Chapter 19
Continuous Quality Improvement (CQI)

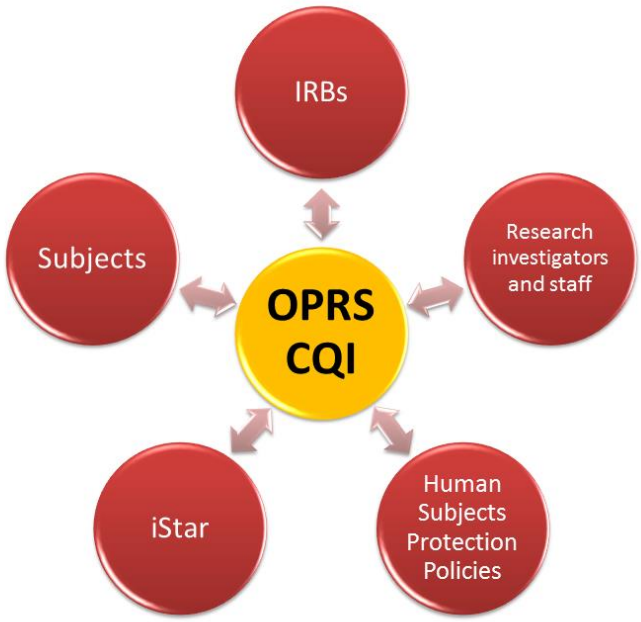
This chapter describes the USC Continuous Quality Improvement Program objectives, activities, and components. A detailed list of quality improvement activities outlines major components of the Program. The chapter concludes with an overview of investigator and IRB assessments and audits.

19.1 The Continuous Quality Improvement (CQI) Program

The Human Subjects Protection Program (HSPP) conducts Continuous Quality Improvement (CQI) activities to measure and improve HSPP effectiveness, quality, and compliance with IRB policies and procedures, and applicable federal, state, and local laws. Outcomes of CQI activities are fed back into the process, resulting in improved protections for human subjects and increased efficiency. The CQI Program:

- develops and maintains USC Human Research Protection Program (HSPP) according to national best practices, regulations and guidelines
- keeps investigators cognizant of rules, corrects procedural errors, and
- increase protections for human research participants
- auditing and assessing investigator compliance with the HSPP policies and procedures and IRB requirements

Continuous Quality Improvement (CQI) Program Diagram



19.2 USC CQI Activities

In addition to developing and maintaining policies, the HSPP creates resources to facilitate compliance in the USC research community. Below is a list of initiatives that make up and support CQI activities:

Human Subjects Teleconferences

Each month OPRS hosts a teleconference for the Health Sciences and University Park IRB Directors and Chairs to share ideas and discuss human subjects protections developments and their impact on the Program.

HSPP Executive Committee

Monthly meetings are held amongst OPRS Executive Director and IRB Chairs and Directors from both campuses to discuss updates to regulations, implementation of new procedures, and best research practices.

Education Sessions

OPRS and the IRB offer educational sessions on introduction to human subjects training, use of the electronic IRB application system and informed consent documentation to the USC research community.

Classroom Education Sessions

OPRS and IRB Student Mentors offer classroom education as guest lecturers to discuss human subjects protections with students (incoming PhD students, medical students, undergrad scholars).

Booklets

OPRS creates many booklets (available in hard copy and online) to educate student and researchers on a range of topics including students and research, conducting research using human subjects, mentoring USC student researchers, informed consent in human subjects research.

OPRS and IRB Website

The website provides the latest information to the USC research community including guidance, consent templates, policies, educational resources, and contact information. Website analytics are reviewed periodically to determine web traffic, reader interest and improve site content.

Listerv Newsletter

OPRS distributes a periodic newsletter to keep the USC research community informed of updates in regulations, policies, best practices, and relevant research news.

Research Coordinator Bulletin

Information specific for coordinators and research support staff is communicated through a coordinator bulletin. Featured topics include educational sessions, coordinator events and networking opportunities, coordinator FAQs, national coordinator resources and articles of interest.

IRB Student Mentor

The OPRS graduate assistant serves as UPIRB liaisons by meeting with student researchers and providing one-on-one assistance and training. The student mentor is a full voting IRB member and represents USC students in IRB deliberations. Student mentors

bring student concerns to policy meetings and also review OPRS documents for student perspective.

Annual IRB Survey

Each year, users of the IRB application system are invited to complete an online anonymous survey to provide feedback about the IRB system and offer suggestions on how to improve the review process. The surveys show trends over time and identify problems and issues. A summary of the survey results is publicly disseminated to the research community on the listserv and HSPP website; detailed results are provided to the Institutional Official and the IRBs. Feedback often results in educational opportunities, policy changes and iStar system process changes.

iStar Development Meetings

Representatives from OPRS, University Park IRB, Health Sciences IRB and Children's Los Angeles IRB meet with iStar personnel twice per month to address iStar upgrades, problems, glitches and solutions. Also, iStar issues and suggestions identified at various stages of the CQI process are addressed and discussed at these meetings.

Policies and Procedures Review and Updates

HSPP Policies and Procedures are regulatory updated by the Human Subjects Working Group (OPRS, HSIRB, and UPIRB). Changes to Policies and Procedures are communicated to the IRB members, IRB staff, investigators, and research staff via the Human Subjects Newsletter. The Policies are available on the HSPP website.

IRB Member and Administration Education

OPRS arranges monthly educational sessions for IRB members as well as periodic IRB administration educational lunches to discuss best practices, upcoming policy changes and other topics.

IRB Community Member Outreach

OPRS hosts annual meetings and teleconferences with community IRB members from many Southern California Institutions to discuss emerging issues and share information. Additionally, OPRS created and regularly updates the "What It Takes to be an IRB Community Member" handbook (https://oprs.usc.edu/files/2013/05/Community-Member-Booklet-5.1.13.pdf). The handbook is nationally praised and has been adapted by various Institutions to supplement community member training.

Collaboration and Networking with Other Institutions

The HSPP collaborates and networks with other Institutions regularly to discuss best practices in policy and guidance development. Additionally, collaborative efforts with local partner Institutions reduce duplicative review of studies conducted at USC and either partner Institution (Children's Hospital Los Angeles and Cedars-Sinai Medical Center).

Flexibility Coalition

The Coalition was originally established to discuss reducing the administrative burden on non-federally funded, no more than minimal risk projects. Teleconferences and in-person meetings are regularly scheduled to share, discuss and brainstorm ideas related to flexibility in the IRB review process. The Coalition is now more than 170 members strong.

Audits

Not-for-cause audits of research studies are conducted by ORPS; for-cause audits are conducted by the HSIRB. OPRS and IRB personnel also conduct assessments of IRB operations and the iStar system to identify trends and issues related to study approval times, IRB and investigator response time, IRB workload, and changes or deficiencies in policy implementation or process. Refer to the rest of this chapter for additional information.

For a list of more CQI activities at USC, visit: https://oprs.usc.edu/files/2013/01/CQI-Efforts-7.2013.pdf

19.3 Audits and Assessments

Audits For-Cause

For-cause audits are reactive, direct, and aimed to investigate or substantiate an allegation or complaint received by the Human Subjects Protection Program (HSPP). Allegations or complaints may be submitted to the HSPP through written correspondence, anonymous phone call, or other avenues. Information received from a sponsor, the FDA, a whistleblower, the IRB, IRB Chair, OPRS, an investigator, or a subject may all lead to a for-cause audit. Audits may also be initiated in response to protocol amendments,

continuing reviews, and other submissions or communications with the IRB. Additionally, funding agencies may request a for-cause audit due to allegations of noncompliance, adverse events, or other causes of concern.

Low-risk/ non-clinical studies rarely warrant a for-cause audit. A main goal of for-cause audits is to collect sufficient information for the IRB to determine a course of action on serious or continuing non-compliance, or reported allegations and complaints. For-cause audits are conducted by HSIRB and OPRS personnel.

Audit Procedures

The IRB Chair or Vice-Chair initiates for-cause audits based on an allegation, complaint, deficiencies found by IRB review activities, and/or information from media or scholarly reports.

The IRB discussion of the allegation and subsequent determination are documented in the IRB meeting minutes.

The following items/processes may be inspected:

IRB (iStar) Application

- Initial applications including the protocol
- Amendment and revisions to the protocol
- Adverse events, unanticipated problems involving risks to subjects or others, protocol deviations, DSMB reports, as applicable
- Continuing Review Progress Reports
- Informed consents and/or other consent/assent documents
- Questionnaires, recruitment materials and other materials used in the study
- Correspondence from the investigator and the IRB
- IRB action letters (approved, approved with contingencies, deferred)

Researcher Files

- Copies of documents submitted to the IRB
- IRB action letters (approval notices)
- Case report forms
- Monitoring logs, enrollment and screening logs
- Correspondence between sponsor and investigators, and/or governmental correspondence
- PI/Staff education certifications/licensure/CVs
- Accrual information including the number of subjects enrolled to date; subjects not meeting eligibility criteria; subjects who either dropped out or were discontinued
- Approvals from other agencies or groups on or off campus (collaborating Institutions or organizations and University Safety Committees such as IBC, Radiation, other)

If the investigator is a student researcher, the IRB may request to have the file inspected in the faculty advisor's office.

Research Case Report Forms (CRF)

These forms are kept in the research staff offices or investigator's office. In most cases the subject's medical records, as a source document, will be reviewed to verify the information on the CRF.

Informed Consent (IC) Documents

- Protocol status (active, closed)
- Version date of the informed consent
- Language version of the informed consent (English, Spanish)
- IRB approval stamp

- Signatures (subject, investigator, witness, legally authorized representative and translator, as applicable)
- Date and time of the signature
- Copy given to the subject
- Short Form Documentation

Observing the Consent Process

Members of the USC HSPP are authorized to observe, or have a third party observe, the consent process and/or the conduct of the research for various reasons. Observation may be required by the IRB for projects requiring additional oversight, or projects that have been reported to have a problem related to the consent process or the conduct of the research.

After an audit/inspection, the auditor will summarize the findings and submit it to the Chair, and/or the IRB. The IRB will make recommendations to address any issues of noncompliance. See Section 20.8 – Procedure for Handling Reports of Noncompliance for more information.

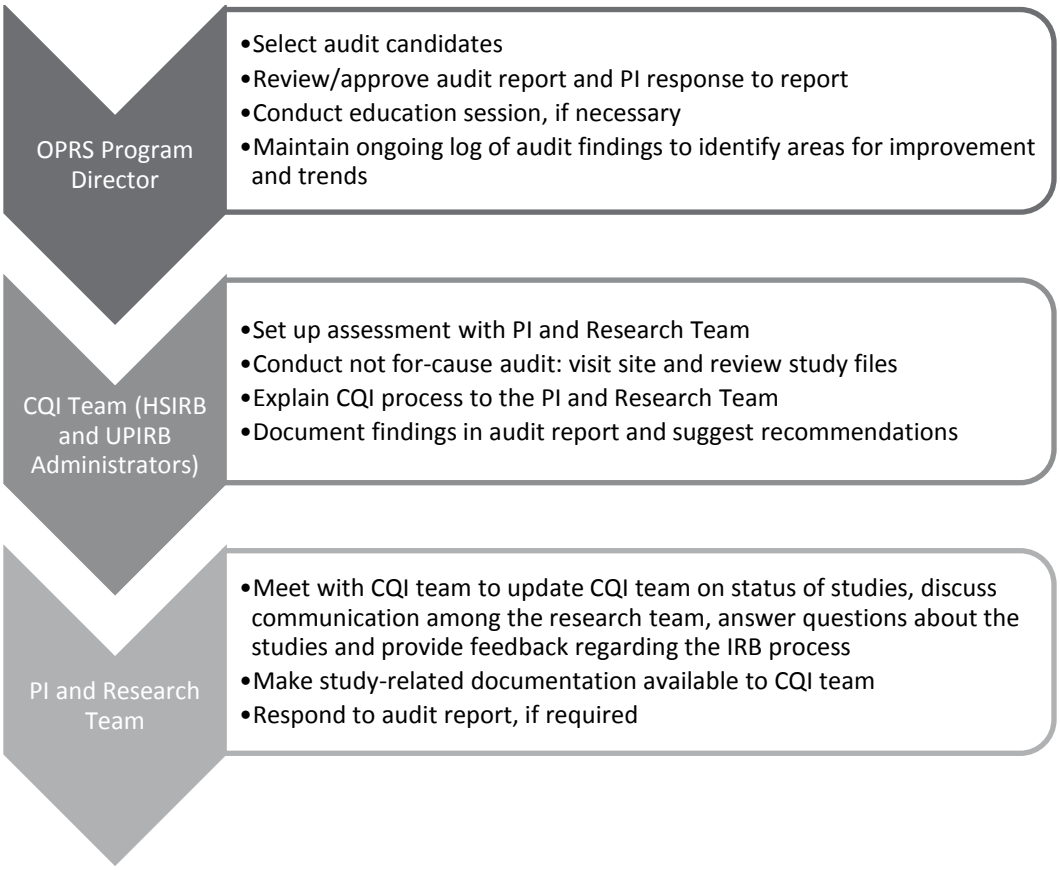
Quality Assessments (Not For-Cause)

Quality assessments are not-for-cause assessments conducted by designees of the HSPP. The assessment team performs up to10 assessments/re-assessments annually. In some cases, a follow-up assessment may be conducted to ensure compliance has been effected. Results of these assessments are educational and not routinely submitted to the IRB unless deemed necessary by OPRS. Research studies are chosen for quality assessment by OPRS/IRB staff using the following criteria:

- Schools and/or departments that submit high volumes of studies to the IRBs
- Investigators who have a high volume of active protocols
- Investigator-initiated protocols
- Studies including vulnerable subjects
- Studies conducted outside of the United States

- Recommendation by IRB staff

Procedures for Investigator Visit Assessment



OPRS notifies the Principal Investigator in writing of being selected for the CQI assessment. The CQI team schedules the assessment with the Principal Investigator (PI) and/or research team. The CQI team may request updated subject enrollment numbers for each IRB approved study to guide the assessment.

During the site visit, the CQI team conducts some of the following activities:

- Interviews the PI/research team to assess their knowledge of the study procedures
- Solicits feedback from researchers on the IRB process
- Inspects documentation that subjects met inclusion criteria

- Inspects study records and storage facilities
- Inspects documents and coding mechanisms used to protect confidentiality
- Reviews documentation of adverse events and unanticipated problems

After the assessment, the CQI team prepares a report summarizing findings or recommendations. Once reviewed and approved by the OPRS Program Director, the final report is forwarded to the PI. If findings are identified, the Principal Investigator must submit a response addressing each deficiency and include an action plan to prevent similar deficiencies in the future. In some cases, a follow-up assessment and/or training session(s) may be required.

If serious and/or continuing non-compliance is found, the CQI assessment report will be submitted to the IRB Chair and/or the IRB. The IRB will make recommendations to correct any issues of serious and/or continuing noncompliance. Refer to Section 20.8 - Procedure for Handling Reports of Noncompliance for more information.

The CQI team maintains a record of audit findings which is also used to identify trends and areas that are difficult or confusing for investigators. OPRS reviews audit findings to determine if improvements to the IRB process, electronic submission system or educational materials can be made to promote investigator compliance. When improvements to the system are identified, OPRS works with the IRB and/or iStar team to implement such changes.

Audits by External Entities

External audits may be conducted by regulatory agencies (FDA, OHRP), a sponsor, or other entities external to USC (AAHRPP). External audits may be conducted for-cause or not for-cause.

For-cause

For-cause audits by entities external to USC may arise from an anonymous complaint, an unanticipated problem reported by the investigator to a sponsor or federal agency (FDA), noncompliance reports, or other. For-cause audits may arise from a self-report or be complaint-driven.

Not-for-cause

Routine, not for-cause audits maybe conducted by entities external to USC. Investigators or sponsors may hire consultants to review a protocol, clinical practices, or other aspects of research. Clinical trial sponsors frequently send trial monitors to verify data integrity and adherence to regulatory requirements.

19.4 Assessments of IRB Processes

OPRS assesses internal IRB processes on an ongoing basis. These are primarily done through iStar-generated reports.

Assessment of the IRB process includes:

- Review of IRB minutes and Full Board meeting agendas, paying particular attention to subject complaints, adverse events, and ad hoc agenda items (miscellaneous problems/issues/suspensions/audits)
- Examination of IRB staff pre-reviews for accuracy, especially for exempt studies approved by the UPIRB staff
- Review of official IRB letters for accuracy, correct regulatory citations, and clarity
- Review of researcher feedback/complaints
- Review of the various forms and guidance documents found on the IRB websites, functionality of the website and hyperlinked documents
- Analysis of IRB processes (Not Human Subjects Research / Coded Data short application, other) to identify process issues
- Monitoring of new IRB staff members for accuracy, and the proper application of regulations and USC policies
- Review of ad hoc items as necessary

Chapter 20:

Reportable Events, Noncompliance, Suspensions and Terminations

Chapter Contents