Setting Standards for Standard Operating Procedures in Oncology Clinical Trials

Theresa Wicklin Gillespie, PhD, RN
Assistant Professor, Dept of Surgery and Winship Cancer Institute
Emory University, Atlanta, GA
Director, Health Services Research
Atlanta VAMC

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?
  - Who needs the SOP – clinical trials? Radiology? Clerical? Others? All of the above?

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

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