

The Personal Flow Cytometer in the Flow Cytometry Core Facility

BD Biosciences

White Paper

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Abstract

Today's flow cytometry core facilities have evolved beyond the simple provision of technical services to furthering their clients' research with state-of-the-art technology and exceptional scientific and technical expertise. According to core laboratory personnel interviewed for this study, these facilities share a service-oriented mission—the need to provide guidance and education as well as technology—and challenging financial constraints. Like most institutions today, they are being asked to do more with less.

The BD Accuri™ C6 personal flow cytometer is a four-color, dual-laser instrument that offers both performance and simplicity. Its combination of low cost, minimal user training, ease of use, and transportability has made it an attractive option, not only for individual labs and research groups, but also for a growing number of flow cytometry core facilities. Core facility directors and managers reported that it is an excellent instrument to train and serve new users, and ideal for self-service use. The BD Accuri C6 eases the staff's training, hand-holding, and maintenance burden, and frees up complex instruments and cell sorters for experiments that need them. It can be used in a laminar flow hood or glovebox or be transported on loan to individual labs.

The core managers appreciated the affordability of the BD Accuri C6, both in initial instrument cost and in total cost of ownership. Affordability for the core translates into lower charge-back fees for users, which can attract a larger user base and thus add revenue streams for the facility. This paper concludes with case studies illustrating how the BD Accuri C6 has helped core facilities fulfill their mission at two universities, a university medical center, and a major teaching hospital.





Figure 1. The first personal flow cytometer: the BD Accuri C6.

Introduction

Since its invention in the late 1970s, flow cytometry has revolutionized research in many areas of the life sciences, including immunology, cell biology, hematology, and oncology. Many flow cytometers are housed in core laboratory facilities that serve scientists across an institution or division. Core facilities provide a broader range of expertise, service, and technological capability than would be feasible for individual investigators.

But flow cytometry core facilities are changing. Largely gone are the days when users would drop off their sample tubes with the operator and come back later for the data, cells, or analysis. Today's flow cytometry core facilities endeavor to make complex experiments possible by providing scientific and technological support for advanced approaches in experimental design, as well as by supporting the adoption of new flow cytometric methodologies. They employ scientists highly skilled in flow cytometry technology and house state-of-the-art instrumentation to help advance biomedical research. These facilities are evolving beyond the simple provision of technical services to become Shared Research Laboratories (SRLs),¹ as exemplified by their mission statements (Table 1).

Table 1. Sample flow cytometry core facility mission statements.

Institution	Mission
Flow Cytometry Core University of Rochester Medical College (URMC)	"To provide investigators with state-of-the-art instrumentation along with the human expertise to support all that is possible now, while pushing the limits of what can be done with flow cytometry." ²
Interdisciplinary Center for Biotechnology Research (ICBR) University of Florida	"To serve as a world-class research support center that provides scientifically knowledgeable, technically superb scientific services..." "Dedicated to initiating and supporting the best of front line technology within the ever-changing and wide-ranging scope of the molecular life sciences." ³

This paper addresses how the BD Accuri C6 personal flow cytometer has helped core facility directors achieve their evolving missions. Interviews were conducted with directors and managers of flow cytometry core facilities that are affiliated with academic research centers.

Commonalities and differences

The core laboratory personnel interviewed share a service-oriented mission—the need to provide both technology and guidance—and challenging funding constraints. Like most institutions today, all are being asked to do more with less.

Customer service orientation

Every core facility strives to provide good customer service—to understand and meet their clients' needs—and help their clients acquire quality data that will advance their research. Without a focus on customer service, a core facility would not exist; clients would simply stop using the resource.

Technology and service

Most core facilities try to forecast and budget for new, advanced instruments to offer better technology than an individual researcher or department could afford. However, not every researcher requires the most advanced instruments, and it is often cost-effective to provide a range of instrument options.



Figure 2. Routine maintenance.

Core facility staff members perform routine maintenance to keep instruments in peak performance.

Core facilities also perform routine instrument maintenance and manage the instruments' service contracts (coordinating visits when needed from manufacturers' field service engineers). They perform regular quality control procedures to keep the instruments in peak performance, even when staff is not present. Service contracts and maintenance costs are generally included in the core facility's hourly instrument charge.

Revenue neutrality

If core facility clients are using National Institutes of Health (NIH) grants to pay for services—as most (if not all) academic core facilities in the US do, according to our sources—NIH guidelines stipulate that the facilities must remain revenue neutral. Factors used to determine pricing include cost of service contracts, supplies, other incidental costs, and instrument depreciation. Personnel costs may also be included, depending on the institution. Charge-back fees cannot be used to fund instrument upgrades, application development, continuing staff education, and many other line items, and must not discriminate between federally and non-federally funded projects.¹ Core facility directors universally struggle to meet this mandate, and institutional support is often crucial.

New instrument funding

Funding for new instruments is typically obtained through grants. In the US, federal funding mechanisms include NIH programs such as the National Center for Research Resources (NCR) Shared Instrumentation Grant (SIG), the National Science Foundation (NSF), and the Department of Defense (DoD). State funds may also be available, such as the Georgia Resource Alliance (GRA). In one instance, researchers submitted a grant proposal to purchase a flow cytometer using a portion of the state's tobacco tax fund.

Alternatively, two or more departments may pool and contribute funds to assist the core facility in obtaining a new instrument. Or researchers may purchase a flow cytometer and house it in the core facility. In this case, the core facility supports and maintains the instrument in exchange for the ability to make the instrument available to others when the owners are not using it.

Guidance and education

Staff expertise at today's core facilities is not limited to technicians who can show users how to load samples or set compensation. They are often trained scientists, highly skilled in flow cytometry technology, who can consult on multicolor experimental design, choice of fluorochromes and reagents, and data analysis techniques.

Typically, core facility staff members train clients on how to use the facility's flow cytometers so that the researchers can access the resources around the clock and run their own samples. Therefore, education of the client base—including expectations of what flow cytometry can be used for and training on appropriate instruments—is a crucial focus of all core facilities. Training can be challenging due to differences in individual learning curves and the wide range of initial knowledge levels.

Doing more with less

Once clients are trained, they are often allowed to access the flow cytometry analyzers at any time, day or night. Increasing reliance on self-service instrument operation helps core facilities achieve their missions in the face of almost universal budget constraints. The use of cell sorters, which generally requires more in-depth knowledge, experience, and even finesse to use, is still typically restricted to trained core staff.

Differences among facilities

Although there are key commonalities among core facilities, there are differences as well. Variables include staffing levels, number and type of instruments (sorters vs analyzers), size of client base, and number of locations within the institution. Some may provide additional services such as formal courses, assay development, and data interpretation. Finally, some facilities house the institution's entire inventory of flow cytometers and sorters, while others do not.

The personal flow cytometer

The BD Accuri C6 is a four-color, dual-laser flow cytometer that offers performance, simplicity, and affordability. Easy to learn and use, it is about the size of a microwave oven, allowing it to be set up in even the most limited lab space. It is also rugged enough to be transported, making it usable in undergraduate teaching labs or classroom demonstrations.



Figure 3. The BD Accuri C6 flow cytometer system.

A state-of-the-art digital signal processing (DSP) system gives the BD Accuri C6 a dynamic range of six full decades. This means that it can finely resolve both faint and bright signals at once and analyze the entire scope of biological variations in a single run, from dim, micron-sized platelets through large, >30 micron, highly fluorescent cell lines. In rare cases in which the fluorescence is off scale, such as cell lines transfected with green fluorescent protein (GFP), easily inserted attenuation filters bring the signals back on scale while maintaining operation of the detectors within their linear range.

The BD Accuri C6 detects this broad dynamic range using standard factory detector settings without the need for optimization or tuning. Users do not need to set voltage and amplifier gains to focus on the high or low end.

Finally, operation is menu driven and intuitive. BD Accuri C6 software was designed with speed of learning and ease of use in mind, based on hundreds of hours observing researchers using flow cytometers. As a result, the software is truly intuitive to use, accessible to novices and proficient users alike. Most new users become fluent with BD Accuri C6 software in less than 30 minutes, assisted only by a 3-page pictorial *Quick Start Guide*.

The combination of low cost, minimal user training, ease of use, and durability has made the BD Accuri C6 an attractive option for a growing number of flow cytometry core facilities.



Figure 4. The BD CSampler™ option.

The optional BD CSampler accessory provides automated sample processing from a 24-tube rack, or from 48- and 96-well plates, further streamlining laboratory workflow.

Benefits of the BD Accuri C6 in the core facility

Core facility managers who purchased a BD Accuri C6 flow cytometer cited several common reasons (Table 2). Selected advantages are highlighted in the text sections and case studies following the table.

Table 2. Summary of BD Accuri C6 benefits for the core facility.

Benefit	Rationale
Ideal to train and serve new users	Simple, approachable, and un intimidating to users. Most operators feel at ease within 30 minutes of instruction. Well suited for simpler assays such as GFP transfection efficiency and screening applications, as well as for more complex 3- or 4-color assays.
Ideal for self-service	Easy to use and easy to learn. No need to adjust voltage or amplifier gains. Forgiving of errors. Data is not lost and can be re-analyzed at any time.
Eases burden on staff	Reduces time spent on training, hand-holding, and maintenance. Staff can concentrate on more complex technical and scientific support and consultation.
Helps balance instrument workload	Frees complex instruments and cell sorters for those experiments that require them.
Transportable	Can be used in a laminar flow hood or glovebox. Can be placed on a lab cart and loaned to individual labs.
Affordable	Total cost of ownership includes instrument cost, staff training, maintenance, service contracts, and supplies. Affordability for core facility translates into lower charge-back fees for users.
Adds revenue streams	Simpler instruments and lower charge-back rates attract a larger user base. Expands flow cytometry access to intermittent users.
User-tracking capability	Restricts access to authorized users only. Facilitates billing and usage reports.

Ideal for self-service

The BD Accuri C6 is forgiving to users. New users can collect data using a simple, preconfigured template, and then analyze the data later with more expert help, without concern over lost data due to improper settings. Data collected on the BD Accuri C6 is not lost, and can be re-analyzed at any time if gating or compensation errors are discovered, or in light of new research findings.

Intuitive BD Accuri C6 software aids researchers in data analysis. For example, a Zoom tool allows researchers to focus (and adjust gates) on very small areas of the data display.

Eases burden on staff

Ease of use, self-cleaning, and standardized performance help reduce staff time spent on training, hand-holding, and maintenance. This can free staff to focus on helping clients with sorting applications as well as developing and analyzing more technically difficult experiments.



Figure 5. Compact and transportable. Weighing only 30 lb (13.6 kg), the robust BD Accuri C6 can be used in a hood or glovebox, or placed on a cart and loaned out to individual labs for intensive, short-term projects.

Affordable

Managers particularly liked the affordability of the BD Accuri C6, citing not only instrument cost but also staff training, maintenance, service contracts, and supplies. For example, the recommended sheath fluid for the BD Accuri C6 is filtered, deionized water, which significantly reduces supply expense and shipping charges. Built-in reliability and low maintenance were also important factors, and the BD Accuri C6 was sometimes purchased to replace outdated analog instruments that had become cost-prohibitive to keep up.

Adds revenue streams

Core managers were pleased with the additional users that the BD Accuri C6 brought to their facility. This includes users new to flow cytometry, those who use it intermittently, and those with simpler applications who might be intimidated by larger machines. An easy-to-use instrument with lower charge-back fees can help these users choose flow cytometry rather than less quantitative or precise methods like qPCR, Western blot, microscopy, or hemacytometry.

User-tracking capability

The User Tracking upgrade for BD Accuri C6 and BD CSampler software allows system administrators to create unique usernames and passwords for each person operating the instrument. In addition to ensuring that only authorized users can access the BD Accuri C6, User Tracking logs each user's sign-in and sign-out. Billing and usage reports can easily be generated.



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ROCHESTER

The BD Accuri C6 helps me fulfill my mission because it helps researchers overcome their fear of flow cytometry while providing analytical data that cannot be provided via other methods, such as microscopy. The BD Accuri C6 gets the researcher hooked on the technology and interested in utilizing flow cytometry further with our higher end instrumentation.

– Tim Bushnell, PhD

Scientific and Technical Director, Flow Cytometry
University of Rochester Medical Center

Case studies

The following case studies illustrate how four different core facilities found a useful place for one or more BD Accuri C6 flow cytometers, as reported by their directors or other key personnel.

University of Rochester Medical Center

Dr. Tim Bushnell runs the central flow cytometry core facility at the University of Rochester Medical Center (URMC). In addition to the URMC core, the university also operates two other flow cytometry cores (one in clinical diagnostics, another in the cancer center) and an independently owned cell sorter. The central flow cytometry core facility has nine cytometers, 400 registered researchers, and routinely serves 50 to 100 clients a week.

Dr. Bushnell purchased a BD Accuri C6 for the core facility to replace an outdated, failing analog instrument that was becoming cost-prohibitive to operate and service. Since purchasing the BD Accuri C6, he has seen researchers become more interested in the benefits of flow cytometry. He attributes this to the unintimidating size and simplicity of the BD Accuri C6; even novices can easily run their samples. Core facility clients can focus on experimental design and data interpretation, as opposed to mastering the instrument.

Immunophenotyping is the most common application at the URMC Flow Cytometry Core, and the high-end BD™ LSR II analyzer is most frequently used for experiments that require 10 to 12 colors. However, many immunophenotyping experiments involving four colors or fewer can be run on the BD Accuri C6. Other applications run on the BD Accuri C6 include cell cycle analysis, apoptosis studies, binding assays, and GFP transfection efficiency.

The URMC core has been servicing an offsite cardiovascular group that owns a capable but complex flow cytometer. A core facility technician has been spending four or more hours a week at this offsite location to run samples, draining the core's staff resources. Dr. Bushnell plans to purchase another BD Accuri C6 for that facility so the researchers, once trained, can run their own samples. The core will then gain use of the higher end instrument as well as recapture the technician's time.

The BD Accuri C6 contributes 40 billable hours per month to the core facility's revenue stream—a significant impact. And its ease of use has helped the facility maximize personnel efficiency.



One of the BD Accuri C6's benefits is that it is very easy to train people in its use. They get over their fear very quickly.

– Steve McClellan

formerly Senior Scientist,
Interdisciplinary Center for Biological Research
University of Florida

(currently Manager of Flow Cytometry and
Imaging Core Laboratories for the Mitchell
Cancer Institute at the University of South
Alabama)

University of Florida

Steve McClellan was formerly a senior scientist at the Flow Cytometry Core Laboratories in the Interdisciplinary Center for Biological Research (ICBR) at the University of Florida. He reports that the ICBR Flow Cytometry Core employs three full-time scientists working in two locations for client convenience. The core maintains three sorters, five analysis instruments, and one high-end live-cell confocal microscope. With 450 registered researchers, the flow cytometry core routinely serves 75 clients a week.

Most of the self-service flow cytometry performed at this facility involves 1- to 4-color assays, which are an ideal fit for the BD Accuri C6. About half the flow cytometry core clients perform 1-color GFP transfection efficiency assays. Other applications include apoptosis, immunophenotyping, and cell cycle studies. The BD Accuri C6 shoulders the burden of these assays, freeing up the higher end cytometers for more complex assays.

Before a client can use any cytometer without supervision, the core facility provides personalized training based on the client's needs. Training on higher end instruments typically requires three or four one-on-one, multi-hour sessions. The BD Accuri C6 reduces training time to 1 to 2 hours, especially if the client plans only 1-color assays. In addition to training, the full-time staff also helps clients design experiments, develop templates, and define settings.

Although sorting constitutes the main revenue source for this flow cytometry core, the BD Accuri C6 contributes to the revenue stream. Many researchers use microscopy to measure GFP transfection efficiency, but it can be difficult to distinguish cellular autofluorescence from true GFP fluorescence. A qualitative result that appears to be 40% positive under a microscope might turn out to be only 20% positive when measured quantitatively by flow cytometry. As word spreads about the BD Accuri C6, researchers are increasingly using it to perform quantitative GFP transfection efficiency assays.

Not all flow cytometers at the University of Florida are administered by the core facility. In fact, there are four other BD Accuri C6 instruments on the Gainesville campus. Mr. McClellan supports an individual laboratory's decision to purchase its own instrument as long as it is routinely used. For researchers who use flow cytometry intermittently, it is generally more cost-effective to utilize the core facility. Mr. McClellan recommends the BD Accuri C6 for core facilities, as well as for higher education institutions that do not currently own a flow cytometer or have a core facility.



ILLINOIS
UNIVERSITY OF ILLINOIS AT URBANA-CHAMPAIGN

When you purchase a flow cytometer, you have to consider the instrument as well as the maintenance costs (service contract and supplies). The BD Accuri C6 is a very good instrument in regards to lifetime cost of ownership.

– Barbara Pilas, PhD

Core Laboratory Director
University of Illinois at Urbana-Champaign

University of Illinois at Urbana-Champaign

All flow cytometers at the University of Illinois at Urbana-Champaign are under control of the flow cytometry core facility, even those housed in individual labs. According to Dr. Barbara Pilas, Director, the facility's instrument experts support, maintain, and troubleshoot all instruments and are available for data analysis assistance. The facility serves about 70 people weekly.

Since this flow cytometry core serves the entire university, its applications are extremely varied, and the core's two sorters and six analyzers are used equally. The staff gives clients one-on-one training to qualify for self-service, and has adopted FCS Express™ (available from De Novo Software) as the standard analysis tool. FCS Express allows clients to analyze data in their labs or offices and, from a revenue perspective, keeps the instruments open for more runs.

The staff purchased two BD Accuri C6 systems not only because they are simple to run, but also because they consider them best-in-class instruments. They are widely used for screening—to answer yes/no questions. Dr. Pilas appreciates how quick they are to start up and run, as well as their portability. “You can move the BD Accuri C6 and it still works!” she marvels. If a researcher is analyzing biohazardous samples, the instrument can easily be moved into a laminar flow cabinet.

When Dr. Pilas purchased the BD Accuri C6 systems for the core facility, she considered not only the initial purchase price but also routine maintenance, service contract, and supplies. Lifetime cost of ownership is crucial since core laboratory charge-back fees include the cost of service contracts, supplies, instrument depreciation, and (depending on the institution) personnel costs. Lower fees entice more people to take advantage of flow cytometry.

In a flow cytometry core, according to Dr. Pilas, all instruments have their place, depending on application. She applauds smaller, cost-effective, easier-to-use instruments such as the BD Accuri C6 because they, in turn, support increased use of the methodology. As flow applications expand, more instruments—including those at the high end—will be needed over all.



BRIGHAM AND
WOMEN'S HOSPITAL

Brigham and Women's Hospital

The flow cytometry core laboratory at Brigham and Women's Hospital serves about 20 researchers weekly. At this institution, independently owned instruments are maintained by the researchers and not by the core.

According to Dr. Grigoriy Losyev, core manager/operator, the core facility trains researchers individually on the use of analyzers. Due to their small staff, they do not assist in assay development or data analysis.

Although sorting is the facility's main revenue generator, Dr. Losyev says that business has increased since the BD Accuri C6 was purchased. He attributes this growth to publicizing the new instrument on the website and its ease of use. The BD Accuri C6 is commonly used for applications such as 1-color GFP transfection efficiency assays.

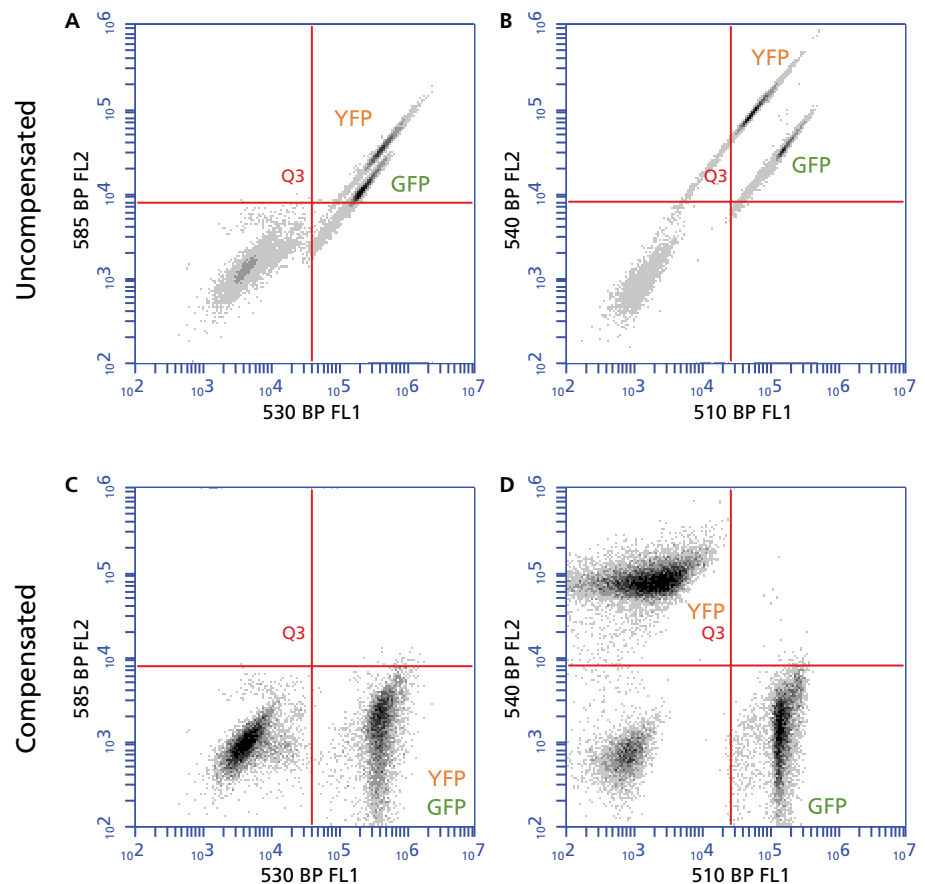


Figure 6. Detection of green and yellow fluorescent proteins.

A, C. Either GFP or YFP signals can be detected in FL1 with the standard BD Accuri C6 filter configuration (530/30 in FL1, 585/40 in FL2). B, D. To detect both GFP and YFP at once, researchers can separate the signals by using the 510/15 filter (Cat. No. 653184) in FL1 and the 540/20 filter (Cat. No. 653528) in FL2. Top (A, B) and bottom (C, D) graphs show uncompensated and compensated data, respectively.

Conclusions

Core directors and managers praise the BD Accuri C6 for its ease of use, ease of learning, versatility, and affordability. Together, they allow the core facility to offer flow cytometry services to both novice and expert users at an affordable charge-back fee. This opens up additional revenue streams for the core and frees more expensive, high-end instruments for more complex experiments.

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Contributors

Dr. Tim Bushnell, PhD
Scientific and Technical Director
Flow Cytometry
University of Rochester Medical Center

Steve McClellan
Formerly Senior Scientist
Interdisciplinary Center for Biological Research
University of Florida

Currently Manager of Flow Cytometry and Imaging Core Laboratories
Mitchell Cancer Institute
University of South Alabama

Dr. Barbara Pilas, PhD
Core Laboratory Director
University of Illinois at Urbana-Champaign

Dr. Grigoriy Losyev
Core Manager/Operator
Brigham and Women's Hospital

