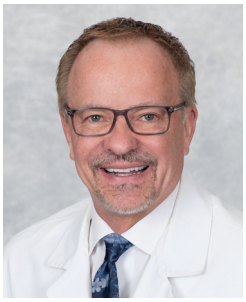
Chapter 10 |

The GOG Foundation, Inc. Quality Control and Modality Committee Oversight



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Introduction

In April 2010, the Institute of Medicine (IOM) evaluated the clinical trial system of the National Cancer Institute (NCI) for the 21st century. It was hoped that reinvigoration of the NCI cooperative group could make it more productive. They produced four overarching goals to guide improvement efforts. In each of these goals, the Gynecologic Oncology Group (GOG) met or exceeded them. The IOM proposed a reorganization of the nation's cancer clinical trials that would significantly change the program's then current structure. Among the changes proposed was the consolidation of the current nine groups studying adult cancers into four multidisciplinary including the consolidation of the operation and data management center.

The legacy GOG adamantly opposed this combination for multiple reasons which have previously been documented. Nevertheless, in March of 2014 the NCI transformed the nine adult groups into a new national organization of four adult groups. The Gynecologic Oncology Group was combined with the Radiation Therapy Oncology Group (RTOG) and the National Surgical Adjuvant Breast and Bowel Project (NSABP) into the NRG Oncology. As a result of this merger the committee structure particularly modality committees were changed and the three groups now had one committee that covered multiple specialties but had similar goals such as surgery, radiation therapy and pathology. It is appreciated that although the common goals were noted, specific intent of the legacy group was still addressed in addition to the overall group of the NRG.

NRG Modality Committee Oversight and Quality Control

The five NRG modality committees represent Gynecologic Oncology, Medical Oncology, Nursing, Pathology and Radiation Therapy. In contrast to the site committee, the modality committees do not initiate new protocols. Members of the modality committees, however, have a direct input into new protocols as they are members on the numerous site committees. The main function of the modality committees is to review the area of protocols that require their special expertise, to make sure that adequate safeguards are in place and that the specific protocol manuals have adequate sections to cover specific therapies as prescribed by the protocols. The evaluation of the protocols by these committees prior to initiation of the protocols is extremely important to properly identify patients eligible for protocols but also to determine feasibility regarding its objective.

Another important role of the modality committees is to perform quality control of the protocols while they are ongoing and at the completion of the protocol in order to determine eligibility and compliance with the protocol. The individual committees will be described separately although the general functions regarding their specific modality are very similar.

Gynecologic Oncology Committee

This committee is responsible for the surgical quality control both prospective and retrospective. The committee is the repository for surgical expertise within the group. The core group maintains continuity and institutional memory with approximately 15% of the membership rotation on and off each year. This allows for new investigators entering the committee structure of the group.
Not only do the members participate in the quality control regarding surgical modality, but that experience is also educational and improves the quality of data that

they may submit from their individual institutions.

All protocol entries that have a surgical requirement to them are reviewed by the Gyn Oncology Committee. All patient entries are reviewed using a a very consistent process. This review is carried out early in the life of a given protocol so that if problems are detected early, they can be corrected by altering the protocol or educating the investigators. The principal investigators are notified quickly, and corrections can be made within their institutions so that errors will not be repeated, maximizing the sacrifice the patients make to participate in the GOG studies. Potential problems can be identified early in regard to protocol requirements and the study chair can correct these if necessary. Review of the surgery by the committee assures consistency across time and studies, which is of particular value to study chairs if they are not surgeons. This early review can be very educational for the individual institutional Primary Investigator (PI) in that eligibility requirements will be reviewed more stringently. The review that the committee performs includes evaluation of NRG forms, dictated operative reports, pathology reports, cytological reports, laboratory reports, imaging reports, and discharge summaries. This ensures that any surgical procedure is in compliance with the surgical standard of the NRG. If after review it is determined that the patient is surgically ineligible, two additional reviewers and the chair must concur.

The NRG surgical standards are maintained in the surgical procedure manual. This manual is not a surgical text or atlas, but rather a statement of the minimum requirements for any given surgical procedure. This manual also lists the usual indications and contraindications for a given surgical procedure. It outlines extent of any given procedure, listing tissue to be removed, the extent of dissection, and the surgical boundaries. Also listed are the expected side effects and complications. Cases entered into NRG protocols are measured against this standard. This insures consistency for all surgical procedures for all NRG protocols. The manual is reviewed at each semi-annual NRG business meeting and revised as necessary. If newer, revised procedures are required for any given protocol, the Gynecological Committee provides the expertise to develop the same. Recent additions to the manual include the procedure for bilateral prophylactic salpingo-oophorectomy and pelvic lymphadenectomy and sentinel node biopsy for vulvar cancer. The applicable surgical procedure for a given protocol is included in the written protocol document as an appendix.

The Gynecologic Oncology Committee has its roots in the very beginning of the GOG. Richard Boronow, MD, chaired an ad hoc committee dealing with surgical issues from the inception of the GOG until the formation of the Modality Committees.

In 1977, Frank Major, MD, became Chair of a standing committee; the Gynecologic Management Committee. This committee was charged with developing the GOG Surgical Procedures manual as a method of standardizing the surgery for patients on GOG protocols. The manual has been maintained and revised as necessary by the subsequent chairmen and members. The second function of the committee is to determine eligibility standards for GOG protocols. The committee also provides quality control for both surgery and eligibility.

Robert Park, MD, succeeded Dr. Major as chair. Dr. Major went on to chair the Sarcoma Committee. Dr. Park served as chair until 1983, when William Hoskins, MD, became chair. Dr. Park went to serve a long tenure as the group chairman.

In July 1984, Harrison Ball, MD, succeeded Dr. Hoskins who went to chair the Ovarian Committee. It was during Dr. Ball's tenure that the committee name was changed to the Gynecologic Oncology Committee. Also during this term, Dr. Ball supervised the formation of the Laparoscopy Subcommittee chaired by John Shlearth, MD. This subcommittee facilitated the incorporation of Laparoscopy into GOG protocols and the group as a whole. Dr. Ball was appointed to the chair of the Corpus Committee in February 1995 and Charles Whitney, MD, became the chairman of the Gynecologic Oncology Committee. Nicola Spirtos, MD,was named Co-Chair in January 2004 and Chair in 2010.

Other notable former members of the committee include William Creasman, MD, Donald Gallup, MD, Paul Morrow, MD, and many others.

Although the Gynecological Oncology Committee is now under the umbrella of the NRG, representatives on that committee from the former GOG serve as co-chair, currently Nicola Spirtos. In many aspects, the future of the legacy GOG continues in a quality control of current surgical protocols and development of new surgical guidelines. An example is the quality control of the surgical aspect of GOG 210. Although the protocol was developed to further evaluate the genetic aspects of endometrial cancer in order to correlate these new criteria of surgical pathological staging was critical. A total of 6,121 patients were enrolled (the largest to date), which required surgical pathological evaluations to make sure surgical protocol was followed. This was carried out by the members

of the legacy gyn surgical committee although now a part of the surgical oncology committee of the NRG.

Medical Oncology Committee

The primary responsibility of this committee is to define the optimal use of commercially available chemotherapeutic agents and supportive care medications being employed in the conduct of NRG protocols. The committee is charged with defining optimal standard management approaches involving the administration of chemotherapy in NRG protocols. The committee also responds to issues regarding unique toxicities experienced by patients participating in clinical trials, and defines how new commercially available chemotherapeutic and supportive medications should be employed in our study population. In addition, the committee formally evaluates all new protocol concepts, which include chemotherapy for any issues or concerns regarding toxicity. These activities have resulted in several recommendations and implementations. The committee has defined required frequency and renal function parameters for recalculating carboplatin AUC dosing. They have developed guidelines for the use of erythropoietin in NRG trials, developed suggested standard steroid prophylaxis for paclitaxel associated hypersensitivity reaction for weekly dosing schedules and evaluated complications associated with Bevacizumab. Dose reduction versus maintenance of dose intensity employing the use of bone marrow colony stimulating factors have been evaluated. These issues relate to the quality assurance activities of the committee. The NRG chemotherapy manual, as developed by the Medical Oncology Committee, serves as the resource for dose frequency as well as toxicity issues involving chemotherapy and NRG trials. This establishes standard statements regarding the use of commercially available chemotherapeutic agents.

The committee regularly includes presentations at the semi-annual meetings on NRG relevant protocol specific topics such as; standards for creatinine clearance determination; safety and monitoring of patients on anti-vascular agents; Carboplatin hypersensitivity reactions; IP Platinum agents and the inhibition of angiogenesis; and assessment of renal function in cancer patients receiving chemotherapy.

Since its inception, the GOG relied on developing a close relationship with the Cancer Therapy Evaluation Program (CTEP) of the NCI. Under prompting from external NCI advisors such as Paul Calabresi, MD, and John Ultmann,MD, the first two directors of CTEP (Stephen K. Carter, MD, from 1970-1975, and Franco Muggia, MD, from 1975-1979) ensured close communication with the NCI and involvement of medical oncologists in generating protocols containing emerging chemotherapeutic drugs. Robert Slayton, MD (with a strong interest in the chemosensitive germ cell tumors); Johannes Blom, MD; H. James Wallace, MD; George Omura, MD; and Tate Thigpen, MD, were among the first medical oncologists to participate in leading protocols containing chemotherapy. William McGuire, MD, a member of CTEP with experience in the NCI intramural program, provided invaluable guidance to the GOG to structure phase I and II studies with new anticancer drugs. In 1977, the group chair, George Lewis, MD and Dr. Thigpen, with the biostatistical input of John Blessing, PhD, launched master protocol 26. James Arseneau, MD, who had emerged from the NCI intramural program, and Tate Thigpen were involved in generating a steady stream of phase II studies with new drugs under the rubric of the Medical Oncology Committee. For example, in the 1989 launch of cisplatin by CTEP, Dr. Thigpen prominently represented the GOG in describing the drug's key role in ovarian and cervical cancers, as well as in germ cell tumors. This became a traditional role in subsequent drug launches by NCI or industry.

The GOG became a major contributor in the clinical investigation of other emerging new drugs as attested by publications in Cancer Treatment Reports and other journals. Hy Muss, MD, joined the group in the early 1980s and became chair of the committee-quality control of drug treatments had become a major responsibility and by 1989, when he left the group to work in breast cancer, he had completed work on the chemotherapy manual that for years remained the backbone for protocol design, until adoption of protocol shells and web-based drug statements. By then, a number of medical oncologists had joined the group contributing expertise in key areas of therapeutics: Robert Young, MD (staging and treatment of early state ovarian cancer); Stephen Williams, MD (germ cell tumors); Bill McGuire, MD (integration of paclitaxel in ovarian cancer); Franco Muggia, MD (anthracycline cardiotoxicity, drug delivery); Gini Fleming, MD (chemotherapy of endometrial cancer); David Spriggs, MD (drug pharmacology); Robert Ozols, MD (optimizing carboplatin in ovarian cancer); and David Alberts, MD (intraperitoneal therapy). In 1993, Developmental Therapeutics was placed under the leadership of Dr. McGuire and Michael Bookman, MD, whereas Medical Oncology – emphasizing treatment safety and quality control functions – continued under the leadership of Dr. Muggia and Dr. Arseneau. Maurie Markman, MD, became the chair of this committee in 1999, and helped delineate carboplatin hypersensitivity reactions, appropriate use of cytokines, issues of dose-scheduling, and assessment and protection of neuropathy following

taxanes and platinums. Dr. Muggia and Paul Sabbatini, MD, are the current Chair and Co-Chair respectively. In addition to reviewing pertinent items at each semi-annual meeting there is one or more certified medical education (CME) presentations on relevant topics. For instance, recently there has been considerable discussion concerning creatine clearance, weight and chemotherapy dosage has been thoroughly reviewed and recommendations made to the group.

In summary, Medical Oncology spurred the successful involvement of theGOG in clinical drug development protocols – now carried forward under the Developmental Therapeutics Committee. Together with other modality committees, it tackles key issues concerning treatment safety, appropriateness of supportive care measures, and quality control.

As previously noted, the Medical Oncology Committee of the GOG is now incorporated into the Medical Oncology Committee of NRG. The legacy Medical Oncology Committee continues to address specific items applicable to gynecologic oncology. They do play a major role in the respective NRG committee in addressing items of interest in regard to chemotherapy. As a legacy committee of the GOG, they recently addressed the role of biosimilar medication, what is the opportunities for bio marker specific treatment. They had been in the process of developing a position paper on carboplatin dose harmonization, and they have recognized the complexity of placebo controls in immunotherapy trials, and we addressed this area. The pharmacy subcommittee of the Medical Oncology Committee continues to be an important aspect of this committee developing pharmacy and toxicity standards, protocol drug information database and forms. The committee also is involved in early phase trial monitoring protocols. Although the modality committees are not responsible for developing protocol, they are intimately involved in partnering with the site committees as new therapy becomes available and developing toxicity profiles. This has been particularly true in the initiation of chemo radiation protocols for gynecological malignancy.

Nursing Committee

The Nursing Committee has been an active committee in the GOG since 1977. From the inception of an informal committee in 1977, under the leadership of Debby Smith, MD, the committee has grown into a separate Modality Committee. Under the leadership of Terry Chamorro, the Nursing Committee was authorized as a subcommittee of the Quality Control Committee. In 1994, the Nursing Committee was established as a separate Modality Committee under the leadership of Sharon Kelly, RN. Leadership of the committee included four GOG nurses:

1977–1979	Debby Smith, RN, UCLA Medical Center
1979–1983	Terry Chamorro, RN, UCLA Medical Center
1983–1997	Sharon Kelly, RN Tufts-New England Medical Center
1997–present	Susan Nolte, CRNP Abington Memorial Hospital

Initially, the Nursing Committee was a subcommittee of the Quality Control Committee, with a primary focus on quality control as related to the process of GOG study development and execution. Specifically, early efforts were directed at: 1. Development of a nursing manual defining acceptable nursing procedures related to GOG protocols; 2. Participating as a review mechanism for the proper definition of the nursing role in each GOG study; 3. Reviewing all studies from a nursing perspective to ensure compliance with protocol requirements; 4. Educating GOG nurses on topics related to GOG protocols to ensure compliance with protocol requirements.

Currently, the Nursing Committee functions as a modality committee within the NRG. As nurses with expertise in the sub-specialty of gynecologic oncology and actively involved in direct patient care and research activities, the members of the NRG Nursing Committee are in a unique position to facilitate quality nursing care. Members are included in protocol development from the concept phase through activation and implementation and are in an optimal position to provide nursing input to all NRG activities.

Pathology Committee

The Pathology Committee's primary responsibility is quality control and quality assurance of the pathological diagnosis of specimens submitted to the NRG. Although the members of this committee do not design or manage protocols, they are involved as members of other committees in protocol design and management responsibility. This is particularly true in which the primary or secondary pathological or translational end point is an important objective of the protocol. The Pathology Committee also has responsibilities to select tissue specimens for the virtual tissue bank protocols; maintain the pathology manual for the NRG; advise the GOG tumor bank; provide a forum for the training and continuing education of NRG pathologists who participate in the quality

control review; and provide a pool of trained pathologists to serve as pathologists and co-investigators of NRG protocols.

The primary responsibility of the committee is quality control and quality assurance. Retrospective review of all pathology reports and representative tissue slides of surgical and cytological specimens are undertaken by the committee.

Members of the committee have also been instrumental in developing protocols to identify biomarkers or translational research. These have resulted in numerous publications. The Pathology Committee also has been instrumental in revising standardizations for different pathological entities that have been accepted by national and international organizations. A good example of this is the grading for endometrial cancer and identification of the role of the squamous component of endometrial cancer.

In the early years when the GOG typically met in Buffalo, few pathologists attended the meetings. Four to six pathologists met outside of regular GOG meetings – usually at member institutions or on neutral territory (e.g., the O'Hara Hilton) to review slides. Alexander Sedlis, MD, was the first Pathology Committee Chair and organizer of these reviews; Jason Norris, MD, was the first referee. These reviews took place on an ad hoc basis, sometimes after clinical trials were completed, and occasionally after a manuscript draft was written. One of the first reviews was of a trial of hormonal therapy in early state endometrial carcinoma. The poor agreements between the clinical and review diagnoses lead to the realization that all cases should be reviewed for the GOG to publish "clean" studies. "Review of all cases" remains the current GOG review model. Until the mid-1980s, pathologists brought their own microscopes to reviews – frequently within strange wooden luggage or other contraptions, making them easily identifiable during registration. By the mid-1980s, rental microscopes were provided for pathologists, and meetings moved from individual hotel rooms to larger conference rooms.

Under the leadership of the Pathology Chairs (Alexander Miller,MD, and Richard Zaino, MD) and the referees (Dr. Norris and Stephen Silverberg, MD) the scope of Pathology Committee activities evolved during the late 1970s and 80s from a review of pathologic diagnoses, to then include a collegial forum of training of gynecologic pathologists. A Delphic system for slide review evolved where an experienced member would team up with a new member to review cases. Drs Norris or Silverberg (past and current referees), adjudicated disagreements. Besides reviewing thousands of GOG slides at a review, formal and informal presentations and discussions of gynecologic pathology always took place, often during dinner meetings. Once it became known that slides were being reviewed at meetings, the numbers of pathologists attending gradually increased to current numbers (approx. 40-70/meeting), keeping pace with the proliferation of GOG clinical trials in the 1980s and 90s. This form of case review improved the diagnostic skills of all participants and provided an effective conduit for dissemination of GOG pathologic criteria to member laboratories. Discussion of problematic GOGprotocol issues by this collegial and diverse group of gynecologic pathologists has influenced pathology practice worldwide – e.g. GOG definitions of primary peritoneal carcinoma have been adopted by the World Health Organization (WHO), the International Federation of Gynecology and Obstetrics (FIGO) and the International Society of Gynecologic Pathologists (ISGYP) via dissemination of the GOG pathology manual and participation of GOG pathologists in these organizations.

As the scope of clinical activities of the GOG began to increasingly include cancer prevention and control, and translational research in the 1990s, the Pathology Committee (Chairs, Dr. Zaino, Jo Benda, MD, and William Rodgers, MD) developed rapid and specialized pathologic review mechanisms, and were key participants in the development of tissue banking, molecular diagnostic and translational research protocols. As the number of studies and patients enrolled on GOG studies increased over time, the number of pathology reviews conducted at each meeting has significantly increased. The number of pathology cases reviewed at recent meetings has exceeded 1,000 cases. Currently Dr. Rodgers is the committee's Chair, and Helen Michael, MD, is the Co-Chair. Six pathologists (G6) have and are reviewing a subject of GOG 210 specimens whose diagnoses have been associated with low reproducibility. This is extremely important as other prognostic factors for endometrial cancer must have an accurate diagnosis before data can be analyzed. In addition to Pathology reviews, the committee continues to evaluate topics of interest such as two grade designation for ovarian cancer with recommendations being made to the group.

The GOG Pathology Committee has been a model for the NRG Pathology Committee. As previously noted, the GOG Pathology Committee has made major contributions identifying pathologic entities which have resulted in improving our ability to better triage and manage our patients. The Pathology Committee has been intimately

involved in the GOG Tumor Bank. The goal for all groups. For several years Dr. Rogers has been the GOG's committee Chair, and currently serves as Chair of the NRG Pathology Committee.

Table 1.

Monitoring	Auditing
Act of overseeing the progress of a clinical trial	Systematic and independent examination of the trial-related activities and documents
100% source document verification of all participants	Snapshot in time of a subset of participants
Ensuring that the study is conducted, recorded and recorded and reported in accordance with: • Protocol • SOPs • GCPs • All applicable regulatory requirements	Determine whether the trial-related activities were conducted and data recorded accurately, analyzed and appropriately reported according to: • Protocol • SOPs • GCPs • All applicable regulatory requirements
Each protocol will outline a data safety and monitoring process and plan	
Some studies may require a data safety monitoring board/committee (DSMB/DSMC)	

Radiation Oncology Committee

This Radiation Oncology Committee pertains to all matters in regard to radiation oncology. The committee is charged with insuring consistency and appropriateness of radiation therapy to patients on NRG protocols as well as compliance with those protocols. The committee reviews radiation therapy treatment details including dose, time, volumes, ports, fraction size for all patients receiving radiation therapy on NRG protocols. This evaluation becomes part of the institution's data for assessment of its performance as a NRG group member. Each of these parameters are evaluated and scored as meeting protocol requirements, minor deviations, or major deviations. This activity serves not only as a quality assurance function but also as an educational function. The committee also maintains and periodically updates a radiation oncology protocol procedure manual. The committee also has representation from the Radiological Physics Center (RPC) in Houston and interfaces with this organization as part of its QA role.

The committee is instrumental in evaluating and adopting new techniques in radiation therapy as they become available. Recently, for instance, is the introduction of high dose (HDR) intra cavitary technique in protocols involving cervical cancer. The committee working with the RPC developed a certification process in which institutions using HDR were required to demonstrate competency.

Quality control and compliance is a major activity of the committee. One important function of the committee is film and dosimetry review, which is carried out on all cases entered into RT containing GOG protocols. Web-based review methodologies have been implemented to further enhance the timeliness and ease of the quality assurance activities.

Committee members participate in the deliberation of all multidisciplinary site committees. This allows radiation oncology members to propose concepts for consideration by the site committees and in many instances the committee members have served as study chair or co-chair for the studies involving RT particularly in study design, directing the ongoing evaluation of case entry material, assisting in analysis of study results, and participating in the publication of those results.

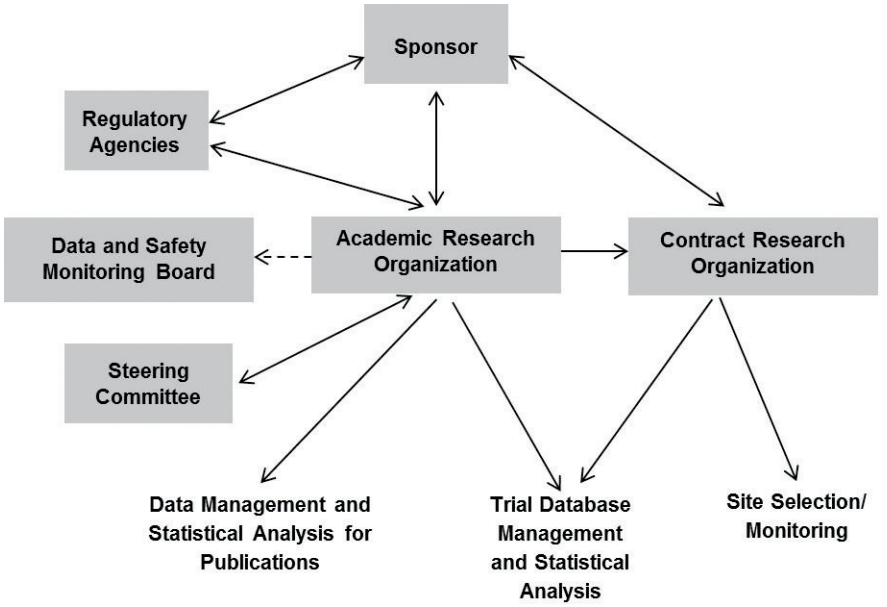
The Radiation Therapy Committee is responsible for the radiation therapy procedure manual which is used to assist in protocol compliance. New procedures are added to the manual as appropriate. These procedures include intensive, modulated RT (IMRT), brachytherapy techniques and imaging-based brachytherapy.

Ivy Petersen, MD, serves as chair of Radiation Oncology committee. In addition to the radiologic oncology reviews educational sessions are also held during the committee's meetings.

Many of the activities of the NRG Radiation Oncology Committee and the legacy GOG Radiation Oncology Committee are mutually complimentary. Currently Sushi Beriwal, MD, is a co-chair on the NRG committee representing the legacy GOG committee. The legacy committee continues to be actively involved in the development of protocols in which radiation therapy and chemotherapy are becoming more common. Adjusting dosage and port size specific to gynecological malignancy are developed in coordination with the radiation oncology committee. The committee continuously updates current practices on imaging and radiation oncology. New techniques are constantly introduced and evaluated as the potential next

generation. The committee also is evaluating artificial intelligence in radiation oncology and what it's future may bring. IMRT, in conjunction with chemotherapy, is currently undergoing evaluation in locally advanced cancers. Ablation radiation therapy for women with oligometastatic gyn cancers are being evaluated. Protocols using anti-PD-L1 as immune-primers concomitantly with extended field chemo radiotherapy have been developed indicating cutting edge protocol development.

Figure 1.



GOG Partners Quality Control, Monitoring and Auditing

Complementary to NRG is GOG Partners (GOG P). In contrast to NRG, GOG P coordinates non-CTEP studies. GOG P has its own Quality and Assessment Committee. Quality assessment is coordinated through study sponsors (IND trials require the sponsor to monitor the study) and is generally maintained through Routine Monitoring Visits (RMV) and audits coordinated together by the Contracted Research Organization (CRO) (Figure 1). Monitoring and auditing of clinical trials have different processes (Table 1) but share common goals to assure that the:

- Rights and safety of patients (i.e., human subjects) are protected
- Reported trial data are accurate, complete, and verifiable from source documents
- Conduct of trial is in compliance with protocol, good clinical practice (GCP) and applicable regulatory requirements

Generally, monitoring is based on risk. Risk Based Monitoring holistically identifies risk of failure. Monitoring is approached to prevent or mitigate risk and delivers a "fit" for the purpose of the study with flexibility to address regulatory needs. It is an extension to smart study design and clinical trial efficiency.

The coordination of quality assessments of sites and study data as well as ensuring compliance in all research areas is the responsibility of the GOG P Quality and Assessment Committee. Institutions and private practices interested in participating on GOG P studies complete applications for review and approval by this committee.

In addition to RMVs, CROs coordinate other types of visits to ensure quality. These include Pre-site Qualification Visits (PSVs), Site Initiation Visits (SIVs) and Close Out Visits (COVs). Common attendees at the SIV include:

Sponsor/CRO
- Clinical Research Associate (CRA)/Monitor
- Medical Monitor
- Project Manager

Site
- Principal Investigator (PI) and sub-PIs
- Research Nurse
- Data Manager
- Pharmacist
- Data Manager
- Regulatory Coordinator
- Biospecimen Coordinator
- Others may attend as appropriate

The purpose of the COV is to: Insure that the study is complete; all investigator obligations have been fulfilled; the data has been retrieved, entered and database locked; and all study related items (including investigational products) have been returned or appropriately destroyed.

Regulatory documents are generally stored in a "Binder" and include:

- All protocol versions and approvals
- All Investigator Brochure versions

- Lab certifications and normal ranges
- All versions of Form 1572
- Curriculums vitae (CVs), licenses and financial disclosures for all Investigators – signed and dated
- All Institutional Review Board (IRB) correspondence
- All sponsor correspondence
- Serios adverse events (SAEs)
- Update Delegation of Responsibility (DRAPs) /signature log as needed

Summary

Clinical trials are becoming increasingly complex, not only in their design, but also in their operations. Close attention to details including quality assessments is necessary to ensure that rights and safety of patients (i.e., human subjects) are protected, data are reported accurately and trials are done in compliance with the protocol, GCP and applicable regulatory requirements.