



Development of Laboratory Biosafety Management: The Taiwan Experience

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Abstract

A stunning laboratory-acquired SARS case broke out in Singapore in September 2003 and, only a couple of months later, a case also took place in Taiwan. The single infection case was diagnosed and confirmed, but did not spread, thanks to the swift inspection and emergency management of Taiwan CDC in December 2003. The CDC is Taiwan's governing authority for prevention and control of communicable diseases, with full responsibility for management against severe biological hazards. Since this incident, we at Taiwan CDC have taken the opportunity to initiate an ongoing revision of the Communicable Disease Control Act and various regulations governing construction standards, occupational safety, fire security and environmental protection in Taiwan, in order to improve the standard requirements and mechanisms of supervising biological safety in laboratories. As a result, the level of biological safety of laboratories in Taiwan has been effectively enhanced through certain management measures of the government.

Through strict inspection of laboratory safety by CDC, along with education, promotion and practical training, all of Taiwan's laboratories for microorganism examinations and related research have made great progress in terms of safety inspection of facilities and equipment, and awareness of safety and personal protection by the operational personnel. Aspects relating to inspection quality and research accomplishments, the physical safety of the research personnel and environmental security have been addressed and constitute a very meaningful and prominent indicator in the course of establishing Taiwan's own laboratory management system concerning biological safety.

A National Biological Safety Committee was formed by relevant government institutions, in collaboration with several private organizations of biological safety for the purpose of policy integration, planning, promotion and implementation. Meanwhile, with complementary measures such as founding of a national information management system for laboratory microorganisms, establishing an accreditation system for labo-

ratory safety, and enhancement in R&D in technology concerning domestic safety equipment, it is expected that the management system of laboratory biological safety would be comprehensive and enable Taiwan to become a meaningful and contributing member towards global biological safety.

Foreword

In December 2003, a laboratory-acquired severe acute respiratory syndrome (SARS) case broke out in Taiwan following on the heels of the first reported laboratory associated incident in Singapore. The Center for Disease Control of Taiwan (Taiwan CDC) immediately assembled an expert team to investigate (WHO, 2003) and found out that a laboratory operator who did not comply with management procedures on accidental spillage caused this single incidence. Fortunately, the affected person did not infect any one else.

One of Taiwan CDC's predecessors, the National Institute of Preventive Medicine of Taiwan, obtained permission in writing from the United States CDC back in 1995 and translated their "Biosafety in Microbiological and Biomedical Laboratories, BMBL" (Third Edition) into Chinese, through which the concept of laboratory biological safety was introduced to Taiwan for the first time. Later, in 1999, our National Science Council established the Principles on Gene Recombination Experiments using guidelines set by the U.S. National Institute of Health as the primary reference, in order to provide protocols to laboratories for gene recombination (National Science Council, 1999). Each institution engaging in such research has to establish a Safety Committee on Biological Experiments to supervise, manage and examine safety concerns around the laboratory.

Similar to the organization of laboratory biosafety in developed countries in Europe and North America, our management of laboratory safety constitutes an area of occupational safety and health under the jurisdiction of the Council of Labor Affairs and other authorities regarding environmental protection and construction. The impact caused by Taiwan's laboratory-acquired case of SARS

in 2003 is significant. Taiwan's CDC is the primary government authority to control communicable diseases with the full responsibility of preventing severe biological hazards. Thus, based upon professional opinions on health, medicine and microorganisms, a reform of the Communicable Disease Control was set into motion. Also, with legislations concerning issues of construction standards, occupational safety, fire fighting and environmental protection, taking a responsibility for improving and monitoring laboratory biological safety at the national level is deemed necessary. It is hoped that certain measures, such as autonomous management of laboratories, periodical inspection by external experts, and education to promote biological safety, will be helpful towards the establishing of a biosafety culture.

Since the accidental laboratory infection at the end of 2003, Taiwan CDC has initiated and implemented the following strategies and measures:

To Facilitate International Exchanges

In January 2004, the World Health Organization (WHO) dispatched an expert team led by Dr. Antony

Della-Porta to Taiwan because of the SARS case (Figure 1). They visited five existing and new constructions of BSL-3 laboratories during their short stay. In addition to the advice given to those individual laboratories, four major measures in terms of general management of biological safety were suggested (WHO, 1993). Soon after, CDC invited two world-class experts in the field, Dr. Thomas Ksiazek from U.S. CDC and Dr. Kazuyoshi Sugiyama from National Institute of Infectious Diseases (NIID) of Japan, respectively, in March and November 2004, to give us a helping hand in inspecting current safety and management of equipment in laboratories of Biosafety Level 3 or above across Taiwan (Figure 2). CDC staff took notes on all drawbacks they found and suggestions they made (Taiwan Center for Disease Control Inspection Team, 2004) in order to assemble a set of guidelines for similar laboratories to incorporate. Also, Dr. Katsuaki Shinohara from NIID in Japan was invited to Taiwan in January 2005 to deliver a keynote speech on how to design and maintain the hardware facilities of BSL-3 laboratories to a group of engineers and laboratory operators. During the same trip, he visited eight newly con-

Figure 1

WHO expertise committee investigated BSL-3 virus laboratory of Taiwan CDC.



Figure 2

Taiwan CDC invited experts from USA CDC and Japan NIID to Taiwan to assist in appraising BSL-3 laboratories.



Figure 3 (right)

Expert of Japan NIID invited to deliver a speech and assist in inspecting BSL-3 laboratories.



structed BSL-3 laboratories and provided valuable suggestions on improving hardware effectiveness (Figure 3).

To Establish Regulations on BSL-3 Laboratory Biological Safety

In response to the future needs of research and to monitor emerging or reemerging infectious diseases such as SARS, health authorities, medical institutions, agricultural administrations, the academia, and biotechnology companies are gradually building up BSL-3 or ABSL-3 laboratories. Presumably, Taiwan will have 21 laboratories at BSL-3 level or above by the end of 2005 (Table 1).

To encourage those responsible for the design and construction of laboratories to follow official guidelines, CDC invited local experts and scholars in September 2003 to write up a set of Biosafety Level 3 Laboratory Safety Guidelines (draft) and published it on the Taiwan CDC global information web (Taiwan CDC web site) for any interested person to download and criticize for further revision until the first edition was officially finalized in September 2004. The guidelines include organization management of BSL-3 laboratories, safety design of facilities, equipment function, inspection, personnel education and training, and internal inspection. In the future, revision and publication of newer editions will be carried out on a periodic basis to comply with the latest international rules.

To Strengthen Biological Safety Consciousness

After Singapore had its laboratory-acquired SARS case in September 2003, Taiwan CDC saw the coming danger and did try to contain the risk. It held seminars in November on both function test of BSL-3 laboratories and safety guidelines of BSL-3 laboratories in an effort to remind participants, who were domestic laboratory operators, of safety control and proper handling of various pieces of equipment in BSL-3 laboratories.

After Taiwan had a laboratory-acquired case in December, CDC immediately gave an order to suspend all laboratories handling the SARS virus across the island, and launched a special safety and response training course using the real scenario to educate the operators of BSL-3 laboratories in order to enable them to acquire

practical experience. The trainees were asked to take an examination and only those who passed the test were awarded a certificate as officially qualified operators when the laboratory reopened for business.

Education and training at each laboratory level are aimed at the operation personnel, engineering and maintenance personnel, laboratory chiefs and biological safety officers to ensure their adequate knowledge about laboratory safety after 2005.

In addition, the CDC also did its best to enhance awareness of biological safety among staff of the examination divisions in medical institutions. All 517 medical institutions designated by the Bureau of National Health Insurance carried out a program of "boosting infection control." To those institutions which carried out regular education and training on biological safety for their new and old staff members and with sound onsite management of pathogenic microorganisms, the Bureau would award a bonus toward their insurance claims in an effort towards emphasizing biological protection and safety to the examination personnel within medical institutions and reducing the potential of laboratory associated infection.

Legislation

While Taiwan CDC amended the Communicable Disease Control Act in January 2004, the concept of biological safety and preservation was included in its Article 32. Based on the Act, the establishment of a set of affiliated rules, i.e., Regulations Governing the Management of Infectious Biological Materials and the Collection for Testing Specimens of the Patients of Communicable Diseases was authorized. The regulations have been on the draft board since 2004. At its draft stage, CDC thoroughly tested the related measures to ensure good feasibility and applicability. With final approval of the Department of Health in August 2005, all 19 articles would be implemented after six months of promulgation period.

Highlights of the regulations are as follows:

1. To establish a management committee of biological safety

The committee of biological safety must be mission oriented that includes (i) to monitor and supervise maintenance, preservation, exchange and usage of infectious

Table 1

Number of established laboratories and new constructions of BSL-3 or above in Taiwan.

Biosafety Level of Laboratories	Before 2003	After 2003	Sum	Total
BSL-4	1	0	1	21
BSL-3	3	15	18	
ABSL-3	0	2	2	

ABSL: Animal Biosafety Level

biological materials, which refer to risky microorganism groups of level two and above; (ii) to review biological safety level of a laboratory from time to time based on the infectious biological materials it deals with; (iii) to advise on handling infectious biological materials and on making improvements after drawbacks of laboratory biological safety are spotted by internal checks; (iv) to guide training for biological safety; (v) to review the plan in response to a biological safety emergency; (vi) to deal with, investigate, and report on accidents concerning biological safety; (vii) to assess laboratory inauguration and closure; and (viii) to appraise unsettled issues regarding biological safety. Through enforcing those missions of the biological safety committee of each unit, an ideal autonomous management will result.

2. Tightening up the qualification of laboratory workers

The regulation clearly stipulates that only those who have taken training from and passed the examination by the laboratory supervisor or senior technician are allowed to handle infectious biological materials in a laboratory operation. In addition, laboratory operators dealing with infectious biological materials of level three and above must take biological safety training duly certified by CDC before their laboratory operation proceeds. Through these stricter qualification measures, accidents due to lack of training could be avoided.

3. Making emergency plans to deal with biological hazards

Each and every unit must develop plans to follow in case of an emergency situation caused by biological hazards. It has to contain (i) an emergency response team with set missions; (ii) accident level certification and risk evaluation (iii) procedures for accident handling, reporting mechanisms, and alarm systems; (iv) storage and management of materials needed in case of emergency; (v) procedures of medical aid for emergency; (vi) standards for personal safety and protection of personnel in the response team; (vii) procedures and measures for urgent evacuation; (viii) governance of damaged areas with means of clearance, integration, and resumption after disaster; and (ix) accident drills and scenario exercises. With such sound emergency plans in place, the unit can expect its personnel to follow correct procedures in case an accident occurs and thus minimize the damage.

4. The regulation of risk levels, managing and reporting on biological hazards

On top of clearly defining the risk levels in its description, managing and reporting procedures on biological hazards have been officially enacted. Taiwan divides biological hazards into three levels depending on the locality where they take place, i.e., (i) within a preliminary or first level protection (such as biological safety cabinets); (ii) within a second level of protection (such as laboratory facilities); (iii) with doubt of spreading into the environment. Regulations for managing and reporting are listed

in Table 2.

5. Managing infectious biological materials

A set of specific regulations for managing infectious biological materials has been officially enacted. It consists of (i) storage sites of any infectious biological materials of level two and above should be put under the care and responsibility of a specific individual, with access control and inventories of level 2 and 3 risk agents; and (ii) use or exchange of any infectious biological materials of level three and above has to be reported to the central authorities in advance. Through strengthening security consciousness of infectious biological materials, we expect all highly infectious biological materials to be kept safely and securely.

6. The central authorities have the authority to order any facility to destroy certain assigned infectious biological materials singly or collectively within a time limit.

7. Regulations regarding import and export of infectious biological materials and testing specimens:

Any importation or exportation of infectious biological materials must apply for and obtain a letter of approval issued by the biological safety committee of the facility, which must then be sent to the central authorities for further approval.

8. Regulations for inspection of laboratories of biological safety level three and above, while they are in operation.

The central authorities can inspect those laboratories of level three or above at any time. Laboratories have a limited time to improve any shortcomings found during these inspections and the central authorities can shut down the operations of such laboratories if the required remedies are not completed within the prescribed time.

9. Inauguration guidelines for newly established biological safety laboratories, level three and above.

It is stipulated that any newly constructed biological safety laboratories of level three or above shall not commence operation prior to receiving approval from the unit's biological safety committee and the CDC. (Table 3)

10. Regulations with regard to reopening of laboratories engaging in biological medicine and microorganism research and having been previously closed for any violation.

Whenever the central authorities have serious safety doubts, they could ask all laboratories or certain ones to stop using specific infectious biological materials or suspend the laboratory operation entirely. Resumption is allowed only after safety is ensured. The inaugurating procedures are shown in Table 4.

11. Regulations with respect to transportation and collection of infectious biological materials and testing specimens from patients of communicable diseases.

In 1999, one of CDC's predecessors, the National Institute of Preventive Medicine, published a booklet written in Chinese called the Handbook of Specimens

Collection for Disease Prevention, which was offered to all medical institutions and health bureaus in Taiwan to follow. The booklet was updated and revised in 2003, and its title was changed to the Handbook for Collecting Specimens of Infectious Diseases. In addition to the original standard operation procedures for the collection of all kinds of specimens, the following were added to it: (i) regulations concerning personnel safety and protection; (ii) rules of personnel physical checkup; and (iii) regulations on the cleaning and sterilization of work environment. They are there to ensure safety in collection and transportation of communicable disease specimens.

To Establish an Interministerial Biological Safety Committee for Policy Synchronization

Biological safety laboratories of all levels are affiliated to or under the jurisdiction of different ministries. For the sake of consistency in policy, Taiwan CDC specifically invited experts, scholars and representatives from the Ministry of National Defense, Ministry of Education, Bureau of Standards, Metrology and Inspection under the Ministry of Economic Affairs, National Science

Council, Council of Agriculture, Environmental Protection Administration, and Council of Labor Affairs to found a permanent Biological Safety Committee in the Department of Health, under the Executive Yuan, in April 2004, which has convened regularly ever since. The Committee’s missions include: (1) to discuss and monitor management policies for biological safety at laboratories and workplaces; (2) to review and advise on management policies for biological materials; (3) to formulate and supervise the policies for transportation safety of biological materials; and (4) to communicate on the interministerial policies of biological safety, integration of resources and manpower and work sharing, as well as common problem solving. It is hoped these undertakings will establish horizontal channels of interconnection among domestic institutions and resolve conflicts of opinion.

To Plan and Organize Private Biological Safety Organizations

To assist the government in promoting policies and education on biological safety issues, biological safety associations have been established in the private sector in

Table 2

Regulations of risk evaluation, management and reporting of biological laboratory accidents in Taiwan

Risk Level	Incident Description	Management	Report
Risk Level 1	It occurs within protective equipments at laboratories, e.g., highly contagious specimens sprayed in biological safety cabinets during experimentation. The consequence does not endanger the lives of personnel immediately.	Handling following relevant hazard management procedures set forth in response plan to biologically threatening emergency.	Reporting to laboratory chiefs with records
Risk Level 2	It occurs outside protective equipments at laboratories, e.g., taking highly contagious specimens that cause spillage on the floor at laboratories; the consequence might endanger the lives of the personnel and contamination within laboratories.	Handling following relevant hazard management procedures set forth in response plan to biologically threatening emergency. If necessary, requesting assistance from relevant authorities is allowed.	Reporting to laboratory chiefs with records. Reporting to central authorities is required while the infection or contamination happens.
Risk Level 3	The spread happens outside laboratories. For instance, severe earthquake inactivates negative pressures at biological safety laboratories of level three. It might vitally endanger the lives of the personnel and contaminate the community and environment outside laboratories with hazards.	Handling following relevant hazard management procedures set forth in response plan to biologically threatening emergency. If necessary, the central authorities have to organize and lead other relevant units to manage the situation.	Reporting to laboratory chiefs with records. Reporting to central authorities is required at once.

Table 3

Inauguration procedures for newly established BSL-3 and above laboratories in Taiwan.

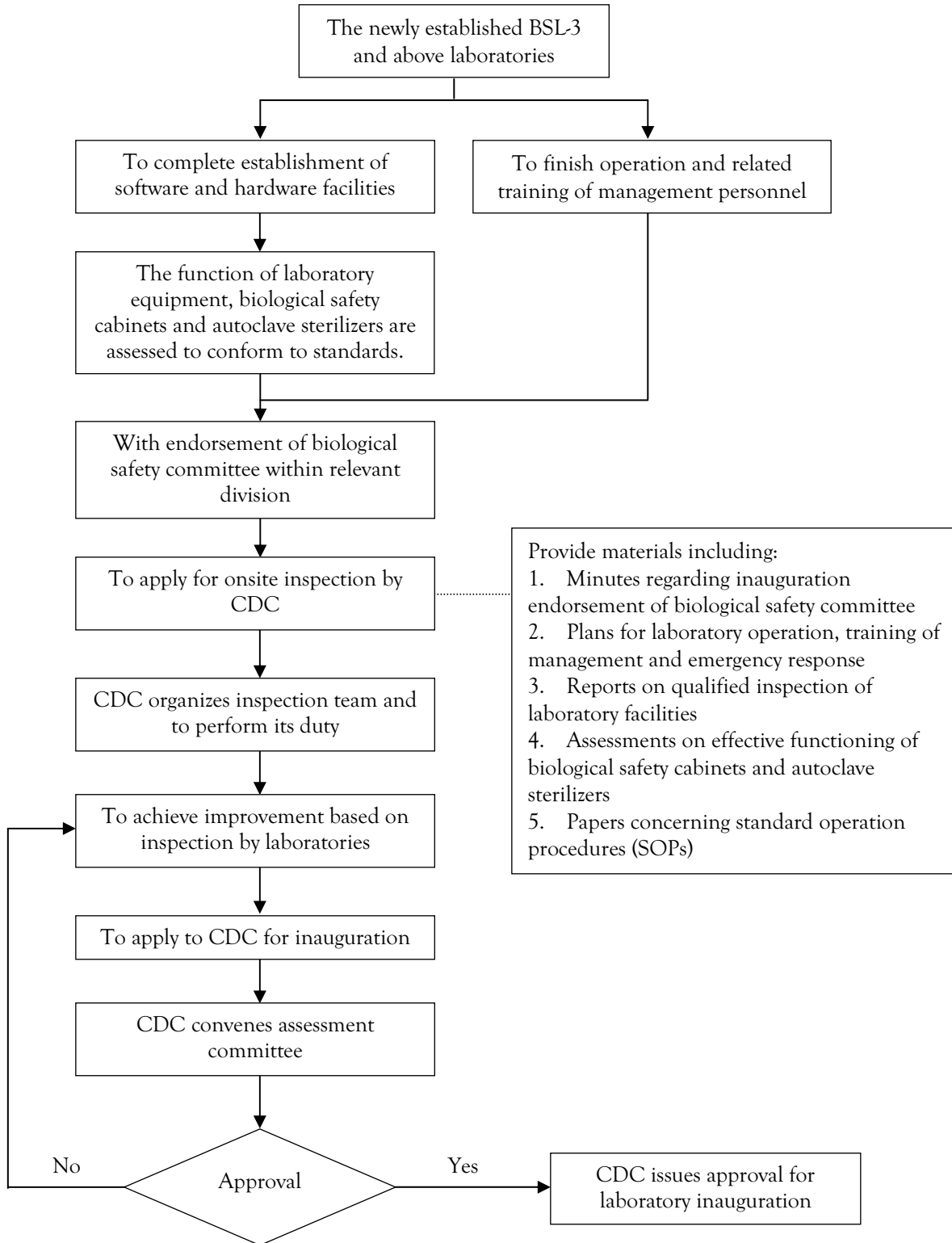
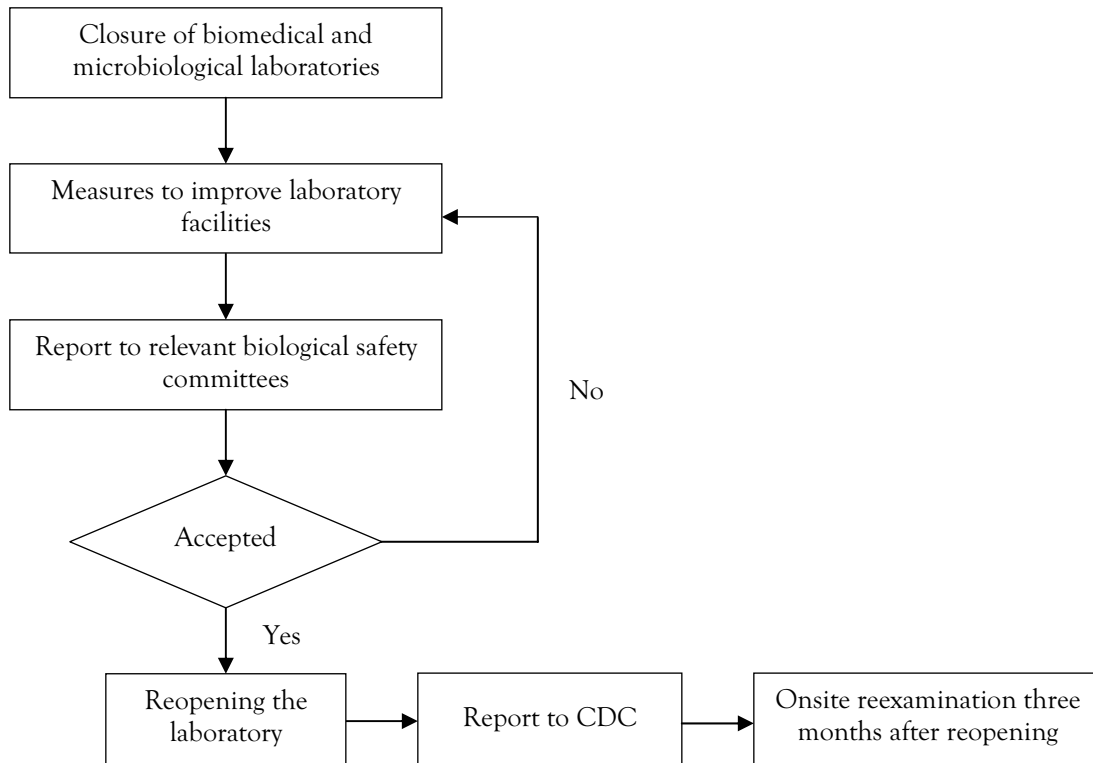


Table 4

Procedures on closure and reopening of biomedical and microbiological laboratories in Taiwan.



developed countries, such as the United States, Japan, and Canada. Taiwan CDC cooperated with the Industrial Technology Research Institute and the Institute of Occupational Safety & Health in early 2005 in a joint effort to materialize the setup of a private organization, the Taiwanese Biological Safety Association (TBSA). It is the founders' hope that TBSA would (1) assist the government to develop policies for biological safety and health; (2) promote education regarding biological safety; (3) enhance the quality of domestic biological safety research; and (4) seek and facilitate international collaborations and exchanges of information regarding biological safety issues. In the future, TBSA is expected to develop useful and specific biological safety knowledge necessary for the nation, to help develop technology concerning biological safety, and to upgrade protection equipment and facility technology.

With the endorsement of the American Biological Safety Association (ABSA) in August 2005, TBSA became an affiliate member of ABSA. Being a member of the global village and, in such an era of advanced technology, Taiwan CDC believes actively participating in relevant international organizations and seminars is essential to acquire the latest information concerning biological safety and security as well as biological terrorism from other countries. We anticipate future attendance at the annual

ABSA conference and active participation in education and training opportunities provided for members to keep us better informed on ongoing biological safety issues.

Prospects for the Future

1. To set up a national information management system for laboratory microorganisms

In order to effectively oversee the current situation of management of infectious biological materials by laboratories at each level, Taiwan CDC began to construct a national system of information management for laboratory microorganisms in 2005. Through the system, goals to be achieved are (i) to keep notice of all events of storage, usage, exchange, shipping in and shipping out of any infectious biological materials of risk level 2 and above; (ii) to take note of the current situation of all domestic biological safety laboratories of level 3 and above in terms of their organization, personnel, and facilities; (iii) to provide Taiwan CDC with background information of those laboratories before inspection; and (iv) to bring about a nationwide operation platform for autonomous management of laboratories at each level.

2. To formulate a suitable accreditation system for institutions engaging in inspection of BSL-3 laboratory safety

So far Taiwan has no system of accreditation regarding inspection institutions of BSL-3 laboratory safety. Therefore, validity and credibility of inspection outcomes (such as laboratory facilities and security of biological safety cabinets) made by inspection institutions and companies cannot be officially recognized. Taiwan CDC plans to entrust the job to some widely recognized institutions of accreditation, such as the Taiwan Accreditation Foundation. Based on the international standard ISO/IEC 17020 (CNS 14725), a system of accreditation is to be established to enhance the technical competence and outcome quality of inspection institutions in order to achieve the goal of safety upkeep of laboratory equipment each year.

3. To upgrade the technical level of locally produced laboratory safety facilities and equipment

All BSL-3/4 laboratories that operated in Taiwan before 2003 were foreign made. Starting from 2004, almost all BSL-3 laboratories have been designed and built by domestic companies under the watchful eyes of experienced foreign advisors. With such a setup, we expect those domestic construction companies would gain the necessary expertise to become independent in the near future. Moreover, the quality of biological safety cabinets produced domestically is quite inconsistent due to lack of national standards. Therefore, in order to enhance the quality of biological safety cabinets made in Taiwan, the Institute of Occupational Safety & Health, Council of Labor Affairs and the Industrial Technology Research Institute will strive to institute some needed national standards and product specifications.

Conclusions

The laboratory-acquired case of SARS in Taiwan sent a shockwave through the nation. However, this incident was a crucial turning point. It led to the seeking and adoption of advice from both national and international experts and scholars and, therefore, acquired invaluable learning experience in biological safety management. This has facilitated the formulation of legislations on biological safety management and the implementation of related measures. Furthermore, founding a central interministerial Biological Safety Committee has helped develop effective horizontal channels of communication within the government. As a result, the undesirable egoism among government authorities could be minimized when promoting policies and regulations concerning biological

safety. Furthermore, with the cooperation of private technical institutions and R&D institutes, a biological safety association has been formed to provide a platform of information exchange between industry, government and academia in the collective efforts to establish a management system of biological safety in Taiwan. It is expected that technical quality within biological safety industries would be enhanced and the personnel health and environmental security could be ensured. The importance of biological safety is no longer ignored with collective change. At the end, contributions to the global vision of biological safety would be made with active participation in international affairs of biological safety.

Acknowledgements

We are deeply indebted to our former CDC Director, Professor Ih-Jen Su (present Director of the Clinical Investigation of National Health Research Institutes) for his generous support and to Taiwan CDC, which regards the establishment and maintenance of a management system of laboratory biological safety as one of its major policies. Besides, the efforts and contributions of the participating ranks and files within CDC, as well as outside experts and scholars, are highly appreciated.

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