The Argentine Experience in Enhancing Biosafety through Good Laboratory Practices

Nidia E. Lucero* and Faustino Siñeriz**

Abstract: Though there may be growing concern about safe laboratory practices in Argentina, there exist lacunae in the development and implementation of effective educational programmes. Efforts of the Argentinean Association of Microbiology (AAM) and the National Institutes of Health in providing training courses have contributed to a healthier work environment. Since the early 1990s, guidelines from the Ministry of Health have been implemented regarding the safe disposal of medical wastes, handling and manipulation of blood-borne pathogens and transportation of biological agents. Also, with World Bank support, Class II biosafety cabinets have been distributed throughout the country to national hospitals and reference laboratories, to provide containment for infectious splashes, and laboratory facilities have been reformed. The ongoing training courses on good laboratory practices have demonstrated that it is possible to change habits, improve motivation to work and act safely. Personnel of the microbiology laboratories should be trained in the proper use of equipment and procedures, including recording accidents. It should be noted that important efforts have been made by national institutions in providing assistance and coordinating biosafety networking in almost all Argentine provinces.

Introduction

Argentina located in the South of South America has a territorial area of 2,791,810 km² with a population of 36 million inhabitants. The country has great climatic variety ranging from the cold regions in the South to the hot areas with extreme drought in the Northwest; there
are five geographical regions: —the humid Pampa, the Northwest, the Northeast, Cuyo and Patagonia which are characterized by major diversities in weather, livestock, agriculture and industries (see Figure 1). The country is divided into 23 provinces and one autonomous city of Buenos Aires — the Nation’s capital, has 1115 public hospitals and a total of 833 public laboratories, classified according to their complexity, namely: — Level 1 low complexity (463); Level 2 medium complexity (235); Level 3 high complexity (126) and Level 4 reference laboratories (9) (see Table 1). Moreover, Argentina has public (35) and private (47) universities, plus public and private institutes where human and animal research projects are in progress.

Microbiologists in clinical and research laboratories process specimens, cultures, toxins and materials that present risks that endanger their health and their work environment. Research in the new biotechnologies and their applications has added potential risks for

<table>
<thead>
<tr>
<th>Argentinian Provinces</th>
<th>Population census year 2001</th>
<th>Public Hospitals</th>
<th>Level 1</th>
<th>Level 2</th>
<th>Level 3</th>
<th>Level 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buenos Aires City</td>
<td>2,729,469</td>
<td>33</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Buenos Aires</td>
<td>13,755,993</td>
<td>174</td>
<td>36</td>
<td>62</td>
<td>48</td>
<td>0</td>
</tr>
<tr>
<td>Catamarca</td>
<td>330,996</td>
<td>44</td>
<td>25</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Córdoba</td>
<td>3,052,747</td>
<td>131</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Corrientes</td>
<td>926,989</td>
<td>40</td>
<td>41</td>
<td>4</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>Chubut</td>
<td>408,191</td>
<td>16</td>
<td>6</td>
<td>6</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Chaco</td>
<td>978,956</td>
<td>90</td>
<td>33</td>
<td>4</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Entre Ríos</td>
<td>1,152,090</td>
<td>60</td>
<td>31</td>
<td>12</td>
<td>11</td>
<td>2</td>
</tr>
<tr>
<td>Formosa</td>
<td>489,276</td>
<td>33</td>
<td>13</td>
<td>7</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Jujuy</td>
<td>609,048</td>
<td>26</td>
<td>2</td>
<td>16</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>La Pampa</td>
<td>298,772</td>
<td>36</td>
<td>10</td>
<td>12</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>La Rioja</td>
<td>287,924</td>
<td>19</td>
<td>13</td>
<td>5</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Mendoza</td>
<td>1,573,671</td>
<td>23</td>
<td>9</td>
<td>5</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Misiones</td>
<td>961,274</td>
<td>23</td>
<td>30</td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Neuquen</td>
<td>471,825</td>
<td>30</td>
<td>12</td>
<td>9</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Río Negro</td>
<td>549,204</td>
<td>32</td>
<td>8</td>
<td>12</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Salta</td>
<td>1,065,291</td>
<td>52</td>
<td>39</td>
<td>13</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>San Luis</td>
<td>367,104</td>
<td>21</td>
<td>20</td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Santa Fe</td>
<td>2,975,970</td>
<td>137</td>
<td>59</td>
<td>31</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>San Juan</td>
<td>617,478</td>
<td>16</td>
<td>12</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Santiago del Estero</td>
<td>795,661</td>
<td>31</td>
<td>16</td>
<td>6</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Santa Cruz</td>
<td>196,876</td>
<td>14</td>
<td>21</td>
<td>13</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Tierra del Fuego</td>
<td>100,313</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Tucumán</td>
<td>1,331,923</td>
<td>32</td>
<td>27</td>
<td>7</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>35,926,728</td>
<td>1115</td>
<td>463</td>
<td>235</td>
<td>126</td>
<td>9</td>
</tr>
</tbody>
</table>

*Note: ND: no data*
research personnel and technicians that handle and use hazardous materials. Safety in clinical laboratories, containment of biological hazards in biotechnology research or production, occupational hygiene, management of new or reemerging disease and the transport of infectious biological materials have been challenges for the Ministry of Health throughout the last decade. Microbiology laboratories are particularly important since their work environments may pose identifiable infectious disease risks for persons in or near them. Laboratory associated diseases have been reported with some of these diseases being attributed to carelessness or poor technique in the handling of infectious materials.\(^1\) Although laboratory personnel are exposed to the risk of infection by the etiological agent they handle, actual rates of infection are unknown or unavailable. Nevertheless, laboratories working with infectious agents have not been shown to represent a threat to the community.

**Epidemiological Situation in Argentina of Disease Risks to Laboratory Personnel**

Although the notification of cases of infectious diseases is underestimated in Argentina and systematic record-keeping may be scarce, the present data from the National Epidemiological Surveillance System (SINAVE), Ministry of Health and Environment (MHE), could reveal disease risks and trends. Low incidence of anthrax caused by *Bacillus anthracis* has been reported in the City and Province of Buenos Aires, Córdoba, Chaco, Santa Fe and La Pampa. And though cases of anthrax decreased from 1995 to 2002; thirty-three cases were registered in 2003. *Bordetella pertussis*, the causal agent of whooping cough has been used in large scale vaccine production operations since 1985 following the compulsory vaccination of children after their sixth birthday as a result of the epidemic of 1984. *Brucella abortus, B. melitensis, B. suis and B. canis* are frequently isolated from human blood and tissues from persons having brucellosis because of their contact with or consumption of food derived from infected animals.\(^2\)

Cases of psittacosis caused by *Chlamydia psittaci*, registered by SINAVE, have increased from 0, 07 to 0, 18 cases per 100,000 inhabitants and infections due to *C. trachomatis* from 11, 2 to 141, 6 cases per 100,000 inhabitants since 1997 to 2002. In a study from a Buenos Aires Hospital, 43 per cent of the patients infected with HIV in serological studies tested positive for the presence of *C.trachomatis*.\(^3\)
The emergence of Q fever has been reported in humans in contact with infected goats. Antibodies against *Coxiella burnetii* have been found in goats imported from Uruguay.  

Human infections resulting from consumption of a variety of food products contaminated with *Clostridium botulinum toxin* decreased over a six-year period from 30 cases in 1997 to 17 in 2002 and 15 in 2003. Tularemia caused by *Francisella tularensis* has not been reported in Argentina. Moreover, the occurrence of legionellosis due to *Legionella spp.* is to date unknown even though some cases identified solely on a serological basis have been reported in the City and Province of Buenos Aires.  

During 2002, 970 patients succumbed to tuberculosis with some 2,56 deaths/100,000 inhabitants. In 2003, 12, 278 new cases were reported (32, 0 cases/100,000 inhabitants); and from amongst 10,350 cases of pulmonary tuberculosis 66 per cent were confirmed by smear microscopy and culture. A study coordinated by: the National Institute of Infectious Diseases (INEl), the National Institute of Respiratory Diseases (INER) and the tuberculosis laboratories network during 1999-2000 have shown that 1.8 per cent of new tuberculosis cases were multi-drug resistant. Data registered during the last 10 years on the occurrence of tuberculosis amongst laboratory personnel engaged in the culture of mycobacterial strains revealed 396 cases per 100,000 individuals exposed.  

Infections caused by *Neisseria gonorrhoeae* in the period 1997-2003 was on average of 16.4 cases per 100,000 inhabitants. In Latin America, the prevalence of gonorrhea is 3 per cent whereas cases of meningitis caused by *Neisseria meningitidis* decreased from 2.9 cases to 1.08 cases per 100,000 inhabitants during the sexennial period of observation.  

In 2002, SINAVE reported 663 cases of typhoid fever caused by *Salmonella typhi*. No cases of plague (*Yersinia pestis*) have been reported in Argentina since 1946 though the occurrence of the disease has been confirmed in Brazil, Bolivia, Ecuador and Peru. *Burkholderia pseudomallei*, the etiological agent of melioidosis often associated with pneumonia or lung abscesses has been reported in Brazil, Ecuador, Mexico, Panama, and Peru but not in Argentina.  

Coccidioidomycosis caused by the fungus *Coccidioides immitis* is endemic in the Andean foothills area from the North to the South of the country. Although the true prevalence in Argentina is unknown, reports of its occurrence in some provinces varies between 9-40 per cent.  

Paracoccidioidomycosis (*Paracoccidioides brasiliensis*) is endemic in the
provinces located in the Northeast of the country; data on the incidence of these diseases is unavailable.\textsuperscript{10}

Histoplasmosis (\textit{Histoplasma capsulatum}) is around 30 per cent in the population living in the basin of the plate river.\textsuperscript{11}

Viral agents other than arbovirus such as Hantavirus are responsible for the Hantavirus pulmonary syndrome a new severe zoonotic disease that has been on the increase throughout 1997-2002 in the Northwest, Central and South regions of the country.\textsuperscript{12} Argentina with no reported cases of avian \textit{Influenza} is on the alert as a result of outbreaks reported in Chile in 2002. With the recent emergence of Coronavirus (SARS-HCoV), travellers coming from Asian countries have been monitored for possible harbouring of the virus.\textsuperscript{13} Though cases of Hepatitis B notified during the period 1997-2003 are stable around 2.6 cases per 100,000 inhabitants, those concerning Hepatitis C in the same period increased over from 0.6 to 2.02 cases per 100,000 inhabitants. The occurrence of Hepatitis D was very low in recent years.\textsuperscript{14}

Lymphocytic choriomeningitis virus (LCMV) is associated with a natural reservoir \textit{Mus domesticus}. Data from a serological survey, using enzyme-linked immunoabsorbent assay (ELISA), in rodents and humans during 1998-2003 in a region of Argentina revealed antibodies in 9.4 per cent of rodents and in 3.3 per cent of humans.\textsuperscript{15} The dispersal of \textit{Calomys musculinus}, an abundant rodent species in Argentina and reservoir of Junin virus that causes Argentine hemorrhagic fever facilitates the spread of the human disease.\textsuperscript{16} Human cases reported to SINAVE from the National Institute of Human Viruses Diseases were 144, 153, 84 and 60 from 2001 to 2004.

The last case of polio due to the wild type of \textit{Polio virus} was in 1984. A decade later Latin America was declared free of polio.

Argentina has a high rate of human immunodeficiency virus (HIV) in the big cities, 25,400 cases were detected in 2002. Eleven cases of Dengue fever were reported to SINAVE in 2001-2002.\textsuperscript{17} Outbreaks of Yellow fever and exotic infections with West Nile Virus and \textit{Venezuelan equine encephalomyelitis} are unknown in Argentina.\textsuperscript{18} In some provinces, such as Jujuy, Misiones, Corrientes, Entre Rios, Santa Fe and Buenos Aires, antibodies against \textit{Rickettsia rickettsii}, \textit{R. prowasekii} and \textit{Ehrlichia chaffeensis} have been detected. No cases of Creutzfeldt-Jacob disease or other human spongiform encephalopathies have been detected.\textsuperscript{19} The absence of the risk of transmission from the bovine form or mad cow disease is due to the rigid stand of the National Service of Health and Agrofood Quality
(SENASA) prohibiting consumption and importation all kinds of animal tissue or food from the UK from the first reported occurrence in that country more than two decades ago. Moreover, most of the cattle are raised in freedom; and recycling of animal parts into animal feed is prohibited. Argentina is ranked as free from BSE among beef exporting countries.

**The Microbiological Laboratories**

The National Administration of Laboratories and Health Institutes (ANLIS) “Dr.C.G.Malbrán” which depends on the Ministry of Health and Environment is comprised of 7 Reference Institutes and 4 Centers dedicated to the diagnosis of infectious diseases, biological production and anti-sera and vaccine quality control. Research and development efforts focus on improving diagnostic methods, determining host-pathogen interaction and reducing the impact of diseases.

The most urgent issues relate to the emergence of new diseases such as human immunodeficiency virus (HIV), which threaten to spread, outbreaks of multi-drug resistant tuberculosis, the rodent-borne pneumonic Hantavirus, hemolytic uremic syndrome, dengue
hemorrhagic fever and other diseases such as brucellosis that seem not to be under control in some Latin American countries. Preventive strategies consist of detection, investigation and promptly monitoring the emerging pathogens, the diseases they cause and the factors influencing their emergence. The public laboratories of the 23 provinces have been integrated into the ANLIS National Laboratory Network Center (NLNC) in order to optimize diagnosis, enhance communication, and to ensure the implementation of prevention programmes. Currently, the NLNC centralizes 833 public laboratories of different complexity (see Table 1). Furthermore, local and federal public health infrastructures have been strengthened in order to implement surveillance and prevention measures.

The annual training courses disseminating new technological developments in the diagnosis of human infections field given to the NLNC members in the last decade have included recommendations oriented to protect occupational health and to improve good laboratory practices. In 2001, a biosafety course with the collaboration of the Public Health Service, Centers for Disease Control and Prevention (CDC-NIH), USA, was provided to 30 professionals. It included advanced training in good laboratory practices that could then be transferred to other laboratory personnel in their province.

A biosafety manual in Spanish was distributed to each province to introduce new knowledge on good laboratory practices in biosafety. In 2004, the Ministry of Health and Environment, the Programme for Surveillance of Health and Control of Diseases (VIGI+A) and the ANLIS investigated the biosafety facilities in the public laboratories of each province. If more modern tools and equipment were required or some adaptation or change was called for these requirements were immediately provided. To date with World Bank assistance and through VIGI+A-BIRF 4516-AR 80 biological safety cabinets have been distributed.

The biosafety conditions of the reference laboratories were reviewed and projects to improve the facilities are now in progress. For example, a biosafety Level 2 laboratory is to be built at ANLIS with access to a biosafety Level 3 laboratory with extra facilities for using experimental animals in biosafe and secure conditions (project VIGI+A-BIRF 4516-AR). With availability of equipment for diagnosis, the development of new diagnostic tools and research projects with viruses, bacteria, fungi, prions, GMOs, or other pathogenic agents responsible of unknown high risk diseases that require a barrier at this level will be possible.
The following pathogen strains that require biosafety Level 2 or 3 practices and containment equipment and are likely to be handled in these facilities are, namely:
- *Bacillus anthracis* (blood, lesion exudates, cerebrospinal fluid [CSF], sputum)
- *Bordetella pertussis* (respiratory secretions)
- *Brucella abortus, B. melitensis, B. suis and B. canis* (blood, semen, animals uterine discharges, fetal membranes)
- *Chlamydia psittaci, C. pneumoniae, C. trachomatis* (blood, sputum, genital and conjunctival fluids, tissues of infected humans)
- *Coxiella burnetii* (blood, urine, milk, tissues of infected animals or humans)
- Toxin of *Clostridium botulinum* (clinical materials, food products)
- *Legionella* spp. (sputum, tissues, pleural fluids)
- *Neisseria meningitidis, N. gonorrhoeae* (CSF, pharyngeal exudates, blood, urethral exudates, synovial fluid)
- *Salmonella typhi* (feces, bile, urine, blood)
- *Burkholderia pseudomallei* (sputum, wound exudates)
- *Francisella tularensis* (respiratory secretions, lesion exudates, tissues from animals)
- *Yersinia pestis* (sputum, blood, feces, CSF, urine)
- *Coccidioides immitis, Paracoccidioides brasiliensis, Histoplasma capsulatum* (clinical materials, animal tissues, mold form cultures and soil from endemic areas)
- *Wild Poliovirus* (workers must be vaccinated with Sabin oral poliovirus to manipulate)
- *Avian Influenza* (materials from infected avian species)
- *Hantavirus* (rodent excreta or bedding, necropsy tissues)
- Dengue (blood, CSF, infected arthropods)
- Yellow fever, Venezuelan equine encephalomyelitis (CSF, urine, exudates)
- Junin *virus* (throat secretion, urine, tissues from humans and rodents)
- HTLV (blood, body fluid)

**The contribution of the Argentinean Association of Microbiology to Biosafety**

In 1988, the Argentine Association of Microbiology (AAM) pioneered the creation of a Biosafety Sub-committee (BSC) to:
— Create awareness for the understanding and the need for biosafety measures; and to
— Develop training activities concerning biosafety practices and protocols to be used in cases of accidental exposure of research personnel to hazardous materials used in microbiological laboratories.

The BSC has prepared yearly symposia, meetings and courses with the collaboration of specialists in the field of human and animal health, and in occupational health sectors (see Table 2) and has offered training programmes and periodic updates that are important for maintaining safety awareness of the laboratory and support staff, including safe shipment of specimens and infectious materials. Concerning the latter point, the risks of accidental infections may result from improper packaging and sealing. A broken or improperly sealed container may lead to contamination of the environment and the infection of personnel.

<table>
<thead>
<tr>
<th>Year</th>
<th>Theme</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>1988</td>
<td>Biosafety in the laboratory</td>
<td>Focus on: Safe handling of pathogens and potential pathogens. Alert sheet that aid recognition of hazardous entities (chemicals, carcinogens, radioactive materials, experimental laboratory animals)</td>
</tr>
<tr>
<td></td>
<td>Special issue</td>
<td></td>
</tr>
<tr>
<td>1990</td>
<td>Biosafety in the laboratory II</td>
<td>Focus on human factors causing accidents and on preventive measures resulting from recommendations of experts dealing with social, psychoanalytic and anthropological elements</td>
</tr>
<tr>
<td></td>
<td>Special issue</td>
<td></td>
</tr>
<tr>
<td>1992</td>
<td>Biosafety manual for laboratory Technician</td>
<td>Emphasis on personal hygiene, protective clothing, hand washing, receipt of specimens, disposal of contaminated materials, and include an emergency first aid guide.</td>
</tr>
<tr>
<td></td>
<td>Technician Special issue</td>
<td></td>
</tr>
<tr>
<td>1995</td>
<td>Safety and biosafety in large Institutions</td>
<td>Describes successful approaches applied to the situations in the laboratories of a hospital, a university and a health institute.</td>
</tr>
<tr>
<td></td>
<td>Special issue</td>
<td></td>
</tr>
<tr>
<td>1998</td>
<td>Transportation and transfer of biological agents</td>
<td>Special packaging and labeling for infectious substances and clinical specimens</td>
</tr>
<tr>
<td></td>
<td>Triple packaging not certified</td>
<td></td>
</tr>
<tr>
<td>2000</td>
<td>Annual training courses</td>
<td>Focus on sterilization with ethylene oxide gas</td>
</tr>
<tr>
<td>2004</td>
<td>Periodical articles in the AAM-Bulletin</td>
<td>Decontamination of the biological safety cabinets and packaging and shipping of biological materials</td>
</tr>
</tbody>
</table>
Since 1998, curators from twelve microbial collections from Argentina organized a National Culture Collection Network that currently links with the AAM-Culture Collection Sub-committee (SCCM) to promote, disseminate and exchange information about aspects and questions relating to preservation methods, quality control, management procedures and biosafety. Recently, a Latin American Federation of Culture Collection (FELACC) was established between SCCM (Argentina) and counterpart members of 4 countries: Brazil, Cuba, Mexico and Venezuela.

Because the microbiologist must be able to exchange microorganisms in a way that presents minimum risk to those who come into contact with them a FELACC Biosafety Commission was created. A safety data sheet must be sent with the microorganisms indicating the hazard group it belongs to and what containment and disposal procedures are necessary. There is extensive legislation concerning the safe handling and distribution of microorganisms at national, regional and international levels but, it is evident that many microbiologists are still unaware of several aspects of these regulations.

**Biosafety Regulations and the Ministry of Health and Environment (MHE)**

One of the areas of biosafety is the implementation of education programmes supporting the wide use of immunization. In 1992, the Ministry of Health and Social Action (MHE), through Law #24151/92 declared the compulsory application of Hepatitis B vaccine for personnel working in the fields of healthcare and who frequently handle blood or blood contaminated materials.

However, during the processing of specimens, the primary strategy in preventing laboratory associated infection is the consistent practice of blood precaution, not only in laboratories where blood, serum, and other specimens are processed from patients with a known diagnosis, but also in all laboratories involved in hematological and microbiological assays of blood and blood products. In 1993, MHE Resolution #228/93 issued recommendations focused on biosafety in microbiological and biomedical laboratories conducting clinical diagnosis or research that involved the handling of biological material, invasive procedures, dental care practices, autopsies and dialysis.

However, when an accident, such as cuts, needle pricks or skin abrasions with instruments possibly contaminated with blood occur, prompt reporting and proper medical consultation are necessary. In
1998, MHE Resolution #19/98 described the prophylactic measures to be taken when accidental exposure to bloodborne pathogens occurs, explicit regulations for reporting accidents due to small cuts, larger accidental wounds or by inoculation with needles or other sharp instruments.

Although all microbiological specimens should be considered infectious materials, knowledge of locally prevalent infectious diseases, indication of the suspected clinical diagnosis and the use of identification labels and disposal bags to flag samples from patients suspected of infectious diseases reinforce the safety awareness of laboratory personnel. Procedures for packaging and shipping hazardous materials properly are often difficult to heed, mainly because of the cost and the difficulty of obtaining containers that must withstand leakage of contents, jolts, pressure changes and other conditions incident to ordinary handling in transportation.

Ministerial guidelines from 1998 describe the procedures for the export of samples of blood, serum or plasma, for diagnosis in certified and accredited institutions as well as for the dispatch of samples of blood, serum or plasma out of the country for histocompatibility studies of patients awaiting organ transplants.

Resolution #145/2003 governs the transport of infectious substances and diagnostic specimens through MERCOSUR countries (Argentina, Uruguay, Brazil and Paraguay). Acceptance or rejection of infectious biomaterials for transport is done on case by case basis following assessment by a Permanent Assessor Committee (CAP).

The disposal of wastes, specimens and contaminated material of human and animal origin needs special considerations concerning the generation, transport, handling, treatment and final disposal of “Dangerous Waste” that includes pathogenic waste. However for the City of Buenos Aires, legislation on the “Generation, handling, storage, collection, transport, treatment and final disposal of pathogenic waste” defines pathogenic waste as blood or blood derivates, microbiological cultures, animal bodies or fluids and any type of waste from facilities working with infectious specimens or specimens suspected of containing infectious materials.

The disposal of untreated waste not only poses a health hazard to workers and a potential risk of contaminating the soil, but also endangers the environment, food production and the people living in close proximity. Another problem is the incineration of waste in
inappropriate equipment that often releases toxic gases into the environment. Moreover, public awareness and knowledge of the potential risks of waste originating from biomedical and microbiological laboratories and the manner in which it can affect human and animal health and the environment, is scarce. This lack is further aggravated by inadequate storage facilities, human and financial resources.

**Response to an Attack with Biological Agents**

The Direction of Emergencies, Trauma and Disasters of the Ministry of Health issued in 2001 guidelines for research and treatment of diseases caused by biological agents that could negatively impact on public health as a result of criminal attempts in some countries to intentionally use chemicals or biological agents to cause illness and spread terror amongst the civilian population. In addressing the possibility of a bioterrorist attack, the surveillance of respiratory distress and hemorrhagic fever syndromes that have been caused by an unknown agent in persons of any age is strongly recommended. Such cases must be reported immediately to SINAVE.

Investigation of the possible source of contamination must begin after reporting to the National Authorities when *Bacillus anthracis*, *Yersinia pestis*, *Francisella tularensis*, toxin of *Clostridium botulinum*, smallpox and hemorrhagic fever virus are suspected. Efforts to enforce biosafety instructions concerning the biohazards samples handled and the use of proper disinfectants are strongly emphasized. These alert bulletins to hospitals emphasize so that appropriate medical care and prevention services be made available. A long list of the antibiotics effective against the most likely bacterial agents to be used in bioterrorism is also communicated.

**Control of Environmental Release and Contained Use of GMOs and GMVOs**

The National Advisory Committee on Agriculture and Animal Biotechnology (CONABIA) is the agency responsible for the control of environmental release and contained use of GMOs and GMVOs as defined in 1991 through Resolution #124 of the Agriculture, Livestock, Fishing and Food Secretary (SAGPyA).

The National Advisory Committee Office of Biotechnology established in 2004 advises and assists in the authorization of biotechnology and biosafety activities, particularly when genetically
modified plant or animal organisms (GMOs) are to be transferred or used. The diversity of ecosystems in Argentina requires a thorough case by case analysis for each request for the release of GMOs. Evaluation of the potential impact on national agro-ecosystems and surveillance and control activities are managed by CONABIA. The use of GMOs in Argentina is regulated by legislation. The environmental release of genetically modified vegetable organisms (GMVOs) is governed by legislation which requires that:

a) The large scale release of GMVOs shall not produce an environmental impact different than what would be produced by a homologous, non genetically modified organism.

b) The appropriateness fit of GMVOs as human or animal food must be approved by National Service of Health and Agrofood Quality (SENASA-SAGPyA).

c) The release of the GMVOs shall not produce a negative impact on international commerce.

Although these regulations were established early and have been useful for the requirements of the last decade, an update is needed to respond to the challenge posed in the applications of the new biotechnology. Technical resources for specific biosafety investigations for individual situations are needed along with an updated legal framework to ensure that prescribed regulations are enforced. Proposals for a National Biosafety Law are now being studied in the National Congress.

**National Service of Health and Agrofood Quality (SENASA-SAGPyA)**

Reemergence of foot-and-mouth disease in Argentina has necessitated the development of tools for the control and eradication of the disease. The absence of outbreaks after January 2002 indicated that the epidemic was controlled. The National Service of Health and Agro-food Quality (SENASA-SAGPyA) implemented the biosafety regulations that govern the handling of foot-and-mouth disease virus (FMDV) strains in the laboratories conducting diagnosis, research and production of vaccine in Argentina. Simultaneously a SENASA-Biosafety Commission inspects, assists and controls periodically the laboratories where FMDV is manipulated. The same commission have supervised the SENASA´s biosafety Level 3 agriculture laboratory (BSL3-A) facility used for FMDV and other exotic disease diagnosis.
The BSL3-A have controlled access, clothing change before entering, shower on exit and walls and ceilings smooth. Floors are monolithic and slip-resistant, all windows are sealed, negative airflow circulates into the laboratory, exhausted air is not re-circulated, and HEPA filter are used in the biosafety cabinet. Frontier autoclaves, treatment of liquid effluents, airlock for fumigation are available and all the biosafety equipment are registered and their performance may be traceable. In addition, SENASA have regulated specific biosafety requirements for laboratories engaged with the production of rabies and encephalomyelitis vaccines.\textsuperscript{26}

**University Biosafety Training Programmes**

The 35 public and the 47 private universities have 65 and 17 biomedical or biomedical related courses, respectively (see Figure 2). A basic training course on good laboratory practices has been included in most of them and biosafety modules designed for specialists in a few during the last decade. Establishing work methods that are well understood and consistently followed have shown to be essential for carrying out orderly and safe laboratory procedures. Practice instruction with an emphasis on good laboratory practices eliminates one of the greatest causes of accidents: the lack of knowledge. The maintenance of equipment and laboratory facilities in good condition helps to prevent risks and improves efficiency. Sources of laboratory infections, biological and chemical laboratory hazards, as well as physical hazards such as fire and electricity are the main topics in the basic course. The use of protective clothing, personal hygiene, proper experimental operations and methods for the disposal of waste (sterilization, incineration or decontamination) are the main instructions given to the students before microorganisms risk group 1 or 2 are handled. Regardless of how well biosafety laboratory training is implemented, the health of the students depends mostly on their own behaviour. Since it is impossible to oversee everything a person does in a laboratory, besides providing direct control, education and motivation to perform the activities safely are also necessary. Training is a powerful influence for biosafety in the laboratory, just as it is in many other areas. Accident prevention depends basically on the willingness of the people to work safely. Since many hazardous conditions and unsafe acts cannot be anticipated; the training courses focus on stimulating the students to use their own common sense and discipline for their protection.
Environmental Microbiology

Students engaged in Environmental Biotechnology research and study need to be trained in safety procedures. Biotechnology is in itself a very wide area attracting students with various backgrounds to the Masters or Ph D. level courses and training. Though a large number had their first degrees as biologists or engineers many of them had never had proper training in microbiological procedures, even less in handling pathogens or prospective pathogenic materials. Students, researchers and personnel when doing biodiversity studies or when developing bioremediation technologies can be exposed to unknown or undescribed microorganisms that should be treated at least as belonging to the P2 group since it is even possible to isolate *Bacillus anthracis* from soil samples. As microbiology is an expensive subject on account of the funds needed for practice in laboratory courses, many universities have
diminished or suppressed laboratory practice in general microbiology thus depriving new students and researchers of the most basic techniques of handling microorganisms properly. In some courses, only P1 organisms are used in laboratory work, so methods to handle pathogens are not taught at all. In some cases, as chemical engineers, some had never had a microbiology course, so it is possible to see chemical engineers, in biotechnology degrees, cultivating P2 organisms without any particular safety precaution or proposing studies using P2 organisms without any idea as how to handle these microorganisms. As a matter of fact, though research with GMOs refers to the widely accepted NIH guidelines, there are no guidelines referring to laboratory practice with unknown microorganisms. Recently, a Society of General Microbiology of Argentina (SAMIG) has been created and these topics are high on the agenda. Derived from the safety guidelines for work places in general (Safety in the workplace) there should be a Biosafety Commission in every research institute or laboratory in universities and research centers. There is also another factor and that is, the compulsory insurance system for job related risks. Until last year, there was a cap to the amount of money to be paid as compensation in the case of death or permanent disability. This cap has been lifted and the victim or the victim’s family can sue to obtain a bigger payment. As a consequence, insurance companies now are making detailed risk assessments and the primes are higher. As most of the research facilities are very old, the authorities find themselves in the dilemma of fostering biosafety methods and the risk of taking the system to collapse because of the lack of funds to refurbish labs and research institutes.

The situation is similar in neighbouring countries. Medical bacteriology and the handling of medical specimens follows similar rules as in Argentina. However, though there has been a general acceptance of NIH guidelines for research and use of GMOs, very little has been done in general microbiology courses and in the precautions needed to work with environmental samples or soil samples.

**Accidents Reported**

In Argentina, reports of laboratory accidents and laboratory-associated infections are scarce. The National Human Retrovirus, Sexually Transmitted Infections and HIV Control Programme have reported seven cases of accidents caused by HIV from 1982 to 2001. A survey of three public hospitals in Buenos Aires City during the year 2000,
revealed that in one hospital, 10-20 per cent of accidents were due to sharp instruments, and that they occurred most frequently with the medical and nursing personnel. In another hospital, accidents of laboratory workers had diminished presumably because the use of gloves, mask and plastic tubes instead of glass tubes had been made compulsory. The third hospital had 38 accidents in the same year; 30 of these were puncture wounds or cuts whereas 8 were due to splashes. These accidents occurred with medical personnel (16), students (9), nurses (8), assistant nurse (3) and laboratory workers (2). The decrease in accidents with laboratory personnel is attributed to the training course, the compulsory Hepatitis B vaccination and the use of protective personnel equipment.

A high degree of precaution must always be taken with any contaminated sharp items such as needles, slides, capillary and scalpels. The risk of contracting an infection with HIV after a cut, skin puncture or blood splash has been estimated as 0.4 per cent. During 2003, 34 parenteral cases of exposure to blood or body fluid were documented by the Occupational Health Department from the Ministry of Health and Environment out of 1512 medical and nursing personnel. One accident in a hand was caused by a sharp instrument and 33 were due to inoculation with needles (30 affected the fingers and 3 the hands).

Figure 3: Fifty six accidents due to inoculation with needles occurred during 2004 among medical and nursing personnel
During 2004, from 110 registered accidents in the same population, 56 were due to inoculation with needles from which 64 per cent affected the fingers, 15 per cent the eyes, 13 per cent the legs, 6 per cent head and neck and 2 per cent arms (see Figure 3) but, the data about complications are not available. Resources such as gowns, gloves and disinfectants are now routinely available and needles and syringes are not washed by hand neither reused.

**Conclusion**

The most effective strategy for the prevention or minimization of laboratory-associated infections is to make certain that only reviewed procedures are consistently carried out. Workers must review protocols to assess whether the good laboratories practice are followed to prevent exposure of themselves, their colleagues and the environment. Unvaccinated personnel involved with handling blood, serum, and other body fluids are at increased risk of being infected with bacterial and viral agents through cuts and wounds resulting from use of needles, syringes, scalpels, surgical knives, drills, and the like. The concern brought about by the spread of AIDS, and the need to use safe methods for handling patients and specimens as a result gave a great push to improving the work places in public laboratories and in the education of the potentially exposed personnel. Such preventive and precautionary action immediately taken by the private sector laboratories has still to be taken seriously by university authorities.

An awareness of the potential infectivity of blood now exists as a result of the widespread transmission of documentation of human immunodeficiency virus infection (HIV) infection as an occupational threat or disease.

Legislation concerning biosafety provides for a practical approach to safety that provides protection against occupational infections and other blood-borne pathogens. However, since prevention strategies do not entirely eliminate the risk of accidental exposure current laboratory safety programmes incorporate a post-exposure evaluation. Microorganisms involved in respiratory infections are assessed in biological safety cabinets. Laboratory-acquired infections such as brucellosis have more often resulted from handling pathogens outside the protective environment of a biosafety cabinet. Furthermore, many of these laboratory acquired infections are not reported nor is data available.
Considerable information has been accumulated on the main routes of worker exposure. The diseases now being tackled are AIDS, Hepatitis B, new strains of hantavirus, re-emergent and multiple drug-resistant strains of *M. tuberculosis*. As a consequence of the threats of bioterrorism, biosafety guidelines now focus on the minimization and eradication of opportunities in the removal from laboratories of biological agents to harm, injure and terrorize people intentionally.

Safe working conditions are the responsibility of many disciplines but ultimately each individual is responsible for her/own safety.

Training in good laboratory practices emphasizes several aspects of biosafety that range from a change in work habits to the use of standardized protocols, that enhances motivation to work and act in a biosafe environment; and that minimizes opportunities for the spread of dangerous diseases.

Several national institutions in the health, food and bioindustrial sectors have contributed to the Argentina experience in enhancing biosafety through the introduction and strengthening of good laboratory practices. The provision of technical assistance, the exchange of information between biosafety network nodes, and the monitoring of research protocols and techniques by the national community of microbiologists and biotechnologists have enriched the evolution the Argentinean experience that is worth sharing with nearby countries within MERCOSUR framework.

This same experience could also be the basis for joint elaboration with other developing countries of the southern hemisphere in combating the hantavirus e.g. in Africa and SARS and avian flu in Asia.

**Endnotes**

5. INER E: Coni.2002.
Asian Biotechnology and Development Review

References


