MHRA Position Statement and Guidance
Electronic Health Records

Executive Summary
There is a legal requirement for all organisations sponsoring and hosting interventional clinical trials on medicines in the UK to comply with the UK Medicines for Human Use (Clinical Trials) Regulations 2004 (as amended). The move within the NHS from paper to electronic health record (eHR) systems has led to significant compliance issues in relation to Good Clinical Practice (GCP). There are potential serious consequences for Trusts that have an inadequate eHR system. These include: Trusts being rejected by commercial sponsors at site selection due to non-GCP compliant systems; the rejection of marketing authorisation applications (MAAs) or journal publications due to an inability to reconstruct the trial; and the unethical recruitment of patients to trials as the systems do not support the robust collection and retention of data. All of these issues may have a negative impact on the selection of NHS sites, and ultimately UK NHS Trusts/ Boards becoming less attractive places to conduct research (and the resultant financial implications of this, as well as reduced access to the latest research and medicines for UK patients). This guide aims to provide clarity for NHS Trust/ Health Boards on how to implement eHR systems compliant with the regulations, and should be used to guide system providers at the project implementation stage and also to make required changes to existing systems to bring them into compliance.

Background
The NHS commitment to the introduction of electronic health records (eHRs) is not new; it was first agreed by the NHS Executive in 1998 from which the National Programme for IT was introduced in 2002. There have been multiple iterations of the approach to be used, ultimately leading to a decision in 2011 to develop a 'connect-all' approach rather than the introduction of a single system. This has led to the implementation of many different systems for the creation and management of clinical eHRs.

Following the subsequent introduction of these diverse eHR systems, the MHRA as a regulator has seen issues in relation to their compliance with the UK Medicines for Human Use (Clinical Trials) Regulations 2004 (as amended) and Good Clinical Practice (GCP) principles. This is also a significant concern for NHS Trusts/ Health Boards and pharmaceutical companies conducting clinical trials of investigational medicinal products.

Purpose
The MHRA supports the move towards eHRs but recognises there is a need to facilitate their regulatory compliance *(in particular see Schedule 1, Part 2(4&9), UK Clinical Trials Regulations 2004 (as amended))*. In response to stakeholder queries on this issue, the MHRA GCP Inspectorate has developed this position statement on points for consideration during the design, build and implementation of an eHR system. The purpose of this guidance is to provide clarity on the regulatory requirements and the MHRA position for Trust/ Health Board Chief Executives and R&D departments, and also for commercial organisations sponsoring clinical trials hosted within the NHS.

Trusts/ Health Boards that are trial sponsors have responsibility for providing a GCP compliant records management system. This means implementing eHR systems that are robust, GCP compliant, and that source data is identifiable for each study (see Regulation 31A(8) UK Clinical Trials Regulations 2004 (as amended)). *Trusts/ Health Boards who act as trial hosts, and thereby are responsible for source records for hosted trials, are*

responsible in the same way as sponsors for ensuring their records management systems are compliant.

It is essential that the Trust/ Health Board has a clear understanding of what the source data are for both sponsored and hosted trials, as a lack of control over the documentation could result in an inability to reconstruct the trial and the trial data being labelled as unreliable. This could have major consequences for the Trust/ Health Board's reputation as a clinical trial site.

It should not be assumed that a provider of a clinical eHR system will have an understanding of GCP, and therefore Trusts/ Health boards should supply the eHR system providers with appropriate user requirements to ensure GCP compliance. This guidance document should be considered along with the Trust/ Health Board requirements for standard health care records and other applicable regulations and guidance (such as data protection legislation).

Ensuring robust, compliant electronic systems from the outset will enable the NHS to continue to be involved in hosting the highest standards of research in the UK. It is recommended that this is achieved by having an R&D representative on eHR project boards, and through the provision of a user requirement specification to the eHR provider at the system development stage that incorporates clinical trial / GCP requirements, as described below.

Compliance Issues

Problems found with the eHR system during GCP inspections:
- Insufficient consideration of quality control (QC) systems and procedures defining how the eHR system will be used to support clinical trial requirements (as detailed in the guidance below);
- Inability to demonstrate investigator oversight due to information in the eHR having been entered solely by the research nurse or via dictation, and subsequent transcription by admin staff. Examples have been seen where the source data has been deleted/ destroyed with no evidence of investigator review of the entry;
- Lack of or insufficient audit trails in the system to enable reconstruction of any changes made to trial data;
- No audit trails to document investigator review of electronic laboratory results, x-rays, scans etc. and/ or such data being stored in an uncontrolled system;
- Paper print outs from the eHR being provided for monitoring or inspection reference that omit information contained in the electronic system;
- Inability to readily access audit trails;
- A lack of control over scanned source data images such as CT scans, and the subsequent uploading into PAC (Picture Archiving & Communication) systems. This includes issues such as data remaining editable (including patient identifiers/ dates of scans etc.) in stand-alone systems without audit trails in place. This has also been seen in relation to images imported from other sources such as referring hospitals.

Problems found with scanning/ transfer from paper to eHRs during GCP inspections:
- Bulk scanning and subsequent disposal of paper medical records (including clinical trial source data) without having a robust QC system and/or process for making 'certified copies' in place. This is required to ensure that the electronic copy is an accurate copy of the source, and to enable verification of the quality of the data;
- Inadequate scan resolution and/ or scanners not fit for purpose;
- Black and white scanning of colour records, resulting in the loss of associated metadata such as the paper health record colour coding system;

- Scanning of paper medical records as PDF files, in no particular order and with missing sections, thereby making trial reconstruction potentially impossible due to gaps in source data;
- Scanning sub-contracted to companies operating to their own QC processes, without adequate checks on whether these processes are sufficient or appropriate.

Guidance and Factors to consider

It is strongly advised that Trusts obtain input from R&D and experienced clinical trial practitioners (such as Principal Investigators, research nurses, data coordinators) on clinical trial source data requirements prior to the introduction of eHR. When establishing an eHR system the following aspects should be considered:

1. For the eHR system:
   - Maintenance of data integrity via ongoing data review, change control processes and clear audit trails;
   - Audit trails for information added to the eHR. Any new information added to the subjects' medical notes (whether paper or electronic) should show when the entry was made and by whom, so that the documentation provides a full audit trial of events (any amendments/ deletions etc.);
   - The investigator should still be able to demonstrate their medical oversight of the trial when eHR systems are used. For example where all entries into the medical records are made by a research nurse it can be difficult to reconstruct the investigator's input. A process should be incorporated into the system to enable investigators to verify the information recorded in the same way a paper record would have been signed and dated. The same principles should be applied to the review of other supporting documentation such as electronic laboratory results, imaging, pharmacy records etc. by the investigator;
   - Where edit functions are in place for images that form part of the health records e.g. to remove subject identifiers and insert subject numbers prior to the image being transferred to the sponsor, QC processes should be implemented to ensure the correct re-labelling of these images (and retention of the original);
   - Access to the system should be available for inspectors and sponsor representatives (e.g. monitors and auditors), which is limited to trial patients. This will enable source data verification of clinical trial subjects whilst protecting the confidentiality of non-trial patients. This should include access to audit trails;
   - System to flag clinical trial patients and search for trial records within the eHR;
   - Appropriate archiving to ensure long term reliability, retrieval and reproducibility of electronic data (and metadata), in line with regulatory storage timelines (note this will be 25 years as standard under the new Clinical Trials Regulation 536/2014);
   - Written procedures in place to cover all of the above processes. These procedures could also be used to assure external sponsors that compliant eHR systems have been implemented;
   - Trusts should have oversight systems in place (usually via R&D) to ensure compliance with these processes and to enable potential serious breaches of GCP to be detected and reported e.g. if source data are lost or destroyed.

The above specifications are in addition to the standard requirements for computer systems used in clinical trials, including:
- physical security;
- restricted access;
- record of roles and access rights;
- data protection;
- back-up of systems;

- system validation and working processes for change control and system failure.

2. For the scanning/ transfer process from paper to e-records:

- A validated process to confirm scanned documents are certified copies e.g. QC checks (to include scan quality, legibility, completeness, page counts etc.) and a documented audit trail of this process. Supporting documentation should include what documents were transferred, when and how the scanning took place and by whom (i.e. metadata);
- Written procedures in place to cover the above processes (these may also assure external sponsors that the system is GCP compliant).

References
'All clinical information should be recorded, handled and stored in such a way that it can be accurately reported, interpreted and verified' (Schedule 1, Part 2(9)); and
'The necessary procedures to secure the quality of every aspect of the trial shall be complied with'
Schedule 1, Part 2(4)), UK Clinical Trials Regulations 2004 (as amended).

'The sponsor and chief investigator shall ensure that the medical files of trial subjects are retained for at least 5 years after the conclusion of the trial'.
Regulation 31A (8), UK Clinical Trials Regulations 2004 (as amended).

ICH GCP 1.22, 1.51, 1.52, 4.9.7, 5.1.2, 5.15.1, 5.18(k)(m), (i) 6.10 - although no legal requirement to comply, sponsors who intend to submit MAAs must comply with ICH GCP. If sites do not comply with ICH GCP references in relation to the source data requirements there is therefore a risk the sponsor will not select the site.

Sources of further guidance
- 'Reflection paper on expectations for electronic source data and data transcribed to electronic data collection tools in clinical trials' (EMA/INS/GCP/4542280/2010) http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2010/08/WC500095754.pdf
- PIC/S Guidance on Good Practices for Computerised Systems in Regulated "GXP" Environments (PI 011-3) http://www.picscheme.org/index.php
- Section 11.5.2 eHR and 14.5 Computerised systems, MHRA GCP Guide 2012.
- MHRA GCP Forum: http://forums.mhra.gov.uk/forumdisplay.php?1-Good-Clinical-Practice-(GCP)