



EUROPEAN COMMISSION
ENTERPRISE AND INDUSTRY DIRECTORATE-GENERAL

Consumer goods
Pharmaceuticals

Brussels, 5 November 2008
ENTR/F/2/SF D(2008) 34961

**GUIDANCE DOCUMENTS
CONTAINING THE COMMON PROVISIONS
ON THE CONDUCT OF GCP INSPECTIONS BY COMPETENT
AUTHORITIES OF THE DIFFERENT MEMBER STATES**

Annex V

**GUIDANCE FOR THE CONDUCT OF GOOD CLINICAL
PRACTICE INSPECTIONS**

Phase I Units

Document History:	
Date of adoption of draft by GCP Inspectors working group:	22 July 2008
Date of publication by the Commission	5 November 2008
Date of entry into force:	= Date of publication + 6 months
Supersedes:	N/A
Reason for Revision:	N/A

Guidance Title: Annex V to Guidance for the conduct of Good Clinical Practice inspections-Phase I Units

Keywords: GCP Inspection, Phase-I units

This document forms part of the guidance documents containing the common provisions on the conduct of GCP inspections. Please check for updates in the Volume 10 of the Rules Governing Medicinal Products in the European Union.

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1. PURPOSE

The purpose of this document is to provide guidance for the preparation of GCP inspections conducted in Phase I Units. The points to consider in this document are specific to these types of units and other guidance documents should be referred to for consideration of those areas common to other types of inspections, e.g. computer systems, archiving and quality systems.

2. LIST OF ABBREVIATIONS

Abbreviations used in the document:

FIH	First In Human
GCP	Good Clinical Practice
ICH	International Conference on Harmonisation
IMP	Investigational Medicinal Product
PI	Principal Investigator
SOP	Standard Operating Procedure
SUSAR	Suspected Unexpected Serious Adverse Reaction

3. INTRODUCTION

Guidance on Phase I trials and in particular First in Human (FIH) studies has been published, with the objective of managing and minimising potential risk to volunteers who take part in these types of studies. This guidance is listed in the references and should be taken into account during the inspection of the Phase I unit.

Appropriately trained and experienced staff are key to the safety of volunteers in Phase I units; competence should be documented and reassessed on a regular basis. Units must have appropriate emergency equipment and procedures for handling medical emergencies must be in place. These procedures should be tested on a regular basis and all staff must be trained in carrying out their responsibilities.

4. DESCRIPTION OF PROCEDURE/REQUIREMENTS

4.1. Protocol and procedural aspects

Points to consider:

- What data is used to make dose escalation decisions. Is this adequate if less than a full cohort
- QC of dose escalation data and interim safety reports

- Clarity of dose escalation and withdrawal criteria
- Documentation of dose escalation decisions
- Knowledge of the PI in relation to pharmacology of the IMP
- Risk assessment and contingency planning e.g emergency treatments, specialist medical staff

4.2. Ethics and regulatory approval

Points to consider:

- Independence of the Ethics Committee
- What documents does the Committee review. Approval of generic screening consent forms
- Approval of advertising
- Documentation of approvals
- Process for submission for Ethics Committee approvals. Updating and maintenance of Ethics Committee documentation
- ICH GCP compliance statement of the Ethics Committee
- List of members of the Ethics Committee
- Annual reporting to the Ethics Committee.

4.3. Quality Assurance and SOPs

Points to consider:

- Written procedures for every aspect of the study process (SOPs)
- Organisation and independence of the QA group
- Training on SOPs, GCP and also specific protocols
- Audits on vendors and suppliers

4.4. Investigator Master File

Points to consider

- Identification and use of source documents
- Storage of medical records
- Long-term archive arrangements
- Documentation of meetings

- Delegation log in place and signed
- Use of Direct Electronic Data Capture methods

4.5. Personnel

Points to consider

- SOP for minimum staffing levels during clinical conduct and medical supervision on dosing days
- Relationship of the Investigator with the Sponsor company
- Adequate staff resources
- Basic life support and advanced life support training
- Qualifications of the Investigators
- Qualification of Bank/Agency staff
- Management of Agency/Bank staff

4.6. Facilities

Points to consider:

4.6.1. Emergency Procedures and Equipment

- Availability and maintenance of emergency medicines and equipment
- Emergency contact numbers provided to the volunteers
- Procedures in case of an emergency
- Alarm points
- Agreement with the local hospital(s) for any services provided
- Fire evacuation procedures

4.6.2. General Facilities

- Security of the facility with respect to unauthorised or limited access
- Back-up power supply
- Storage of samples. Monitoring of the fridges and freezers
- Maintenance, service and calibration of instruments/equipment

- Facilities for archiving, laboratory and pharmacy.

4.6.3. *Volunteer Care*

- Procedures for testing for use of illegal drugs (drugs of abuse)
- Measures in place to ensure compliance of the volunteers with the protocol
- Monitoring of subjects
- Facilities for meals. Documentation of meals
- Leisure facilities for lengthy stays/overnight stays
- Identification of subjects during their stay
- Documentation of medical history

4.7. Sampling

Points to consider:

- Documentation of processing of samples within the unit prior to shipment to the laboratory
- Facilities equipped and resourced to handle the capacity of samples
- Procedures for collection of urine samples
- Procedures for sample management e.g. collection, processing, consideration for missed and late samples, aliquoting, labelling, tracking, storage and shipment
- Clocks – easily visible and synchronised.

4.8. Investigational Medicinal Product

Points to consider:

- Authorisation/Licence(s)
- Blinding, if applicable
- Storage and access control
- Packaging and labelling
- IMP administration
- Compliance with the randomisation list, if applicable
- IMP accountability

4.9. Recruitment and Consent

Points to consider:

- Recruitment strategies
- Volunteer database
- Collection and verification of volunteer medical histories
- Contact with the subject's primary physician/family doctor
- Procedures to prevent 'over-volunteering'
- Routine screening procedure
- Subject records
- Procedures taken to verify the identity of the volunteers
- Procedures for payment
- Procedures for taking consent
- Training of the recruitment staff
- Recruitment of staff from the facility/institution

4.10. Contracts

Points to consider:

- Contracts in place prior to study start
- Management and documentation of collaborations with other departments/organisations

4.11. Insurance and indemnity

Points to consider:

- Provisions in place for insurance and indemnity
- Indemnification of the investigator
- Professional indemnity insurance for nurses, if applicable

4.12. Confidentiality

Points to consider:

- Confidentiality agreements for Agency staff, consultants etc

- Procedure to ensure volunteer identifiers do not leave the unit (e.g on sample labels, adverse event documentation etc)

4.13. Adverse Events

Points to consider:

- Recording of adverse events
- Follow- up and counselling
- SUSAR reporting to Ethics Committee/Regulatory Authorities
- SUSARs information provided to investigator(s)

5. FORMS NEEDED FOR THIS PROCEDURE

Not Applicable

6. REFERENCES AND RELATED DOCUMENTS

- Directive 2001/20/EC on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use.
- Directive 2005/28/EC laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the requirements for authorisation of the manufacturing or importation of such product
- CPMP/ICH/135/95: “Note for Guidance on Good Clinical Practice”.
- Annex 13 to the EU Guide to Good Manufacturing Practice.
- ABPI Guidelines for Medical Experiments in Non-Patient Human Volunteers, 2007
- Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products (CHMP/SWP/294648/2007)