

GUIDANCE FOR AUDITING QUALITY SYSTEMS OF INDEPENDENT ETHICS COMMITTEES IN EUROPE

The European Forum for Good Clinical Practice



‘where science and ethics meet’

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1. Introduction

This document has been developed following research and discussions by the Ethics Working Party of the European Forum of Good Clinical Practice (EFGCP). It defines guidelines and recommendations to establish a quality assurance programme for Independent Ethics Committees in Europe.

Following review by EFGCP of 'The Procedures for Ethical Review of Protocols for Clinical Research Projects in the European Union' and the publication in 2007 (ISSN: 1364-9027) responses to the question asked 'Is there an ongoing quality assurance process (e.g. audits, inspections, internal standard operating procedures) for research ethics committees' provided an almost universal answer of 'no'. There were a few exceptions but most countries had no system in place.

ICH GCP (CPMP/ICH/135/95) defines audit as 'a systematic and independent examination of trial related activities and documents to determine whether the evaluated trial related activities were conducted, and the data were recorded, analysed and accurately reported according to the protocol, sponsor's standard operating procedures (SOPs), Good Clinical Practice (GCP), and applicable regulatory requirement(s)'. The key words defining the process of audit are 'systematic' and 'independent'. The challenge here may be the independence of the auditor and this will need to be carefully considered. At present, there are no established guidelines or recommendations in operation within Europe to assist Independent Ethics Committees in establishing their quality systems. (Note: IEC reviews in Asia promoted by WHO, refer to "surveys" and "surveyors" in place of "audits" and "auditors").

This guidance document builds upon the earlier EFGCP document "European Guideline for Auditing Independent Ethics Committees", 2002. Others have also published similar guidance in this area such as; Dent, N. J. and Sweatman, W. J. F; "Can Non-Regulators Audit Independent Ethic Committees (IEC), and If So, How?", Quality Assurance Good Practice and Law Journal, January - March 2002, Volume 9, No.1 pp 43-54.

The aim of this document is also to provide a complimentary guide to support the *Guidelines and Recommendations for European Ethics Committees* previously published by EFGCP in 1997.

By introducing a quality system within an Independent Ethics Committee, this will assist in raising standards of the committee and thereby provide greater protection for human subjects participating in biomedical research.

What is the Purpose of Internal Audit?

Internal audit forms an important part of a quality system. As part of a quality system, Standard Operating Procedures (SOPs) are established which define both quality control review at key steps and quality assurance which is a random process of reviewing by audit. The aim of audit is to standardise

processes and practices which would ultimately improve the overall quality function of Independent Ethics Committees. During the process of audit, the adherence to internal procedures, ICH GCP, European Directives and any country-specific guidelines or regulations are reviewed.

The Audit Approach

The role of Independent Ethics Committees has been defined in ICH GCP, in Directive 2001/20/EC and during national implementation. The auditing approach must be focussed on established guidelines and legal requirements. This document aims to act as a guidance to identify the minimum requirements as defined by EFGCP.

The process of accreditation of Independent Ethics Committees has not been defined in this document. If this route is introduced in the future within Europe, this would not reduce the need for the establishment of a quality system within the Independent Ethics Committee. In fact, the role of Quality Assurance would considerably assist in this process.

What Types of Internal Audits can be conducted?

Internal audits are likely to fall into one of the following categories:

- Documentation review (to include but not limited to: review of documents provided to Independent Ethics Committee members, CVs and training records of members/expert reviewers, minutes of meetings and agendas, files on projects reviewed/approved/declined, indemnity documents)
- Process review (to include but not limited to: the approval process, circulation and review of documents, independence of voting, assessment of suitability of investigators and sites, process for annual safety report reviews, review of Suspected Unexpected Serious Adverse Reactions (SUSARs), process for substantial amendments, processes for interaction with Regulatory Authorities/ other Ethics Committees/Advisory Committees)
- Facility review (to include but not limited to: storage of documents, fire, security, long-term archiving).

2. Glossary

Accreditation

A system of accreditation or certification of Independent Ethics Committees by a suitable body that has the authority and appropriate procedures and qualifications to determine that a Committee qualifies for accreditation.

Applicant

A qualified researcher undertaking the scientific and ethical responsibility for a research project, either on his / her own behalf or on behalf of an organisation/ firm, seeking a decision from an Independent Ethics Committee through formal application.

Appointing Body

The organisation that appointed the Independent Ethics Committee such as a Health Authority, Institution or Governmental Authority.

Audit

A systematic and independent examination of clinical trial-related activities and documents to determine whether the evaluated trial related activities were conducted, and the data were recorded, analysed and accurately reported according to the protocol, standard operating procedures (SOPs), Good Clinical Practice (GCP), and the applicable regulatory requirement(s). In the context of this document, an audit refers to a systematic and independent examination of the constitution and practices of an Independent Ethics Committee.

Auditee

The audited party. In the context of this Guidance, auditee refers to the Independent Ethics Committee being audited and / or the representatives of the Independent Ethics Committee and / or may be any partners that the Independent Ethics Committee interacts with.

Auditor

A suitably qualified and trained person responsible for carrying out an audit and for reporting the findings.

Audit Certificate

A document presented by the auditor confirming that an audit has taken place (if available).

Audit Findings

The results of audit based on the scope of the audit and the materials reviewed by the auditor. The audit findings should refer to specific observations made by the auditor and supported by objective evidence. Audit findings express the auditor's conclusions regarding specific procedures or systems audited and evaluated as being compliant or noncompliant with the appropriate requirements and the impact on the work of the Independent Ethics Committee.

Audit Plan

A plan setting out the specific practices, resources, activities, and time lines relevant to a particular audit or a group of related audits.

Audit Report

A written evaluation by the auditor of the results of the audit.

Conflict of Interest

A conflict of interest arises when a member (or members) of an Independent Ethics Committee hold(s) interests with respect to specific applications for review that may jeopardise his/her (their) ability to provide a free and independent evaluation of the research with a focus on the protection of the trial participants. Conflicts of interests may arise when a member of an Independent Ethics Committee has financial, material, institutional, occupational or social ties to the research.

Community

A community is a group of people understood as having a certain identity due to the sharing of common interests or to a shared proximity. A community may be identified as a group of people living in the same village, town, or country and thus, sharing geographical proximity. A community may be otherwise identified as a group of people sharing a common set of values, a common set of interests, or a common disease.

Decision

The response (positive, conditional, or negative) by an Independent Ethics Committee to an applicant following the review of an application.

Good Clinical Practice (GCP)

A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and the rights, integrity, and confidentiality of trial participants are protected.

Investigator

A person responsible for the conduct of the clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator.

Independent Ethics Committee (IEC)

An independent body (a review board or a committee, institutional, regional, national or supranational), constituted of medical / scientific professionals and non-medical / non-scientific members, whose responsibility it is to ensure the protection of the rights safety and well-being of human participants involved in a trial and to provide public assurance of that protection, by, among other things, reviewing and approving /providing favourable opinion on, the trial protocol, the suitability of the investigator(s), facilities, and the methods and material to be used in obtaining and documenting informed consent of the trial participants. The legal status, composition, function, operations, and

regulatory requirements pertaining to Independent Ethics Committees may differ among countries, but should allow the Independent Ethics Committee to act in agreement with the requirements of ICH Good Clinical Practice.

Protocol

A document that describes the objective(s), design, methodology, statistical considerations, and organisation of a trial. The protocol usually also gives the background and rationale for the trial, but these could be provided in other protocol reference documents.

Protocol Amendment

A written description of a change to, or formal clarification of, a protocol.

Quality Assurance (QA)

All those planned and systematic actions that are established to ensure that the trial is performed and the data generated, documented (recorded), and reported in compliance with Good Clinical Practice (GCP) and the applicable regulatory requirements(s).

Quality Control (QC)

The operational techniques and activities undertaken within the quality assurance system to verify that the requirements for quality of the trial-related activities have been fulfilled.

Sponsor

An individual, company, institution, or organisation which takes responsibility for the initiation, management, and / or financing of a clinical trial.

Standard Operating Procedures (SOPs)

Detailed, written instructions to achieve uniformity of the performance of a specific function.

3. Assigning Auditors/Auditor Qualifications and Training

Auditors should be assigned based on the following qualifications/experience and training:

- Suitable experience and education
- Independence
- Formal regular appropriate training
- Understanding of the clinical trial process
- Up-to-date knowledge of EU regulations and guidelines and national laws and requirements

Suitable experience and education:

- It is desirable that auditors be educated to University level or have equivalent experience in medicine, pharmacy, pharmacology, toxicology or other related field. The level of education is required to allow for effective communication with persons involved in clinical trials.
- Auditors need to be familiar with the healthcare systems in the relevant Member States and where appropriate, third countries and to be familiar with basic medical terminology.
- Auditors must have had training in auditing techniques either from attendance at a course(s) and/or by being accompanied and mentored by experienced auditors.
- Auditors must be provided with a job description to document their roles and responsibilities and any ongoing training requirements.
- Up to date records of qualifications, training and experience must be maintained.

Independence:

- Auditors must report, at the highest level to the body that has sponsored the audit, usually the Appointing Body. Preferably they should not be in a reporting structure in which the Chair of the Independent Ethics Committee is their superior. Auditors, if assigned from an external source (i.e. not directly working for the relevant Independent Ethics Committee) must initially sign a statement provided by the Ethics Committee to show they have no conflict of interest, any financial or other links with the Independent Ethics Committee and parties to be audited so that they can be provided with full access to all auditable documents. The auditor should also sign a confidentiality agreement to be allowed full access to documents.

Formal regular appropriate training:

- Auditors must undertake regular GCP training / updates which must be documented in their CV/training records. The number of hours on GCP training will vary depending on whether there have been significant

changes to GCP regulations since the last training was completed. Training should be completed when any new GCP directives / guidelines or other documents are issued, either at a European or national level.

- It is desirable to have training on the relevant parts of the GMP requirements of Annex 13.
- Other appropriate training and training needs must be assessed regularly. Auditors must take action to maintain and improve their skills.
- The level of training required must be sufficient to ensure competence and skills required for the planning, execution, reporting and management of audits. Ideally, the course agenda and training materials should be permanently filed.

Understanding of the clinical trial process:

- Auditors must have knowledge of principles and processes that apply to the development of a medicinal product and clinical research.
- It is recommended that auditors should have at least 1-2 years experience in GCP auditing. The clinical trial process should then be well understood.
- Additionally, regular training should also be documented in the Auditors CV/training records.
- Auditors need to be familiar with procedures and systems for recording clinical data, have a knowledge and understanding of current technology, IT systems, data handling and archiving techniques.
- Auditors must have up-to-date knowledge of applicable EU and national legislation and guidelines applicable to the conduct of clinical trials and the granting of a marketing authorisation.
- Training needs to be conducted on a regular basis or when any new regulations or guidelines are published.
- The course agenda and training materials must be filed in the auditor's training records.

4. Audit Planning

Elements of planning for an audit can be incorporated into an audit plan. An audit plan should include:

- **Scope**
To identify the intent, purpose, location, date (if known) of the audit activities and any relevant study identifiers.
- **Contacts**
To identify the key personnel involved in conducting the audit (both auditors and auditees)
- **Agenda**
Outline of detailed activities e.g. facility tour, identification of interviewees.
- **Documentation to be Reviewed**
To identify the documents to be available for review
- **Audit History**
To outline the audit history as relevant to the auditor- e.g., describes past interactions
- **Letter/Communication**
Auditees should receive a letter of introduction with a confirmation of the audit dates and brief synopsis of activities to be conducted
- **Provision for Responses**
Description of how responses are to be made (e.g. inclusion of action plan) and the expectant timeframe.

5. The Conduct of an Audit

An audit of an Independent Ethics Committee should be conducted according to a previously agreed audit plan that follows the following procedures:

5.1 Opening Meeting

It is anticipated that at a minimum, an officer (i.e. chairperson, assistant chairperson or secretary) will be present at the opening meeting. The audit begins with an opening meeting between the auditor and representative(s) of the Independent Ethics Committee.

The auditor leads the opening meeting and introduces the agenda:

- Introduction of all attendees
- Review of the purpose and scope of the audit

- Review of the agreed audit plan
- Confirmation of the agreed audit plan requirement of availability of the documents and facilities to be reviewed
- Discussion of the current practices (e.g. SOPs / working practices / organisation document including frequency of meeting / members / meeting minutes) of the Independent Ethics Committee and the impact of any guidelines, laws, or regulatory requirements on those practices
- Clarification of Independent Ethics Committee representative availability during the audit and contact arrangements
- Clarification of availability of identified interviewees during the audit
- Confirmation of the time and date for the closing meeting
- Clarification of any unclear details from the audit plan
- Clarification of to whom the report should be sent.

5.2 Document Review

The auditor should review the documents required for the audit as well as the manner in which documents are filed and securely stored, including previous editions of any procedures or earlier SOPs. Some of these documents may have been reviewed by the auditor in advance of the audit visit bearing in mind the requirements of confidentiality and privacy.

5.2.1 Documents Referring to the Constitution and Standard Operating Procedures of the Independent Ethics Committee

The auditor should review the documentation referring to the constitution and standard operating procedures (SOPs) of an Independent Ethics Committee. These SOPs should include the following information:

- Authority under which the Independent Ethics Committee was established and relationships to institutions (i.e. hospitals)
- A statement (dependant upon national laws) that the Independent Ethics Committee follows ICH Good Clinical Practices Guidelines (requirement ICH GCP 5.11.1.b), relevant laws and regulatory requirements, and appropriate national and international guidelines
- Terms for the appointment of members (for example, duration, renewal procedure, disqualification, and resignation and replacement

procedures) including reserve members and specialists identified to provide advice as needed

- Conditions of appointment (for example, withdrawal from the decision-making process if there is a conflict of interest); willingness to publicise his / her full name, profession, and gender; agreement to declare any financial reward or equivalent from Independent Ethics Committee work to officials of the committee, and the signing of confidentiality agreements)
- Procedure for making the appointment including the individual or party that makes the appointment, selection of candidates (for example, by consensus, by majority vote, or by direct appointment)
- Provisions and conditions for expedited Independent Ethics Committee review and approval, e.g. “chairman’s approval”
- Membership requirements, including the duties, responsibilities and training of members
- Quorum requirements, including the minimum number of members of Independent Ethics Committee to be present, the minimum distribution of professional requirements, and gender requirements; and back up arrangement to ensure that there are always enough members to take decisions
- Procedures for submitting an application for the review of the proposed clinical research, including the need for the name and address of the Independent Ethics Committee required to provide the decision, the number of copies to be submitted, the language of the core documents to be submitted, the required format, the deadlines for review dates, the means by which the applicants will be informed of any incompleteness, the fee structure for considering an application and follow-up (if applicable)
- Required documentation to be included in the application, including the application form, the protocol, the current (or the latest available) investigator’s brochure or equivalent describing recent pharmacological and toxicological data if absent from the protocol, for post-registration studies a summary of the product characteristics, recent curriculum vitae (signed and dated) of the investigator(s) which should include ICH GCP training, recruitment of trial participants documentation including any advertisement material, all rewards and compensations to the trial participants, informed consent forms in core and local language (if appropriate), indemnity agreements for liability, other documentation that may influence decisions made by the Independent Ethics Committee (such as diary cards and questionnaires for trial participants), previous decisions by other Independent Ethics Committees that may influence the decision of the reviewing Independent Ethics Committee

- Meeting procedures, including the preparation of the agenda, the minting of the meetings, invitations of guests to the meeting (including sponsors, investigators, and specialists that may provide advice on occasions or assist in the review of a particular protocol with consideration for possible conflicts of interests and confidentiality agreements as warranted)
- Actions necessary for the enrolment of trial participants in emergency treatments (for example, Independent Ethics Committee recommendations of investigator handling informing the local community and / or next of kin in the case of trauma or stroke)
- Decision-making procedure, including whether the decisions are by consensus or vote, the manner of specifying conditional decisions, management of ambiguous decisions and the manner of documenting the reasons for negative decisions. The procedure for documenting the appeals and the outcome of the appeal
- Procedures to assess safety of a study (whether industry sponsored or non-commercial sponsored study), e.g. how safety reports are handled (SAEs / SUSARs / annual safety reports), how they are received from the investigator / sponsor and if there are any requirements for reports from other sites / countries
- Procedure for communicating with other Independent Ethics Committees and Regulatory Authority(ies)
- Procedure for communicating a decision which should include a dated and version controlled document stating the name of the Independent Ethics Committee (including if it is a central or local Independent Ethics Committee); the exact title of the research project / clinical trial; a list of the documents reviewed, their date and version number; the name and title of the applicant; the date and place of the Independent Ethics Committees decision; a list of members present during the vote (can be listed by role); a clear statement of the decision made with any advice or comment; and the signature and date of the chairperson of the Independent Ethics Committee or in his / her absence by another official of the Independent Ethics Committee but never a non-voting member of the ethics committee. In the case of a positive decision, confirmation that all amendments have been duly regarded and brought to the attention of the full committee by the chairperson. In the case of a negative decision, the reasons for a negative decision are clearly stated. [A full committee should review all individual amendments submitted to the committee involving patient safety and welfare.] Additionally, cycle times should be considered
- Procedures for the notifications of completion or premature study terminations

- Continuing review (including frequency, determined by the nature of the study) but recommended to be at least annually
- If procedures exist for Independent Ethics Committee visits to sites for monitoring purposes
- Processes for the development, maintenance and revisions of procedures
- Documentation and archiving procedures, including an inventory of all documents archived and the length of storage of the documents based on their SOPs and on the national legislation. These documents should identify the author, authorisation, date of release, and the date of future review of the documents. In addition, earlier editions of these documents should be available to the auditor when relevant.

Additionally, the following documents should also be reviewed during audit:

- Listing of current and previous members of the Independent Ethics Committee
- Curriculum vitae of current members of the Independent Ethics Committee; a description of the requirements for holding the office of the chairperson, his / her deputy (if appropriate), secretary, and treasurer (the secretary should be defined carefully to avoid confusion between a secretary who is a voting member of the Independent Ethics Committee and an administration clerk who helps prepare the documents and arrange for dispatch of correspondence) and confidentiality agreements
- Record of all incomes and expenses of the Independent Ethics Committee (including honorariums, payments, and reimbursements made to members and staff); budget review should evidence financial support of the responsible Authority
- Description of the responsibilities and duties of the members of the Independent Ethics Committee (for example, announcement of meeting dates, last dates for submission, agenda of meetings, minutes, sending notification of decisions, filing and archiving) and structure (e.g. minimum number of members, affiliations and gender diversity, procedures for appointing external experts)
- Registration of applications, including the process whereby incoming material is dated, version controlled, checked for completeness, filed, the applicant informed of the expected date of review, and the Independent Ethics Committee members informed of the review date
- Maintenance and tracking of records including written, verbal, or electronic communications

- Review procedures (i.e. selection of reviewers, allowance of expedited reviews) and timelines including frequency of Independent Ethics Committee meetings
- Agendas of all Independent Ethics Committee meetings relevant to the audit plan with parallel reviews of meeting minutes
- Elements of the review of the application, including considerations such as: the completeness of the information and documentation, the suitability of the investigator(s) and supporting staff and the site, adequate provision for monitoring the conduct of the study, the adequacy and comprehensibility of the written and oral information to be provided to the trial participants, relatives and other legal guardians, or representatives, the means of recruitment of trial participants, provisions for receiving and responding to queries and complaints, provisions for compensation / treatment in the case of injury / disability/ death of a trial participant attributable to participation in the study, insurance and indemnity agreements covering the liability of the investigator by the sponsor, scientific design, study conduct and ethics- e.g. measures taken to ensure the confidentiality of personal participant information and the rewards and compensation for trial participants
- Review Independent Ethics Committee procedure for determining the suitability of investigators and support staff
- Review Independent Ethics Committee procedure for determining the suitability and quality of facilities
- Review Independent Ethics Committee procedure for examining the arrangements for rewarding or compensating investigators and the relevant aspects of any agreement between the sponsor and the site
- Minutes of all Independent Ethics Committee meetings relevant to the audit plan (including time, date and place of the meeting, members present, third parties present, points of discussions, decisions made [including how the decision was made], signature and date of the chairperson or his / her deputy)
- Whether the Independent Ethics Committee requires documentation of the registration of the submitted trials to be in a publicly available clinical trials registry.

5.2.2 Audit Specific Applications (sample) Made to the Independent Ethics Committee.

Auditors should review the applications submitted to the Independent Ethics Committee as well as the manner in which those applications are handled. The materials that are to be reviewed should be established in the audit plan

and agreed to by the Independent Ethics Committee. An auditor assigned by an Appointing Body may not review confidential documents that are outside of the scope of the audit plan.

The following documents should be considered:

- Materials submitted by applicants (including protocols, informed consent materials, advertising materials, information regarding potential conflicts of interest, information regarding incentives for trial participants, the curriculum vitae of investigators, insurance certificate, safety reviews, as applicable)
- Correspondence regarding applications, decisions, and follow-ups
- Copies of the decisions and advice provided to applicants.

5.3 Interviews

The auditee(s) would normally be members and staff of the Independent Ethics Committee. Some or all of the members of the Committee may be involved (possibly including lay members). The auditors may also interview others that interact with the Independent Ethics Committee (Investigators, institution representatives; etc) as appropriate. Auditees will be interviewed to provide information to the auditor explaining the roles and processes of the Independent Ethics Committee.

5.4 Tour of the Facilities

The auditor should observe the facilities for the reception, handling, filing and archiving of applications to, and the records of, the Independent Ethics Committee.

5.5 Storage and Archiving of Audit Documents

An archive should be suitably designed and constructed to accommodate the materials to be archived and to ensure their integrity. A building, room, fire-resistant safe, filing cabinet or other appropriate storage can be designated as an archive. The following factors should be considered as part of the archive designation:

- A secure location to prevent unauthorised access to the retained materials, e.g. by the use of locks or electronic entry systems.
- An archive should be able to withstand the elements of weather. Consideration may need to be given to specific local conditions such as a risk of flooding.
- Storage should occur in areas with minimum variation in temperature and humidity if stored for long period of time. Data tapes should be kept in accordance with EC Guidelines for GMP i.e. duplicates tapes in fire-proof safes or in off site storage.
- A risk assessment relating to the entry of pests (e.g. rodents, insects) into the archive should be undertaken. If appropriate, a monitoring program should be implemented.
- Fire precautions are usually according to national legislation, local by-laws and building regulations. A minimum requirement is for automatic fire detection and extinguishing system or fire detection and provision of readily accessible fire fighting equipment. Smoking must be forbidden. Water is not advisable but is better than having no precautionary systems. Dry powder, carbon dioxide or halon substitute extinguisher can be used and to consider automatic, non-aqueous extinguishing systems.

Retention of Materials

The retention period set for trial materials should take account of all legal, regulatory, operational, national, historical or fiscal requirements that apply to the organisation.

Destruction of Material

Measures should be taken to prevent accidental or premature destruction of documents. There should be defined procedures for managing the destruction of materials that include:

- Processes for identifying materials that have reached the end of their retention period
- Approvals by appropriately qualified individuals needed for the destruction to occur
- How the destruction will be carried out, that ensures the materials confidentiality is maintained
- Records of destruction should be retained

Electronic Records

An electronic record is defined as information recorded in electronic form which requires a computerised system to access or process. The risk of

obsolescence media, software, file format) of electronic records presents special challenges for their long term retention.

To ensure that essential information remains complete and retrievable throughout the retention period, a migration strategy is essential. The strategy must ensure that the data transferred remains complete and accurate. The migration procedures used must be validated. Electronic records should be maintained in a designated archive. Procedures must be in place to ensure they are managed appropriately throughout their lifecycle.

Contract Archive Services

The use of contract archive facilities is permissible but it must be ensured that they are satisfactory and that records may be made available if requested. The contract archive organisation should have documented procedures for operations.

There should be a formal, documented, agreement with the contract archive that details the level and conditions of service to be provided. This agreement should include:

- Specific location of archive facilities to be used
- Process for authorising use of alternative archive facilities
- Transportation of material to and from the archive
- Chain of custody of materials
- Access rights to stored material
- Storage conditions within the archive facility and required monitoring
- Period of storage
- Method of retrieval/access
- Method of return/disposal including authorisation requirements

Business Continuity and Disaster Recovery

A disaster recovery plan describing the steps to be taken in the event of damage to the archive or archived materials should be in place. The types of event to be considered in the plan should be determined by an assessment of the exposure risks which are likely to be most dependent on the archive location and environment. Examples of the risks to be considered should include but not be limited to fire, flood, pest infestation and structural damage due to, e.g. subsidence, forced entry of the archive by unauthorised persons.

5.6 Closing Meeting

At the end of the audit, the auditor should hold a meeting with the auditees, who would normally be officials of the Independent Ethics Committee and members of the committee. A representative of the Appointing Body may also attend this meeting. The main purpose of this meeting is to present audit findings to the auditee(s) to ensure that the results of the audit are clearly understood and there is no misunderstanding by either the auditees(s) or the auditor. It is an opportunity to ask questions but it is not the place for

protracted discussion, to argue with the auditors, or to report how the audit findings will be addressed (that should be done in the written response to the audit report). The closing meeting should be of a supportive nature rather than one of conflict.

6. The Audit Report

The audit report should reflect the execution of the audit. It should be dated and signed by the auditor and contain, at the minimum, the following items:

- Scope and objectives of the audit (these should include that the conduct of the Independent Ethics Committee meets those aspects of ICH GCP and local regulations relating to Independent Ethics Committee)
- Identification of the auditor (s)
- Identification of the auditee(s) and the representative(s) of the auditee
- Audit plan
- Identification of the facilities, persons interviewed, and the documents reviewed
- Audit methodology
- Findings of the audit
- Recommendations for corrective actions or areas of suggested revisions in practice
- Timeframe for responses
- Audit report distribution list
- Signature and date of the auditor.

The audit report is strictly confidential and should be retained securely and only shared with the auditor(s), auditee(s) and the Appointing Body. Due to the sensitive nature of the audit report, some Independent Ethics Committees Standard Operating Procedures require that the audit report is destroyed (by confidential waste means) after the corrective and preventative actions have been put in place. The documentation of the completion of the corrective and preventative actions should be retained securely by the auditees for the period required by their local procedures for retention of other Independent Ethics Committee documentation.

7. Audit Follow-up

7.1 Corrective and Preventative Actions

The auditor should determine with the auditees and the sponsor of the audit, who would be the most appropriate person to respond to each of the findings. The auditee is then responsible for determining, initiating, and completing corrective and preventative actions according to the findings of the audit report. These actions and a time period for completion of the actions, should be communicated to the auditor within a pre-determined time period following the receipt of the audit report.

Corrective Action and Preventive Action plans (often referred to as CAPA) should be explained.

Definitions:

Corrective Actions that are taken can be in isolation; for example the errors or inconsistencies that the auditor put forward from the sample audited were corrected by the auditees.

Corrective Actions can also be taken in a systemic way; for example a systematic check was made across the entire system or set of studies, to check for similar errors to the ones identified in the audit sample and corrections were made.

Preventative Actions (taken in a systematic fashion) would be defined as actions that were put in place to prevent recurrence of all similar errors across an entire system or set of studies. Examples might be: implementing a new training program, re-training the staff, creating and implementing an SOP (Standard Operating Procedure), implementing a new Quality Control (QC) process across the entire system or set of studies, etc.

7.2 Follow-up

In order to derive the greatest benefit from an audit, it is necessary for the auditees (with the help of others) to produce a comprehensive CAPA that addresses the audit findings, puts in place systems which make the reoccurrence of similar issues unlikely and periodically monitors the system to see that the CAPA is effective. Such implementation of a CAPA will increase the quality of the operations of the Independent Ethics Committee and will produce assurance to the regulatory bodies.

Ideally, the auditor and the sponsor of the audit would determine if the responses to the audit were acceptable and determine if the audit can now be considered “closed”.

If a follow-up audit is thought to be appropriate, an audit plan should be prepared and agreed to by the auditor and the auditees.

7.3 Audit Certificate

The auditor may provide the Independent Ethics Committee with an audit certificate.

The purpose of the audit certificate is to confirm that an audit was performed and completed. It does not reflect a positive outcome of the audit. The audit certificate should include the following:

- Name and affiliation of the auditor
- Name of the Independent Ethics Committee audited
- Type of audit (i.e., audit of an Independent Ethics Committee)
- Audited system (for example, general review or specific to a project or clinical trial)
- Audit dates

The audit certificate may be appended to the Clinical Study Report (see Appendices of the ICH Guideline “Structure and Content of Clinical Study Reports” adopted by the EU as CPMP/ICH/137/95 Note for Guidance on Structure and Content of Clinical Study Reports).