Taiwan Epidemiology Bulletin

October 18 , 2011/ Vol.27 / No.20

# Outbreak Investigation Express

## Investigation on the First Local Japanese Encephalitis Confirmed Case in Taiwan in June, 2011

Hsin-Fan Chien, Shu-Hua Huang, Chi-Chuan Huang, Sheng-Tang Wei, Li-Jen Lin

Fifth Branch, Centers for Diseases Control, Taiwan

The Taiwan Epidemiology Bulletin series of publications is published by Centers for Disease Control, Department of Health, Taiwan (R.O.C.) since Dec 15, 1984.
**Publisher :** Feng-Yee Chang
**Editor-in-Chief :** Yi-Chun Wu
**Executive Editor :** Li-Gin Wu, Hsiu-Lan Liu
**Telephone No :** (02) 2395-9825
**Address :** No.6, Linshen S. Road, Taipei, Taiwan 100 (R.O.C.)
**Website :** http://teb.cdc.gov.tw/
**Suggested Citation** :
[Author].[Article title].Taiwan Epidemiol Bull 2011;27:[inclusive page numbers].

**Abstract**

One suspected Japanese encephalitis case was reported at a local hospital in Kaohsiung City on June 8th, 2011, a 63 years-old housewife who lived in Hunei District, Kaohsiung City. The illness started on June 3rd, showing symptoms of fever, headache, neck stiffness, and coma. She was then admitted to the hospital on June 7th. Because the case conformed to the Japanese encephalitis reporting criteria, it was reported, and specimen collection was performed on June 7th. The CDC confirmed the case on June 13th: it was the first local Japanese encephalitis case in Taiwan this year. The patient with a history of diabetes mellitus and hypertension lived in a townhouse with three stories. There's a dovecote on the top of a neighboring house, and also a pigsty about 600 meters away, with emitted waste water from the pigsty silting in the surrounding forest area. Right on the day the case was confirmed, the health units implemented prevention measures including reinforcing health education and advocacy to the local people, visiting hospitals and clinics, urging children of the right age to have Japanese encephalitis inoculations, and hanging mosquito lamps over high risk areas. Till June 30th, the patient of the case was conscious, but still had poor concentration, speech impediment, and dystonia in need of improvement. The district was monitored till July 3rd (double of the latent period of the disease,) and no new case was discovered afterwards.

**Keywords:** Japanese encephalitis, Culex tritaeniorhynchus

**INSIDE**

**Original Article**

# A Norovirus-associated Gastroenteritis Outbreak in a school in Yilan County, 2010

Ming-Chih Liu[1],Dah-Shyong Jiang[1]
Yi-Ting Shen[1],Wan-Ching Chen[2]
Hsuan-Chih Lin[2],Wang-Chin Cheng[3]

1. Field Epidemiology Training Program, Centers for Disease Control, Taiwan
2. First Branch, Centers for Disease Control, Taiwan
3. Sixth Branch, Centers for Disease Control, Taiwan

**Abstract**

In September 2010, a gastroenteritis outbreak in School X was reported to Taiwan Centers for Diseases Control, involving 425 of the 2,199 students (attack rate = 20.1%). The most common symptoms were diarrhea (90.8%), abdominal pain (61.9%), and tenesmus (23.5%). Some patients had vomiting (8.9%). The average duration of illness was 4.3 days. Among those who had diarrhea, 72.9% had watery diarrhea and more than 60% had stool passage twice per day at least. Among those who had symptoms, 47.9% had sought medical consultation and 0.6% had been hospitalized. Stool specimens of 1 student and 2 restaurant workers were positive for norovirus but there was no pathogens detected in the water samples. Because of the two-peak appearance of the epidemic curve and the scattering of patients in different classes, the outbreak could be resulted from a combination of common-source exposure and human-to-human transmission. Risk factors could not be identified, but the number of patients ceased increasing after implementation of aggressive control measures. Norovirus is highly contagious in populous institutions and schools. A comprehensive surveillance and reporting system and early intervention might be helpful in controlling outbreaks, but environmental sanitation and hand hygiene are of fundamental importance.

**Keywords:** norovirus, outbreak, human-to-human transmission

**Background**

On September 7, 2010, the 1st branch of Taiwan Centers for Diseases Control (Taiwan CDC) received a notification from School X in Yilan County, reporting that about 40 students presented with symptoms including diarrhea and abdominal pain since September 6. Because these patients not only clustered temporally and geographically, the number had also surpassed the baseline daily absenteeism of 7 to 8 students, an outbreak was highly suspected. The number of patients gradually increased and a food-borne disease could not be ruled out, so an outbreak investigation was soon conducted by the First Branch and Field Epidemiology Training Program (FETP) of Taiwan CDC, and the Public Health Bureau of Yilan County on September 9. Reexamination was done on September 13.

**Investigation Purposes and Methods**

The purpose of this investigation was to evaluate the extent of this outbreak, to find out the pathogen, and to assess the effects of control and preventive measures. Field investigation included an assessment of the school environment, interviews with school administrators and students. Questionnaires were administered to all students and the results were analyzed statistically. Anal swabs and stool specimens were collected from symptomatic students and sent for bacterial culture (including *cholera, shigellae, enterohemorrhagic E. coli, salmonella, and vibrio*) and viral detection /isolation (including *rotavirus* and *norovirus*). Ground water was sampled for detection of *shigellae* and norovirus. The residual chloride level of tap water was also tested.

**Questionnaire**

Questionnaires were administered to all students to collect data on demographic characteristics, clinical symptoms and medical consultations, history of food intake, and personal hygiene. A case patient was defined as a person with diarrhea more than twice in a day, or had at least two of the following gastroenteritis symptoms, including abdominal pain, tenesmus, nausea, and vomiting. Patients with respiratory symptoms were excluded. Teachers were asked to help us distribute and retrieve the questionnaires. A retrospective cohort study was used to evaluate the risks of consumed food and water. Epi-Info was used to do statistic analysis.

**Results**

There were 1,459 junior high school students, 740 senior high school students, 167 teachers or administrators, and 19 restaurant workers, indicating a total number of 2,385 people in this school. Ninety percent of the students lived on campus and went home on weekends. Based on their grades, boarding students left the school either on Friday afternoon or on Saturday noon. The dormitory was separated into 3 buildings and each room could accommodate 8 students. Boarding students were required to study in the classrooms until 10 to 11 pm every night. Air conditioners were installed in all classrooms and dormitory rooms. There was no group activity held between the beginning of the fall semester on August 30 and the beginning of this outbreak. Tap water was used for drinking and cooking while ground water was used for other daily routines. The distances between ground water well and septic tank and sewer were more than 15 meters. Different from other schools, there was no hand-washing facility outside each classroom. Students who would like to wash their hands had to go to the toilets at both ends of the corridor. The school food court was a cafeteria with hand-washing facilities and soap at the entrance. Roommates of the same dorm room also shared a same restaurant table. Restaurant workers were required to wear masks while working. Because the school located at remote area, there was no restaurant nearby. In addition to the cafeteria, students could buy foods or drinks only in a convenience store.

Questionnaires were administered to 2,199 students and 2,113 were retrieved. The response rate was 96.1%. A total number of 425 students met the case definition and the attack rate was 20.1%. Case patients were found in all 50 classes but one. Among these patients, 265 were males and 160 were females. The male to female ratio was 1.66. Common symptoms included abdominal diarrhea (90.8%), abdominal pain (61.9%), and tenesmus (23.5%). The average duration of illness was 4.3 days. Among those who had diarrhea, 72.9% had watery stool and more than 60% had defecation twice to thrice per day. Other symptoms included headache (16.7%), dizziness (14.4%), decreased appetite (11.9%), fever or chills (10.1%), nausea (9.9%), and vomiting (8.9%). Among those who had symptoms, 47.9% had sought medical consultations and 0.6% had been hospitalized. The proportion of students claiming that they had washed their hands before dining was not statistically different between case patients and non-case students (71.5% versus 73.6%). The proportion of hand-washers who used soap was 41.6% in case patients and 43.7% in non-case students; the different was not significant either. The proportion of students who washed their hands after using toilets was 97.6% in both groups. Compared the personal hygiene between case patients and non-case students using Chi-square test, the differences were not statistically significant. The p-value of unconsciously touching the mouth or nose was 0.06, with a relative risk of 1.04 (95% confidence interval: 0.999~1.09). Among the 425 respondents, 379 could recall the date of onset. The daily number of patient was shown in an epidemic curve (Figure). For those who had onset before September 12, the data was collected via questionnaire (yellow bars); for those who ha onset after September 13, the data was collected by the school administrators (green bars). The result of the analysis on the risks associated with personal hygiene was illustrated in Table.

**Table Results of analysis of the risks associated with personal hygiene**

| Risk Factors | | Case patients | Non-case students | Relative Risk (95% Confidence Intervals) |
|---|---|---|---|---|
| Unconsciously touching the mouth or nose | Yes | 306 | 1136 | 1.04 (0.0999-1.09) |
| | No | 119 | 552 | |
| Usually wash hands before dining | Yes | 304 | 1243 | 0.98 (0.93-1.03) |
| | No | 121 | 445 | |
| Usually wash hands after using toilets | Yes | 415 | 1648 | 1.00 (0.87-1.15) |
| | No | 10 | 40 | |
| Usually use soap to wash hands | Yes | 177 | 738 | 0.98 (0.94-1.03) |
| | No | 248 | 950 | |
| Brush your teeth almost everyday | Yes | 417 | 1650 | 1.03 (0.90-1.18) |
| | No | 8 | 38 | |
| Take a bath almost everyday | Yes | 417 | 1661 | 0.97 (0.80-1.16) |
| | No | 8 | 27 | |
| Drink water from drinking fountains | Yes | 398 | 1574 | 1.01 (0.93-1.10) |
| | No | 27 | 114 | |
| Drink water from wash basin | Yes | 3 | 18 | 0.93 (0.78-1.11) |
| | No | 422 | 1670 | |
| Drink bottle water | Yes | 124 | 508 | 0.99 (0.95-1.04) |
| | No | 301 | 1180 | |

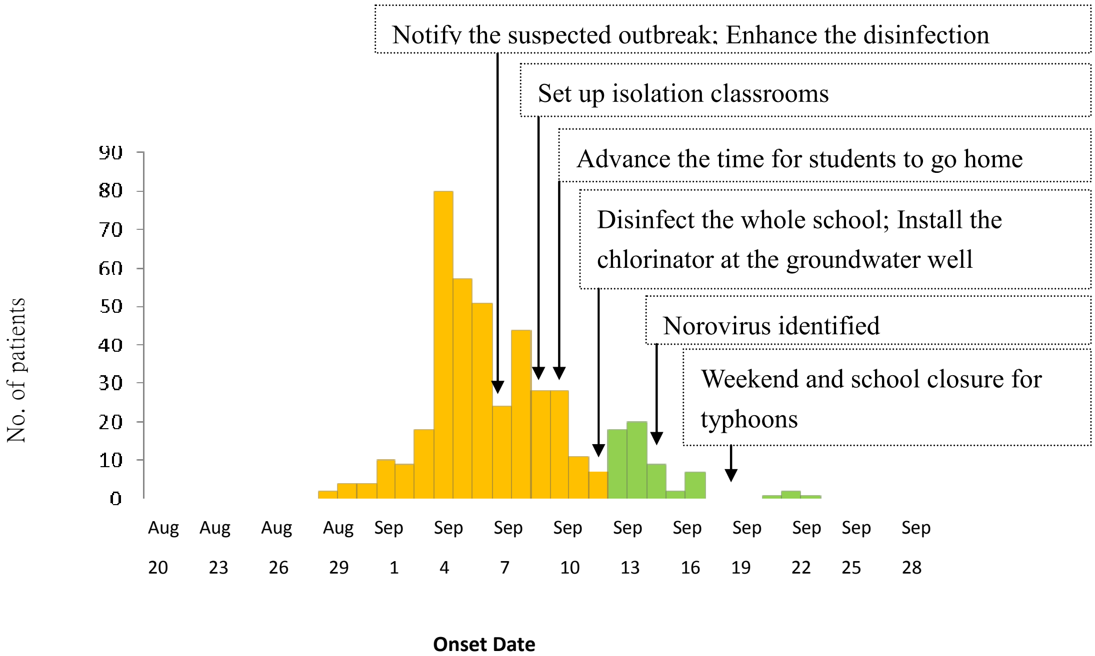



**Figure Daily number of patients in School X. (n=437)**

Note:For those who had onset before September 12, the data was collected via questionnaire (yellow bars); for those who had onset after September 13, the data was collected by the school administrators (green bars)

About the laboratory examinations, 5 fecal specimens and 11 anal swabs were collected; one of them was positive for norovirus. Among the restaurant workers, 2 fecal specimens were positive for norovirus; one of them came from someone who once had mild symptoms while the other was from an asymptomatic employee. There was no *shigellae* or norovirus identified in groundwater. Although *E. coli* could be found in the groundwater, the amount was within acceptable range of tap water. The residual chloride level of the tap water in the kitchen was 0.48-0.6, which was also within the acceptable range of 0.2-1.5μg/L.

As for the control and preventive measures, the school authority had helped the students to seek medical consultations and had encouraged the symptomatic students to go home. Those who were not able to go home were isolated in designated classrooms. Air conditioners were turned off to avoid transmission via door knobs. Students were also asked to wear masks because some had upper respiratory infections. In response to this outbreak, the school authorities hired a cleaning company to do environment sweep, which used to be managed by students. Generalized disinfection was done on September 6, September 7, and September 12. Door knobs, desks, chairs, and stair handles were cleaned by bleach water. The school shuttles were required to be disinfected immediately after transporting a sick student. Education about norovirus was done before the laboratory results were available. To eliminate the virus in the environments, bleach water with a higher concentration was recommended. Antiseptic containing phenol should be equipped in the toilets and students were required to wash their hands with soaps before meals and after using toilets. To prevent transmission of other gastroenteritis pathogens, chlorinators were also recommended to be set at the groundwater pipes. One week after notification of this outbreak, norovirus was identified while the number of cases has become less than the average absenteeism in the past. There was no new epidemics observed, so the outbreak formally ceased on September 24.

**Discussion**

During outbreaks, the pattern of epidemic curve could help us figure out the pathogens and transmission mode. In the case of prolonged but intermittent exposure to a common pathogen, several irregular peaks could be observed; while a plateau occurred in a continuous exposure. In outbreaks caused by point source exposure, there would be a sharp rise immediately followed by a decline. Multiple waves could be observed with progressively taller peaks and similar intervals in-between in outbreaks which are spread from person to person [1]. Because of the initial peak identified on September 4, a food-poisoning event with point source exposure was suspected (Figure 1). As the number of new cases increased in the following 2 weeks, the epidemic curve turned out to be different from anyone of the typical patterns in the literature. Food poisoning became unlikely with such a prolonged course, while the gradual declining peaks were not compatible with the pattern of person-to-person transmissions. More information would be necessary to evaluate the mode of transmission in this outbreak.

Human specimens collected in this outbreak were positive for norovirus, but the most common symptom among symptomatic students was diarrhea, which is different from the past notion that vomiting should have a higher proportion. In recent literature, the major symptoms in norovirus infection were found to be quite different in patients below and beyond the age of 16. More than 90% patients had nausea, but the proportion of patients with diarrhea was significantly higher than that of nausea in those older than 16-years-old (71.5% versus 64.1%). On the other hand, the proportion of patients with nausea was significantly higher than that of diarrhea in those younger than 16-years-old (80% versus 52%) [2]. Therefore, clinical presentations of the same virus infection still varied. In Taiwan, norovirus is the pathogen in 72% of the gastroenteritis outbreaks. Common symptoms included diarrhea (83.9%), vomiting (36.0%), fever (14.9%), abdominal pain (8.1%) and nausea (3.0%) [3]. Although the attack rate of this outbreak was 20.1% according to our investigation, the extent could be larger because of the possible asymptomatic infections.

Norovirus could be transmitted from person to person, via food, water, contact with contaminated environmental surfaces, or inhalation of the droplets of vomitus [4-7]. In food poisoning, the number of patients should stop increasing within 3 days, which was not the case in this outbreak. So food poisoning was less likely. Considering the water used in this school, although ground water without chlorination was used to wash and clean, the distance between the well and septic tank was adequate and the well was appropriately covered. Norovirus was not detectable in groundwater. The drinking water was tap water and the level of residual chloride level was conforming to standards. About students' drinking habits, there was no significant difference between case patients and non-case students. An outbreak caused by contaminated water could be excluded. Two restaurant workers were positive for norovirus; one had onset of symptoms on September 4, while the other was asymptomatic. Because the onset date of symptomatic worker was the same as that of most sick students, he was less likely to be the source of the first wave in this outbreak. In contrary, the asymptomatic restaurant worker was not identified as a carrier or suspended from work until the fecal specimen was examined; the asymptomatic carrier could be the source of this outbreak and might lead to propagation of this epidemic. Because all students stayed in the classrooms and used air conditioners for more than 12 hours daily, and 90% of the students lived in the dormitories, they had frequent and close contacts. Despite most students claimed that they did wash their hands before meals and after using toilets, only 40% use soaps. Besides, there were no hand-washing facilities outside the classrooms. More than 2,000 people would have to wash their hands before meals using less than 10 wash basins outside the school cafeteria. During field investigation, less than half of the students were observed to wash their hands correctly using soaps; most of them only used water and washed for seconds. Considering the close and frequent contacts, as well as poor personal hygiene, an outbreak caused by person-to-person transmissions was most likely. However, the analysis on personal hygiene and hand-washing habits did not reveal any significant differences between case patients and non-case students, indicating that poor hand-washing habits did not result in an increased relative risk of infection. Unconsciously touching the mouth or nose was one of the indicators of poor personal hygiene, the p-value was 0.06 and the relative risk was 1.04. Although not statistically significant, norovirus transmitted by this behavior from contaminated environmental surfaces was possible.

In gastroenteritis outbreaks, it takes time to confirm the pathogen. New and effective laboratory examinations have been published in recent years, one of them could detect norovirus within 15 minutes using a special reagent, with a sensitivity of 83% and specificity of 100% [8]. Because there was no false positivity or cross-reactivity with other viruses that frequently cause human gastroenteritis such as rotavirus, astrovirus, sapovirus, or adenovirus, it offered good potential for further research. Currently, the application was limited because it only detected GII genogroup. Vaccination was also a field with excellent potential. Chimpanzees were found to have similar immune responses as humans after acquisition of norovirus infection, and vaccines made by virion-like particle inoculated intra-muscularly could lead to sufficient protection. This research could be a good reference of human norovirus vaccine [9].

Norovirus is highly contagious; a very small amount of virus could cause disease. Higher concentration of bleach water (1,000 ppm for environment and 5,000 ppm for surfaces contaminated by body fluids or blood) was required to eliminate norovirus, compared with other pathogens that cause gastroenteritis [10]. Alcohol can only destroy viruses with envelopes. Since norovirus do not have envelopes, alcohol should not be used to disinfect. Norovirus plays an important role in outbreaks worldwide, and experts provided some recommendations for its infection control [11-12]. First, contact isolation can prevent human-to-human transmission. Second, wash hand with soap for at least 20 seconds after contacting with patients or contaminated surface. If the cook was infected by norovirus, food-handling should be stopped immediately and restart 48 to 72 hours after recovery. In addition, norovirus can not be reproduced in food, so cooking thoroughly can prevent its spreading. If the outbreak persisted continuously, temporary closure of the institution is one of the preventive measures. Norovirus can spread via contaminated water [13-15], which is preventable by using bottle water or boiled water. South Korea researchers surveyed their groundwater and found norovirus in water with proportion of 21.7% in summer and 17.3% in winter [16]. Water quality surveillance may contribute to prevent norovirus infection. If cost-effectiveness was concerned, hand hygiene and disinfection are the best ways for infection control [17].

In this outbreak, we learned that aggressive control and preventive measures are effective even before the identification of the risk factors and pathogens.

## Conclusion

Gastroenteritis outbreaks often occur in populous institutions and schools, and norovirus is the most common pathogen which can be easily transmitted person-to-person and lead to propagation of the epidemic. Major symptoms are different in patients with different demographics. Implementation of surveillance and early intervention can interrupt the transmissions. To prevent outbreaks, hand hygiene and environmental cleanliness are of greater importance.

## Acknowledgement

We appreciate the 1st branch, the Research and Diagnostic Center of Taiwan CDC, as well as Yilan County Public Health Bureau. We also thank the medical officers (Dr. Song-En Huang, Dr. Tsung-Wen Kuo, Dr. Wan-Chin Chen, Dr. Huai-Te Tsai, Dr. Chia-Ping Su, and Dr. Yu-San Chien) for assisting us to analyze the collected data.

## References

1. Torok M. Focus on Field Epidemiology, Volume 1, Issue 5: Epidemic Curves Ahead. North Carolina Center for Public Health Preparedness. Available at: http://cphp.sph.unc.edu/focus/vol1/issue5/1-5EpiCurves_issue.pdf
2. Götz H, Ekdahl K, Lindbäck J, et al. Clinical Spectrum and Transmission Characteristics of Infection with Norwalk-Like Virus: Findings from a Large Community Outbreak in Sweden. Clin Infect Dis 2001;33(5):622-8.
3. Lin CH. Analysis of surveillance data of diarrhea cluster events between 2005 and 2006 in Taiwan. Taiwan Epidemiology Bulletin 2007;7:23-31.
4. Koopmans M, Vennema H, Heersma H, et al. Early identification of common-source foodborn virus

outbreaks in Europe. Emerg Infect Dis 2003;9(9):1136-42.

5. Marks PJ, Vipond IB, Carlisle D, et al. Evidence for airborne transmission of Norwalk-like virus (NLV) in a hotel restaurant. Epidemiol Infect 2000;124(3):481-7.
6. Marks PJ, Vipond IB, Regan FM, et al. A school outbreak, of Norwalk-like virus: evidence for airborne transmission. Epidemio Infect 2003;131(1):727-36.
7. Koh SJ, Cho HG, Kim BH. An outbreak of gastroenteritis caused by norovirus-contaminated groundwater at a waterpark in Korea. J Korean Med Sci 2011;26(1):28-32.
8. Bruggink LD, Witlox KJ, Sameer R, et al. Evaluation of the RIDA®QUICK immunochromatographic norovirus detection assay using specimens from Australian gastroenteritis incidents. J Virol Methods 2011;173(1):121-6.
9. Bok K, Parra GI, Mitra T, et al. Chimpanzees as an animal model for human norovirus infection and vaccine development, Proc Natl Acad Sci U S A. 2011;108(1):325-30.
10. Taiwan Centers for Disease Control. Norovirus infection control guideline. 2007. Available at http://www.cdc.gov.tw/public/Data/812116593971.pdf.
11. Thornton AC, Jennings-Conklin KS, McCormick MI. Agents in outbreaks of acute gastroenterolitis, Disaster Manag Response 2004; 2(1): 4-9.
12. Patel MM, Hall AJ, Vinjé J, et al. Noroviruses: a comprehensive review. J Clin Virol 2009;44(1):1-8.
13. Kim SH, Cheon DS, Kim JH, et al. Outbreaks of gastroenteritis that occurred during school excursions in Korea were associated with several waterborne strains of norovirus. J Clin Microbiol 2005; 43(9):4836-9.
14. Parshionikar SU, Willian-True S, Fout GS, et al. Waterborne outbreak of gastroenteritis associated with a norovirus. Appl Environ Microbiol 2003; 69(9): 5263-8.
15. ter Waarbeek HL, Dukers-Muijrers NH, Vennema H, et al. Waterborne gastroenteritis outbreak at a scouting camp caused by two norovirus genogroups: GI and GII. J Clin Virol. 2010 Mar;47(3):268-72.
16. Lee SG, Jheong WH, Suh CI, et al. Nationwide groundwater surveillance of noroviruses in South Korea, 2008. Appl Environ Microbiol 2011;77(4):1466-74.
17. Lee BY, Wettstein ZS, McGlone SM, et al. Economic value of norovirus outbreak control measures in healthcare settings. Clin Microbiol Infect 2010;17(4):640-6.

## Biosafety and Biosecurity

# The Commissioning Process and Activation for New Laboratories above Biosafety Level 3

Wei-Shi Tsai, Wen-Chao Wu, Jer-Jea Yan

Fifth Division, Centers for Disease Control, Taiwan

There were 3 laboratories above biosafety level 3 (BSL-3) in Taiwan when the global severe acute respiratory syndrome (SARS) epidemic broke out in 2003. In order to respond to the next wave of SARS epidemic and other emerging and re-emerging infectious diseases, domestic testing or research organizations built BSL-3 laboratories gradually. Also, because the laboratory infection of SARS occurred at that time, the issue of biosafety management for the laboratories with high containment levels has begun to be taken seriously. Besides compiling the "Safety guidelines for biosafety level 3 laboratories" (Revision 2.0 has been accomplished in 2011) [1], the Centers for Disease Control, Taiwan (Taiwan CDC) set "The commissioning process and activation for new laboratories above BSL-3" [3] based on the Paragraph 2, Article 11 of "Regulations governing the infectious biomaterials and specimens collection from patients of communicable diseases" [2] that states "The newly established laboratories above BSL-3 should obtain approval from the Institutional Biosafety Committee before operation and should report to the central competent authority for records".

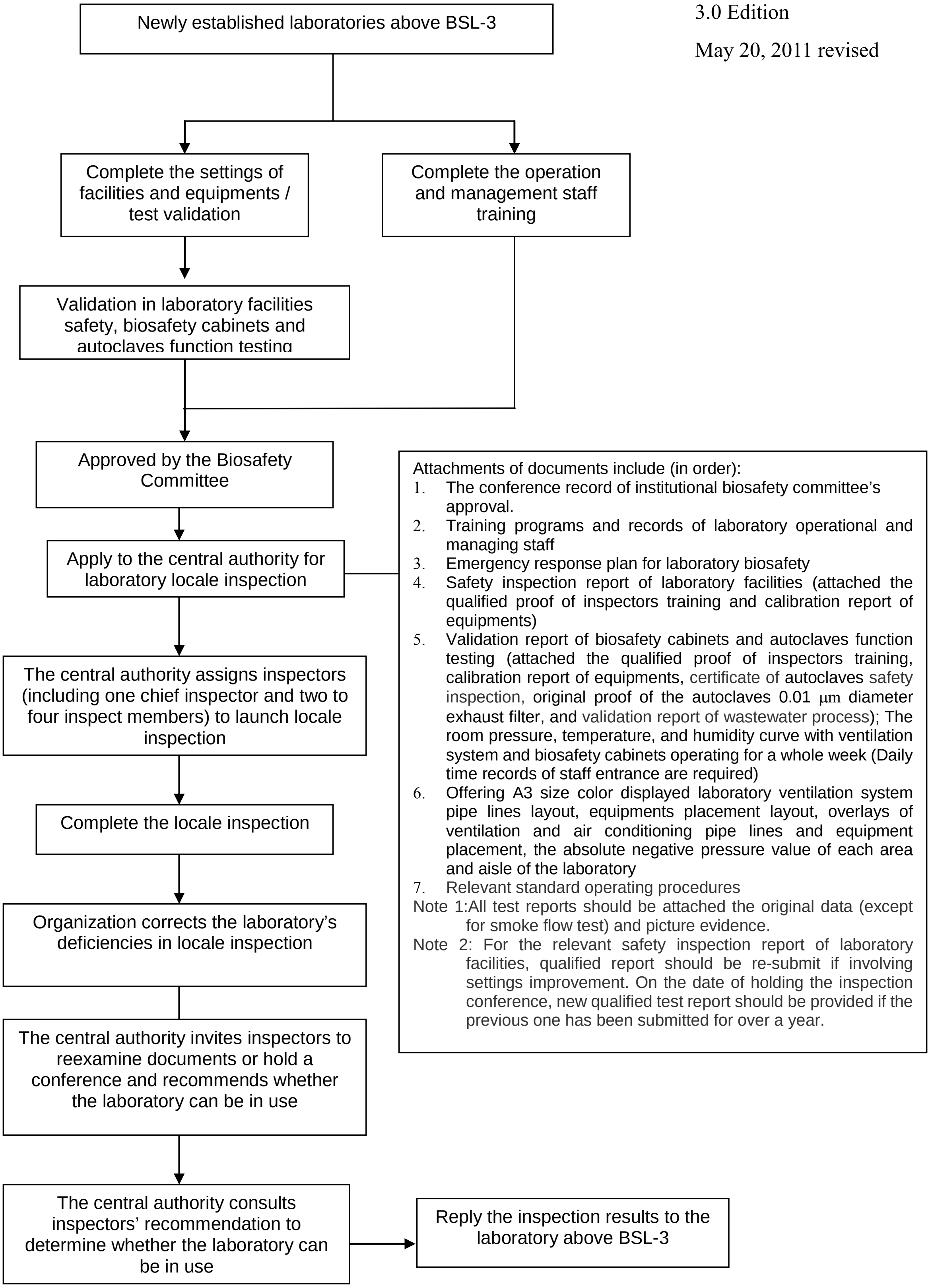
Taiwan currently enables the established laboratories above BSL-3 by approving ex post facto. Newly established laboratories whenever completed the relevant settings of facilities and equipments, and tested by the security validation, also approved by the Biosafety Committee, can follow the commissioning process (Table ) to apply for an activation approval from Taiwan CDC by submitting the documents and test reports including laboratories' management practices, moving direction design, standard operating procedures, and equipments and ventilation/air conditioning design. After receiving the application documents, Taiwan CDC will assign three or more experts in the biosafety field as inspectors to review the submitted documents and inspect on-the-spot, and then will request the applicants to improve and reply for the deficiencies. When inspectors reconfirm the applicants' correction reports, Taiwan CDC will hold a "commissioning inspection conference for newly established laboratories above BSL-3 applications," to review the applicants' presentation and inspectors opinions to determine the laboratories' occupancy.

To help applicants avoiding incomplete documents that lead to delay the activation, the currently practical problems of certifying process are listed as follows. (1) The improvement period varies. Recently, some applicants delay the improvement period in laboratory deficiencies; consequently, the earlier laboratory test results became overdue for more than a year and hence cannot reflect the real conditions, making time consuming and money expending. (2) The revised "Safety guidelines for BSL-3" (2.0 edition) has clearly stated that the continuous operation period of ventilation system and biosafety cabinets been modified from two weeks to one week. The room pressure, temperature, and humidity curve (with daily time records of staff entrance during operation are required) should be marked at the significant change sites for inspectors to make judgment. (3) The applicants submitted the unclear or incomplete information caused

**Table Commissioning process for new laboratories**

3.0 Edition

May 20, 2011 revised



replenishment although the laboratory blueprints have been well-defined in forms. (4) To facilitate review, some of the test report supporting information (such as fumigation validation by bio-indicator color change) should be presented in colored photographs but not in black-and-white photographs or copies.

To date, 19 BSL-3 laboratories and a BSL-4 laboratory have completed the commissioning applications in Taiwan. For the already activated laboratories above BSL-3, organizations should implement self-management, and Taiwan CDC will also arrange regular check to maintain biosafety management. In addition, BSL-3 laboratories can submit proposal to Taiwan CDC according to "The process of closure and reactivation for certified laboratories above BSL-3" [4] if the laboratories need to be suspended for routine test, operation needs, or operating cost maintenance, and Taiwan CDC will inspect immediately or arrange in annual check to confirm the reactivation documents and inspection records.

In Summary, the process of "new activation" or "closure and reactivation" is simply to confirm the work safety of laboratories above BSL-3 and ensure the staff's health.

**References**

1. Taiwan CDC. Safety Guidelines for Biosafety Level 3 Laboratories. 2nd edition, 2011.
2. Taiwan CDC. Regulations governing the infectious biomaterials and specimens collection from patients of communicable diseases. Collection of communicable disease control acts and regulations. Communicable Diseases Control Act compilation 6th edition. Taipei; Centers for Disease Control, Taiwan: 2009;47.
3. Taiwan CDC. Commissioning process for newly established laboratories above BSL-3 (Appendix E). Available at: http://www.cdc.gov.tw/public/Attachment/15231342371.doc
4. Taiwan CDC. The process of closure and reactivation for certified laboratories above BSL-3. Available at: http://www.cdc.gov.tw/public/Attachment/09916165071.doc

# Introduction of Current European Union Biosafety and Biosecurity Regulation

Chih-Heng Liao

Department of Laboratory Accreditation,
Taiwan Accreditation Foundation

**Key Element of European Union biosafety legislation**

European Union biosafety legislation focuses on the prevention of risks related to the handling and transporting of the dangerous biomaterials by the workforce. In addition to common European Union (EU) directives and regulations, the members of EU have already addressed in many national laws, ordinances, and regulations, expect to prevent the exposure of dangerous biomaterials as well as to protect human beings, animals, and plants, further, the regulations for dangerous biomaterials disposal was also drafted [1].

The core of European Union biosafety legislation includes: (A) Directive 2000/54/EC drafted by the European parliament and of the council of 18 September 2000 for the protection of workers from risks related to exposure to biological agents at work [2]; (B) Council Directive 90/219/EEC revised on 26 October 1998 based on Directive 98/81/EC of 23 April 1990 on the contained use of genetically modified microorganisms [3]. The major issue of Directive 2000/54/EC includes: link the risk assessments to the biological agents and classify the pathogens into 4 risk groups; conclude related measures and levels of laboratory prevention as well as industrial processes protection; competent authority would be informed in advance while biological agents higher than level 2 are used for the first time; the employers should preserve the name list of workers engaging with biological agents higher than level 3, and the authorities are authorized to acquire the list.

To protect human health and environmental safety, Council Directive 90/219/EEC on the authority and utilizing regulations of genetically modified microorganisms was revised. It referred to the similar skeleton of Directive 2000/54, including risk assessment of biological activities and four containment levels to guard the laboratory activities, glasshouses, growth-rooms, animal house and other activities, as well as other protection measures. Before starting the authority that mentioned above and utilizing regulations, competent authority should be informed in advance; furthermore, the first time the biological agents higher than level 2 and biological agents higher than level 3 at each subsequent use, competent authority should be informed additionally; before biological agents higher than level 3 are used, prior approval by competent authority should be obtained.

**Biological facilities of concern**

Directive 2000/54/EC and Council Directive 2000/54/EC have answered the EU members of the key questions about biosafety and biosecurity, including: (A) Do you know which dangerous biomaterials are used in the laboratory? (B) Do you know who handles these materials? (C) Is it in control while laboratories handled the materials? The answer to the first question should be positive, because these two directives had demanded that before the laboratories start working, competent authority should be informed. The answer to the second question should also be positive, because the workers were under the exposure of high risk biological agents which were higher than level 3. Finally, the competent authorities of each EU members have the responsibility to implement the inspection and other regulation measures to obey the Directives certainly.

**Transport of dangerous biological material**

Council Directive 94/55/EC of 21 November 1994 [4] on the approximation of the laws of the Member States with regard to the transport of dangerous goods by road (including 6 amendments and revises) detailed-stated the necessary regulations about dangerous biological material transportation. Council Directive 95/50/EC [5] on uniform procedures for checks on the transport of dangerous goods by road was revised by Directive 2001/26/EC with referring to elements of European Agreement concerning the International Carriage of Dangerous Goods by Road (ADR). While Member States drew up the regulations of transporting dangerous goods related to infectious biological materials by railroad, except following RID regulations, they should also follow the Council Directive 96/49/EC of 23 July 1996.

**Biosecurity: Green Paper on Bio- preparedness**

In July 2007, "Green Paper on Bio-preparedness" was published by Commission of European Committee [6]. The purpose of the Green Paper was to promote debates and start the consolation process about how to reduce biorisk on European level, and to enhance bio-preparedness. The paper related to improve security and maintain the present EU legislation, resolution, and advice, also, it brought up how and who to improve biosecurity and bio-preparedness of the member states. Problems presented in the paper are now under discussion by brain trusts. In the meantime, EU CBRN Inventory in 2002 and Bio Inventory in 2007 were renewed by General Secretariat of the Council and the Commission Services. Bio Inventory collected all directives, regulations, resolutions, advices, and other measures responded to biosafety and biosecurity issues by EU Member States or European Parliament. According to advices to the Green Paper by over 80 governmental and non-governmental organizations, the results discussed by brain trusts, and renewed Nuclear-biochemical Inventory, the Council and the Commission developed a written policy to prepare for the community improvement, which was finished in 2009. The written policy will become the future foundation of measures for improving biosecurity in EU Member States.

**Laboratory biorisk management standard (CWA 15793:2008) [7]**

To ensure the effectiveness of the laboratory biorisk management function, the 31st working group of European Committee for Standardization (CEN) for Laboratory biosafety and biosecurity, established a laboratory biorisk management standard in 2007. The paper was discussed by not only 76 countries but also WHO. During public consultation stage, 33 stakeholders including Argentina, Canada, Europe, Russia, Taiwan, and the United States, had offered related proposal. Eventually, the final protocol file was published by CEN in 2008.

Laboratory biorisk management standard (CWA 15793:2008) utilizes the knowledge and the operation method of management system to induce the concept of continuous improvement. The nature of the standard is adopted the cycle of quality, as known as PDCA (plan–do–check–action), the principle of quality control, to implement and operate, including affirming biorisk management policy, planning biorisk management measures, implementing and operating, taking regular check and corrective action, inspecting and improving, in the end, by the biorisk management review to ensure each process in management and operation effectiveness. The standard mainly aimed to management/ placement and risks related to disposal of biological agents and toxins in the laboratory and facilities to draw up a necessary risk control demands, to aid agencies or laboratories to establish and maintain biorisk management system, to control or reduce the related risk of the workers, communities, people, and environment, that was direct or indirect exposed to biological agents or toxins, to an acceptable level, further, to effectively input biorisk management policy to fulfill the request. Meanwhile, appropriate management skeleton can be offered by auditing the biorisk management system with independent third-party verification or validation, to facilitate the operation in organizations or laboratories, to establish the laboratory biosafety and biosecurity guideline and fine operation, and appropriateness and effectiveness of practice-related training, moreover, to increase the knowledge of biosafety management of the workers.

The operational requirements of management system offered by the standard applied to common situations, and can be used in all organizations/agencies disposing biological agents or toxins, no matter what kind or what scale of the disposed biological agents or toxins are. However, the document is not a technical document aiming on biosafety operation. It isn't used to replace the international standards, regulations, or demands like Laboratory biosafety, instead, it is an auxiliary document to assist the above standards to achieve the process.

## References


1. Germany on behalf of the European Union, European Union Legislation and Recommendation Related to Biosafety and Biosecurity. Available at: http://www.unog.ch/80256EDD006B8954/(httpAssets)/C4BD641FF55084A1C12574A2004242B0/$file/Germany+EU+legislation+and+recommendations+to+implement+and+improve+biosafety+and+biosecurity+WP.pdf
2. Official Journal of the European Communities, The protection of workers from risks related to exposure to biological agents at work, 2000/54/EC. Available at: http://www.biosafety.be/PDF/2000_54.PDF
3. Council of the European Communities, Contained use of genetically modified micro-organisms, 90/219/EEC.Available at:http://ec.europa.eu/health/files/eudralex/vol-1/dir_1990_219/dir_1990_219en.pdf.
4. Official Journal of the European Communities, The approximation of the laws of the member states with regard to the transport of dangerous goods by road , 94/55/EC. Available at: http://www.efma.

org/PRODUCT-STEWARDSHIP-PROGRAM-10/images/9455EC.pdf

5. Council of the European Union, Uniform procedures for checks on the transport of dangerous goods by road, 95/50/EC. Available at: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CONSLEG:1995L0050:20050103:EN:PDF
6. Commission of European Committee, Green paper on bio-preparedness, 2007. Available at: http://ec.europa.eu/food/resources/gp_bio_preparedness_en.pdf
7. European Committee for Standardization (CEN), Laboratory Biorisk Management Standard, CWA 15793; 2008.