



## From Training to Safe Behaviour to Avoid Accidents and their Consequences

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### Editorial

Biocontainment facilities in which we handle dangerous pathogens of risk groups 3 and 4 are highly complex buildings. Complexity is not only architectural, in the materials and in the engineering solutions, which has an undeniable complexity in costs of construction, commissioning and maintenance. Complexity is also organizational, with a procedural base, and this complexity in procedures carries with it the need for educated and well-trained staff. If the biohazard is in the centre, the focus, of the activities of the facility, this is the only safe way, a priori, to work.

Furthermore, throughout the life of a biocontainment facility, the experimental activities and the nature of the pathogens related to them can be very varied. The diversity of these pathogens currently handled may follow in time or temporarily coincide in the facility. All this evolution, unexpected at the very beginning, and fuelled by the requirements of the own Administration or by the needs of private companies or sponsors, has a potential deep impact on biosafety.

An increase or expansion of activities in a BSL3 (or BSL4) facility should raise concern among Direction that an expansion in the laboratory workforce would result in an increased number of accidental exposures, some of which might lead to actual infection. The main objective of Direction and the Biosafety Committee must be to markedly reduce their incidence as a result of the standardization of laboratory design, proper biosafety practices, and last but not the least employee training.

However, each BSL3 facility is unique and each biosafety and biosecurity training program will have unique aspects depending upon their research focus (animal diseases, zoonotic diseases, mainly airborne pathogens, not air-borne pathogens) and the program must necessarily create processes that facilitate and safeguard research but at the same time demonstrate biosafety competency.

Under the worldwide BSL system, research on each species of infectious agent is assigned to 1 of 4 biosafety levels, based on the threat the research poses to laboratory workers, especially when exposure occurs by the aerosol route. Research on BSL3 agents (virus or bacteria) which can cause lethal disease in humans but for which countermeasures exist in the form of vaccines and antibiotics, requires BSL-3 practices, which include restricted laboratory access, performance of all manipulations in biosafety cabinets (BSC), and the use of personal protective equipment (PPE) but it is mainly founded in the previous own expertise in a BSL2 environment, which should be characterized by a good and extensive microbiological training of the personnel, the proper use of BSC to prevent aerosol exposure, and other measures regarding how to act in case of incidents, spills and splashes and so on. In BSL3 there is not a "space suit" approach, in which all personnel wear positive-pressure plastic suits to prevent any

possible aerosol exposure. If we act in an improper way, the likelihood to be infected is, in my opinion, higher in a BSL3 environment than in BSL4, if we forget, for a moment, the consequences of such infection.

In the following paragraph I will discuss, in a general way, how my institute, CReSA, faces such biosafety training and hypothetical accidents.

### Basal Biosafety Training

Basal biosafety is achieved by reading the general Biosafety level 3 manual and accompanying SOPs detailing safety practices and procedures applying to each laboratory and common procedures (way of entry and exit, chemical and hazardous waste handling, transfer of infectious substances, emergency contact information). Computers are available in each laboratory, which enable electronic access to these various SOPs and protocols. Each principle investigator is also responsible for ensuring his/her personnel follow all procedures as outlined in the approved biosafety manual. Nevertheless, Biosafety and Management Biosafety Committees conduct post-training monitoring to ensure full compliance with SOPs. Retraining is mandated for individuals who deviate from approved protocols and could imply total restriction of access to BSL3 facility (temporarily or permanently).

### Specific Biosafety Training

Specific training have to include information about the infectious agents to be used, routes of exposure, symptoms, medical surveillance, appropriate PPE, incident response, post-incident response, post-exposure medical surveillance, how to report such exposures and incidents and follow-up procedures. In a specific experiment, personnel should be trained on facility equipment, and how this equipment interact with samples and modify (increase or decrease) the hazard.

Any change in an experimental procedure reported to the Biosafety Committee will lead to a new risk assessment analysis and, if proceed, additional training should be provided.

As part of initial and refresher training, all personnel must review and sign laboratory manuals to acknowledge their existence and location as needed for consultation of procedural or safety concerns, and for review of any updated material. By signing, personnel acknowledge that they have been advised of the hazards associated with this research, that they have been properly trained in the handling of the biological agent following BSL-3 guidelines, and that they agree to adhere to these regulations.

Prior to beginning work in a BSL-3 (or BSL-4 laboratory), it is mandatory that personnel have documented experience working in BSL2 laboratory (in the same facility or in an external one) in that area

of research. When working with highly dangerous pathogens additional training (how to use and wear N-95 respirators or how to wear, use and care Powered Air Purifying Respirator (PAPR)) should be required at the discretion of the Direction of the facility (or Biosafety). In addition to own BSL3 Laboratory Manual, other biosafety guidelines (BMBL 5th Edition published by the CDC; the WHO and the Canadian guidelines) are available on-line and in print. We are not reluctant to use web-based approaches, but we are case-by-case responders. If we consider a free web-based format is useful for some personnel (providing more individualized training on biosafety and biosecurity concepts), we encourage them to follow and report in a written format the completion of the training. Biosafety keeps a record with the web courses and the "attendants". Over the long term, this approach will reduce cost but the main handicaps are related to the ownership and the likelihood these courses were kept forever in a free format.

A third and probably more critical component of the training program is the hands-on training which provides time for the trainer to check the knowledge but also the practice and/or ability of the trainee with the previously studied biosafety and biosecurity principles and practices. Ideally, as biosafety and biosecurity risks increase, the trainee / trainer ratio should decrease. In our case, this hands-on training is provided by the Biosafety (or delegated personnel) as this position is occupied by a scientist. A smaller ratio student-teacher approach stresses thinking and reasoning approaches rather than rote memorization and focuses on the risks at hand. This is especially important for basic research, which is not a static process. Instruction provided should require productive behaviour and/or appropriate feedback. Each hands-on training session should be documented as to time and tasks covered with space for comments and concerns noted. Amount of time or number of sessions required for hands-on training will vary based on the individual's prior level of expertise.

So, as a general conclusion of biosafety training programs, they have to be designed with people, facilities and processes in mind. These things support the successful management and implementation of such a large and complex training (1) continuous assessment and (2) proper implementation, and (3) development of a self-supporting culture of compliance.

CRESA do not perform a behavioral health screening looking for alcohol and drug abuse. However, we try to detect symptoms of anxiety and depression among staff and mainly the likelihood that the employee will follow safety rules, and the employee's general attitudes toward safety, by daily observation and checking. As in Spanish regulation vaccination is not mandatory, CRESA only strongly recommend its employees to be vaccinated, but not oblige them.

Working in couples in a BSL4 (or BSL3) environment, at all times while biological work is doing, does not protect "per se" the facility (and the staff) from an accident. A similar degree of control and quick intervention could be achieved by video monitoring systems or by presence of staff in surroundings labs (if they are provided with big windows which allow to see inside), rather than by the presence of a fellow scientist. In any case, seems of common sense that the standard biosafety practice should be to perform a risk assessment before any activity is undertaken. This approach will be quite different when kinds of experimental activity or pathogen involved (zoonotic or non-zoonotic) are assessed. A 2-person rule could be inappropriate for an activity with food and mouth disease, or African swine fever

virus, simply because the best approach is not to have rules that are not objectively assessed.

A surveillance video monitoring and data storing can protect us from unauthorized access and loss of materials, but their effectiveness for ensuring proper handling of pathogens is quite limited (again proper microbiological and safety training poke their heads). At the end, a careful selection, training and monitoring of staff is the main foundation of biosafety and biosecurity. Even the most sophisticated controlling system pales against it.

### But at the End, an Accident

We can think in three ways of an exposure to a pathogen in a BSL3 environment: an accident such as an animal bite or a skin puncture by a contaminated needle that the worker reports to a biosafety officer; a similar event but not reported by the employee; or an unrecognized exposure, such as contact with infectious material without wearing proper PPE, or removed from biocontainment without adequate inactivation or improper labelling.

It is therefore essential to monitor the health of all employees for the occurrence of illnesses, as this will be the only way to track the latter 2 cases of potential exposures, when null report or adventitious infection occurs. And this monitoring implies to instruct our workers to monitor their own health status but also require tracking attendance and responding to any unexpected absences by Biosafety assessments. A main drawback, however, has to be considered as the initial signs and symptoms of some severe laboratory-acquired infections resemble those of mundane illnesses such as colds, or gastroenteritis.

### Evacuation of Exposed Personnel

As administration of care should begin as soon as possible, depending on circumstances, the exposed laboratory worker should be directly sent to hospital isolation. The way to proceed also has to include situations in which a worker in biocontainment becomes ill from an unrelated medical condition (such as a heart attack or stroke). The ways to perform it (evacuation from inside) have to be formally written and periodically assayed. A working relationship with local responders, currently reluctant to enter in a BSL-3 or BSL-4 facility, should be initiated and maintained with total transparency in terms of information and practical procedures. However, we have not set up corridors to transport exposed personnel through highly populated residential areas or along heavily trafficked roadways, or special isolation systems, because of the known latency period between exposure and any clinical manifestation of an infection that might make the patient potentially infectious to others, as they don't have the short time frame needed to mobilize the potential exposed to hospital. The need for responsible escorts has been solved by one from Biosafety and/or Laboratory management.

Emergency 24-hour medical contact information is readily available on all pathogens data sheets allocated in all CRESA laboratories but also in the CRESA intranet. To maximize compliance, procedures for reporting possible exposures (and the algorithms for post exposure management) are extremely short with one, no more of two steps, so that they are not viewed as too time-consuming or onerous. This procedure works all days around the year and the formal report is executed by the Biosafety

CRSA has a formal memorandum of agreement with a referral hospital for managing employees with an occupational exposure to a BSL-3 pathogen. The established hospital setting is the single one destination for our potentially infected employees. The hospital has not been constructed following standards approximating a corresponding containment laboratory, as it is ours facility. But at that moment, in an accident outcome, we are looking for a state-of-the-art medical care to the patient and if accommodations and specialized standard operating procedures are in place to handle such patients, and we could collaborate to set up of such rules, the hospital would meet acceptable minimum standards.

Our standard operating procedures request employees to report immediately to the Biosafety any known or possible exposure to an infectious agent. Our workers know this request will not lead to any disciplinary action, or advice in their own work record. In fact we promote to inform about suspicious or uncertain exposure, and battle against “wishful thinking” by the employee that his or her risk of

acquiring infection a particular exposure is minimal. With respect to this last point, we encourage our employees to discuss with the Biosafety why they arrive to such conclusions because is a indirect way to discuss about bioafety, risk evaluation and assessment, minimal dose, etc. We try to create a no punitive, supportive atmosphere, in which reporting should be recognized as a team that enhances the safety of the lab for everyone.

As a general conclusion, the most means of dealing with the problem of accidental laboratory infections is to prevent their occurrence through a combination of engineering controls, training in proper microbiological techniques (starting at BSL2 level), encouraging employee vaccination, and implementing an active biosafety program. If an exposure occurs despite these each facility must have a program in place to deal promptly with any eventuality, so as to protect the exposed individual and the rest of the community.