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## Bio-Medical Light Microscopy Imaging Facility Management

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Turning microscopic specimens into data involves using microscopes and often image analysis hardware and software. Such items may be beyond the reach of an individual laboratory. For example, a confocal/multiphoton laser scanning microscope can cost roughly \$800,000 with an annual maintenance fee on the order of \$60,000. An imaging facility may have additional fluorescence microscopes with digital cameras, along with specialized equipment, such as motorized fluorescence stereomicroscopes, automated stage tiling microscopes, slide scanners, slide makers, and high quality/poster printers. Ideally, the facility will be connected to the entire campus via centralized file servers through Gigabit Ethernet (at about \$100,000 per building). Information about such facilities can be found on various web sites.<sup>1-4</sup> Many facility managers communicate through the [confocal listserv](#) where postings on many topics can be found. Besides listserv signatures, many facilities can be found by doing Internet searches, as can all items discussed below.

### PLANNING

Before setting up a microscopy facility, an institution should think about the mission of the facility, its location relative to users, amount of space and infrastructure, and who will direct, staff, and use the equipment. Location is not a trivial consideration, and a poor choice can doom a facility. After the mission statement is agreed upon and published, policies on cost structure, access, and who does what is put into place. These should be posted on the facility website. Facilities, even with charge-back fees, rarely generate enough revenue from local users to fully recover operational costs. Administrators should not look upon facilities as potential profit centers, but rather should see the hardware and staff as technology infrastructure and resources that facilitate the research goals of the institution. Regarding hardware, systems usually have a computer with a Windows based operating system. Macintosh users should be prepared to adapt.

### ORGANIZATION

To start a facility, the available money, annual operating budget, and space will dictate the scope of the operation. The user community should be consulted through a needs-assessment survey and in meetings to determine what should go in the facility (or even if there should be one). The Director of an academic facility should be a faculty member who is knowledgeable about microscopy, but who will not monopolize the facility and staff for his/her own research. Typically, the institution pays 10% of the Director's salary to run the facility. The Director should have an advisory board that meets regularly during the year for review and planning. The board should not rubber stamp the Director and should have real input into how the facility is managed. A crucial role of the board is as an honest broker that can rationalize to institutional administrators the worth of subsidizing the facility with institutional funds. The facility staff will usually include one or more individuals who manage day-to-day operations, including educating faculty and users on which instruments will best answer their research questions, train (and retrain) users, track usage, maintain equipment, interact with vendors for annual preventive maintenance, learn new applications, and potentially run experiments for users.

## **INCOME AND COSTS SCHEDULE**

Methods of generating income include charging individual labs a set monthly or annual access fee for access to basic equipment, and an hourly fee for expensive equipment. Because the annual costs can be easily estimated, an initial fee schedule can be determined and then modified as income versus outflow becomes more apparent. Publicly funded resources are not allowed to generate a budget surplus, but arrangements (e.g., accumulated depreciation) can be made to set aside income to fund future needs, such as upgrades or new instruments. Some facilities charge less for off-hour operation and more when staff is required to setup or carry out experiments. "Bulk" pricing for labs that make heavy use of a system is not economically viable and may breed discontent among other users. A requirement associated with federally funded instruments is that the fee schedule applies to all users.

The fee structure should be explained to each new faculty member and user, and a cost-center number for billing should be obtained for each user. Exceptions can be made for faculty without current grant support so they can "prime the pump" with imaging data for grant and manuscript submissions. Evaluation of imaging goals for such users by the advisory board may be a good mechanism for waiving fees for well-planned experiments without incurring the ire of paying customers.

Once the equipment is in, the two biggest recurring direct budget items are salaries and maintenance contracts on hardware and software. A "consumables" budget should also be agreed upon within the institution. By totaling the annual estimated cost, then dividing by an estimate of the hours used, an hourly rate can be derived. Be ready to make adjustments as reality sets in, but give the facility a year to develop a user base and pass through lulls, such as summer vacation. At the facility one of us managed, with \$760,000 worth of equipment, the maintenance contracts totaled about \$25,000 per year and we had an additional \$20,000 "consumables" budget for purchasing supplies, additional fluorescence filter sets, low - end scientific digital cameras, new software, new computers, new computer peripherals, and disks. Useful supplies might include QA/QC fluorescent microspheres, calibration microscope slides, and commonly used reagents, such as DNA counterstains and mounting media. If a large enough user base exists, negotiating with a supplier of commonly used reagents may get you an "in house" freezer plan. This would provide an immediate source of commonly used materials, such as secondary antibodies, nuclear stains, mounting media, membrane and organelle labels, and other supplies.<sup>5</sup> Objective lenses are not intended to be consumables but are sometimes treated as such. Repairing a \$6,000 plan apochromat 63x/1.4 NA oil immersion lens costs \$3,000.

## **TRACKING USE**

Access is best tracked by a combination of institutional scan card access to the facility, and computer login and/or sign in/out sheets at each station. Commercial or freeware<sup>6</sup> calendars can be used for tracking usage and billing. Even for equipment that is not billed, usage for each equipment and staff should be summarized for monthly reports to the Director and annual presentations to the advisory board and to the institution's senior research administrator. The annual usage/billing data can be used to justify budgeting for new equipment, upgrades, maintenance fees, and promotions. Access to the most expensive equipment is often limited to institutional business hours. If access is available on evenings and weekends, a policy defining how experienced the user needs to be to get access is needed. Facilities funded through shared instrumentation grants or other government funds usually have both usage/cost recovery and data archiving requirements. As a facility manager, you should operate on the assumption that you will be audited; you really do not want to get in trouble because you could not find a computer file.

## **SPECIFIC CONCERNS**

Certain questions must be addressed when considering an imaging facility. Does (will) your space have the necessary room, power, HVAC, and Ethernet connections? Remember to consider future needs. The layout of your space needs to be thought out carefully to enable productive work with minimal disruptions from people walking through experiments, room lights going on and off, or distracting conversations. Exits need to be well marked and aisles kept clear of chairs, carts, gas tanks, and cables so that staff, users, and visitors can get out safely in the event of emergency. Does the electrical system provide clean power? Does it work 365/24/7? Even hospitals with mandated always-on power experience blackouts. Key equipment should be powered through an uninterruptable power source (UPS), available from several sources. Does the HVAC maintain constant temperature (few do)? A heavily instrumented room may exceed design range, especially with several people in the room. Are the air ducts organized correctly to avoid drafts and dust blowing on the equipment?

Vibration can affect your experiments. If you see a standing wave in your cup of coffee or petri dish, you have a vibration problem. Ideally, only the microscope and items directly bolted to it should be on the anti-vibration surface (tables that isolate are easy to find, those that do so and leave the equipment ergonomic are not). It is best to place all ancillary equipment (i.e., filter wheels, beam-splitters, spinning disk confocal attachments, intensifiers, digital cameras) on an optical rail to enable easy component changes while maintaining alignment. Cables should be suspended off the table by elastic supports to dampen transmission of vibrations from a source to the scope. Will your facility be used for intravital microscopy or pathogen research? If so, you need to plan for how to contain and clean up after such experiments. Some people are allergic to mouse or rat dander so clean up is critical. Are the animals going to be under anesthesia the entire time they are in the facility? If gas anesthesia is being used, how will it be vented? Will you require copies of all animal care committee paperwork before permitting a researcher to bring animals to the facility? Handling lab animals always requires gloves. If the facility equipment is normally used ungloved, it should continue to be used this way during experiments. This implies either a lot of ungloving/regloving or multiple researchers. Are the extra hands going to come from the researcher's lab or will the facility staff assist (and provide oversight to make sure the glove/bio-safety policy is followed)? Do the facility staff need animal care training?

Finding staff for a facility can sometimes be done locally, but excellent resources for trained personnel include the Confocal listserv, International Society for Analytical Cytology (ISAC), and Microscopy Society of America (MSA). Ads in certain journals may be appropriate for certain positions.

A common way to find out what equipment to buy is to visit other facilities, either locally or during travel to meetings and speaking engagements. The confocal listserv again is a valuable resource for these types of questions. Visits and needs assessments go hand in hand. Visits also help build bridges for collaborations, mentorship, and access to complementary equipment. Most facilities managers are happy to show off their gizmos. Identifying the good, the bad, and the ugly is done by communicating with local vendors, querying other facilities, and attending meetings to kick the tires and get a sense of the organizations standing behind (or not) the local salespeople. After-purchase support can be a huge bone of contention in some venues, so be sure to ask people about their experiences with vendors. The big biomedical meetings are where new imaging equipment is introduced. These include American Society for Cell Biology, Neuroscience, Biophysics, and Federation of American Societies for Experimental Biology. Smaller meetings/tradeshows, such as The Histochemical Society, International Society for Analytical Cytometry, and Microscopy Society of America, may also be worthwhile. There are several excellent courses offered in advanced light microscopy that can help the Director or a staff member get up to speed on new equipment and techniques, plus network with course faculty and other users. For microscopy courses, see the Confocal listserv.

## **SAFETY**

Safety is everyone's business. In addition to having sharps and biosafety trash available (and not overflowing), you should train everyone on the hazards of arc lamps and lasers. In practice, the risks of eye damage from a 100+ Watt arc lamp or explosion of a high pressure bulb may be greater than from lasers. Institutions usually require non-ionizing radiation training for the manager and staff. If lasers are not enclosed, then laser safety training may be required for all users. Laser physics labs have signs posted; the classic is: "do not look at laser with remaining eye." Staff of microscopy and flow cytometry labs sometimes becomes cavalier with their 50-W laser or especially with their 1-W, 80-MHz, multi-photon laser. This energy source puts out 100-fs pulses, resulting in 125,000-W peak power that may be invisible (current multi-photon lasers are tunable from 700-950 nm, with invisible light above 800 nm).

Insist on the use of fiber coupled lasers or at least enclose all laser light paths in tubing. Explain to each user the dangers and oversee them (and watch yourself). "Off-the-shelf" confocal instruments come with this protection, but homemade or modified systems may need special attention. Fires from lasers, arc lamps, or any other malfunctioning equipment are a very real possibility. Users need to be educated not to place paper (or anything else) on such equipment. Any smoking equipment could potentially trigger an overhead sprinkler system, which could in turn cause water damage. Our closest call was allowing the unfiltered output of a 300-W arc lamp's light guide to touch a wooden desktop. Within a second, smoke started rising from the illuminated spot of wood.

*Pathogen controls:* are users permitted to bring live pathogens or live animals into part or all of the facility? What is the policy regarding lab coats and gloves? Users typically glove up to protect their specimen from themselves (i.e. RNase or bacterial contamination), but rarely think about protecting other users and staff from their specimens. At hospital new employee orientations, more time may be devoted to hand washing than to lab safety. It is hard enough to get MDs to wash hands,<sup>7, 8</sup> getting researchers to un-glove before touching door knobs and computer keyboards/mice is just as difficult. Clear policies and training on the use of gloves should be implemented with full support from the research administration.

Microsoft Outlook can be used for equipment and staff calendars/reservations, but email serves as a major entry point to computer viruses. Backing up key files and periodically making a "disk image" of all facility computers can mitigate against computers failing or becoming infected. A general facility policy is for files to go out, not in. Image files from other acquisition devices can be placed on a virus-scanned file server for analysis. A file server and blank recordable CDs and DVDs can be used to export results.

## **WEBSITE**

Any modern facility should have a website, either intranet or Internet. Intranet-only allows for informality, quicker posting, and avoids the need for organizational approval. Internet access enables the entire world to see what you have. One site, Molecular Expressions,<sup>9</sup> already has a huge amount of informational content. A simple "confocal facility" Internet search will find many sites, some with current, others with out of date, information. At the least, the site should contain information on what is available, who is allowed access, who to contact to get access, and what the basic charges and policies are. Be careful with verbiage. If you have too many policies, no one will remember (or even read) them, so keep it simple. The most contentious issues in running a facility are fee structure and recovery, access, data control, and safety, both hardware and biological.

## **TRAINING**

*Learning and Unlearning Curves:* Most users are focused on the thing they study and want to spend the minimal time and thought to get the image they need. There are three ways to provide for use of advanced instruments, such as confocal/multiphoton: 1) spend the time to climb the long, shallow learning curve to understand what is happening when a good image is produced, 2) learn only those buttons and knobs that get the required image, or 3) ask the facility staff to setup (and run?) the instrument. Blank stares and yawns usually follow the first approach, and large fees and excessive staff time follow the last. A brief overview of the system and a few principles, followed by emphasis on doing what the investigator needs may be the most efficacious approach. Remember, however, that these are intelligent, educated people, so terms such as “spectra,” “objective,” and “resolution” should not be avoided. One of the most basic problems for new users is the confusion surrounding the green of fluorescence versus the green from a laser.

## **AUTHORSHIP**

Authorship for both academic publications and especially patentable inventions should be defined by the institution, and whoever has the final decision should be defined. At the least, the facility and/or staff must be acknowledged for every publication containing data from the facility. All documentation should be available online. Facility-specific tips should be produced for major applications and be available online and in binders by each instrument. Many graduate students, postdoctoral fellows, medical residents/fellows, faculty, and fellow staff are not native English speakers, thus understanding training or advice may be problematic. If you value your equipment, you will become attuned to who gets the message and who does not and act accordingly.

## **TOURS AND DEMONSTRATIONS**

*Presentations and Tours:*<sup>10</sup> For a VIP tour, we recommend personalizing the title page. VIPs include past, present, and future financial donors/sponsors, Presidents, Deans, advisory committees, seminar speakers, faculty and staff recruitments, and just about everyone else. Tours are a type of outreach. If you are asked to participate in a VIP tour, find out who the tour is for, communicate to make sure that your facility is a useful stop, find out what the goal is, and what should and should not be presented. Provide best contact information for the liaison (and get their pager and cell phone in return). Make sure that the hallways are clear and make reservations to block out all instrument access for several hours before and for a few hours after the scheduled stop. Communicate with users and neighbors about the need to shut down access for a few hours and on the need to keep the hallways clean and quiet on the day of the tour.

Clean up (or mark up!) whiteboards in the hall and conference room. Plan ahead for the number of visitors to be expected, but be prepared in case there are more. If possible, hallways with large professional prints of interesting (but non-controversial) images from your facility will impress VIPs on the way in and out, and give something for overflow crowds to check out while waiting their turn. Have something interesting on each microscope but do not expect anything from the visitors. Time is money; if you have a 10-minute slot, show a few slides, light up an instrument (multicolor sequential scanning on a confocal microscope is good), and be prepared to answer questions (keep noisy equipment off so you can hear the questions).

A set of application-specific PowerPoint presentations and/or web pages should be available for meeting potential clients (faculty and users). When you meet with clients, listen for their needs and communicate how your facility will help them. Get your (and sibling facilities) on campus seminar series or set up your own. Having so many users that you are too busy is a better problem to manage than an unused facility.

## SUMMARY

We have tried to provide insight into setting up and running a light microscopy facility. Many of these issues — such as scheduling and data management — can be shared with flow cytometry, electron microscopy, small animal imaging, microarray, and other facilities. Discuss your issues with the people in other campus facilities, as well as other microscopy facilities. The success of your facility ultimately rests with what your users take away from it: training, data, and insight into their experiments.

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