Setting Standards for Standard Operating Procedures in Oncology Clinical Trials

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Objectives

- Review elements of and criteria for standard operating procedures (SOPs) in clinical practice and clinical trials;
- Examine and evaluate examples of SOPs used in academic, community, and private practice settings
- Design a customized or template-developed SOP for a specific area of clinical trials conduct or management
Why are Standard Operating Procedures Important in Clinical Trials?
Definitions of Terms

- Standard Operating Procedure
- Protocol
- Guideline
- Clinical Pathway/Algorithm

STOP

GO
What are SOP’s?

- Standard Operating Procedure
- Protocol

Goals:
- Consistency across individuals, sites, procedures
- Replicability
- Generalizability of results
- NO deviations from standard
How Do SOP’s Differ from Guidelines or Algorithms?

- Guidelines or pathways recommend specific interventions or actions.
- Recommendations are not requirements.
- Deviations based on individual provider preference or individual patient requirements are expected and allowed.
- Results from guidelines subject to adherence levels that may vary widely.
Application of SOP Concepts to Clinical Trials in Varied Settings

- Prevention Trials
  - Assessment of chemoprevention compliance, e.g. pill count
- Cancer Control/Behavioral Oncology Trials
  - How to manage missing data on QOL forms
- Therapeutic Trials
  - Obtaining informed consent: Who? How?
- Investigational Drugs or Devices
  - Returning partially-used medications
- Palliative Care Trials
  - Data quality standards
Areas of Clinical Trials Oversight and Operations Benefiting from or Requiring SOPs

- Continuum of cancer clinical trials:
  - Concept development
  - Protocol development
  - Regulatory affairs: IRB, contracts, budgets
  - Protocol implementation
  - Subject recruitment
  - Informed consent
  - Intervention delivery: drugs, devices, regimens
  - Data collection, entry, submission
  - Reporting requirements: SAE’s, follow-up
  - Audits: preparation, conduct (internal, external)
Protocol Development

- Format
- Elements
- Level of detail
- Template-driven
Regulatory Affairs

- IRB – when, how, how often, where?
- Informed consent – what, how, who?
- Budget for sponsored trials – for what, how, when, by whom?
- Approvals by other internal or external review groups
Protocol Implementation and Compliance

- Critical for consistency of study
- What parts of protocol need further clarification, planning, details for local implementation?
- Example: Chemotherapy given on trial
  - How are orders generated?
  - How are dose and/or schedule modifications made?
  - Who controls modifications?
  - Who monitors compliance?
Patient and Family Education and Informed Decision-Making

- Informed consent document
  - Guidelines vs SOP for development, e.g. reading level
  - Elements & format
- Informed decision-making process
  - Who is involved with DM process?
  - How is informed DM process conducted?
- Evaluation of informed consent
  - How is DM process and outcome evaluated and documented?
Data Collection and Data Management

- Protocol outlines what data are collected and when
- SOP details who, what, when, where, how for local implementation of trial
- Examples:
  - Documentation of oral medication compliance
  - Documentation of care given off-site or by other providers (e.g. GYN exams)
Investigational Drugs and Devices

- Sponsor and protocol may specify
- NCI guidelines for IND receipt, distribution, inventory control

**LOCAL issues:**
- Who in pharmacy or local practice responsible?
- How are drugs to be returned handled?
- Who monitors investigational devices for OR?
Biological Specimens

- Protocol or sponsor delineates what specimens are to be collected and when
- SOP covers how to be implemented locally
  - Who draws?
  - Who collects specimen(s)?
  - How are specimens stored temporarily?
  - How are specimens processed?
  - How are specimens stored long-term?
  - How are specimens shipped to central repository?
Reporting Adverse Events

- Protocol or sponsor outlines SAE reporting
- SOP deals with local SAE and AE reporting and follow-up
  - Who generates SAE reports?
  - What criteria used for reporting?
  - What group(s) receive the reports?
  - What happens next?
    - Revision of consent documents?
    - Notification of subjects of new information?
    - Need for reconsent?
Internal Quality Assurance and External Audits

- Sponsor or protocol may define external auditing procedures and frequency
- Need for internal monitoring and QA
  - How often? Number of cases? Who does it? How communicated to others?
- Need for preparation for external audit
  - Who, how, when is pre-audit conducted?
- Need for follow-up after an internal or external audit review
  - How will deficiencies be addressed?
Staff Development

- Who is responsible?
- How delivered and how often?
- Local vs Off-site?
- Documentation of educational initiatives
- Measuring impact on clinical trials quality
Recruitment, Publicity, and Community Outreach

- IRB may outline what materials need prior review
- Local implementation
  - How are approved recruitment materials distributed?
  - Who generates, reviews, implements recruitment & PR materials?
  - Who is responsible for community outreach?
  - How is outreach specifically done?
Scope and Detail of SOPs Indicated in Oncology Clinical Trials

- Quality of conduct of trial and data collected are key
- SOPs designed to ensure quality
- Level of detail often predicts success
- If SOP is not followed, value is questionable
Essential Elements of SOP Development

- Purpose of SOP
- Developer(s) of SOP
- Local review
- Elements to include based on purpose
  - Who, what, when, where, how
- Must incorporate all individuals, sites, levels involved with procedure
  - Inpatient, outpatient, clinical trial office/staff, pharmacy, laboratory, radiology
Responsibilities for Development and Monitoring of SOPs

- Clinical trial staff
- Input from PIs, administrators, clinical leaders and managers
- Input from patients and family members as appropriate
Continuous Quality Improvement and SOP Review and Revisions

- Do SOPs get put into a notebook and never seen again?
- How are SOPs used?
- How & how often are they reviewed?
- How are revisions made? By whom?
- How are revisions reviewed? How often and by whom?
- CQI loop is on-going
Application of Material to SOP Design

- Template-driven
- Customized SOP
Example #1: Specimen Collection and Storage

- **Pre-collection**
  - Generation of specimen collection packets
  - Who prepares, what goes into packet
  - Collection devices (tubes), labeling, storage of packets, medium (esp if tissue)
  - Working with OR & Pathology staff if collecting tissue

- **During collection**
  - Who draws or collects specimen?
  - e.g. does lab draw if pt having routine bloodwork?
  - Store in refrigerator, on wet ice, etc.
  - Picking up from gross room or Pathology if fresh tissue
Specimen Collection and Storage

- Post collection
  - How is specimen processed?
  - Done in lab, in clinical trial area?
  - Who processes? Labels?
  - Interim storage prior to shipping?
  - Stored in what freezer? Where? How long?

- Shipping
  - How often are specimens shipped?
  - Delivery services: pickup times, places
  - Shipping materials needed, access
  - Who ships? Who monitors delivery post-shipping?
Example #2: Measurement of Indicator Lesions

- Prime area for QA monitoring
- Prime area with potential for deficiency on audit
- Requires close collaboration between clinical trials staff, radiology dept, individual radiologists, clinicians, clerical staff
- Protocol states: “Measure target lesions q 2 cycles” – how will this be done at YOUR site?
Measurement of Indicator Lesions

- Assessment
  - How are radiology requisitions done?
  - How often are measurements inaccurately documented or not documented at all?
  - Who is responsible for measuring? How involved are they in trials?
  - Is there a consistent person in Radiology for development of SOP?
Measurement of Indicator Lesions

- **Planning**
  - Buy-in from all key parties: PI, other clinicians, radiology leadership and others, clinical trial staff, clerical staff for requests
  - Can you use a protocol measurement form?
  - Do you need to develop a new form?
Measurement of Indicator Lesions

- Implementation
  - Use of the measurement form
  - Ex: attach measurement form to requisition for specific lesion(s)
  - Ex: attach complete table of all lesions with measures from baseline to current date
  - Ex: request measure of specified lesions on requisition
  - Ex: request comparison of current study to previous study OF xx/xx/xx
Measurement of Indicator Lesions

- **Evaluation**
  - Does the plan work? How will you know?
  - Monitoring of outcomes: who does it? How often?
  - Reporting of findings to all involved parties
  - CI loop again
Example #3: Audits and Pre-Audits

- Assessment
- Planning
- Implementation
- Evaluation
- Application to participant study sites
PreAudits and Audits

- Assessment
PreAudits and Audits

- Planning
PreAudits and Audits

- Implementation
PreAudits and Audits

- Evaluation
Summary

- SOPs represent a key area for quality assurance in clinical trials
- SOPs are often not developed or followed
- SOPs are often overlooked due to lack of time or lack of attention to importance
- SOPs are critical for local implementation of protocol
- SOPs are part of quality improvement loop
Application

- Development of SOPs for your site
- Application of information to individual research settings


Moody LE, McMillan S. Maintaining data integrity in RCT. *Nurs Res* 51: 129-33, 2002