

SOP 11: Quality Assurance

Background/Objectives

It is the main objective of CESAR to improve the treatment of cancer patients by conducting studies required for the approval of new anticancer drugs. It is therefore important that all observations and findings are properly documented for verification. This supports the reliability of the data and ensures that the conclusions presented are correctly derived from the raw data.

The quality assurance measures required by CESAR, the pharmaceutical industry and the national associations for medical oncology jointly form a comprehensive quality assurance program.

Monitoring

Studies are monitored by the sponsor's monitors in accordance with the guidelines defined in the sponsor's own SOPs. The procedure is to be specified in detail in the study protocol (see 'SOP 03: Preparation and Structure of Trial Protocols'). This applies also to the situation of CESAR-sponsored studies.

Quality Assurance by the Sponsor/Inspection by Relevant Authorities

The quality assurance department of a sponsor's institution or a corresponding auditor that has been contracted by the sponsor is entitled to conduct audits at the participating investigators' institutions and, if appropriate, at the data center (if study data are analyzed at the center). A statement to this effect must be included in the study protocol (see 'SOP 03: Preparation and Structure of Trial Protocols'). Audits follow the procedures specified in the sponsor's SOPs. Drug regulatory authorities to whom the data of a study have been submitted, as well as the authorities in charge of the monitoring of clinical studies in the respective territory of study conduct are entitled to inspect

the investigational sites as well as the original records of the study.

System Audits of CESAR

Auditors

The Project Review Committee (PRC)/Quality Assurance Committee (QUAC) appoints 2 auditors who may be but must not necessarily be members of the respective working group. No person may serve as auditor for an audit at his own institution.

Conduct of a System Audit

The auditors will arrange a date for the audit at a member's institution 4 weeks in advance. The system audit comprises the following items (see also 'SOP 1: Clinical Investigations in CESAR'):

- Local Ethics Committee;
- adequate staff for/with
 - Patient care by physicians and other authorized (e.g. nursing) personnel,
 - A local representative (medical doctor) available,
 - Performing specialist examinations (e.g. radiography),
 - Documentation,
 - Drug accountability (storage, distribution and return of trial medication);
- Adequate facilities for performing clinical studies with
 - Access to hospital beds for inpatient observation,
 - Direct access to an intensive care unit,
 - Resuscitation equipment,
 - Quality assurance implemented for diagnostic procedures (e.g., participation in quality assurance programs);
- Adequate facilities for keeping of the study materials (study files/trial medication) in a secure, limited-access area;
- Adequate facilities for the archiving of the study documentation after completion of a study;

- 100% source data verification for at least 5 study patients;
- Protocol violations (patients not eligible or not evaluable for investigator-related reasons);
- Timely reporting of serious adverse events or other adverse events with an obligation for expedited reporting;
- Evaluation and verification of a list of patients entered on phase I/II studies (by indications).

Support of the Quality Assurance Committee by the Data Center

The data center will issue a quarterly status report on CESAR's studies. This report will include incremental information on recruitment rates as well as information regarding items 7–9 ('Conduct of a System Audit') for all participating institutions. The members of the QUAC will routinely receive this report as a monitoring tool and as an aid for planning and conducting an audit.

Reports

After a system audit, the auditors will send a report to the audited member, the Chair of the working group and the data center.

Study Evaluation Meetings/Response Evaluation Meetings

After closure of a study and prior to closure of the data base for statistical analysis (see 'SOP 9: Statistical Design and Analysis') a response evaluation meeting will be held. At this meeting of investigators, the case reports of all patients

entered on the study will be presented. The documented findings of imaging procedures such as conventional radiography, computed tomography, ultrasound, and magnetic resonance imaging will be verified by re-evaluating the corresponding source documentation (i.e. x-ray films, etc.).

Evaluability and tumor response will be decided on in consensus with stringent interpretation of the study protocol and the criteria specified therein. If such consensus decision deviates from the primary assessment of the investigator, the corresponding entry in the Case Report Form (CRF) will be corrected accordingly, either by correcting the original CRF or by writing a notice of change that will be attached to the CRF. Special care has to be taken that a copy of the corrected CRF or the notice of change is included in the documentation to be retained by the investigator and that the data base of the study is corrected accordingly.

In addition, the meeting shall discuss all aspects of the study that are relevant for the quality of the results and data analysis. The results of this meeting will be considered in the statistical analyses, the final report, and publications of the study.

Any disagreement about the evaluation of study data among the quality assurance representatives of the sponsor, and CESAR will be resolved by consensus at the study evaluation meeting.

Such meetings of investigators will be convened by the Coordinating Investigator (CI). Attendance is mandatory for an authorized investigator from each center involved in the study. In addition, the CI may invite experts such as radiologists or other oncologists.