ARTICLE

Building a Quality Management System in a Core Facility: A Genomics Core Case Study

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Core facilities are key resources supporting the academic research enterprise, providing access to innovative and essential technologies and expertise. Given the constraints placed on core facilities as recharge centers and the ever-changing research environment, an important competitive differentiator that can support rigorous and reproducible approaches in core labs is the implementation of a quality management system (QMS). This paper describes a systematic approach to building a QMS in a genomics core facility at the University of North Carolina School of Medicine. This model is based on principles of the International Organization for Standardization 9001 system with initiatives focused on process mapping, training (communication, customer service, performance management, development of standard operating procedures, and quality audits), root cause analysis, visual control boards, mock quality audits, and continuous improvement through metrics tracking and "voice of the customer" exercises. The goal of this paper is to share practical step-by-step recommendations and outcomes of this core facility QMS that are generally applicable to academic core facilities, regardless of technical focus. Application of these good laboratory practice principles will foster "competitiveness through compliance" and promote outstanding interdisciplinary research between academic cores and their nonacademic pharmaceutical and federal research partners. Additionally, implementation of the QMS qualified this core to apply for federally funded contracts, thereby diversifying its types of projects and sources of revenue.

Key Words: process improvement, Six Sigma, good laboratory practice

INTRODUCTION

Many factors drive scientific progress, but high on this list are constant advances in technologies and the ubiquitous need to pool resources and technical knowledge among diverse teams of researchers. Core facilities directly address these issues by providing access to innovative and essential know-how and equipment that would otherwise be cost-prohibitive to individual laboratories or departments. In this respect, all academic core facilities share the overarching mission of providing expert services and consultations at affordable costs. This shared mission dictates shared core requirements,[1] including supportive expertise, cost-effective access to equipment and state-of-the-art applications, acceptable turnaround times for supported services, and generally open access to all scientists. Operational funding is typically through user fees, and cores often receive major institutional investments to ensure availability of cutting-edge technologies. In addition, given the dual nature of core facilities as both research laboratories and small businesses, they require unique skills for their management that include general business expertise such as accounting, customer service, and marketing as well as advanced technical knowledge idiosyncratic to the specific research endeavor.[2]

Effective institutional infrastructure and long-term strategic planning enable adaptation to a constantly changing research environment. A forward-looking organization will anticipate technological advances and offer these to the research community. This is achieved through close monitoring of shared services and a sustainable investment plan for assessment, acquisition, upgrading, and ongoing maintenance of equipment, software, informatics, and data storage. Ph.D. scientists lead the operations of core facilities and direct core staff who are generally a mix of Ph.D., M.S., and B.S. trained scientists. By consolidating expertise, continuing education of core staff helps to maintain access to technological advances. Federal guidelines for rate determination for core services only allow cost recovery and prohibit acquisition of new equipment with an internal operating surplus. Thus, the ability to demonstrate return on investment to guide institutional investment is critical to the success of core facility growth. Over the past decade, several institutions conducted studies to assess core facility management approaches,[3] consolidation efforts,[4] and

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performance standards.[2] Recently, results of a survey of core facilities were published showing that most core labs use best practices and provide services that support rigorous and reproducible research, including access to well-maintained instruments and key training on design of experiments and data management and analysis.[5] Encouraging best practices and evaluating performance ("measure what you manage") of core facilities are necessary pursuits that strengthen reputations, drive customer loyalty, and enable future growth.

However, given the requisite constraints placed on core facilities and the ever-changing research environment, an important competitive differentiator that supports rigorous and reproducible approaches is the implementation of a quality management system (QMS) (Table 1). A QMS is defined as a formalized system that documents processes, procedures, and responsibilities that guide an organization's activities to meet customer and regulatory requirements. More than simple documentation, QMS refers to the entire system of internal processes, people, and performance that ensures optimal conduct and delivery of services, underpinned by a continuous improvement mindset. Operations driven by a QMS not only fulfill the core's primary responsibility to academic researchers but make the facility attractive to potential external customers, including pharmaceutical companies and federal agencies that could benefit from good laboratory practice (GLP) services and technological innovation. Commonly associated with pharmaceutical development and manufacturing,[6] a QMS is seldom a top priority for an academic core facility because it is not required for operating a core and establishing and maintaining a QMS requires significant effort.

The value of standardization of next-generation sequencing workflows and establishment of QMS in sequencing laboratories has been described. Endrullat et al.[7] emphasized the need for sample quality control, validation of workflows in clinical applications, and definition of standards for the bioinformatics pipeline and data handling. Although adherence to GLP standards in academic biomedical research core labs is not required, GLP-like standards in "-omics" core labs engender confidence in the scientific enterprise, standardize workflows, thereby ensuring reproducible results, and enhance traceability of data and associated documentation.[8] Recently, the establishment of a QMS in a next-generation sequencing research environment was described.[9] The design process and subsequent application of this QMS provided significant opportunities for operational improvement in the core. Positive outcomes included staff motivation and effectiveness, elevated customer confidence, more published articles, and an increase in the number of international author affiliations.

This paper describes a case study using a systematic approach to building a QMS in a genomics core facility at the University of North Carolina (UNC) School of Medicine. This model is based on principles of the International Organization for Standardization 9001 system,[10] which specifies requirements for QMS when an organization 1) needs to demonstrate its ability to consistently provide products and services that meet customer and applicable statutory and regulatory requirements and 2) aims to enhance customer satisfaction through the effective application of the system. Guidelines include initiatives focused on process mapping, training, root cause analysis (RCA), visual control boards (VCBs), mock quality audits, and continuous improvement through metrics tracking and "voice of the customer" (VOC) exercises. Training encompasses communication, customer service, performance management, development of standard operating procedures (SOPs), and participating in quality audits. Six Sigma tools,[11] which are designed to improve processes to enhance customer satisfaction and bottom-line results, were also utilized to implement process improvement and process control before, during, and after QMS implementation. The goal of this article is to share practical step-by-step recommendations, examples, and outcomes of this core facility QMS that can be applied at other institutions in core facilities. The QMS enables outstanding interdisciplinary academic research and

TABLE 1

QMS terms

Term	Definition
Root cause analysis (RCA)	Tools and techniques used to uncover cause of problems
SIPOC	Process mapping tool focused on Supplier, Input, Process, Output, Customer (SIPOC)
Six Sigma	Tools used to improve processes to enhance customer satisfaction
Standard operating procedure (SOP)	Step-by-step instructions for complex routine operations
Swim lane	Process flowchart used to visualize duties and responsibilities
Quality management system (QMS)	Formalized system that documents processes, procedures, and responsibilities
Visual control board (VCB)	Communication tool used to manage and track process performance
Voice of the customer (VOC)	Tool used to capture expectations and frustrations of customers

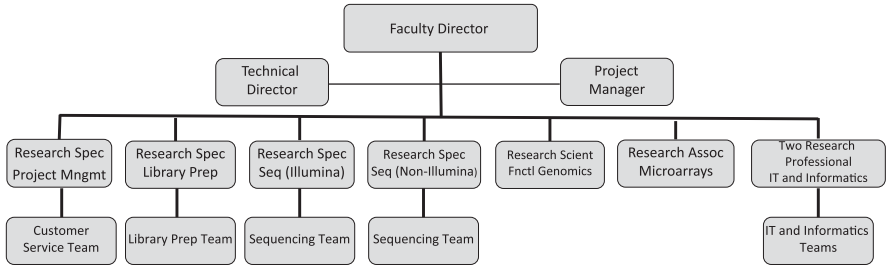

FIGURE 1

Organizational chart for UNC HTSF.

"competitiveness through compliance" for nonacademic pharmaceutical and federal research partners.

MATERIALS AND METHODS

The High-Throughput Sequencing Facility (HTSF) at UNC is a state-of-the-art next-generation sequencing facility featuring modern instrumentation from Illumina, Oxford Nanopore, Perkin Elmer, Agilent, Affymetrix, 10X Genomics, and BioNano Genomics. Currently serving more than 135 internal and external academic users in addition to federal agencies, the core has experienced growth in staff, instrumentation usage, and customer demand. The HTSF was formed in 2007 as a research-focused experimental facility for next-generation sequencing technologies. The HTSF evolved through consolidation of multiple smaller cores providing stand-alone services (including Sanger sequencing, microarray, and functional genomics, all in existence for more than 10 years). More than 25 employees work in the core, and it is organized under functional managers with a technical director and a faculty director (Fig. 1). These core mergers created growing pains, including implementation of a new management structure, challenges with on-time delivery and quality, and a reluctance to adopt new processes. In 2017, following repeated core facility errors and obvious customer dissatisfaction, a systematic process of core improvement was initiated at the request of the Vice Dean for Research in the UNC School of Medicine and with the support of core leadership and key stakeholders.

Using a Six Sigma–based framework, process improvement was initiated to drive the facility to new levels of performance. The primary improvement framework of Six Sigma has 5 key components: define, measure, analyze, improve, and control (DMAIC).[11] Using DMAIC as a roadmap, a stepwise process was followed and is detailed below and in Fig. 2.

Step 1: Discovery (Define and Measure)

To understand the challenges of the core facility from the inside, structured interviews were conducted with the core management, including all supervisors and customer service staff. Interviews were conducted with each individual in a confidential manner to gather feedback on day-to-day core operations, challenges and barriers, customer base, and ideas for improvement. Likewise, select customers of the core were interviewed to assess their level of satisfaction, perceived timeliness of core deliverables, quality of data, and ideas for improvement. This valuable feedback from core personnel and customers was synthesized and informed subsequent training and organizational principles that were required for improved operations of the facility.

Step 2: Process Mapping (Measure and Analyze)

A full-day workshop was conducted and included all HTSF employees (N = 25). Team building exercises focused on teamwork and communication were conducted in small groups of 4–5 team members, followed by detailed presentations from each functional area of the core, including sample submission, library preparation, quality assurance and control workflow, flow-cell design, sequencing, and data processing. This educational session ensured that all core employees understood the various steps in the process from beginning to end. An overview of the Six Sigma principle of SIPOC (supplier, input, process, output, customer)[11] was provided to orient the team to the concepts of

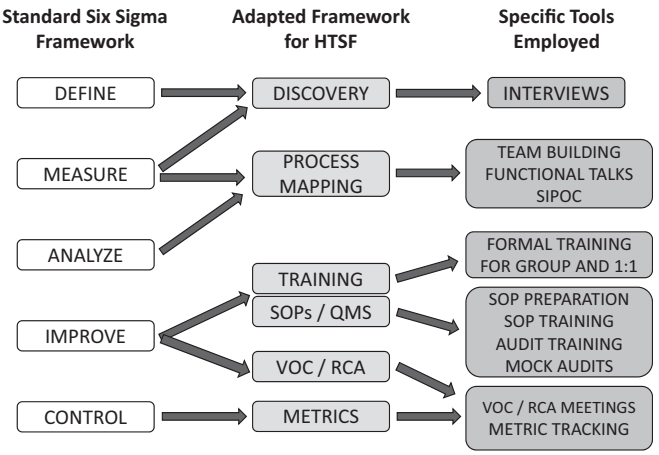

FIGURE 2

Six Sigma framework adapted for UNC HTSF. The DMAIC framework was adapted and specific tools were developed or utilized for HTSF process improvement.

process mapping[12, 13] using a "swim lane" approach. Teams of 2–4 core staff mapped out the current state of their respective functional areas on white boards with colored Post-It notes, drawing the connections and dependencies of all high-level process steps. A spokesperson from each team presented the process map to the full core group, and process improvement opportunities (barriers and inefficiencies) were identified and highlighted for future action. An example of a SIPOC-based process map for the sequencing workflow is presented in Fig. 3.

Step 3: Training (Improve)

Based on feedback from core employees and UNC core customers, training modules were developed to address specific areas of focus, including performance management, communication, customer service, QMS requirements, preparing SOPs, and preparing for a quality audit (Table 2). These training sessions were provided to all core staff members, with the exception of performance management training, which was provided exclusively to supervisors. The training format included lectures and participatory exercises to reinforce key learnings. Additionally, one-on-one training was provided to team supervisors and focused on team dynamics, setting expectations, communication, accountability, and operational excellence.

Step 4: SOPs and QMS Infrastructure (Improve)

The core had multiple protocols and work instructions but lacked formal SOPs. Based on guidance from an external corporate customer regarding the essentials of a quality system required for the core to perform services, an SOP template and an SOP portfolio were put in place. These documents include naming and numbering conventions (Fig. 4). Team members were assigned to draft SOPs by area of expertise, followed by 2 levels of review and signature to formalize and approve each SOP. The SOP categories were organization, customer focus, facilities and safety, personnel, purchasing and inventory, equipment, process management, documents and records, information management, nonconforming event management, and assessments. The team constructed a table of SOP contents, and SOPs were saved to a core intranet location, allowing access to all core personnel. SOPs were also printed and stored in 3-ring binders, available in each of the 3 laboratories comprising the core.

Following completion of the HTSF SOPs, all core personnel were required to read SOPs that were directly or peripherally related to their functional area and to certify their completion of training through signing off in an electronic database. This served multiple purposes: 1) retraining all staff on all procedures in their area of responsibility, regardless of years in job; 2) initial training for new core staff during their onboarding process; 3) formal documentation of the training records of core staff; and 4) identification of new SOPs that should be written based on gap analysis of process flows.

Quality audits are conducted by internal or external quality auditors and involve a systematic review of a QMS through interviews, lab tours, SOP reviews, and compliance assessments. In anticipation of a quality audit of HTSF, training was provided to core management and staff, focused on the following areas: what is "fair game" for auditors, what is off-limits to auditors, the importance of management alignment to the QMS, "do's and dont's," what to say and what not to say, behavior during an audit and a general audit schedule to set expectations. Following this training, core staff were instructed to ensure that facilities, staff, processes, and equipment should be audit-ready. Following the practice of "inspect what you expect," mock audits were conducted during which all core labs were closely inspected and core staff were quizzed on protocols, SOPs, health and safety, and customer service. Core staff were instructed on proper responses to queries from auditors and given examples of common mistakes, areas requiring additional improvements, and likely scenarios.

Step 5: VOC and RCA (Improve and Control)

By definition, core facilities are both research laboratories and small businesses, with a customer base made up primarily of professional academic scientists. Commercial contract research organizations and analytical services firms may offer similar services at competitive rates, performed under existing QMS and GLP with quicker turnaround

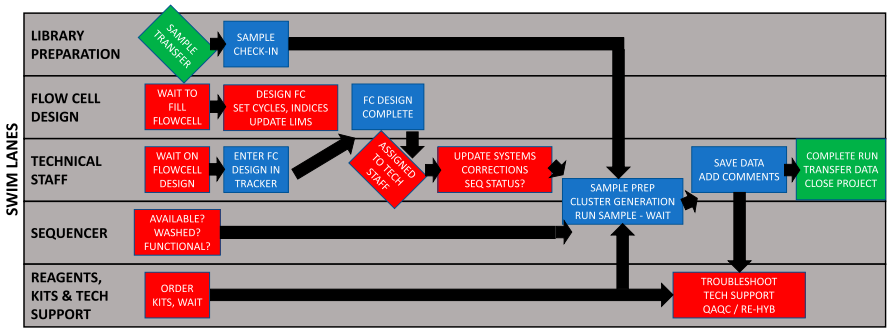

FIGURE 3

SIPOC-based process map for sequencing workflow. Each horizontal "swim lane" represents a component of the HTSF workflow. Green boxes, start or end of process; blue boxes, process step; red boxes, process step with potential wait time; diamond shape, handoffs. FC, flow cell; QAQC, quality assurance quality control; RE-HYB, re-hybridization

TABLE 2

Training modules

Training module	Contents
Performance management	Definition
	Competitive assessment *vs.* coaching or development
	Dealing with poor performers
	Setting goals
	Talent development plans
	Performance appraisals
	Recognition ideas
Communication	7 C's of communication
	Communication in writing, face-to-face
	Active listening
	Common mistakes
	Effective meetings
	Dealing with unhappy customers
Customer service	Who are our customers?
	Who impacts our customers?
	What do our customers expect and deserve?
	Communication (internal and external)
	Technique for dealing with unhappy customers
QMS requirements	Details of quality system essentials (organization, customer focus, facilities and safety, personnel, purchasing and inventory, equipment, process management, documents and retention, information management, nonconforming events, assessments, continual improvement)
How to prepare SOPs	Review of SOP template and discussion of required detail for each section (see Fig. 4)
Preparing for quality audit	Planning for an audit
	What is "fair game" for auditors?
	What is off-limits to auditors?
	Management alignment to QMS
	Do's and don't's during an audit
	Communication and behavior during an audit
	Basic agenda for 1-day audit (opening meeting with management, tours of labs, review of SOPs, interviews of core staff, closing meeting with management)

times, providing viable alternatives to core customers. This tension creates the need for academic core facilities to develop "whole-package" services[14] and to value the customer relationship. One way to demonstrate this value is to always say "yes" to customer requests unless the existing technology does not support the research initiative.[1]

Occasionally, factors including reagent quality or availability, technical errors, poor sample quality, or equipment malfunction lead to customer dissatisfaction. In the HTSF core, when projects are delayed or a customer does not receive the expected data at the expected time, a VOC meeting is conducted to gather feedback, and to ensure continuous improvement. These 1-hour, facilitated meetings are structured around the agenda in Table 3. The benefits of VOC meetings are numerous and include strengthened scientific partnerships, documentation of nonconformances and remedies (required in QMS), retention of the customer, and identification of gaps in existing procedures or new SOPs that should be prepared. A VOC meeting that we conducted this past year involved 2 projects from the same laboratory. Three scientists from the investigator's lab met with 7 HTSF staff members, including the faculty director, technical director, and functional managers, in a facilitated setting to provide candid feedback and specific concerns with their samples. The lab requested timely status updates on sample or library quality, improvements to the laboratory information management system (LIMS) customer interface, timely communication if delays are anticipated, and knowledge of which technician in the core is handling their samples at each phase. Each customer concern was discussed in detail, and the entire team agreed on the most pertinent issues and brainstormed solutions. Four action items were decided and assigned owners and a timeline for completion. Following the meeting, the

STANDARD OPERATING PROCEDURE SOP Outline	Document Number ABC-XYZ-001	Version Number 1.0
	Effective Date XX/XX/XXXX	Page 1 of XX

1.0 Purpose
The purpose of this SOP is to demonstrate the outline of an SOP.

2.0 Scope
This SOP applies to all SOPs that will be created for CORE NAME HERE.

3.0 References/Related Procedures
This SOP is related to all other SOPs associated with the Quality Management System in CORE NAME HERE (LIST SOP NAMES)

4.0 Responsibilities
Directors, managers, research associates, technicians and administrative personnel have the responsibility to format SOPs as described in this document.

5.0 Definitions
SOP – written procedure that ensures the quality and integrity of the data generated during the course of a project.

Attachments – referenced within an SOP (e.g., diagram showing flow cell loading, equipment diagram, etc.)

6.0 Procedure
This section describes the SOP outline procedure in enough detail that a familiar person could follow the step by step directions without additional training. What, how, when, why? Use subheadings and numbering system.

7.0 Safety
Any safety concerns should be listed along with countermeasures to avoid exposure or injury (e.g., exposure to hazardous chemicals, heat/cold, machine parts, etc.)

8.0 Attachments
Any attachments that are needed to make the SOP complete should be included here as a list with names.

9.0 Revision History
Include current version name, number and effective date with reference to any previous versions.

FIGURE 4

SOP template used by HTSF when building the QMS. This template is an example of a suitable SOP outline that will satisfy the requirements of a formal QMS for a core lab.

facilitator distributed detailed meeting minutes, including the agreed action items, to all attendees. Two weeks later, the facilitator followed up with the team to determine the status of action item completion and updated the meeting minutes to reflect 3 out of 4 items completed. Additional improvements were put in place by the core following this process, including an instructional video for customers on how to optimize use of the LIMS for placing new orders or checking status of existing projects.

RCA refers to a wide range of tools and techniques used to uncover the cause of problems, including *what*, *why*, and *how*.[15, 16] As part of a QMS, RCA is a key problem-solving process that can be used to address nonconformances and has the added benefits of formalizing change management, increasing operational excellence, and improving customer satisfaction (Table 4). Common RCA tools include Five Whys Analysis, Failure Mode and Effects Analysis, Fault Tree Analysis, Fishbone Diagram, and Current Reality Tree.[11] In practical terms, HTSF has used RCA to address various issues, including a lost customer sample, failure to deliver a project on time, customer submission of samples with poor quality, how to deal with custom projects, and a sequencing run failure. Any RCA meeting includes key stakeholders closest to the problem and is facilitated by an individual with training in conduct of RCA. The customer may or may not participate in the RCA, depending on the circumstances surrounding the issue. To ensure an effective RCA, the meeting should be conducted as soon as possible after the event to prevent loss or alteration of the data or details. In general, RCA meetings in HTSF follow a prescribed agenda: 1) agreement on the problem statement and desired outcomes, 2) conduct of RCA using one or more tools (*e.g.,* Five Whys), 3) identification of root cause, 4) discussion of and agreement on mitigation strategies, 5)

TABLE 3

VOC meeting agenda template

1. A customer provides feedback to gathered team of relevant core staff and managers
2. A facilitator records feedback on whiteboard, flipchart, or computer
3. The participants agree to main themes related to issues with the project
4. The participants discuss possible improvements and brainstorm solutions
5. The team decides on action items and appropriate follow up and agrees on next steps
6. The facilitator provides meeting minutes and action items to participants and follows up with the core and the customer to ensure actions have been taken

assignment of time-based action items to participants, and 6) follow-up with customer once action items are completed. Typically, mitigation strategies involve educating customers, improving laboratory processes, solving vendor challenges, or enhancing communication. Frequently, weaknesses in procedures are identified, which require SOP revision, approval, and training by core staff. During the "define and measure" phase of the HTSF process improvement initiative, an RCA was conducted regarding a project that was delayed by several months, resulting in customer dissatisfaction. We conducted a Five Whys exercise with the core directors and functional managers to identify the root cause or causes for the significant project delays. Rework due to poor quality of the samples submitted by the customer was identified as the initial cause of the delays, but further questioning revealed the following: poor quality DNA libraries were caused by bad reagents; newly constructed libraries were poor quality, so a third set of libraries were made, but a barcode was duplicated, which the customer and the core failed to detect; failure to detect the barcode error was due to libraries being submitted at 2 distinct times; the dual submission did not raise any warnings because the library kit being used was rare and not included in the LIMS database; and the technician was unaware of how to capture this in the database due to a lack of training and lack of SOP addressing this issue. Mitigation strategies included customer education, a new communication process with vendors to identify bad reagents, new SOPs and retraining of staff, and assignment of a technician to maintain integrity of the LIMS database, including entry of new library kits and how to deal with multiple submissions for one project. RCA has proven to be a key continuous improvement tool in HTSF that has reduced the number of errors over time.

Step 6: Metrics (Measure and Control)

Tracking performance metrics as a component of a QMS allows one to "measure what you manage" and is critically important to demonstrate the effectiveness and efficiency of core facilities and to justify institutional funding requests for equipment and personnel. Turpen et al.[2] proposed 8 categories of core performance evaluation: general management, research and technical staff, financial management, customer base and satisfaction, resource management, communications, institutional impact, and strategic planning. The approach with the HTSF core is to track the "metrics that matter"—to customers and to research administrators. These metrics include number and type of samples submitted, number of libraries produced, number of sequences produced, expenses and revenue, customer satisfaction, number and type of nonconformances, customer publications and grant applications, new services offered, and on-time delivery.

RESULTS AND DISCUSSION

Two fiscal years (FYs) have elapsed since this QMS was instituted in the UNC HTSF. The operational improvements resulted in overall financial growth, improved

TABLE 4

How to conduct an RCA

1. Core management and staff associated with the project (consider including the customer who was impacted) meet to discuss nonconformance
2. Team agrees on problem to be addressed and desired outcomes of the meeting
3. Conduct RCA using suitable tools (e.g., Five Whys, Fishbone Diagram, *etc.*) and document discussions and outcomes
4. Discuss and prioritize mitigation strategies
5. Assign time-based action items to core staff or customer
6. Follow up with customer once action items are completed; update document to demonstrate resolution

management of all core functions, enhanced focus on the needs of customers, competitiveness for external contracts, and addition of the latest technological advancements in genomics research. Total revenue grew 74% between FY17 and FY19. During these same periods, total expenses grew 14% in FY18 and 31% in FY19. Expenses were predominantly associated with increased personnel costs, service contracts for equipment, and research supplies associated with greater volume of samples. The core ended both FY18 and FY19 with a positive balance, mitigating the need for cost-cutting measures to manage deficits. Core usage and output increased between FY17 and FY19 (Fig. 5). The number of samples submitted increased 40% between FY18 and FY19, and the number of libraries prepared increased each year (39% between FY17 and FY18 and 17% between FY18 and FY19). The total number of sequencing runs performed by the core remained relatively steady, but efficiency and output were improved by the addition of the Illumina NovaSeq 6000 platform in FY18. The number of samples that were sequenced was significantly higher in FY19 than prior years.

Once the QMS was in place, the UNC HTSF was prequalified to apply for federally funded contracts to provide RNA sequencing services for translational projects associated with sponsored clinical trials. To complete qualification, the core was subjected to a full-day quality audit conducted by a third-party operations and technical support contractor to certify that the core was governed by a QMS, followed GLP, and had robust reporting and quality monitoring infrastructure in place. Minor gaps were identified during the assessment, which were subsequently remedied by the core. Since the fall of 2017, the HTSF has been awarded 5 federal contracts worth more than $10 million, transforming the financial performance of the core. Additional benefits included improvements in workflows, efficiency, communication, metrics tracking, problem solving, and operational discipline. Two additional quality assessments were performed in FY18 and FY19, with only minor findings, resulting in drafting of new or improved SOPs and adjustments to the sample submission processes. To improve sequencing workflows, a VCB was put in place in the sequencing facility, using a whiteboard and dry erase markers. Projects are organized by analyst and by day of the week in horizontal workflow swim lanes. Twice-weekly meetings at the VCB are used to update project status and assigned analysts. The VCB also includes metrics, lab maintenance schedule, work schedule calendar, and a section for urgent or delayed projects.

	FY17	FY18	FY19
Total number of samples submitted	7195	6538	10,800
Total number of libraries prepared	5812	9474	11,322
Total number of sequencing runs	2160	2494	2342*
Total number of projects	124	135	135

FIGURE 5

HTSF metrics for FY17–19. Performance metrics for the core, including sample input, library and sequencing output, and number of customers using the core. *, reflects NovaSeq 6000 platform usage increase of ~5-fold between FY18 and FY19, accommodating more samples per run compared with other sequencing platforms.

Continuous improvement is a process with no "finish line," and the ongoing control phase for HTSF has included RCAs, VOC meetings, retraining as necessary, and extensive functional upgrades to the LIMS based on customer feedback. Overall, the organizational discipline required to deliver on time and on budget for the federal contracts has improved core function for all academic customers, resulting in streamlined procedures, competitive pricing models, and the addition of new sequencing equipment to keep up with demand and with technological advancements. An additional benefit of process improvement and control in HTSF is evident in the working relationships with other cores. HTSF is often one of the final cores involved in a multicore workflow (*e.g.,* tissue procurement; biobanking; embedding and histology; tissue isolation; cell sorting; DNA or RNA extraction; library preparation, quality control, and sequencing by HTSF; and bioinformatics). The "handoffs" must be effective for projects involving multiple cores and lacking a central project manager. HTSF personnel have been instrumental in defining or improving core-to-core processes with upstream cores to ensure timely consultations, seamless handoffs, and on-time delivery. The net effect of these process improvements is satisfied customers who are unaware of the "nuts and bolts" of the cores' inner workings.

One of the challenges of introducing process improvement in general and a QMS specifically in academic core labs is overcoming resistance to change. The thesis of "this is right because we've always done it this way" must be addressed through discussion, training, and negotiation. Concepts such as process mapping, Six Sigma, QMS, RCA, and VOC must be demystified and explained in practical terms. Support of senior leaders and core directors is an

essential component to ensure adoption of new models by core personnel. At UNC, this process improvement and control methodology has been utilized across multiple core research laboratories, regardless of technology or size. Cores that have benefitted the most include those that are highly transactional with multiple process steps and sample handoffs, such as the Animal Histopathology Core, Systems Genetics Core, Translational Pathology Laboratory, Human Pluripotent Stem Cell Core, Tissue Procurement and Cell Culture Core, and Tissue Procurement Facility. Combined, these cores have experienced almost 50% improvement in account balances, comparing FY18 with FY19, demonstrating that improved efficiency supports improved performance. Although extensively utilized to improve manufacturing organizations over the past several decades, process improvement based on the Six Sigma framework is essentially agnostic to the industry to which it is applied. In the UNC School of Medicine, Six Sigma approaches have been successfully applied to improving operational excellence in multiple cores, and specifically in the HTSF, the implementation of a QMS has been a differentiating factor in eligibility for large federally funded contracts. Core labs in academic institutions are likely to benefit from the systematic approach to process improvement described in this manuscript, ensuring that cores can continue to share expertise, cutting edge technology, and analytical services with a quality-based workflow that will overcome competition and drive the scientific enterprise into the future.

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