ARTICLES

Standard Operating Procedures for Clinical Research Personnel – Part 11

The Quality Assurance Journal

Wendy Bohaychuk* and Graham Ball

GCRP Consultants, Lakehurst General Delivery, Ont., Canada KOL 2JO

Summary

This is the eleventh in a series of articles containing proposals for wording and content of standard operating procedures (SOPs) for clinical research activities conducted by sponsors and Contract Research Organisations (CROs). The procedures include those required by the International Conference on Harmonisation (ICH), the Food and Drug Administration (FDA), many other guidelines and regulations, and 'best practice' observed by the authors. The model forms require modification for actual use. In this article, SOPs are presented for selection of CROs (SOP 326) and selection of clinical laboratories (SOP 327). (The full text of all 101 SOPs is available from the authors.)

Key Words

GCP; SOP; CRO; clinical laboratory

SOP 326. Selection of Contract Research Organisations

Policy

It is the policy of the sponsor to select CROs which work in conformance with the current international standards of good clinical practice (GCP). Therefore, it is a requirement that a careful evaluation of a candidate CRO is performed prior to placing an assignment.

[This SOP is primarily concerned with assessment of a CRO with regard to the monitoring activities in a clinical study. Assessment for other activities (e.g. data management) requires specialised SOPs relevant to those activities.]

Procedures

326.1. The [Title] will be responsible for the assessment of a CRO to be used for a clinical study.

326.2. The assessment and selection processes must be undertaken several months before the planned start of the clinical study.

326.3. If the CRO is known to the sponsor, the [Title] should consult with other departments to discuss previous experience with the CRO. An assessment visit is still necessary for each new study (and an assessment visit report must be prepared) to ensure that no important factors (e.g. personnel and equipment) have changed significantly.

326.4. If the initial contacts look promising, an assessment visit will be organised by the [Title]. More than one visit will probably be necessary. An agenda will be prepared by the [Title] and forwarded to the CRO at least two weeks before the planned visit.

326.5. A confidentiality agreement with the CRO must be agreed and signed prior to providing any specific information on the medication/device to be studied (e.g. full protocol, investigator brochure) and prior to the assessment visit.

326.6. At the assessment visit, the [Title] should assess all items noted in Form 326-1. If the [Title] does not feel competent to address some items (e.g. technical details), assistance must be sought.

* Correspondence to: Wendy Bohaychuk, GCRP Consultants, Lakehurst General Delivery, Ont., Canada KOL 2JO.
E-mail: wbohaychuk@gcrpc.com

DOI: 10.1002/qaj.168

326.7. The assessment of a CRO should be documented by the [Title] using Form 326-1.
326.8. The [Title] will be responsible for the selection of a suitable CRO after review of the assessment reports.
326.9. The decision to use a CRO will be authorised by the [Title].
326.10. The [Title] will be responsible for negotiating the terms of the contract with the selected CRO.
326.11. All contracts must include the names and duties of the sponsor personnel as well as the CRO so that shared responsibility is recognized.
326.12. The responsibilities agreed by the CRO and the sponsor must be clearly stated in the contract, and should include the following:

- Allocation of responsibilities;
- Monitoring strategy;
- Financial arrangements (including timing and condition under which payments will or will not be made);
- Project timing;
- Reference to specific guidelines and regulations;
- Description of legislative jurisdiction;
- Provisions for amendments to the contract;
- Time period during which the contract is valid;
- Requirements for documentation (e.g. format, frequency) of all activities;
- Specific contact names;
- Confidentiality.

326.13. Legal advice should also be sought in preparing the contract.
326.14. All initiation and progress review visits to a CRO must also be documented.
326.15. The [Title] must inform the [Title] of all relevant information (e.g. selection, contracts) that must be entered into the clinical study tracking schedule in accordance with SOP 109.
326.16. After internal approval by the [Title], two original copies of the contract will be sent to the authorised representative of the CRO for signature. One copy will be retained by the CRO study archives: the other copy will be retrieved by the [Title] and retained in the sponsor study archives.
326.17. The [Title] will ensure that Form 326-1 is archived in the sponsor study archives.

Related SOPs:

SOP 324. Confidentiality agreements

Suggestions for Forms:

Model contract with CROs, Authorization to use CROs

Form 326-1. Initial Assessment of Contract Research Organisations

Please complete a separate form for each visit. Please provide a comment for all 'No' and 'NA' (not applicable) responses.

Sponsor/CRO name:
Study medication/device name:
Project name/code number:

Study/protocol number:
Study/protocol version number and date: (dd/MMM/yy)
Study/protocol title:

Planned commencement date (first study subject to be entered): (dd/MMM/yy)
Planned completion date (last study subject to be completed): (dd/MMM/yy)

Date of report: (dd/MMM/yy)
Date of selection visit: (dd/MMM/yy)
Name of CRO:
Address of CRO:
Place (address) of selection visit:

(Form designer: The information below should be recorded in columns for each person present at the selection visit meeting.)
Details of CRO personnel present at the selection visit meeting: name, title, study function/responsibilities.
Details of sponsor personnel present at the selection visit meeting: name, title, study function/responsibilities.
Were all relevant staff present at the meeting? [] Yes [] No [] NA [] Comment
If not, specify and describe action:

The following items were discussed and/or demonstrated at the selection visit meeting:

Range of services:

- Protocol preparation; [] Yes [] No [] NA [] Comment
- CRF preparation; [] Yes [] No [] NA [] Comment
- Monitoring; [] Yes [] No [] NA [] Comment
- Data management; [] Yes [] No [] NA [] Comment
  Specify:
- Study medication/device preparation; [] Yes [] No [] NA [] Comment
  Specify:
- Study medication/device management; [] Yes [] No [] NA [] Comment
  Specify:
- Regulatory affairs; [] Yes [] No [] NA [] Comment
  Specify:
- Clinical laboratory;[‡] [] Yes [] No [] NA [] Comment
  Specify:
- Clinical report preparation; [] Yes [] No [] NA [] Comment
- Other; [] Yes [] No [] NA [] Comment
  Specify:
- Experience in therapeutic area; [] Yes [] No [] NA [] Comment
  Specify:
- Experience as a CRO; [] Yes [] No [] NA [] Comment
  Specify:
- Previous experience with sponsor; [] Yes [] No [] NA [] Comment
  Specify:
- Subcontracting; [] Yes [] No [] NA [] Comment
  Specify:

[‡] It is not usual that the same CRO which undertakes monitoring or data management would also provide clinical laboratory facilities. Only brief notes would be expected here in terms of the relationship of the CRO to a local or central clinical laboratory. If the CRO were also responsible for clinical laboratory services, a more comprehensive assessment, as noted in SOP 327, would need to be undertaken.

General:

- Confidentiality; [] Yes [] No [] NA [] Comment
- Background and purpose of study; [] Yes [] No [] NA [] Comment
- Investigational status of study medication/device; [] Yes [] No [] NA [] Comment
- Investigator brochure; [] Yes [] No [] NA [] Comment
  Specify version provided:
- GCP; [] Yes [] No [] NA [] Comment
  Specify guidelines/regulations discussed:
- Declaration of Helsinki; [] Yes [] No [] NA [] Comment
  Specify version discussed:
- Investigator responsibilities; [] Yes [] No [] NA [] Comment
- Local regulatory requirements; [] Yes [] No [] NA [] Comment
  Specify:
- Notification of regulatory approval; [] Yes [] No [] NA [] Comment
- Indemnity provisions; [] Yes [] No [] NA [] Comment
  Specify:
- Insurance provisions; [] Yes [] No [] NA [] Comment
  Specify:
- Budget; [] Yes [] No [] NA [] Comment
  (Request and attach budget estimate.)
- Overall financial payment schedule; [] Yes [] No [] NA [] Comment
  Specify:
- Investigator grant and payment schedule; [] Yes [] No [] NA [] Comment
  Specify:
- Costs of overheads, if any; [] Yes [] No [] NA [] Comment
  Specify:
- Proposed study timeframe (initiation, enrolment, completion);
  (Request and attach time estimate.) [] Yes [] No [] NA [] Comment
- Publication policy; [] Yes [] No [] NA [] Comment
  Specify:
- Ownership of data; [] Yes [] No [] NA [] Comment
- Plans and responsibility for analysis of data; [] Yes [] No [] NA [] Comment
  Specify:
- Plans and responsibility for final clinical reports; [] Yes [] No [] NA [] Comment
  Specify:
- Ownership of any special equipment provided by sponsor; [] Yes [] No [] NA [] Comment
  Specify:
- Standardised procedures for multicentre studies; [] Yes [] No [] NA [] Comment
  Specify (e.g. use same equipment, organise special training):
- Availability to attend startup meeting (if undertaken by sponsor); [] Yes [] No [] NA [] Comment
  Specify who will attend:

Facilities:

- Number of other studies currently ongoing at facility; [] Yes [] No [] NA [] Comment
  Specify:
- Number of other studies previously conducted at facility; [] Yes [] No [] NA [] Comment
  Specify:
- Type of other studies currently ongoing at facility; [] Yes [] No [] NA [] Comment
  Specify:
- Type of other studies previously conducted at facility; [] Yes [] No [] NA [] Comment
  Specify:
- Location of facility (proximity and ease of access to investigators, study subjects); [] Yes [] No [] NA [] Comment
  Specify:
- All staff bound by confidentiality agreement; [] Yes [] No [] NA [] Comment
- Security; [] Yes [] No [] NA [] Comment
  Specify:
- SOPs describing security systems available; [] Yes [] No [] NA [] Comment
- Facilities for communication with sponsor; [] Yes [] No [] NA [] Comment
  Specify:
- Procedures for telephone contact documentation; [] Yes [] No [] NA [] Comment
- Fax contact management (e.g. photocopy thermal-sensitive fax paper); [] Yes [] No [] NA [] Comment
- Facilities for communication with investigators; [] Yes [] No [] NA [] Comment
  Specify:
- Procedures for telephone contact documentation; [] Yes [] No [] NA [] Comment
- Fax contact management (e.g. photocopy thermal-sensitive fax paper); [] Yes [] No [] NA [] Comment
- Space (office, wards, etc); [] Yes [] No [] NA [] Comment
  Specify:
- Equipment; [] Yes [] No [] NA [] Comment
  Specify:
- Up-to-date maintenance records; [] Yes [] No [] NA [] Comment
- Up-to-date service contracts; [] Yes [] No [] NA [] Comment

---

SOPs and QA systems:

- SOPs were reviewed; [] Yes [] No [] NA [] Comment
- SOPs were adequate; [] Yes [] No [] NA [] Comment
  Attach a list of SOPs reviewed. Provide details of deficiencies noted in the SOPs. (A full review of SOPs may be necessary depending on the range of services provided by the CRO, and intended to be used for the current study.)
- There was evidence that staff were required to comply with SOPs; [] Yes [] No [] NA [] Comment
- If required, CRO able to adopt sponsor SOPs; [] Yes [] No [] NA [] Comment
  Specify the SOPs:

- Internal auditing; [] Yes [] No [] NA [] Comment
  Specify:
- QA organisation; [] Yes [] No [] NA [] Comment
  Specify:
- Responsible QA personnel; [] Yes [] No [] NA [] Comment
  Specify:

Personnel:

- Organisation chart; [] Yes [] No [] NA [] Comment
  Obtain a copy and attach.
- Personnel qualifications; [] Yes [] No [] NA [] Comment
  Obtain CVs and attach.
- Personnel job descriptions; [] Yes [] No [] NA [] Comment
  Obtain copies and attach.
- Personnel experience; [] Yes [] No [] NA [] Comment
  Obtain evidence and attach.
- Personnel training (previous and ongoing); [] Yes [] No [] NA [] Comment
  Obtain evidence and attach.
- Personnel language skills; [] Yes [] No [] NA [] Comment
  Specify:
- Personnel fluency in English; [] Yes [] No [] NA [] Comment
  Specify:
- Responsibilities for overall study coordination; [] Yes [] No [] NA [] Comment
  Specify:
- Responsibilities for recruitment; [] Yes [] No [] NA [] Comment
  Specify:
- Responsibilities for randomisation of study subjects; [] Yes [] No [] NA [] Comment
  Specify:
- Responsibilities for review of data in CRFs; [] Yes [] No [] NA [] Comment
  Specify:
- Responsibilities for collection and storage of biological samples; [] Yes [] No [] NA [] Comment
  Specify:
- Responsibilities for storage/dispensing of study medication/device; [] Yes [] No [] NA [] Comment
  Specify:
- Responsibilities for maintenance/calibration of equipment; [] Yes [] No [] NA [] Comment
  Specify:
- Current personnel workload; [] Yes [] No [] NA [] Comment
  Specify:
- 24-hour availability of CRO personnel; [] Yes [] No [] NA [] Comment
  Specify:
- Proposed personnel assignment for study; [] Yes [] No [] NA [] Comment
  Specify:

Study subject population:

- Inclusion/exclusion criteria; [] Yes [] No [] NA [] Comment
- Source of study subjects (e.g. investigator's patients or referred study subjects); [] Yes [] No [] NA [] Comment
  If referred, specify means of obtaining adequate medical history:
  If referred, specify means of informing primary care physician:
- Potential number of study subjects; [] Yes [] No [] NA [] Comment
  Specify:
- Recruitment procedures; [] Yes [] No [] NA [] Comment
  Specify:
- Potential recruitment rate; [] Yes [] No [] NA [] Comment
  Specify:
  Obtain and attach evidence (e.g. signed and dated printout of anonymised patient population to support proposed recruitment).
- Screening procedures; [] Yes [] No [] NA [] Comment
  Specify:
- Payments to study subjects; [] Yes [] No [] NA [] Comment
  Specify:
- Advertising; [] Yes [] No [] NA [] Comment
  Specify:

Ethics requirements:

- Informed consent procedures; [] Yes [] No [] NA [] Comment
  Specify:
- Internal procedures for reviewing consent documents; [] Yes [] No [] NA [] Comment
  Specify:
- Access to central/local ethics committee/IRB; [] Yes [] No [] NA [] Comment
  Specify:
- Relationship with central/local ethics committee/IRB; [] Yes [] No [] NA [] Comment
  Specify:
- Identification of local/central committee/IRB; [] Yes [] No [] NA [] Comment
  Specify:
- Identification of any central committee review requirements; [] Yes [] No [] NA [] Comment
  Specify:
- Ethics committee/IRB approval procedure; [] Yes [] No [] NA [] Comment
  Specify:
- Ethics committee/IRB documentation required; [] Yes [] No [] NA [] Comment
  Specify:
- Ethics committee/IRB documentation of membership; [] Yes [] No [] NA [] Comment
  Specify:
- Ethics committee/IRB documentation of working procedures; [] Yes [] No [] NA [] Comment
  Specify:
- Usual waiting period for review/approval; [] Yes [] No [] NA [] Comment
  Specify:

- Continuing review requirements (e.g. protocol amendments, safety data); [] Yes [] No [] NA [] Comment
  Specify:
- Ethics committee/IRB requirements at end of study; [] Yes [] No [] NA [] Comment
  Specify:
- Consequences if investigator is a member of ethics committee/IRB; [] Yes [] No [] NA [] Comment
  Specify:
- Fee to be paid to ethics committee/IRB (if any); [] Yes [] No [] NA [] Comment
  Specify:

Protocol:

- General details of protocol and procedures; [] Yes [] No [] NA [] Comment
- Compliance with protocol and amendments (if any); [] Yes [] No [] NA [] Comment
- Consequences of protocol violations; [] Yes [] No [] NA [] Comment
- Study subject evaluation procedures; [] Yes [] No [] NA [] Comment
- Study subject visit schedules; [] Yes [] No [] NA [] Comment
- Concomitant medications/devices; [] Yes [] No [] NA [] Comment
- Criteria for completion or early termination; [] Yes [] No [] NA [] Comment
- Recording study subject dropouts or withdrawals; [] Yes [] No [] NA [] Comment

---

CRFs:

- Procedures for completing CRFs; [] Yes [] No [] NA [] Comment
- Rules for correction of CRF entries; [] Yes [] No [] NA [] Comment
- Procedures for review of CRFs; [] Yes [] No [] NA [] Comment
- Signature requirements; [] Yes [] No [] NA [] Comment
- Requirements for timely submission of CRFs to data management; [] Yes [] No [] NA [] Comment
- Method of submission of CRFs to data management; [] Yes [] No [] NA [] Comment

---

Safety data:

- Review of known AEs (in accordance with investigator brochure); [] Yes [] No [] NA [] Comment
- Definitions of all categories of AEs; [] Yes [] No [] NA [] Comment
- Procedures for reporting AEs; [] Yes [] No [] NA [] Comment
- Procedures for recording AEs; [] Yes [] No [] NA [] Comment
- Procedures for reporting SAEs; [] Yes [] No [] NA [] Comment
- Follow-up of AEs and SAEs; [] Yes [] No [] NA [] Comment

Monitoring requirements and procedures:

- Direct access to source documents; [] Yes [] No [] NA [] Comment
  Confirm that direct access is acceptable: [] Yes [] No
  Confirm that direct access is understood: [] Yes [] No
- Source document verification procedures; [] Yes [] No [] NA [] Comment

- Documentation required in source documents; [] Yes [] No [] NA [] Comment
- Need for accurate, legible records; [] Yes [] No [] NA [] Comment
- Data query procedure; [] Yes [] No [] NA [] Comment
- Frequency of monitoring (schedule); [] Yes [] No [] NA [] Comment
- Availability of investigator and other site personnel during visits; [] Yes [] No [] NA [] Comment
  Specify:
- Available working area for monitor at sites during visits; [] Yes [] No [] NA [] Comment
  Specify:
- Access to other facilities at sites (e.g. pharmacy, clinical laboratory); [] Yes [] No [] NA [] Comment
  Specify:

Clinical laboratory requirements:

- Reference ranges; [] Yes [] No [] NA [] Comment
  Obtain and attach copy (signed and dated) and specify date of reference range:
  Specify frequency of update of reference ranges:
  Specify responsibility for update of reference ranges:
- QA of laboratory (e.g. evidence of accreditation, certification, participation in proficiency testing, maintenance and control of analyzers); [] Yes [] No [] NA [] Comment
  Obtain and attach copies and specify documents retrieved:
- Procedures for collection of clinical specimens; [] Yes [] No [] NA [] Comment
- Procedures for handling specimens; [] Yes [] No [] NA [] Comment
- Procedures for storage of specimens; [] Yes [] No [] NA [] Comment
  Specify storage area and conditions:
- Clinical laboratory protocol (if relevant); [] Yes [] No [] NA [] Comment
  Specify version:
- Handling of test kit (if applicable); [] Yes [] No [] NA [] Comment
- Special equipment (if applicable); [] Yes [] No [] NA [] Comment
  Specify:
- Maintenance of equipment; [] Yes [] No [] NA [] Comment
  Specify schedule and responsibility:
- Review and completion of clinical laboratory reports; [] Yes [] No [] NA [] Comment
- Filing of clinical laboratory reports; [] Yes [] No [] NA [] Comment

---

Management of clinical study medication/device:

- Study medication/device preparation or reconstitution (if necessary); [] Yes [] No [] NA [] Comment
  Specify:
- Labelling arrangements; [] Yes [] No [] NA [] Comment
  Specify:
- Packaging arrangements; [] Yes [] No [] NA [] Comment
  Specify:

- Shipping arrangements (e.g. address, responsibility for receipt); [] Yes [] No [] NA [] Comment
  Specify:
- Randomisation procedures; [] Yes [] No [] NA [] Comment
- Blinding (masking) provisions; [] Yes [] No [] NA [] Comment
- Dosing schedule; [] Yes [] No [] NA [] Comment
- Dosing instructions; [] Yes [] No [] NA [] Comment
- Dispensing requirements; [] Yes [] No [] NA [] Comment
  Specify individual responsible for dispensing:
  Specify dispensing procedures for out-patients (if applicable):
  Specify dispensing procedures for in-patients (if applicable):
- Requirements for separate storage for investigational study supplies; [] Yes [] No [] NA [] Comment
  Specify acceptability:
- Storage requirements; [] Yes [] No [] NA [] Comment
  Specify provisions for storage:
- Temperature control; [] Yes [] No [] NA [] Comment
  Specify method:
- Temperature recording; [] Yes [] No [] NA [] Comment
  Specify procedure:
- Control of other environmental requirements (e.g. light, humidity); [] Yes [] No [] NA [] Comment
  Specify method:
- Recording of other environmental requirements (e.g. light, humidity); [] Yes [] No [] NA [] Comment
  Specify method:
- Security requirements (e.g. locked access); [] Yes [] No [] NA [] Comment
  Specify:
- Procedures for assuring accountability; [] Yes [] No [] NA [] Comment
  Specify:
- Documentation of accountability; [] Yes [] No [] NA [] Comment
  Specify:
- Expiry dates; [] Yes [] No [] NA [] Comment
- Final disposition; [] Yes [] No [] NA [] Comment
  Specify planned procedure:
- Final destruction; [] Yes [] No [] NA [] Comment
  Specify planned procedure:
- Emergency randomisation codebreak procedures; [] Yes [] No [] NA [] Comment
- Storage/security of codebreak envelopes; [] Yes [] No [] NA [] Comment
- Documentation of codebreak; [] Yes [] No [] NA [] Comment
- Time during which pharmacist is on duty, and availability if not 24 hours; [] Yes [] No [] NA [] Comment
  Specify:
- Designated research pharmacist; [] Yes [] No [] NA [] Comment
  Specify:
- Maintaining records of shipment; [] Yes [] No [] NA [] Comment
- Maintaining records of receipt; [] Yes [] No [] NA [] Comment

Computer systems:

- Documentation of validation of hardware and software; [] Yes [] No [] NA [] Comment
- Up-to-date maintenance records; [] Yes [] No [] NA [] Comment
- Up-to-date service contracts; [] Yes [] No [] NA [] Comment
- SOPs available for testing and validation procedures; [] Yes [] No [] NA [] Comment
- Hardware and software compatible with sponsor systems; [] Yes [] No [] NA [] Comment
  Specify:
- Capability for data transfer; [] Yes [] No [] NA [] Comment
  Specify:

Maintenance of study records:

- Documents required to be archived; [] Yes [] No [] NA [] Comment
- Location of source documents; [] Yes [] No [] NA [] Comment
  Specify:
- Availability of lockable and fire-resistant files for paper and electronic media; [] Yes [] No [] NA [] Comment
  Specify:
- Policies of medical records department (e.g. long-term provision, policy if patient dies or moves, policy if investigator dies or moves, etc); [] Yes [] No [] NA [] Comment
  Specify:
- Time periods for retention of documents; [] Yes [] No [] NA [] Comment
  Specify:

Audits/inspections:

- Sponsor audits of CRO; [] Yes [] No [] NA [] Comment
- Sponsor audits of study sites; [] Yes [] No [] NA [] Comment
- Regulatory authority inspections; [] Yes [] No [] NA [] Comment
- Requirement to notify sponsor of impending inspection; [] Yes [] No [] NA [] Comment
- Has the CRO been inspected by a regulatory authority? [] Yes [] No [] NA [] Comment
  If so, specify when:
  Specify the findings:
  Specify steps taken to correct deficiencies:

Responsibility for report: name, title, signature, date: (dd/MMM/yy)
Supervisor review: name, title, signature, date: (dd/MMM/yy)

Decision to use CRO: [] Yes [] No
Requirements/action before final contracts can be signed:
Authorization by: name, title, signature, date: (dd/MMM/yy)
If CRO selected, next planned visit date: (dd/MMM/yy)
To be conducted by: name, title

Archiving: Sponsor Study Archives, CRO Study Archives (if CRO selected)