Safe Science

Applying safety in a modern research laboratory

By Maureen Modica

APPLYING SAFETY in a modern research laboratory is the personal responsibility of each researcher as well as the collective responsibility of the entire research community in any given laboratory setting. Modern research laboratories are complex environments with inherent safety, health and environmental risks. However, these risks can be greatly minimized by good laboratory design, careful preplanning of each research project and daily integration of good science and safe work practices.

New Trends in Laboratory Design

Planning, designing and constructing a new or renovated laboratory in today's ever-changing research environment is no simple task. Open, flexible and generic labs are among the major trends in modern lab design (Photo 1, p. 26). The open design concept is desirable because it can:

- support multiple types of research experiments within the same space;
- accommodate large numbers of researchers;
- allow customization of individual bench spaces due to interchangeable and mobile components;
- sustain both long-term and short-term research projects;
- provide an ergonomically sound work space with use of adjustable benches and casework;
- promote greater collaboration among researchers.

The safety challenges posed by these spaces may include:

- greater risk of cross-contamination or incompatible chemical experiments being conducted simultaneously when bench space is shared among different researchers over multiple shifts;
- increased likelihood of blocked exit routes, electrical panels, safety showers, eyewash stations and fire extinguishers due to the mobility of casework and equipment;
- fire safety considerations relative to the quantity, use and storage of flammable liquids in the large open lab;
- increased need for routine and reliable preventive maintenance of shared equipment such as centrifuges and autoclaves due to the increased hours of uninterrupted use.

Professional collaboration among researchers is an integral part of the success of many projects. Many new laboratory designs include spaces such as lab entry niches (Photo 2, p. 26) that promote casual interaction among researchers. A minor safety risk posed by the design shown in Photo 2 is the proximity of food and beverages to the lab. Aside from the risk of taking food or drinks into the lab, careful cleaning and maintenance of this area would be necessary to avoid microbial growth or pest infestation.

Separate, dedicated support zones that adjoin the primary lab space and house large equipment such as upright freezers, liquid nitrogen cylinders, centrifuges, ice makers, incubators, autoclaves, glassware washers and other specialized equipment are generally included as part of the open design concept. Separate support zones also can be dedicated to high-risk or sterile operations such as tissue culture work in biological safety cabinets, potent drug ingredient work in isolators, or work with toxic, corrosive, reactive or flammable substances in chemical hoods. Separation of support operations and high-risk procedures improves the efficiency and quality of life in the primary lab while preserving the safety of the researcher in the performance of these high-risk procedures.

However, dedicated support zones require careful planning to address specific ventilation, electrical and regulatory compliance needs. For example, if a support zone is dedicated to house 50 high performance liquid chromatography units that are expected to generate

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substantial quantities of a flammable mixture of methanol and acetonitrile waste, consideration must be given to the intrinsic safety of the room as well as compliance with hazardous waste regulations. Support zones that are used for cryogenic storage of cell cultures in liquid nitrogen repositories may require additional ventilation and, in some cases, oxygen monitoring. In most support zones that house typical equipment such as freezers, centrifuges and incubators, emergency backup power is generally required.

Flexible casework systems are another popular trend in modern research lab design. They consist of movable assemblies that allow easy interchangeability of components and adjustable positions for improved ergonomic design. Other features include separate but adjoining desk space, energy efficient lighting systems and use of large windows with filter screens to improve aesthetic value while minimizing solar load. Debate continues among safety professionals over the proximity of desk space to bench operations. There are documented incidents in which researchers working at a computer near a bench operation have been caught off-guard and injured by an experiment gone awry. In these situations, it is rare that the researcher will continue to wear PPE including lab coats and safety glasses while seated at the computer. But since many research projects involve more and more computer applications, it is difficult to separate the two operations.

Several new lab design layouts are now including core office space that adjoins the lab space but is not part of the lab. Windows with shades are often installed in the offices to allow researchers to view lab operations from their office space or draw the shades for privacy. Other features in core office space include skylights for natural sunlight and windows that overlook an atrium or other building areas to regain the aesthetic value lost as a result of being away from the perimeter windows. From a safety perspective, core office spaces are desirable because they eliminate the risk of performing low-hazard work (computer work) in a high-hazard area (lab). In addition, many researchers carry the dual role of researcher and professor, and may have students in street clothing entering the lab space and waiting to see the professor. A core office space eliminates some of this unnecessary traffic in the active lab area.

It is essential that research institutions have a design review system which includes input from the SH&E department to ensure that these safe design features are incorporated into every newly renovated or constructed laboratory. In addition, new design features should be continually evaluated from the operations and maintenance perspective, as well as from the researcher's perspective.

Codes, Regulations & Standards

Federal, state and local codes, regulations and standards apply to nearly all phases of laboratory design, construction and use. Regional building codes that have long been used in the U.S. for building construction have given way to international codes adopted in whole or in part by most states, such as those from International Code Council (www.iccsafe.org). Challenges posed by these new standards are being realized as universities and large research institutions implement them in new building construction.

OSHA's Laboratory, Hazard Communication and Bloodborne Pathogens standards, as well as several other general industry standards for fire protection and emergency response, apply to research laboratories. In addition, Nuclear Regulatory Commission (NRC) and state-specific radiation standards apply to all laboratories that use radioisotopes, X-ray equipment and sealed radioactive sources. Research laboratories involved in drug research are regulated by the Food and Drug Administration and the Drug Enforcement Agency, which requires implementation of good laboratory practices and special registration, accountability and security of controlled substances.

Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) is a private, nonprofit organization that manages a voluntary accreditation and assessment program for research institutions involved in the care and use of animals in research. The guidelines for animal facilities in the program are found in *Guide for the Care and Use of Laboratory Animals* (Institute of Laboratory Animal Research, Commission on Life Sciences & NRC, 1996). Participation in the AAALAC accreditation program by research institutions with vivariums and other animal facilities lends credibility to the institution by demonstrating its commitment to responsible animal care and use.

Centers for Disease Control and Prevention (CDC)/NIH's (2007) *Biosafety in Microbiological and Biomedical Laboratories* is the prominent resource for determining the biosafety level of individual laboratory operations that may involve infectious materials, human cell lines or bloodborne pathogens. The packaging and shipment of dangerous goods through the U.S. Postal Service or other delivery services is regulated by the International Air Transport Association, CDC and the Department of Transportation. Dangerous goods include infectious substances, diagnostic specimens, genetically modified organisms and dry ice (IATA; CDC; DOT).

Medical waste regulations apply to laboratories that generate medical waste, sharps and other biological agents. EPA regulations under the Resource Conservation and Recovery Act (RCRA) apply to labs that generate hazardous chemical waste. RCRA compliance has been a key emphasis over the past decade, primarily in the academic research community (EPA).

Finally, several noteworthy consensus standards and guidance documents, such as the ANSI/AIHA Z9.5-2003, Laboratory Ventilation and *Prudent Practices in the Laboratory: Handling and Disposal of Chemicals* (NRC, 1995), apply to research laboratories.

Laboratory Equipment

Laboratories have many unique functions and uses that require unique and sophisticated equipment. Although some experiments and equipment may be

Abstract: *Modern research laboratories are complex environments with inherent safety, health and environmental risks. These risks can be greatly minimized by good laboratory design, careful pre-planning of each research project, and daily integration of good science and safe work practices.*

(Counter-clockwise from top left) Photo 1: Open, flexible and generic lab spaces are a new trend in modern research labs.

Photo 2: A laboratory entry niche with blackboard and small break area allows professional collaboration among researchers.

Photo 3: New energy-efficient chemical hood with multiple safety features.

Photo 4: Strobic Air® laboratory exhaust system provides low maintenance, odor control, noise control and discharge plume up to 350 ft high.

similar in cell biology, molecular biology and biomedical research labs, they may be vastly different from the experiments and equipment used in surgical, gross anatomy or organic chemistry laboratories. Industry-specific research labs may require scaled up pilot plant operations, rather than benchtop scale, which can present special equipment and space challenges. Chemotherapy drug research may require a dedicated suite equipped with airlocks, special ventilation controls and glovebox containment or isolators for potent drugs. Vivariums and other animal facilities may need to be equipped with microisolator cages, cage washers, sterilizers, surgical equipment and other special animal care equipment. Recent trends in nanotechnology research also may require specialized equipment. Due to the unique requirements of these research applications, safety and health considerations often must be evaluated on a case-by-case basis.

Aside from specialized needs, many research laboratories have standard equipment such as chemical hoods, centrifuges and refrigerators/freezers. Let's take a closer look at these pieces of equipment and their safety benefits and risks.

Chemical Hoods

The chemical hood is the primary engineering control in a laboratory for containing and removing chemical gases, vapors, mists and fumes. New chemical hoods are designed to afford energy efficiency as well as protection against exposure to airborne chemicals.

The chemical hood pictured in Photo 3 features both a vertical and horizontal sash with four sliding panels. This multifunctional sash allows excellent flexibility for moving apparatus in and out of the hood. It also allows good personal protection when one of the smaller panels is used as a barrier between the experiment in progress in the hood and the researcher performing the experiment. The researcher can place his/her arms around the side of the panel to conduct manipulations inside the hood, while maintaining full protection of the eyes, face and body. This hood is also equipped with other safety features such as electrical cord bypass ports, sash stops, flammable and acid storage cabinets, airfoil sill and a hood monitor with audible and visual alarms.

One of the energy-efficient technologies with new chemical hoods is the use of proximity detectors that sense when someone is standing near the hood. If no one is standing in front of the hood, the ventilation to the hood is decreased by approximately 50%. This is an excellent energy conservation feature, but it raises the safety concern of experiments that may need to distill, heat up or otherwise remain in the hood for extended periods without constant oversight by the researcher.

New lab hood designs also must consider the exhaust fans connected to the hoods, which are generally located on the roof of the building. Maintenance of these exhaust fans by maintenance personnel can result in exposures to chemical, radiological or biological hazards. An alternative to the traditional single exhaust fan for each chemical hood is the concept of manifolding exhaust hoods together and exhausting through a single, larger fan system. Strobic Air® is one alternative system that provides a low-maintenance, direct-drive fan, low-profile and relatively small footprint, and internal and external exhaust stream dilution for odor control and effective stack height up to 350 ft (Photo 4).

Although chemical hoods are considered a primary engineering control for eliminating exposure, the surrounding lab activities and the actions of the researcher may compromise its function. If supply air diffusers are located too close to the hood, they may interfere with hood operation. In addition, if a lot of activity or movement occurs near the hood, the resulting airflow may cause eddy currents around the researcher at the hood and compromise the face and capture velocity. The researcher also must be cautious to not overload the hood with extraneous equipment or chemicals. A cluttered hood can seriously compromise the airflow patterns and negate the hood's safety features.

In addition, safety features such as proximity sensors and hood monitors must be calibrated and maintained. It is also a good standard practice to conduct periodic smoke testing and face velocity measurements of chemical hoods. A new practice being adopted during the commissioning of new laboratory hoods is containment testing by the ANSI/ASHRAE 110-1995 standard, Method of Testing Performance of Laboratory Fume Hoods (ANSI/ASHRAE, 1995), which includes both qualitative and quantitative analysis of hood containment.

Biological Safety Cabinets

The biological safety cabinet (BSC) has features similar to a chemical hood with a few critical exceptions. Where the air in the chemical hood is exhausted to the outside, most BSCs are designed to filter and recycle a portion of the air and exhaust the remainder into the room. BSCs contain either high-efficiency particulate air (HEPA) or ultra-low-particulate air filters for both the recycled and exhausted air. BSCs also provide a laminar airflow across the work area that provides protection from cross-contamination. Laminar flow BSCs are designed to provide three primary types of protection:

- personal protection from harmful or infectious agents inside the cabinet;
- product protection to avoid contamination of the work, experiment or process;
- environmental protection from the contaminants within the cabinet.

Several types of BSCs are available, however, the type most commonly found in modern research labs is the Class II series (Photo 5) because it offers good containment for many biosafety Level 2 and 3 agents.

Safety considerations for BSCs include good ergonomic design, good aseptic (sterile) technique and limited use of flammable liquids or open flames inside the cabinet. Fires in BSCs have been reported that stem from the use of open flames to sterilize inoculation loops, as well as from flammable vapor (typically 70% ethanol used to sterilize the cabinet work surfaces) igniting in the non-explosion-proof fan compartment. Use of flammable liquids should be strictly limited to alcohol wiping of surfaces before and after each procedure. Use of alternate sterilants and disinfectants should be investigated, and storage of flammable liquids inside the cabinets should be prohibited. Electric incinerators, glass bead sterilizers or presterilized disposable inoculation loops offer a safer alternative to the use of open flames for sterilization of inoculation loops, needles and the lips of culture tubes.

Good aseptic technique is critical in preventing cross-contamination of product material and contamination of surfaces outside of the cabinet. Each BSC should be tested and certified at least annually to ensure continued proper operation. If a cabinet is relocated, the seal in the HEPA filter compartment may be breached and recertification would be necessary.

Another safety concern is potential exposure to formaldehyde during decontamination of BSCs using heated paraformaldehyde. Decontamination is generally required when a BSC is moved, decommissioned, known to be contaminated or requires internal repair and/or HEPA filter changeout (CDC & NIH, 2007). Although different decontamination protocols exist, the proven standard is the paraformaldehyde protocol. It is critical that a reputable and qualified microbiological decontamination firm conducts this process to avoid formaldehyde infiltration of adjacent spaces.

Photo 5 (top): A Class II biological safety cabinet used for tissue culture work in a new research center.

Photo 6 (bottom): The result of an explosion in a high-speed ultracentrifuge caused by the use of an improper rotor.

Centrifuges

Centrifuges and ultracentrifuges are capable of reaching speeds of 100,000 rpm, which can subject the rotors to powerful mechanical stresses that can lead to metal fatigue over time. Centrifuges are designed to withstand a rotor failure, however, incidents such as that shown in Photo 6 have caused significant damage. The primary causes of rotor incidents are:

- failure to put the lid on the rotor;
- failure to secure the lid;
- failure to secure the rotor to the drive.

Centrifuges have built-in safety features such as interlocks, but also require good preventive maintenance for safe operation. Preventive maintenance includes routine visual inspection of rotors by users, periodic nondestructive testing by the manufacturer or qualified vendor, and maintenance of a logbook that records the hours of use for each centrifuge rotor. This information will help determine when rotors need to be derated (permanently lowering its speed) or retired from use altogether.

Photo 7 (top): A typical steam autoclave operates at 270 °F and 30 psi.

Photo 8 (bottom): An unexplained explosion of an autoclave caused significant contamination and damage.

Autoclaves

Typical steam autoclaves operate at 270 °F and 30 psi (Photo 7). The extreme heat and high pressure pose a risk of burn injury. Before using an autoclave for the first time, it is essential to become familiar with its operating procedures and safety features. A user must never attempt to interrupt a cycle, and should only use metal trays with minimal water, rather than laboratory plasticware, for more rigid support. Although modern autoclaves have sophisticated safety interlocks that prevent the door from being opened during the operating cycle, sufficient residual heat exists in the chamber and equipment trays at the end of the cycle to cause a serious burn injury. Documented autoclave explosions such as that pictured in Photo 8 also have occurred. Annual servicing and maintenance of autoclaves is an essential component of an effective lab safety program.

Refrigerators, Freezers & Cold Boxes

Standard refrigerators are common equipment in laboratories and are generally used to store temperature-sensitive media, drug products and specimens. One of the most common hazards associated with refrigerators in labs is the use of a standard refrigerator to store toxic or flammable chemicals, as shown in Photo 9. Flammable-safe refrigerators should be used whenever flammable liquids are stored inside refrigerators. Explosion-proof refrigerators, which require hard wiring into explosion-proof junction boxes, should be installed whenever flammable vapors are present in the lab environment in the immediate vicinity of the refrigerator.

Ultra-low freezers—both upright (vertical) and chest (horizontal) types—are also common equipment in support zones of modern labs. Safety concerns primarily involve the proper use of cryogenic gloves, safety glasses/faceshields and lab coats while retrieving samples from freezers. Some ergonomic concerns may arise during the retrieval of large quantities of materials stored in freezers, particularly the chest type that require bending at the waist. Liquid nitrogen freezers require special operating procedures including required PPE during liquid nitrogen filling, retrieval of samples and storage.

Since cold boxes are essentially large refrigerators with recycled cooled air, it is important to prohibit the storage of toxic and flammable chemicals inside them. One common misconception among researchers is that it is acceptable to store dry ice in a cold box to retard the rate of sublimation (transformation from the solid state to gaseous CO_2). Dry ice has a surface temperature of -80 °C and a cold box offers little help in retarding sublimation. The CO_2 given off by the dry ice inside a cold box can easily exceed the OSHA permissible exposure limit of 5,000 ppm (AIHA Laboratory Safety & Health Committee).

Other materials that should not be stored or used inside cold boxes (or warm boxes) include mercury thermometers, gas cylinders and flammable liquids (Photo 10). Broken mercury thermometers are more dangerous in a warm room than a cold room, where the higher temperature will support vaporization of the mercury and contribute to a toxic environment. If the contents of a gas cylinder are released inside a cold room, an asphyxiation hazard, fire hazard or toxic environment may exist depending on the gas in the cylinder. Flammable liquids used in cold rooms may pose a fire hazard, particularly if operations inside the cold room are left unattended.

Safety Equipment

Safety Showers & Eyewash Stations

Older research centers have safety showers and eyewash stations located in corridors that are accessible to several laboratories. Modern research laboratories have moved these emergency safety devices back inside the labs. It is common to see eyewash stations at sinks in the labs (Photo 11). Maintenance of these emergency systems is critical to ensure proper operation in the event of an emergency. Following installation of a new eyewash station, it is important to check the water pressure to make sure it is not too strong or too weak.

In one new eyewash station design, the eyewash is flush with the wall and is activated by pulling down a handle. This is ideal for aesthetics and space constraints, but is often overlooked by lab occupants if it is not demonstrated to them. In some open lab areas, this type of safety shower/eyewash station is located in an alcove, which can be prone to improper storage. It is imperative that the space around these units is kept clear. A key safety issue with eyewash stations and safety showers is a good preventive maintenance program that includes routine flushing and inspection of the components. Researchers should not only become familiar with the location of the nearest safety showers and eyewash stations, they should also understand the operation of these devices.

Gas Shut-Offs

Emergency gas shut-off switches are a relatively new safety feature in modern research laboratories. These switches allow remote shut-off of gas in the laboratory in the event of a fire. There can be more than one gas shut-off within a single lab or a central shut-off switch in a remote location such as the exit corridor. Experience with these switches has revealed several concerns that may not be immediately apparent:

•The standard mushroom-type switch may be prone to accidental activation by a researcher leaning against it. The switch shown in Photo 12 had to be retrofitted with a protective sleeve to prevent such incidents.

•Some switches may be tied into the emergency power system. They may be activated when monthly load tests of emergency backup power are per-

Photo 9 (above): A standard refrigerator being used for storage of toxic and flammable chemicals.

Photo 10 (right): Dry ice, flammable liquids and liquid nitrogen should never be stored in cold boxes.

formed. Since the switches have a built-in safety feature that requires a manual reset when activated, this may cause some delay in returning service to the laboratories in question.

•Once the switch is activated and the area is deemed safe to return to service, it is critical to check that all stopcocks and gas valves are shut before the switch is reset.

•If more than one switch is present in the lab, it is useful to know which gas lines would be affected by each switch. In some cases, the switches may be tied into gas lines in adjacent labs in addition to the lab in which they are located.

Health Hazards & Physical Hazards

Chemical, Biological & Radiological Materials

Some of the most common risks in laboratories revolve around the chemical, biological and radiological materials used in specific scientific protocols. These can be carcinogens, teratogens and mutagens, and may be in the form of liquids, solids and gases. The chemical composition along with the physical properties of the chemical must be fully understood before performing full-scale laboratory manipulations.

Chemicals can be controlled in the laboratory by implementing a lab safety plan or chemical hygiene plan that includes a chemical review process and standard operating procedures that incorporate chemical safety for specific lab experiments. In addition, the chemical hygiene plan should include procedures for chemical handling, transport, storage and disposal.

Centralized chemical purchasing systems, centralized chemical supply rooms and routine laboratory inspections help keep chemical inventories in check. Research institutions can flag certain highly toxic, reactive or regulated chemicals in their computerized chemical purchasing systems by limiting quantities that may be ordered, or by requiring approval prior to placing the order. These systems also offer a means to track and trend chemical purchases and use. Chemical control can also be achieved with a central chemical supply room that not only provides new chemicals when needed, but also accepts unused or partially full containers when they are no longer needed. This type of system promotes minimization of chemical waste and limits excessive chemical storage in laboratories.

Because of the risk of fire resulting from several commonly used reactive chemicals, this class of chemicals should be strictly controlled. Water-reactive chemicals such as sodium, potassium and lithium react violently with water, releasing heat and, in some cases, explosive byproducts. Other reactive chemicals such as those that form peroxides as they age (e.g., butadiene, cyclohexene, ethyl ether) may explode when exposed to heat, shock or friction. Lab experiments using reactive chemicals must be carefully designed to include emergency procedures, availability of emergency equipment and training for all employees using the chemicals. In the case of reactive metals, a standard ABC dry chemical fire extinguisher is not appropriate. A Class D fire extinguisher must be used.

For radioisotope users, a radiation safety program is required with strict adherence to provisions of NRC and/or state regulations. A comprehensive program that includes

Photo 11 (left): Eyewash at lab sink with proper pressure and flow.

Photo 12 (above): This emergency gas shut-off switch required installation of a protective sleeve to prevent accidental activation by researchers leaning against it.

Every researcher must understand that it is a matter of teamwork and personal responsibility to maintain a safe laboratory environment.

medical surveillance, training, exposure monitoring, wipe testing, waste management and inspections is essential. For biological agents, special precautions must be taken based on CDC and NIH guidelines as well as site-specific programs.

Lab experiments that involve biological organisms, human cell lines or human blood are best controlled by adherence to the biosafety procedures set forth in *Biosafety in Microbiological and Biomedical Laboratories*, which establishes engineering controls, facility design features and work practices for biosafety Levels 1-4 (CDC & NIH, 2007). Control procedures also are identified in an exposure-control plan that is often a companion document to the chemical hygiene plan. The exposure control plan defines specific procedures such as use of biosafety cabinets for aerosol-producing operations, autoclaves for sterilizing equipment and waste materials, biohazardous waste containers for contaminated items, and sharps containers for needles, razors, glass pipettes, microscope slides and other sharps that come in contact with infectious materials.

The best defense against exposure to the health hazards in laboratories is to incorporate safety procedures directly into the laboratory protocol. A review process for highly toxic materials should be implemented to prevent acute and/or chronic illness from exposure. Industrial hygiene monitoring, radiation exposure monitoring and medical surveillance are all important components of a lab safety plan that addresses health hazards. In addition, certain biological indicators, post-exposure treatments and first-aid measures should be explored before working with extremely dangerous materials.

General precautions that should be taken for all types of potential laboratory exposures include initial and refresher safety training, emergency preparedness and good housekeeping. Training not only should include OSHA compliance but also should extend into the practical and hands-on demonstration of common safety devices in labs (e.g., hoods, hood monitors, safety showers, fire extinguishers). Researchers should also be familiar with emergency phone numbers and spill-response procedures.

Laboratory Culture

The final—and perhaps most important—element in applying safe science to research laboratories is the behavior of the researcher. Every researcher must understand that it is a matter of teamwork and personal responsibility to maintain a safe laboratory environment. The principal investigator and/or laboratory manager is a role model for other laboratory staff and essentially dictates the safety standard (or lack thereof) by his/her own actions in the lab. Few researchers deliberately violate safety rules, but may unknowingly encourage greater risk in the laboratory by insisting on long working hours, encouraging staff to work alone or by becoming so intensely focused on the research that the surrounding lab environment becomes cluttered and unsafe.

Another laboratory culture issue that may impact safety is increasingly diverse and multilingual research settings. When multiple cultures coexist in research labs, the collaboration may be outstanding but sometimes the safety message quite literally gets lost in translation. Along with the language barriers, acceptable safe practices in another country may not be compatible with safe practices in the host country.

One last laboratory culture concern is when a researcher makes a mistake that may endanger other lab workers and fails to report it or correct it out of fear of severe criticism or disciplinary action. The laboratory culture must support and encourage reporting of adverse events so that the overall safety and health of all lab workers is protected. Once it is understood that safety and science can go hand-in-hand without repercussions, the end product will be productive, insightful and safe. ■

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