

Section 28:

Quality Assurance Office for Clinical (QACT)

28.1 Introduction and Purpose

The QACT at DFCI was established in 1986 as the Quality Control Center (QCC). The QCC was charged with creating a standardized data management system for clinical trials. Over time the role of the QCC has expanded to include a variety of tasks, such as registering participants to clinical trials, developing Case Report Forms (CRFs), generating frequency and descriptive summaries for investigators, and generating vital statistical reports for DFCI and its partners.

In 1997, the Dana-Farber /Partners Cancer Center (DF/CC) was established, uniting DFCI with BWH and MGH as one comprehensive adult oncology center. In 2000, BIDMC, Children's Hospital Boston, Harvard Medical School, and Harvard School of Public Health joined with the DF/PCC to form the Dana-Farber/Harvard Cancer Center (DF/HCC). As a result, the DF/HCC Clinical Trials Support system was established, and the QCC was renamed the Quality Assurance Office for Clinical Trials (QACT). The QACT has been designated as the central facility for coordinating clinical trials across these multiple institutions.

28.2 Mission

The QACT is responsible for review of systems for clinical trials that are conducted across DF/HCC institutions. Through the DF/HCC Medical Director of Clinical Trials Operations and the senior vice-president of research at DFCI, the QACT reports to senior management on the status of clinical research management.

28.3 Functions of the QACT

Specific QACT responsibilities include:

- Registration of participants on clinical trials
 - o Up-front registration of participants to all therapeutic trials and selected ancillary trials
 - o Development of eligibility checklists
 - o Eligibility and consent checking
 - o Randomization of participants to treatment arms, when applicable
 - o Monitoring of Phase I dose-escalation trials
 - o Protocol accrual monitoring
 - o Providing statistics for the DF/HCC

- Data computerization and quality control of oncology protocols initiated within the DF/HCC
 - o CRF design

- o Database table design and maintenance as well as eDC implementation
- o Development of protocol-specific quality-control procedures to maintain data integrity
- o Maintenance of database documentation
- o Report preparation

- Internal clinical research auditing
 - o Performance of internal audits for ongoing clinical trials
 - o Presentation of final audit reports and audit summary results to the DF/HCC Audit Committee
 - o Training to improve protocol and regulatory compliance

- Meeting/project coordination
 - o Clinical Investigations Leadership Committee (CLC)
 - o Audit Committee
 - o Clinical Trials Operations Committee (CLINOPS)
 - o DSMB for high-risk Phase I, I/II, and II trials
 - o DSMB for large randomized trials
 - o Multi-center Coordinating Committee (MCC)

- Management of a master research Listserv for dissemination of information to DF/HCC clinical research staff

28.4 Participant Enrollment in Clinical Trials

Prospective Participant Registration by the QACT

Prior to the initiation of treatment, all protocol participants are registered in the QACT Protocol Registration System. The registration system is a computerized registry of all patients on DF/HCC oncology protocols, and it serves as a master list for various departments for summary statistics, drug dispensing, NCI reporting, and auditing.

This centralized registration process allows for the reporting of a variety of statistics. It also allows for the monitoring of accrual rates, which is vital in determining whether a protocol will meet the accrual objectives that are outlined in the protocol.

An investigator, treating physician, research nurse, or study coordinator is responsible for registering a participant with the QACT. Registration involves faxing a completed protocol specific eligibility checklist and signed participant consent to the QACT.

Information in the QACT Protocol Registration System is transferred in real time to the BWH computing system and CH Chemotherapy Order Entry (COE) for electronic chemotherapy order entry. If an MGH participant is registered, a manual link is also necessary to the Enterprise Master Patient Index (EMPI) computing system. This manual link is the responsibility of the registrar. Linking to these systems ensures participant safety by verifying that participants are eligible and have consented to participation in a clinical trial or non-protocol treatment.

Registration information is also transferred every night to the Ingres database system. The protocol system coordinator and data analysts use the information for statistical reports.

If a participant is not registered, the treating physician cannot order drugs. Likewise, if a participant is not removed from protocol, the physician cannot order non-protocol therapy.

Retrospective Registrations

Retrospective registrations for therapeutic protocols are not allowed. For some minimal-risk trials, where a high volume of participants is recruited daily, registrations are accepted retrospectively in batches by fax or mail. In these cases, the study team prospectively needs to seek approval from the QACT Director.

Eligibility Checking Process

Protocol-specific eligibility criteria are established to identify the target population and ensure participant safety. When an investigator identifies a potential trial candidate, he or she must confirm in detail if the candidate is eligible to participate in the trial. The QACT eligibility checklist ensures that all inclusion/exclusion criteria are verified prior to protocol enrollment.

The completed eligibility checklist is faxed to the QACT along with the entire signed consent document. The QACT registrar confirms that all fields on the checklist are thoroughly completed and that all values are within the acceptable range allowed by the protocol. The QACT does not register a participant until all eligibility tests have been completed and all values are made available to the QACT.

All tests that are required to determine eligibility must be completed within the time frame specified in the protocol.

If a time frame is not specified in the protocol, tests must be completed as follows:

- Lab tests required for eligibility must be completed within *14 days* prior to trial enrollment by the QACT.
- For protocols requiring measurable disease, baseline measurements must be completed within *14 days* prior to trial enrollment by the QACT. Examples: flow cytometry, HLA typing, fluid cytology, tumor markers, and hormones (CEA, CA-27-29, CA-125).
- Non-lab tests required for eligibility must be performed *30 days* prior to trial entry. Example: Radiological scans.
- For bone marrow transplant (BMT) protocols and non-protocol treatment plans, eligibility tests must be completed within *42 days* prior to enrollment by QACT. The extended period of time is allowed to facilitate insurance approval while ensuring participant safety.

Development of Eligibility Checklists

When a research protocol is activated or amended, the QACT registrar generates a new checklist or revises an existing eligibility checklist from the protocol document, which is found on Oncology Protocol System (OncPro). For cooperative-group trials or industry-sponsored trials that may generate their own checklists, the QACT develops a “front sheet” to capture additional information not found on the checklist, such as patient demographics, lab values, test dates, and randomization arms for randomized trials or dose levels for Phase I dose-escalation trials.

The registrar notifies the OHRS online team that a checklist has been generated. In the case of front sheets, the cooperative group or sponsor’s checklist is scanned online by the OHRS online team.

In the event that an eligibility checklist is not required by the protocol, a QACT registration form is put online to capture patient demographics for patient registration in the QACT. The protocol system coordinator or registrar comments in the QACT Clinical Research System that a checklist is not required.

Consent Checking Process

Investigators have an obligation to obtain informed consent from a participant (or the appropriate legally authorized representative) before enrolling him or her in a clinical trial. Written consent must be documented on the valid IRB approved consent, which can be found in OncPro. All pages of the consent must be faxed to QACT along with the eligibility checklist for participant registration, unless the protocol specifies differently. If that is the case, the protocol system coordinator or protocol registrar enters an appropriate comment in the QACT Clinical Research System. If a consent form has embedded questions, all questions must be answered for the form to be considered complete.

An expired or invalid consent form is not accepted by QACT. If this happens, the protocol registrar notifies the registering person and/or the person who obtained consent that the participant must be re-consented before he or she can be registered. Non-protocol treatment regimens do not require the consent form to be IRB-approved.

All pages of the consent form must bear unique patient identifiers.

[DF/HCC SOPs](#) indicate which individuals can obtain written informed consent from a participant. An attending physician (non-trainee) who has an active NCI 1572 on file with the CTEO/QACT and NCI *and* has current human participant protection training must obtain informed consent for a therapeutic trial. Otherwise, the signature page must be co-signed by an attending with an active NCI 1572 on file in the CTEO/QACT. For non-invasive minimal risk protocols, PIs can request to delegate the duty of obtaining consent by prospectively sending written notification to the protocol registrar, as designee for the QACT Director.. The protocol registrar documents this in the QACT Clinical Research System.

The signature of any staff member on the consent means that he or she was involved in the consenting process and that the participant was presented with a clear explanation of the protocol and given the opportunity to ask questions.

28.5 Randomization Process

The protocol registrar is responsible for randomizing participants to treatment arms for some non-industry-led and non-cooperative group trials. The protocol system coordinator is instructed by the statistician in the Department of Biostatistics Sciences how to conduct the randomization. The protocol system coordinator then documents the instructions in the QACT Clinical Research System, to which the protocol registrar will refer. The protocol registrar documents the randomization assignment in the QACT

Clinical Research System, unless the protocol is blinded. If the protocol is blinded, the protocol registrar conveys the randomization assignment to the appropriate departments (e.g., pharmacy) as directed by the randomization instructions.

28.6 Phase I Dose-escalation Trials

The protocol registrar is responsible for monitoring all non-industry-led and non-cooperative group Phase I trials. The dose-escalation schema for the protocol is documented in the QACT Clinical Research System by the protocol system coordinator, adding “DOSE-ESCALATION (QACT),” for the protocol registrar to refer to. Patient registration is denied if the specified waiting period between and within cohorts has not been met. The IRB must approve revisions to the protocol if additional patients, cohorts, or dose-levels are to be added. The protocol registrar ensures that the dose-escalation schema is followed exactly as it is written and appended in the protocol.

28.7 Single Patient IND

Single patient IND protocols are also known as ‘compassionate use’ or ‘individual,’ and were previously referred to as ‘interim approvals.’ An individualized IRB approved consent form must be signed and faxed to the QACT. Data collected through this process can’t be used in analysis of the protocol it may refer to.

28.8 Non-protocol Standard Treatment Registration

Some participants may be registered on a standard regimen not part of a clinical trial. The regimen may be commercially available drugs or a specific procedure. QACT designates the treatment plan by assigning a three-digit number.

28.9 DF/PCC Network Affiliate Registration

For DF/PCC network affiliates, consent must be obtained on a current, IRB approved consent form from the IRB of record for the affiliate institution, and the completed QACT-generated eligibility checklist must accompany the consent.

The protocol registrar does not register a participant from a non-DF/HCC institution, unless that hospital is named on the front sheet of the protocol and the IRB from that hospital has approved the protocol for use.

If a hospital must be added to the provider directory in the QACT Clinical Research System, a request must be made to the Access Management Department.

28.10 Industry-led and Cooperative-group Registration

For industry-led and cooperative-group trials, often registration must occur at the sponsor/cooperative-group level before registering with the QACT. Registration in the QACT must still occur before treatment is administered. The QACT cannot register a participant from an outside hospital on a sponsored trial unless the hospital’s name appears on the front sheet of the protocol and adequate IRB-approval has occurred.

For participants enrolling in a CALGB trial for treatment at a DF/HCC institution, the QACT-generated front sheet (or checklist) must accompany the consent. For participants treated at a non-DF/HCC

institution, the CALGB checklist and confirmation of registration must accompany the IRB-approved hospital consent.

28.11 Non-patient Volunteer Registration

Non-patient volunteers undergoing invasive procedures or administration of pharmacologically active substances must sign a consent form and are registered in the QACT. Blood draws are exempt. Bone marrow aspirates are not exempt.

28.12 Electronic Confirmation of Registration

System generated electronic confirmation of registration is automatically sent to the registering person, PI, treating physician, and trial contacts for protocol patients. Hard copies are generated upon request.

When a name is not in the QACT Clinical Research System, a request to add it to the provider directory must be sent to the Access Management Department.

28.13 After-hours Registration

Normal business hours for the QACT are 8:30 AM to 5:00 PM. Patients are enrolled and randomized in clinical trials or non-protocol treatment during normal business hours, unless an emergency arises in which a participant must be treated before the next business day.

After-hours registration involves calling the QACT main number, (617) 632-3761, selecting option one, leaving a detailed description of the participant's eligibility and a call-back number, and faxing the signed consent form and completed eligibility checklist to the QACT. Registration occurs off-site after normal business hours. A QACT registrar on call will contact the caller to complete the registration.

28.14 Removing a Participant from a Research Study

When a participant will no longer be treated and/or followed on protocol and no further data will be collected from him or her, the QACT registrar must be officially notified via telephone, fax, or email. The trial number, the reason the participant is being removed from the trial, the effective date, as well as the date treatment ended (if known) must be specified. The protocol registrar then removes a participant from trial by updating his or her record in the QACT Clinical Research System.

The categories for removing a participant from protocol are as follows:

- Cancelled (never began treatment)
- Ineligible
- Completed protocol requirements
- Unacceptable toxicity
- Progressive disease/relapsed

- Withdrawal of consent
- Withdrawal of consent but agrees to be followed
- Died (specify date of death)
- Lost to follow-up
- Other (specify)_____

Due to a chemotherapy-order entry safety mechanism that is built in to the QACT Clinical Research System, a participant can't be registered to more than one therapeutic trial at the same time but can be enrolled in multiple minimal-risk ancillary trials at any given time. If a participant is not removed from a therapeutic protocol, the physician cannot order non-protocol therapy or register the participant to a second therapeutic protocol. If the participant must be treated on a different therapeutic trial but the off-trial date is unknown, in the Clinical Research System the protocol registrar will enter 1 day prior to the registration date of the new trial and will document the reason as "other – switched to other protocol."

If the date of death is not in the participant display banner in the participant record, it is advisable to send that information to Health Information Services (HIS).

28.15 Protocol Closure Notification

The Protocol Closure Form must be sent to OHRS. The OHRS notifies the QACT registrars when a protocol is closed to enrollment for any reason. The QACT protocol system coordinator updates the Clinical Research System with this information.

For trials open to accrual prior to 2009, paper copies of the registration documents (eligibility checklist and consent document) are maintained by the QACT. For trials open to accrual after 2009, electronic copies of the registration documents (eligibility checklist and consent document) are maintained by the QACT. When deemed appropriate, protocol registration files are moved to an off-site storage facility. If those records are needed, the QACT Director must be notified and a copy of the documents will then be retrieved.

28.16 Protocol Completion/Termination Notification

To formally complete a protocol file, investigators must notify the IRB when a protocol is terminated or completed or after data analysis is complete by submitting a final Continuing Review form. QACT then receives electronic notification from OHRS, and the protocol system coordinator or protocol registrar updates the QACT Clinical Research System.

28.17 Reports Available from the QACT

There are various reports available from the QACT relating to accrual statistics for protocol and non-protocol patients. The protocol system coordinator or protocol registrar must be contacted if a report is needed.

QACT reports include:

- Participant accrual reports, which can be generated for any protocol, contain a summary of

information about each participant registered on the protocol. The lists are generally sorted chronologically by date registered, but they can also be sorted alphabetically by patient name or in order of hospital medical record number.

- Special protocol accrual reports present accrual by periods across protocols or by specific categories such as disease sites, phase, and sponsor.
- Protocol population accrual figures (race, gender, ethnicity, and service area) are useful for grant applications.
- Reports with various other specifications are provided upon request.

28.18 Protocol Accrual Monitoring

The protocol system coordinator monitors accrual on a constant basis and notifies the study team when the protocol is nearing target accrual. Additional accrual monitoring occurs through the Scientific Progress Review Committee (SPRC).

28.19 Case Report Form (CRF) Design

Cancer treatment is largely based on clinical research. Therefore, careful and accurate collection of protocol and non-protocol data is essential to reliable answers to scientific questions posed in research protocols.

The CRF is a data-gathering tool developed by the QACT data analyst. CRF design refers to the process of identifying what data must be gathered to meet trial objectives. The data analyst refers to the protocol document to identify information that must be collected for computerization and data analysis. Not all required data specified in a protocol need to be computerized in the research database/Ingres system. However, all required data must be documented in a patient's medical record.

During CRF design, the study team works together to agree on what specific data ought to be collected to meet the trial objectives.

The Forms Design Process

CRFs are computerized by the QACT using Visio 4 software. The data manager for participants enrolled in a given protocol completes them. CRFs typically include:

- On-trial form
- Treatment form
- Lab form
- Summary form
- Follow-up form
- Other protocol-specific forms

Generally, the data analyst coordinates study team meetings to facilitate the forms development process. The study team and data analyst work together to choose the specific data points they would like to collect. The QACT data analyst drafts preliminary forms, referring to the protocol document during the process. Pertinent sections include planned objectives, eligibility criteria, treatment plan, expected toxicities, dose modifications, follow-up, measurement and response assessment, and statistical considerations. The data analyst incorporates QACT standards and coding conventions into each CRF. The study team is asked to review the preliminary draft forms. During this review, the data analyst advises the study team to be critical of whether the forms properly reflect the statistical and data gathering needs of the protocol and whether data has been neglected. Once all parties have approved the CRFs, the forms are finalized by the Department of Biostatistics and published on OncPro.

Unless the protocol states differently, forms are due as shown in this sample:

SAMPLE DUE DATES FOR PROTOCOL FORMS	
On-Trial	Within two weeks of subject registration
Treatment	Every three months during treatment unless it is a Phase I trial, then after every cycle
Summary	Within one month of treatment completion
Follow-up	At least every six months while the protocol is open, depending on the protocol
Other Forms	As specified in the protocol or on the forms themselves

Study teams are encouraged to approve and finalize forms at the time of trial activation for prospective data collection. For in-house trials, the CRFs must be created early in the process. The data analyst generally waits until three to five participants have accrued to a trial to have some data reflected on forms before the paper forms are finalized and database tables are set-up by the database administrator. This is to test the forms for appropriateness and accuracy. The forms process is complex, and it can be costly to make major changes to the database once it has been set up.

The QACT is not responsible for CRF design for all protocols. Some cooperative groups and industry sponsors provide CRFs for the study coordinator to complete, and in this case, the group computerizes the data. These forms differ in complexity and design from QACT-generated CRFs but serve the same purpose of summarizing a subject's protocol treatment, including information needed for analysis of the protocol as well as preparing an FDA submission for drug approval.

Data Collection

Data collection involves reviewing medical information that has been abstracted by a Study Coordinator and transcribed onto CRFs, retrieving data from affiliate hospitals and gathering information from various databases. Ultimately, the PI assumes the overall responsibility for data that are collected. The QACT data analyst is assigned to a protocol to organize the data collection process, to manage the Ingres database, and to ensure the quality of the data that are being collected for statistical analysis and report

writing.

QACT performs quality assurance for most in-house protocols and is active in the data collection process. All therapeutic DF/HCC protocols are quality controlled by the QACT. Cooperative-group trials (CALGB, NSABP, RTOG, COG, GOG, and others), most industry-sponsored protocols, and any other protocols for which collected data are sent to a source other than the DF/HCC for analysis are not included in this process.

Paper CRFs should be completed using *permanent black ink* to ensure a good copy, and the study coordinator must submit the *original* to the QACT for computerization. Whiteout should *not* be used to correct mistakes; instead, all errors must be marked with a single line drawn through the mistake and noted with initials and date the correction was made. The study coordinator must keep a copy of the completed CRFs for the research file.

The QACT expects the study team to meet regularly (at least four times per year) to review the progress of the trial. Data should be submitted to the QACT according to the protocol schedule or as instructed on the CRF and should be submitted to the QACT on an ongoing basis rather than in bulk. All CRFs are date-stamped upon receipt in the QACT.

Computerization of Data

After any problem areas have been clarified and the first three to five patient forms are received, the QACT data analyst creates a protocol database with help from the database administrator and biostatistician to flag range errors. This process takes approximately one week to complete.

Before data is computerized, the data analyst performs quality-control measures on the CRFs that are submitted to the QACT. For example, the data analyst reviews CRFs for legibility and checks for data consistency as well as improper use of values. Data-cleaning programs can also be used to check for inconsistent data. Any discrepancies are listed in a query report to the study coordinator. All queries should be answered within one week.

Electronic Data Capture (eDC)

Electronic Data Capture through Phase Forward's program *Inform* is being implemented to replace over time the current Ingres database that is used to computerize data. Disease programs are being introduced to the new system on a gradual basis. Once eDC is rolled out in a disease or discipline-based program all new protocols will be managed in this system. Some of the process above will not be applicable in Inform. A team including Information Services (IS), QACT and the study team create the electronic case report forms. The data is keyed directly in to the system by the study teams. Many logical checks are built into the protocols ensuring that data will be available sooner for analysis.

Data Requests

Biostatisticians require ample time to conduct a thorough review of all the trial endpoints and issues. Last-minute requests for data analysis should be avoided. Data requests must be made in writing to the QACT assistant director and have the approval of the PI. The request form must be filled out completely to expedite the request. A minimum of one week for programming should be allowed, depending on the request. If the data request has not been processed and keyed, allow two to four weeks. All requests require programming time and effort; therefore, careful consideration should be given to the request information in advance.

Incomplete Forms/Missing Forms/Queries

The QACT data analyst is responsible for generating missing forms reports on a regular basis to monitor the data collection process. In addition, the data analyst can request missing information or data in one of two ways:

Individual or participant-specific query. For individual forms with missing or questionable data, the data analyst will notify the study coordinator electronically. A copy of the query and the reply is kept in the QACT, and the database is corrected with the appropriate information once the response is received. To document this process, the data analyst maintains an Excel spreadsheet consisting of minimal information due to privacy reasons.

Formal data request. The QACT uses a computer program to notify the study coordinator of missing forms and/or information across all protocol patients on a given trial. This allows the data analyst to request information from the study coordinator if a specific CRF's survival or relapse information is overdue.

If forms are queried, the data analyst performs corrections in the database. The biostatistician analyzes all protocol data after the data analyst updates the database. The biostatistician will work with the data analyst to check all fields for missing data or inappropriate ranges, account for all eligible patients, and close the database once analyses are complete.

28.20 Documentation and Storage of Data

Documentation Procedure

Each protocol computerized in the QACT has an associated binder, which includes a copy of the protocol, important correspondence relating to the forms (excluding data queries that do not pertain to the interpretation of the forms), SAS programs, coding conventions, and the CRFs. The binder may also include an updated protocol-patient accrual list.

Storage Procedure

Once the CRFs have been reviewed, submitted, and appended to the database, they are filed at QACT. The study coordinator should keep in their research file a copy of all CRFs submitted to the QACT. CRFs are the written record documenting information that has been computerized. Whenever computerized data looks questionable or more specific information is required, the forms can be referenced as a backup.

All forms for a given protocol are stored on-site at QACT while that protocol is active. Forms collected for protocols that are inactive or for which data are not being analyzed are housed at an off-site storage facility.

The Department of Biostatistics conducts nightly backups of all computer data in Ingres. Those tapes are stored off-site. The QACT conducts nightly backups of all computer data stored in the QACT.

28.21 Accrual-monitoring Program

Accrual monitoring is managed by the Scientific Progress Review Committee (SPRC) based upon information provided by the QACT. Protocols are monitored for slow accrual, rapid accrual, and zero accrual. The SPRC has the authority to close a trial for accrual problems.

28.22 Internal Auditing

The DF/HCC internal auditing system oversees the compliance of the clinical trial process. The purpose of the internal audit system is to assure a high standard of quality for DF/HCC protocols by systematically evaluating:

1. Protocol Compliance
2. Protection of Human Research Participants
3. Institutional SOPs, ICH Good Clinical Practice Guidelines and Federal Regulations Compliance
4. Data Accuracy
5. Investigational Drug Handling

Each Clinical Research Auditor selects a minimum of two protocols a month to audit. All active DF/HCC protocols are eligible for audit, including those protocols sponsored by NCI, pharmaceutical industry or other sponsors. The following rubric is used for prioritizing protocols to audit:

- Gene transfer protocols are audited annually.
- In-house intervention & NCI/NIH funded protocols are audited a minimum of once in their lifetime. Priority is given to high-risk studies. Disease and discipline-based programs are chosen on a rotating basis and a protocol is eligible after five participants have been accrued, unless the target accrual is less than 10 participants.
- Industry and Cooperative Group trials: Annually, a minimum of one industry and cooperative group trial will be audited per disease or discipline-based group.
- DF/PCC Network Affiliate hospitals are audited annually after at least two participants are entered on trial(s).
- For cause audits of protocols requested by CLC, IRB, DSMC or DSMB including re-audits.
- Protocols identified as rapidly accruing by the Accrual Monitoring Program (expected duration less than one year or accrual rate is 1.5 times faster than expected).
- Protocols identified as having new DF/HCC Overall PIs or new clinical research investigators per the DF/HCC SOPs QA-722 and QA-723.

Each disease site will be audited every three to six months to ensure protocol compliance. An Overall Principal Investigator (PI) who is audited once during the year may be audited a second time during the year on a different protocol.

The Clinical Research Auditor selects protocols from a list of eligible studies and disease sites. The auditor attempts to distribute the audits evenly among the various disease programs and protocols including multi-modalities.

The Clinical Research Auditor uses the protocol document as the basis for judging protocol compliance. The specific areas are:

- Regulatory

- Informed Consent
- Registration and Randomization
- Eligibility
- Pre-Therapy Requirements
- Treatment Administration
- On-Study Evaluations
- Response Evaluations
- Adverse Events
- Data Collection
- Investigational Drug Handling

The DF/HCC Audit Committee reviews the audit findings and approves or disapproves of the violations and audit rating. The Overall PI is requested to correct any major violations identified during the audit and respond in writing with a corrective action plan. The Audit Committee will also review the corrective actions plans from the Overall PI. Documentation is maintained in the QACT audit files.

The QACT provides a resource document entitled, the [Clinical Trials Audit Manual](#). The Manual describes the auditing process in detail. All clinical researchers and data management staff are advised to become familiar with the importance of and the procedures for audits. Seminars are arranged annually through the Clinical Trial Education Office (CTEO) to familiarize staff with the audit process and assist them in preparing for an audit.

28.23 DF/HCC Data and Safety Monitoring Board (DSMB)

The DSMB for large randomized trials was formed in accordance with NIH/NCI requirements. The purpose is to monitor trial progress and potential risks to participants enrolled in protocols that are developed by DF/HCC investigators. Board members are by majority external to DF/HCC with few clinicians and biostatisticians from across the DF/HCC. The DSMB meets semiannually and reports findings to CLC and the IRB.

28.24 DF/HCC Data and Safety Monitoring Committee (DSMC)

The DSMC for pilot, phase I, I/II, and Phase II trials provides ongoing monitoring for high-risk clinical trials initiated and conducted by DF/HCC investigators to ensure the safety of trial participants as well as to evaluate the ongoing status of the trial. Membership is appointed by the senior vice-president for research and includes:

- Voting members:
 - 3 medical oncologists
 - 1 ad hoc physician as needed (i.e., radiation oncologist, surgeon)

- 1 biostatistician
- 1 nurse
- 1 pharmacist
- Chair will be one of the physicians
- Non-voting member:
 - 1 coordinator for meetings

The QACT serves as administrative support to the committee. Information that has to be provided to the committee includes: current participant accrual, reporting of all adverse events including, any response information that is available, and a summary provided by the study team. Other information (e.g., scans, laboratory values, participant charts) will be provided if requested by the committee. Minutes are kept and recommendations are made to the study teams and reported to the IRB and CLC. All trial and participant information must remain confidential. All DSMC members sign a confidentiality and conflict of interest (COI) statement related to the trials being discussed. Members will recuse themselves from the discussion and voting if a conflict exists for a given protocol.

Protocols that require monitoring are high-risk DF/HCC-initiated protocols. The study team, SRC, pediatric SRC, IRB, and/or CLC identify them. High-risk protocols may include, but are not limited to, gene-transfer trials, vaccine trials using live or attenuated viruses, new therapies being tested for the first time in humans, trials initiated within the DF/HCC but conducted at multiple centers outside the DF/HCC, or trials that are exceptionally complicated or intensive. Most high-risk sponsored trials initiated outside of the DF/HCC have their own monitoring committee. If these trials do not have a DSMC and if the DF/HCC review committee determines that an increased level of monitoring is required, then they will also be reviewed by this committee.