS at the time of consent and screening. [redacted] dated 14 October 2020 [redacted] which required to send a GP Letter 'once the subject has passed screening' and then 'check and register the suitable subject as applicable on the TOPS'. Therefore, subjects who consented but were screen failed were not registered, despite the HRA website (https://www.hra.nhs.uk/about-us/committees-and-services/the-over-volunteering-prevention-system accessed on 07 July 2021) stating 'volunteers should be registered on TOPS when they attend a unit for a screening exam'. For example: • For subject [redacted] on the [redacted] trial, the consent form was signed on 01 September 2020 at screening but the subject was not registered on TOPS until 07 September 2020 when eligibility was confirmed. The subject could potentially attend another unit during this interval. • There was inconsistency for registering subject [redacted] (previously [redacted] on the [redacted] rial in TOPs. They were registered on 23 September 2020 as 'never dosed' [correctly] then registered on 14 October 2020 but not as 'never dosed'. The subject was then subsequently re-screened on 23 November 2020 which resulted in recruitment but was not re-entered into TOPS for the screening event, instead relying on the previous registration. • In the [redacted] trial, Subject [redacted] was screen failed for the [redacted] and [redacted] trials and Subject [redacted] was screen failed for the [redacted] trial but these were not showing on their TOPS records.

Inspected Organisation's Response 01	
Evaluation & Root Cause	[redacted]
Corrective Action 1:	
Preventative Action 1:	[redacted]
Listing of CAPA evidence provided	

[redacted]

MHRA Review 01

[redacted]

Inspected Organisation's Response 02

[redacted]

MHRA Review 02

[redacted]

A4	**Subject Identification & Recruitment** Subject [redacted] was dosed in the [redacted] trial despite participating in another FIH at another Phase 1 Unit two months previously. It is noted that GSK were not aware of this at the time of inclusion of the subject, however the review of previous trial participation was not robust enough to detect this. The subject reported on the [redacted] completed on 14 October 2020) that their last dose in a clinical trial was November 2019 and their last follow-up visit was January 2020. However this did not correspond with their TOPS record (accessed on 19 October 2020) which did not indicate inclusion in a trial in 2019 but did show the FIH trial at another Phase 1 Unit. [redacted] dated 14 October 2020 [redacted] did require the Recruitment Team/Physician to 'clarify any ambiguities with the subject' but not what next steps would be required if they did not.

Inspected Organisation's Response 01

Evaluation & Root Cause

[redacted]

Corrective Action(s)	[redacted]
Preventative Action(s)	
Listing of CAPA evidence provided	

MHRA Review 01	[redacted]

Inspected Organisation's Response 02	
Corrective Action:	[redacted]
Due Date:	

MHRA Review 02	[redacted]

A5	**Subject Medical History** Subject [redacted] was dosed in the [redacted] trial despite participating in another FIH at another Phase 1 Unit two months previously. GSK were not aware of this at the time of inclusion of the subject. An updated Health Verification Form E was sent to the subject's GP on 16 September 2020 (although was not required as a version from within a year was completed on 06 February 2020) and a response was completed on 22 January 2021 which indicated that the subject had been in another trial in August 2020 and 'not to be in another trial for three months post-completion'. This version of the Health Verification Form E, GP Report and the [redacted] had not been provided to the PI for the [redacted] trial at the time of the inspection for his review as [redacted] dated 14 October 2020 [redacted] only required PI/ Sub Investigator review of medical history in relation to trial specific inclusion/exclusion criteria.

Inspected Organisation's Response 01	
Evaluation & Root Cause	[redacted]

	[redacted]
Corrective Action(s)	
Preventative Action(s)	
Listing of CAPA evidence provided	

MHRA Review 01	[redacted]

Inspected Organisation's Response 02	
Corrective Action:	[redacted]
Due Date:	

MHRA Review 02	[redacted]

A6	**Training** [redacted] was rota'd onto overnight cover on 26 October 2020 when her Basic Life Support (BLS) training had expired. Training was completed on 23 October 2019 and not again until 24 February 2021 despite the certificate including 'valid for one year' (as per document request [redacted]). Planned Deviation [redacted] to SOP [redacted] stated that 'ALS and ILS courses have been cancelled since the start of the lockdown during the COVID-19 pandemic. This has led to staff being unable to attend a course and subsequently exceeding the time limit for renewing their certification. The UK Resuscitation Council has granted a 6-month extension to ALS and ILS certification for those that expire in 2020'. However, this did not cover the BLS training that [redacted] had completed.

Inspected Organisation's Response 01	
Evaluation & Root Cause	[redacted]

	[redacted]
Corrective Action 1:	
Preventative Action 1:	
Listing of CAPA evidence provided	

MHRA Review 01 [redacted]

The following are observations and recommendations to which no response is required.

Observations and Recommendations

Quality Systems

- SOPs referred to the MHRA Phase I Accreditation Scheme Requirements but not the current version [referred to [redacted] dated 28 October 2015 whereas the current version is [redacted] dated 09 April 2021]. For example, [redacted] dated 14 October 2020 [redacted] It is recommended that the current version of the Phase I scheme, [redacted] 09 April 2021, is assessed to determine if any SOP are to be updated or document if no update is required.

Staff Delegation and Responsibilities

- The task of 'confirm dose following dose progression meeting' was delegated to the role of Sub-Investigator in the [redacted] trial. This was a FIH trial but the role was assigned to physicians who were not FIH PIs, including [redacted] and [redacted] It was noted that the Site Signature and Delegation of Responsibilities Log also contained a section for 'Principal Investigator Designee for Delegation' which was only delegated to FIH PIs. It was recommended that the documentation is updated in order that tasks are not repeated throughout the document and that FIH PI tasks are not inadvertently delegated. *It was noted that no confirmations of dose had been completed by non-FIH PIs.*

Subject Identification & Recruitment

- The inspectors were informed in document request [redacted] that [redacted] dated 14 October 2020 [redacted] section [redacted] stated 'check the subject's Health Verification Form has been completed within the last year; if not, request completion of an updated Health Verification Annual Update Form or medical history summary from their GP'. However, this was not written clearly in the RAMPCT for the [redacted] trial where section [redacted] required 'a GP verification form dated no earlier than 12 months prior to start of trial' which is ambiguously written.

Training

- Historical tracking records for life support training status was not retained and only the current status was available. It was recommended to retain the historical tracking records as this can provide evidence that can be quickly reviewed to assess training requirements being met for staff in the unit between accreditation inspections.

Appendix III – GCP Inspection Statement

Medicines & Healthcare products Regulatory Agency

MHRA Regulating Medicines and Medical Devices

GCP INSPECTION STATEMENT

Inspection Number	INSP GCP 5866/37356-0010
Purpose of Inspection	Statutory GCP Systems and Phase I Accreditation Inspection
Type of Inspection	Onsite
Organisation Inspected	GSK Clinical Unit Cambridge (CUC)
Organisation Address	Addenbrooke's Centre for Clinical Investigation (ACCI), Addenbrooke's Hospital, Hills Road, Cambridge. CB2 0QQ
Organisation Type	Commercial Sponsor and Phase 1 Clinical Research Unit
Dates of Inspection	05 to 08 July 2021 (Onsite) 16, 23, 27 and 28 July 2021 (1.5 days of remote office based inspection for [redacted] and [redacted])
Lead Inspector	[redacted] Inspector
Accompanying Inspector(s)	[redacted] Inspector [redacted] Inspector
Date of Inspection Statement	21 March 2022

The organisation has provided corrective and preventative actions in response to the inspection report. These have been reviewed by the GCP Inspectorate and are considered acceptable. This inspection can be considered closed.

In summary:

There were no "critical" or "major" findings identified during this inspection.

The factual matter contained in the GCP Inspection Report relates only to those things that the Inspection team saw and heard during the inspection process. The GCP Inspection Report and Inspection Statement are not to be taken as implying a satisfactory state of affairs in documentation, premises, equipment, personnel or procedures not examined on this occasion.

Statement Issued by

[redacted] Inspector, MHRA