

松本城

MATSUMOTO Castle

The first place attacked
by Sarin June 1994



Regional Biosecurity Workshop

Singapore May 28-30, 2007

山は高く険しい



ジャンダルム

(日本北アルプス)



National Institute of Infectious Diseases
Takeshi KURATA (Toyama Institute of
Health)

History of Biosafety in Japan

Started at National Institute of Health (Japan)
(MHLW)

(Present: National Institute of Infectious
Disease)
1975 Establishment of Biosafety Committee

1976 Risk Classification of Microbiological
Pathogene

1976 Summary Data on Biohazard 1

1978 Summary Data on Biohazard 2

1981 Regulation on the Safety Control of
Laboratories handling Pathogenic Agents

1981 Establishment of Maximum Safety Laboratory
(BSL-4) : NID

Academia, Ministry of Education, Culture,
Sports, Science and Technology (MEXT),

MHLW

1979 Rules for handling genetically modified living
organisms (MEXT)

1993 Biosafety Guideline (Japanese Soc. Virology)

1993 Handling Rules of Microorganisms (Institute of
Animal Health, Ministry of Agriculture)

1998 Biosafety Manual for handling Microorganisms
(MEXT)

1999 Biosafety Guideline (Japanese Soc.
Bacteriology)

Continued

1999 Law Concerning the Prevention of Infection
and Medical Care for Patients of Infection

2002 Establishment of Japanese Biosafety
Association (JBSA)

2004 Law Concerning the Conservation and
Sustainable Use of Biological Diversity through
Regulation on the Use of Living Modified
Organisms

2006 Safety and Security Science and Innovation
Strategy (Council for Science and Technology
Policy, Cabinet office)

2006 Revised LCPIMCPI for Antiterrorism

- Regulation of Possession, Use and Transport:

The Japanese Biological Safety Association (JBSA) : founded in 19 Jan. 2002.

- To improve and develop the level of biosafety, JBSA steps up the research on biosafety-safety management, safety equipments and laboratory facility to handle pathogenic agents, and spreads knowledge of biosafety by education and training.
- To researcher for microorganism, animal science, biosafety officer in laboratory or hospital (diagnostic lab.) or manufacturer for biological products, and engineer for safety equipments, laboratory facility designer, maintenance staff, disinfection staff, medical doctors, veterinary doctors, clinical laboratory staff, health administration staff and other related persons who are interesting in biosafety.

The Japanese Biological Safety Association (JBSA) : founded in 19 Jan. 2002.

JBSA activity

To achieve the purpose, the work below is performed.

- 1) annual meeting, scientific meeting etc.
- 2) newsletter and journal in future etc.
- 3) biosafety education and training course etc.
- 4) affiliation to related national or international associations
- 5) the others

The Japanese Biological Safety Association (JBSA) : founded in 19 Jan. 2002.

President: Takeshi KURATA (NIID, Toyama Institute of Health)

Board of directors;

Aikichi IWAMOTO (Institute of Medical Science, Tokyo University)

Atuo KITABAYASHI (Yashima.Eco/System Co.Ltd)

Toshihiko KOMATSU (NPO; Bio Medical Science Association)

Yuko SAGARA (Yokohama City Hospital)

Kazuyoshi SUGIYAMA (NIID)

Koichi YAMANISHI (NIBIO)

Haruo WATANABE (NIID)

Membership; 240

Secretariat:

Division of Biosafety Control and Research, NIID

1-23-1, Toyama, Shinjuku, Tokyo 162-8640

Tel: 81-3-5285-1111 ext.2420, Fax: 81-3-5285-1184

www.nih.go.jp/niid/meetings/index.html

ksugi@nih.go.jp

Membership of JBSA

MHLW



Quarantine stations



Regional Health administration

University/ College

National Institute of Infectious Diseases (NIID)



Company:
Pharmaceutical,
diagnostic lab, BSC
and other equipments
manufacture,
maintenance,
construction,
disinfection, others

Membership 230
(supporting member 14)

N. I. of B.Med. Innovation

Institute of Science

Research Institute
of Tuberculosis and
Hospital

Incorporated foundation
(biological substance
manufacture) etc.



al

NPO Bio-medical
Science Association



Others

Cooperation with domestic organization

- National Institute of Infectious Diseases (NIID)
(Biosafety management, international cooperation, translation of WHO guidance etc., training program and material)
- Regional Institute for Health (RIH)
(Biosafety management, training program and material)
- Japan International Cooperation Agency (JICA)
(Influenza and Biosafety training course from 2007)
- Other academic Association (Virology, Bacteriology, Infectious disease, Clinical Microbiology, Vaccine etc)
(symposium, seminar)
- NPO Bio-medical Science Association (BMSA)
(training program and material)
- Others

Cooperation with international organization

- American Biological Safety Association (ABSA)
- European Biological Safety Association (EBSA)
- Asia-Pacific Biological Safety Association (A-PBS)
- WHO;HQ/WHO;WPRO
- Others

JBSA Annual Conference

- Foundation meeting (Jan. 2002) Tokyo
- 2nd Annual meeting (Nov. 2002) Tokyo
- 3rd Annual meeting (Nov. 2003) Tokyo
- 4th Annual meeting (Nov. 2004) Yokohama
- 5th Annual meeting (Nov. 2005) Yokohama
- 6th Annual meeting (Nov. 2006) Tokyo
- 7th Annual meeting (Nov. 2007) Tokyo

JBSA Symposium

- 1st Symposium (2002)
“Biosafety and Bioterrorism”
- 2nd Symposium(2005)
“Biosecurity”
- 3rd Symposium(2005)
“Transport of Pathogen”
- 4th Symposium(2007)
“Revision of Infectious Disease Law”

5th JBSA meeting (2005)

The Special Session for Biosecurity

1. Principles and Requirements for Biosecurity in the US, and Recommendations on Global Codes of Conduct
Barbara Johnson, DOD, US
2. Biosecurity and Bioterrorism Preparedness in Canada
Maureen Ellis, PHAC, Canada
3. The Status of International Biosecurity
Reynolds Salerno, SNL, US
4. Planning for a Successful Containment Laboratory
Maureen Ellis, PHAC, Canada

6th JBSA meeting (2006)

The Special Session for “Pathogenic Bacteria from Biosafety point of view”

1. *Bacillus anthracis*

S. Makino, Obihiro University

2. Plague

H. Takahashi, NIID

3. Tularemia

O. Fujita, NIID

4. *Clostridium botulinum* toxin

S. Ozaki, Osaka Prefecture University

1st Asia-Pacific Symposium (2006) by JBSA - Biosafety in Asia-Pacific -

1. Current situation of Biosafety in Japan
2. Activity of ABSA
3. Activity of A-PBS
4. Current situation of Biosafety in Taiwan
5. Current situation of Biosafety in Korea
6. Strategy for Biosafety in WPRO

1. Risk assessment for implementation of Biosafety
2. Biosafety in field collection and presumptive analysis of highly infectious pathogen samples

Regulation on the Safety Control of Laboratories handling Pathogenic Agents, NIID

1. Risk Classification of microbiological agents
2. Relation of risk groups to biosafety levels, practices and equipment
3. Facility requirements at the four biosafety levels

4. Biosafety Guidelines

1) Risk assessment

2) Basic laboratory BSL-1, 2

3) Containment laboratory BSL-3

4) The maximum containment laboratory
BSL-4

*All laboratories have the own operation
manual

5. Laboratory animal facilities ABSL-1 to 4

6. Guidelines for laboratory certification

Good Microbiological Techniques

- ① Laboratory techniques
- ② Emergency procedures
- ③ Disinfection and sterilization
- ④ Rules on transport of microbiological agents including other infectious substances (domestic and international)

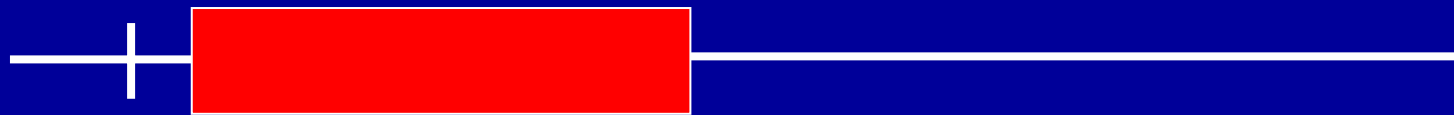
Safety Organization and Training

- ① Biosafety Office (permanent and temporary members): Responsible for all issues on biosafety and biosecurity
- ② Training Course : bimonthly, including English course
- ③ Reporting System
 - Material Transfer Agreement
 - Permission and reporting of pathogen for handling, transfer, acceptance, etc.
 - Reporting on accident in the laboratory
 - Other issues

B & C Terrorism

Experiences in JAPAN

Outbreak of Disaster by B/C Terrorism



N, C

Victims appear immediately after Exhalation / Bombing



B

Victims appear after certain Incubation period
(4-14 days)

Bioterrorism and Chemical Terrorism done by AUM Cult Group in 1990s

1. Biomaterials were made by only one DVM with few-years experience in a graduate school
2. Chemical materials (Sarin) were made by one chemist, who had also few-years experience in a university chemical institute

(1) AUM CULT GROUP – What They Have Done

Bioterrorism

- 1990. April : Spray of Botulinum Toxin From Car Window using Electric Fan
- 1990. May : Spray of Botulinum Toxin From Car Window using Electric Fan
- 1993. June : Spray of Botulinum Toxin From Car Window using Electric Fan
- 1993. June : Distribution of Spore (B. Anthracis)
- 1993. Sep : Distribution of Spore from Car Window at HQ. Office of Kanagawa Prefecture and at the outside area of the Emperor's Palace in the Center of Tokyo
- 1995. March : Spray of Botulinum Toxin

(2) AUM CULT GROUP –What They Have Done

Chemical Terrorism

1994. June : Spray of Sarin by a motor fan through a car window (Matsumoto City)
Seven people who lived down the leeward died
1995. March : Sarin was sprayed at the same time through staging plastic bags filled with Sarin in the subway wagons, 3 different lines, at 5 Kasumigaseki stations. HQ Area of Beurocracy, Tokyo.
Twelve People died and > 5000 injured.

Why AUM Cult Group Could Operate Terrorism

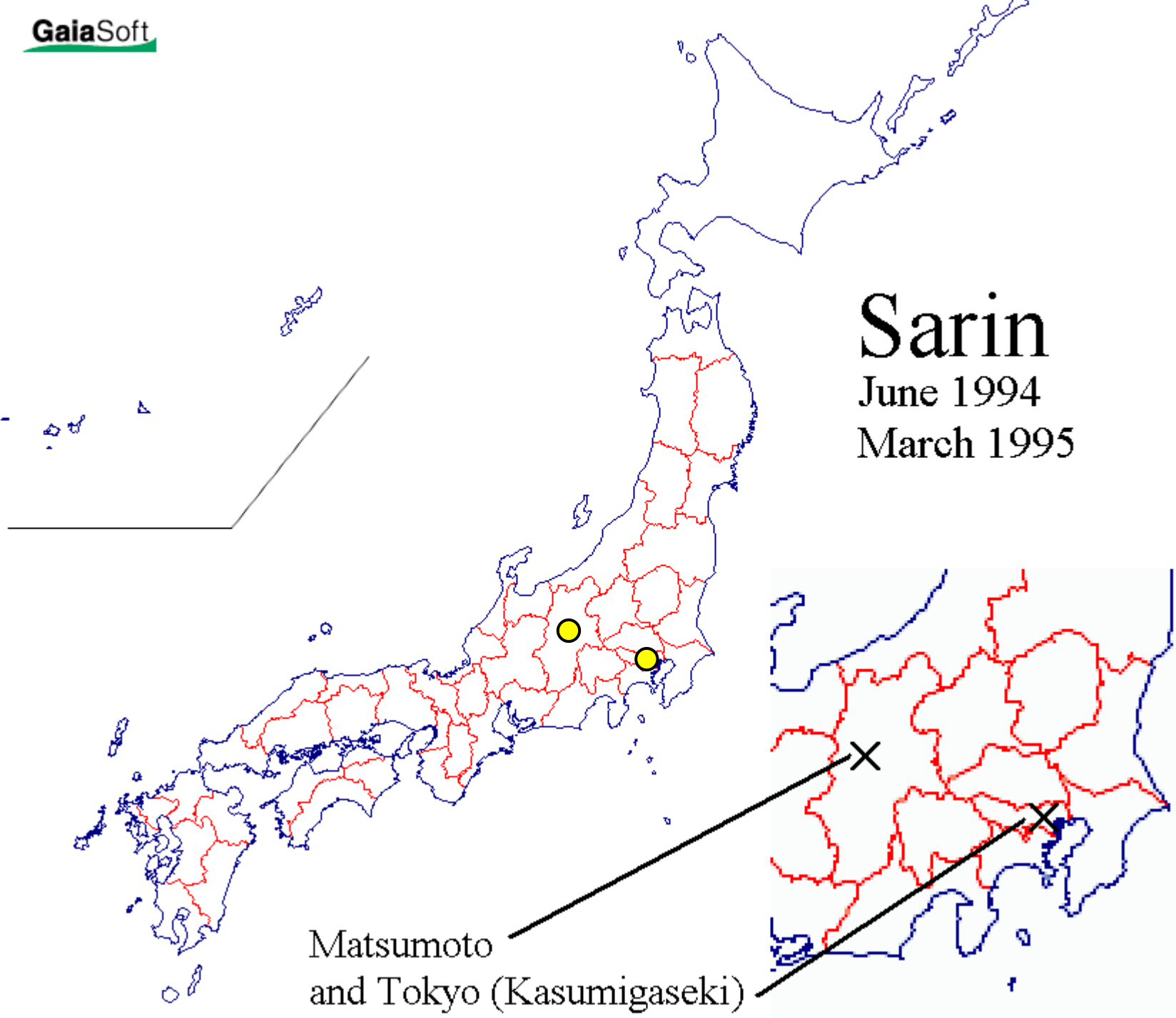
AUM is (was) one of the real cult group, which had been authorized as a religious group by the Government. Once authorized as a religion, the group is not required to pay tax, even they collect any amount of money by any means. And all their performances are recognized as religious activities, and the government even police can't has any right to control religious groups.

Nobody can touch religious activity in Japan!!

Sarin

June 1994

March 1995



Matsumoto
and Tokyo (Kasumigaseki)

Tokyo Subway Sarin Gas Attack in 1995

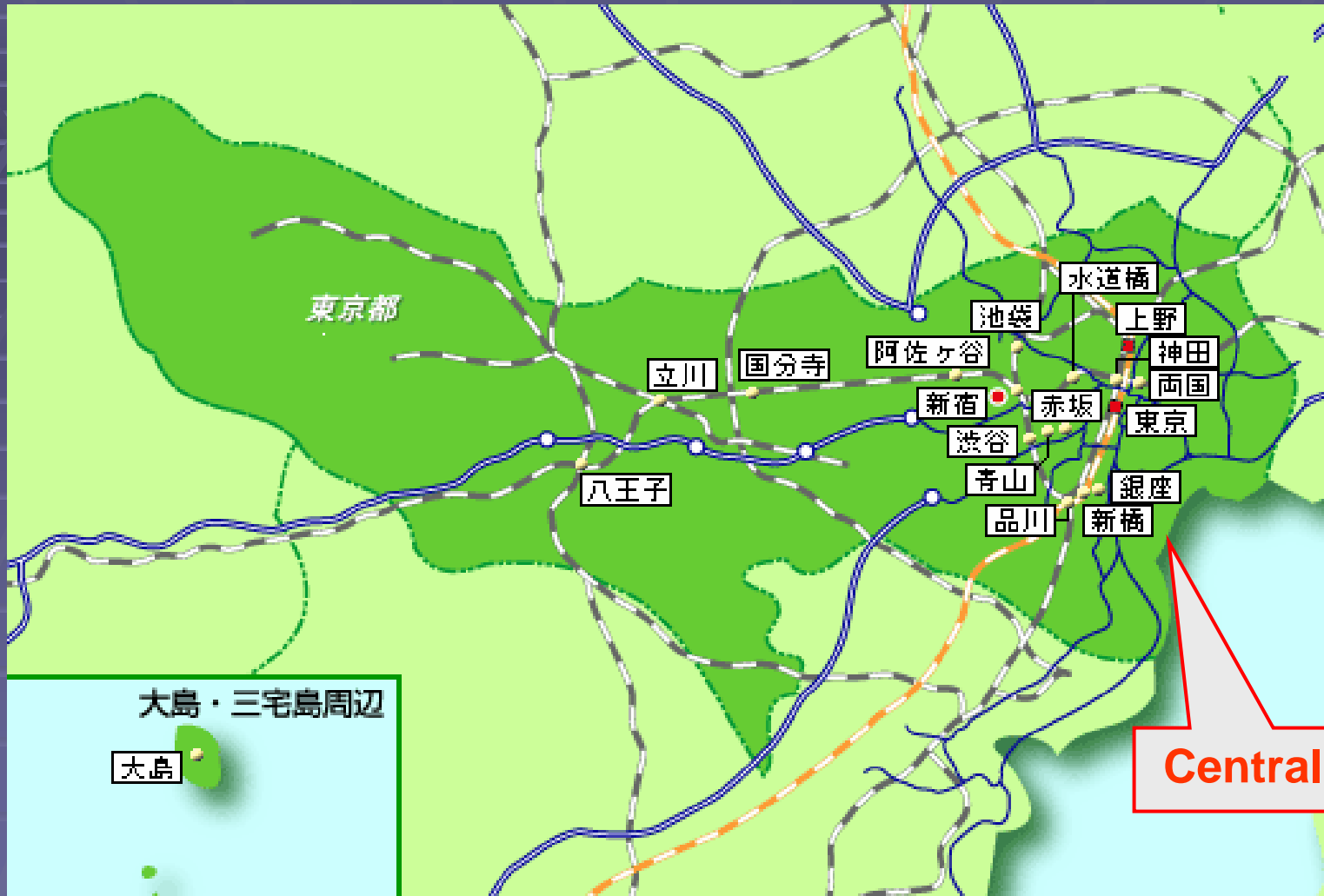
Fire Suppression Division,
Tokyo Fire Department

東京消防庁

Tokyo Subway Sarin Gas Attack in 1995

- (1) Outline of the Incident
- (2) Response to the Incident
- (3) Lessons Learned from the Incident

Tokyo Metropolitan Map



Area :2,187Km²
Population:12,300,000

Tokyo Fire Department Resources



Personnel 17,988

Fire Station 80

Fire Station Division 2

Fire Station Branch 207

Fire Apparatus 1,859





TOKYO HAZ-MAT Unit (1990 ~)



Infrared ray gas analyzer



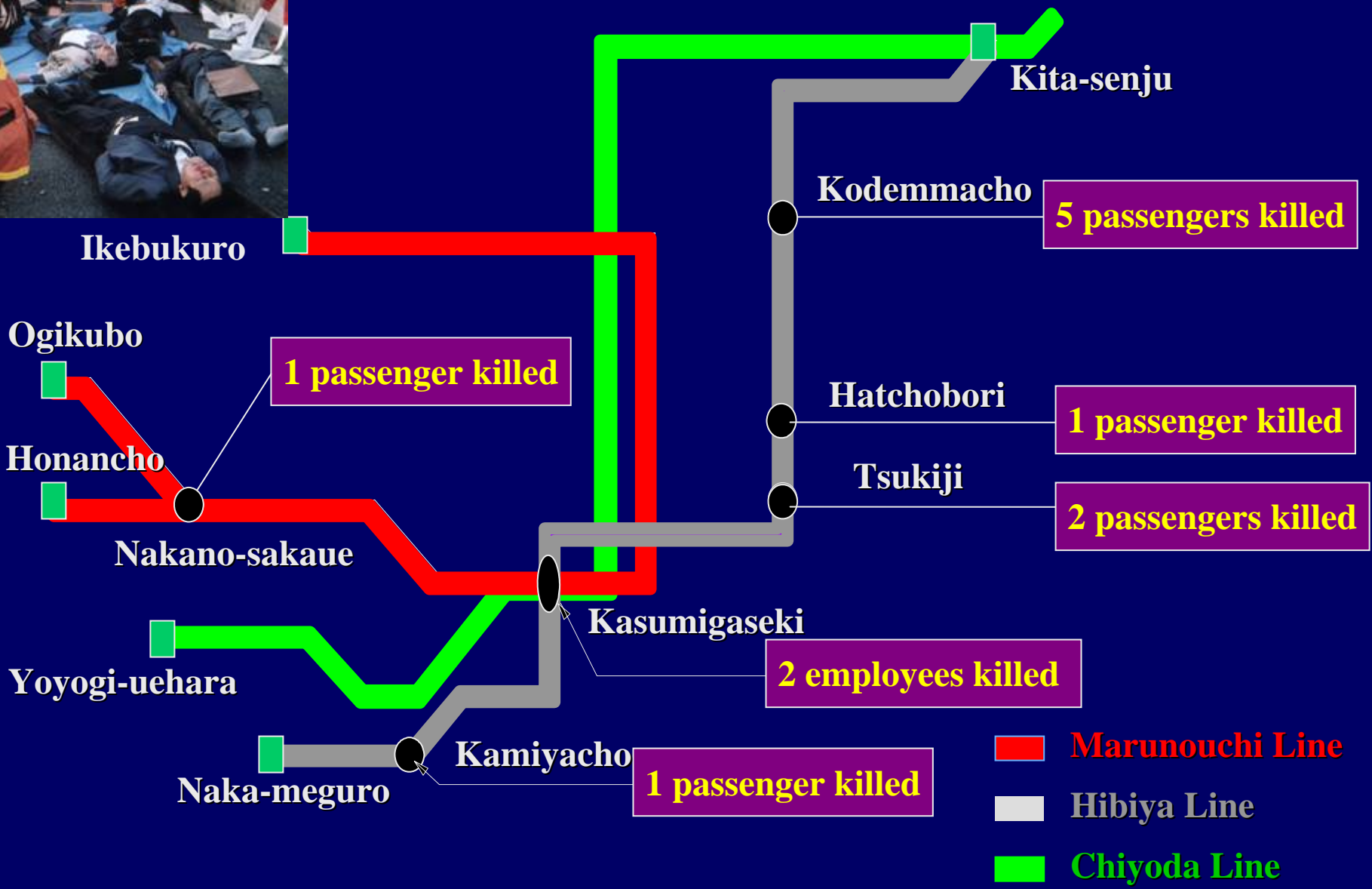
Tokyo Subway

Outline of the Subway Sarin Attack

- Known at - 8 : 09 a.m on March 20, 1995 (1st 119 call)
 - Where occurred: Within the premises of the subway in Tokyo
 - Method employed in the crime: To prick a bag containing sarin liquid (about 900ml) with the tip of an umbrella
 - Number of death - 12
 - Number of injured - 5,501
- * Indiscriminate terrorist attack, using sarin gas, a deadly poison
- * Occurred within the premises of the subway, a closed space
- * Sarin gas was dispersed in multiple terrorist attacks



Casualties



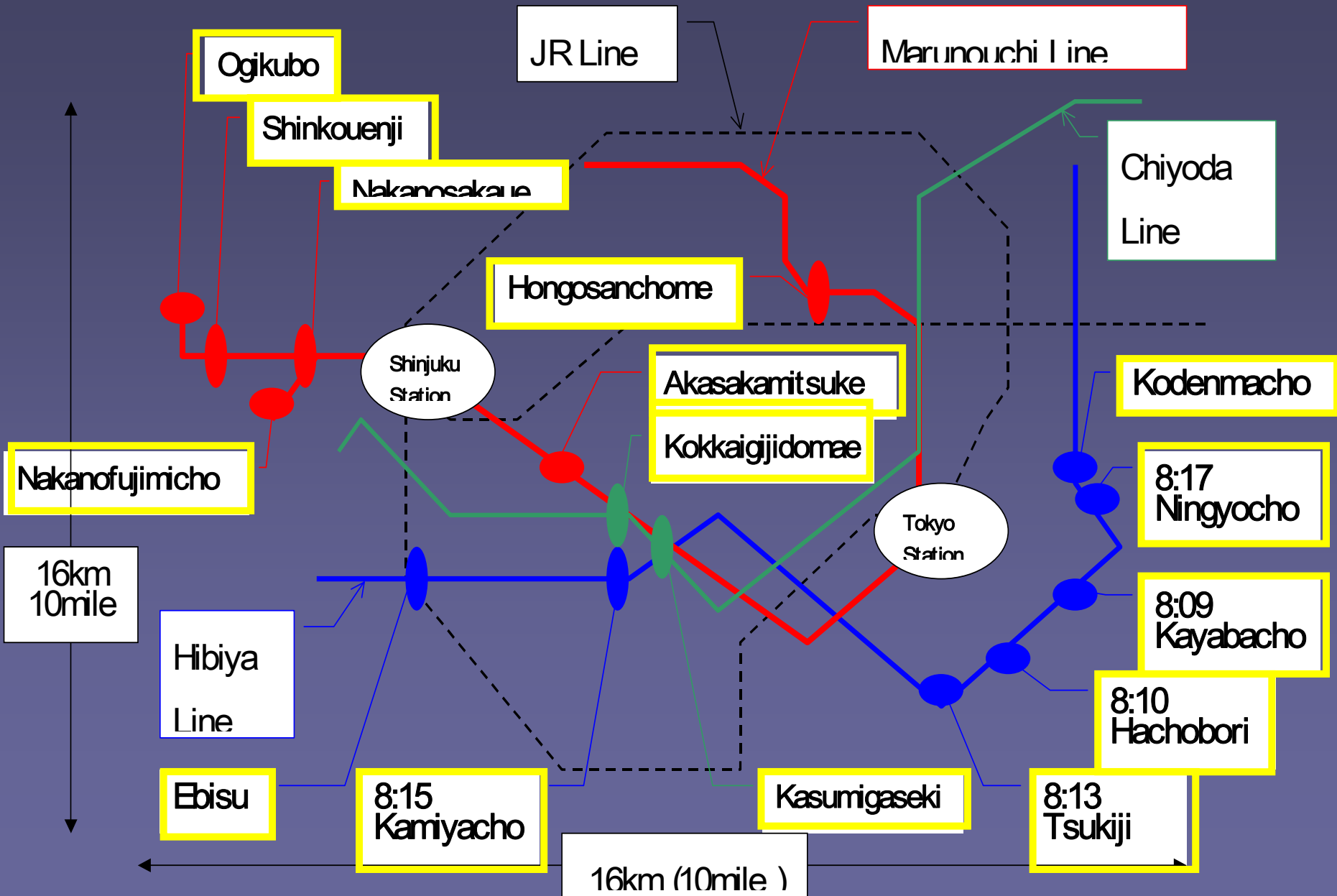
- █ Marunouchi Line
- █ Hibiya Line
- █ Chiyoda Line

Outline of the Actions Taken by the Tokyo Fire Department

- Units in action – 340 units in total including Haz-Mat Units, pump units and EMS Units
- Rescue and Relief of the Injured
- Analysis / Cleansing of Poisonous Gas
- **Number of Transported – 688**
- **Number of Rescued – 692**
- Number of firefighters in action – 1,364
- Number of injured firefighters - 135



Subway Stations the TFD Responded to



Actions of the Headquarters of the TFD

- The headquarters commanded fire stations where spare ambulances were made available for potential response.
- The headquarters ordered on-site fire personnel to secure the safety of themselves and prevent a secondary disaster.
- The headquarters provided information regarding chemical substances to all fire stations and on-site fire personnel.



東京・地下鉄サリン事件



除染による二次三次災害の防止



地下鉄サリン事件における自衛隊との連携活動

汚染車両の除染状況







Injury of fire personnel

- Number of firefighters in action – 1,364
- Number of injured firefighters - 135
 - inside the subway station - 101
 - above ground - 34
- Number of firefighters transported - 52
- Number of firefighters hospitalized - 43

Major Actions Taken on the Day of the Subway Sarin Attack (Tokyo Metropolitan Government / Japan Self Defence Forces)

【March 20th】

- 8:09 a.m.
- 8:14 a.m.
- 8:17 a.m.
- 8:27 a.m.
- 8:30 a.m.
- 8:42 a.m.
- 8:55 a.m.
- 9:00 a.m.
- 9:00 a.m.
- Around 11:00 a.m.

by the telephone c



nd Chiyoda

ommodation of

als

11:17 a.m. TV news announced, “The poison is highly likely to be sarin gas.”

12:50 p.m. The Govenor of Tokyo requested the Japan Ground Self-Defence Force to dispatch anti-disaster teams.

- Related institutions were busy taking countermeasures against the sarin attack until the night.
- Number of people affected by the suspension of subway operations: 1,108,000 (total for three lines)

【March 21st】

1:22 a.m. Japan Ground Self-Defence Force completed the cleansing of the Kodenmacho Station.

5:00 a.m. All the subway lines started their normal traffic service from the first trains as scheduled.

Operational Lessons Learned

- Necessity to introduce reinforced detection/protection equipment against chemical agents
- Necessity for education and training for incidents involving chemical agents such as sarin gas
- Necessity to improve decontamination systems for preventing secondary contamination
- Necessity for the cooperation with related institutions such as the police/hospitals and experts



Bioterrorism

B. Anthracis

***Bacillus anthracis* Incident, Kameido, Tokyo, 1993**

Hiroshi Takahashi,* Paul Keim,† Arnold F. Kaufmann,‡ Christine Keys,† Kimothy L. Smith,†
Kiyosu Taniguchi,* Sakae Inouye,* and Takeshi Kurata*



Figure 1. Spraying scenes from the Aum Shinrikyo headquarters building (photographs taken July 1, 1993, by the Department of Environment, Koto-ward).



Figure 2. Fluid collected from the Kameido site cultured on Petri dishes to identify potential *Bacillus anthracis* isolates.

Figure 3. Multiple-locus, variable-number tandem repeat analysis genotype of all 48 Kameido isolates and the Sterne strain of *Bacillus anthracis*: *vrrA*, 313 bp; *vrrB1*, 229 bp; *vrrB2*, 162 bp; *vrrC1*, 583 bp; *vrrC2*, 532 bp; CG3, 158, bp; pX01-att, 129 bp; pX02, no amplification.

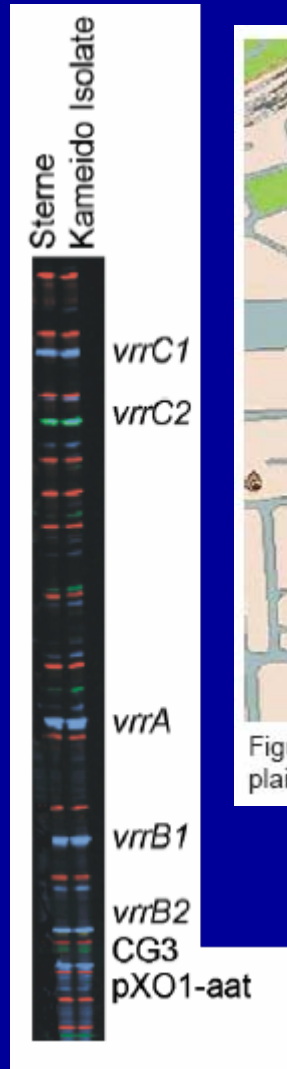
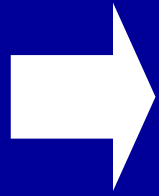


Figure 4. High-risk area for infection, based on foul odor complaints.



Complete Lack of Risk Management of Japanese Government !!

(1998, E&RE Inf. Dis. Conference,
Atlanta)

In AUM cult group only one person
(Ph.D.) had the experience handling
viruses in some institute of a national
university

This indicated bioterrorism will be
caused quite easily and in any places by
ordinary citizens !!

International Collaboration

1. Global Health Alert Network (MHLW)
Global Biosecurity Action Group Net
 2. Global Biosecurity Laboratory Net (NIID)
 3. WHO, US CDC, Pasteur Institute, China & Korea CDC, Taiwan CDC and other foreign National Health Institutes
- NIID (MHLW) is responsible for Surveillance Activities of Infectious Diseases and NIID is responsible for Laboratory Surveillance of the Pathogens causing Infectious Diseases, in collaboration with local health laboratories and quarantine offices

Biosafety and Biosecurity (2006-2007)

Amendment of Law Concerning the Prevention of Infections and Medical Care for Patients of Infections – will be approved by Japanese National

↳ Parliament

Define for possession, use and transfer of selected biological

agents

- * Original law is a rather voluntary reporting based system of infectious diseases. But the purpose of the revision of the law is for prevention of bioterrorism through regulation of biological agents.

LAW CONCERNING THE PREVENTION OF INFECTIONS AND MEDICAL CARE FOR PATIENTS OF INFECTIONS.

Third Revision 2006

Purpose : Prevent people from the Bioterrorism through regulation of microbiological pathogens.

Regulation : Strengthen management of pathogens to secure from the following points.

- ① possession
- ② storage
- ③ use
- ④ transportation

In these items, standard has been set and contravention to the law, even facility, devices, registration of pathogens, documentation and etc, will be punished, fine or imprisonment. Even you have no distribution of pathogens intentionally !

Specified Pathogens

Dec 08, 2006

Group I 6 Genus

Group II 5 Genus + 1 Toxin

Group III 23 Genus

Group IV 15 Genus + 1 Toxin

49 Genus. 79 Strains and 2 Toxin

There is no exact correlations
on BSL-1~4 level between this law and
International classification

Legal Duty and Penalty to the Person Who Handle Pathogens

	GI	GII	GIII	GIV
The Mimiter's Assignment for Possession and Import	⊙			
Permission for Possession and Import		⊙		
Report for Possession and Import			⊙	
Protection Rule of Infection	⊙	⊙		
Designation of Responsible Person	⊙	⊙		
Training / Education	⊙	⊙		
Decontamination	⊙	⊙		
Documentation	⊙	⊙	⊙	
Facility (Standard)	⊙/○	⊙/○	○	○
Rule of Storage	○	○	○	○
Reporting of Transport	⊙	⊙	⊙	
Reporting of Accident	⊙	⊙	⊙	⊙
Emergency Measure	⊙	⊙	⊙	⊙

Safety and Security Science and Innovation Strategy (Council for Science and Technology Policy, Cabinet Office)

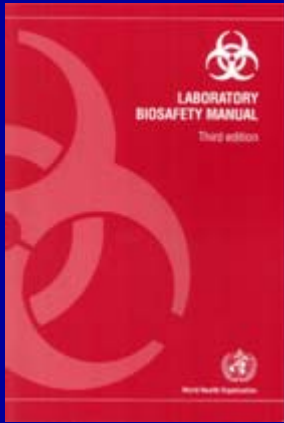
2006

1. Security Innovation by needs for practice
2. Promotion of International collaboration – especially antiterrorism measures
3. Fostering of capable researcher and technologists for the purposes
4. Implementation of the surveillance activity
5. Development of rapid and reliable detection methods, vaccines and drugs

Code of Ethics for Misuse of Scientific Knowledge, Research and Resources (Proposed by IUMS)

The Statement on Ethics of Scientists has been Approved by the Science Council of JAPAN on October 03, 2006

To promote ethical conduct of research and training in the areas of biosecurity and biosafety so as to prevent use of microorganisms as biological weapons and therefore to protect public health and to promote world peace



Classification of Agents



Risk Group	VIRUS	BACTERIA	FUNGUS	PARACYTE
Level 1	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Level 2	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Level 3	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
Level 4	<input type="radio"/>			

National (Regional) Classification of Micro-organisms by Risk Group

1. Pathogenicity of the Organisms

2. Mode of transmission and host range of the organism.

These may be influenced by existing levels of immunity in the local population, density, presence of appropriate vectors and standards of environmental hygiene.

3. Local availability of effective preventive measures. Prophylaxis by immunization or administration of antisera, sanitary erasure, food, water hygiene, control of animal reservoirs.

4. Local availability of effective treatment. passive immunization, postexposure vaccines and use of antimicrobials, antivirals and chemo therapeutic agents, possibility of the emergence of drug-resistant strain.

Biosecurity Strategy on Pathogens

Law concerning anti-bioterrorism



- **USA** 2003 active
Possession, Use, and Transfer of select Agents and Toxins



- **UK** 2001 active
Anti-terrorism, Crime and Security Act 2001
Part 7 Security of Pathogens and Toxins

Regulation on Biosafety

- Directive 2000/54/EC of The European Parliament and of the Council of 18 September 2000 on the protection of workers from risks related exposure to biological agents at work



Each country has made domestic law based on the Directive

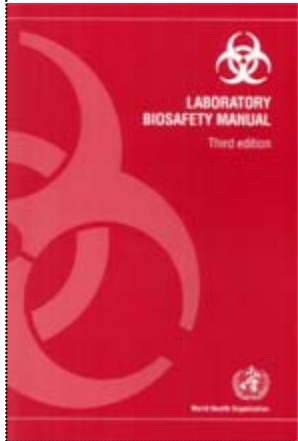
- **China** 2004
Prevention and therapeutic law on communicable diseases, China.



International Standard on Handling Pathogens

Biosafety

○ WHO



***Laboratory
Biosafety
Manual 3rd
Edition***

○ 米国CDC



***Biosafety in
Microbiological
and Biomedical
Laboratories
(BMBL) 4th
Edition***
5th Edit on web

Biosecurity

○ WHO

Laboratory biosecurity (Laboratory Biosafety Manual Part II)
9.Labortory biosecurity concepts

Laboratory biosecurity guidance (Biorisk management)

○ USA CDC ***Laboratory Security and Emergency Response Guidance
for Laboratories Working with Select Agents***

Japan

Law Concerning the Prevention of Infection and Medical Care for Patients of Infection (2nd revision)

Approved at the Parliament

Dec. 2006

Will be active in June 2007

Discrepancy of Classification of the Pathogens

NIID	LCPIMCPI	CDC	WHO*
Level 1	Group 1	BSL-1	Risk G 1
Level 2	Group 2	2	Risk G 2
Level 3	Group 3	3	Risk G 3
Level 4	Group 4	4	Risk G 4

* WHO doesn't specify the agent

Select Agents were classified into 4 Groups

- I Usually forbidden to possess, use, import, etc. except for diagnosis and research necessary for public health.
- II Need permission of the Minister of Health, Labour and Welfare to possess, use, import etc.
- III Report to the Minister for possession, use, import, etc.
- IV Follow the rule for storage, use, disposal, etc.

(1種 isshu)

Group 1 (6)

Forbidden: Possession, use, import, transfer, etc.



Ebola virus

Crimean Congo virus

Variola virus

Marburg virus

Lassa virus

South America hemorrhagic fever virus

(Guanarito, Junin, Machupo, Sabia)

例外

・ 国、又は政令
で

定める法人

・ 試験研究

厚生大臣指定

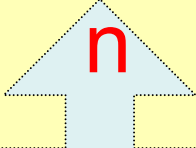
Group 2 (6)

Need permission for possession and import and control of transfer



Permissio

- Plague
- SARS Corona virus
- Anthrax
- Tularemia
- Botulinus
- Botulinus toxin



許可基準

- ・ 検査、治療、医薬品等の製造、試験研究

基準に適合する旨
厚労大臣の許可

Group 3 (21)

届出

Need report of possession, import, transfer

Report

Q fever Coxiella

Rabies virus

MDR MTb

Coccidioides immitis

Monkey pox

HFRS

Nipha virus

Brucellosis

B virus

Burkholderia mallei, pseudomallei

Venezuelan, Eastern and Western
Equine Encephalitis

Rocky Mountain spotted fever,
Typhoid fever, Spotted fever
japonica rickettsia

Tick-borne Encephalitis and
hemorrhagic fever virus

Hendra virus

Rift valley fever virus

HPS virus

Group 4 (16)

Follow the handling rule

遵守

Westnile fever virus

H2N2 influenza virus

Yellow fever virus

Chlamydia psittaci

Cryptosporidium

Cholera

Mico. tuberculosis,
excluding MDR-MTb

Polio virus

Shigella

Typhus-Palatyphus

Enterohemorrhagic E coli.

Dengue virus

Avian influenza virus

Japanese encephalitis
virus

Shiga toxin

What We Need Now ?

- Emerging & Re-Emerging Infectious Diseases
- Biodefence

Strengthen the Active Surveillance

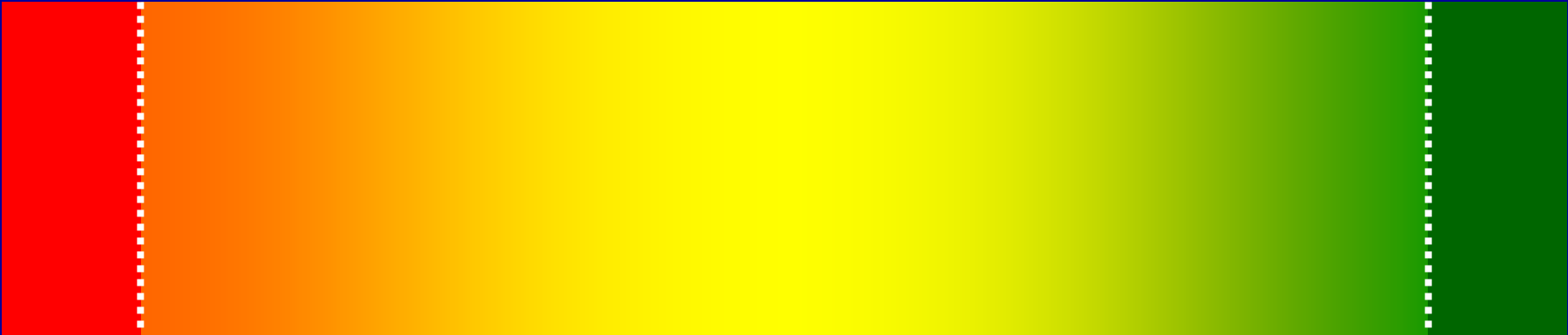
Promotion of Basic Research
of Pathogens Including
Genetic Analysis

Enhancement of the Basis
of Infrastructure Preparation
(Facility, Devices, Personnel,
Training, Information Network
– Domestic & International)

Technical Development

- ① Vaccine for Prevention
- ② Diagnosis Technology
- ③ Drug / Therapy

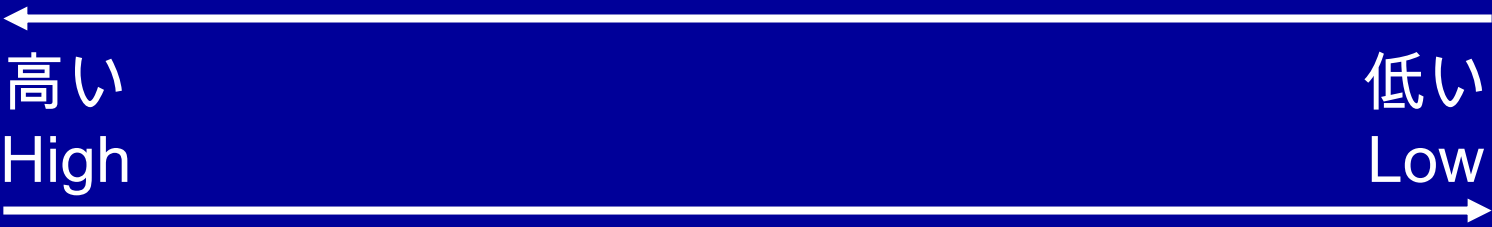
Safety and Security



危険 Danger

リスク Risk

安全 Safe



○ 危険性(Danger)

former use



安全性 (Safety)

Present use

○ バイオハザード対策

Biohazard Measure (old usage)



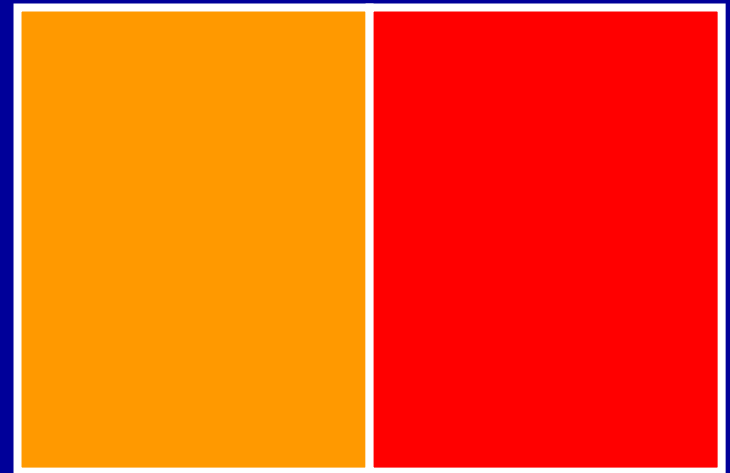
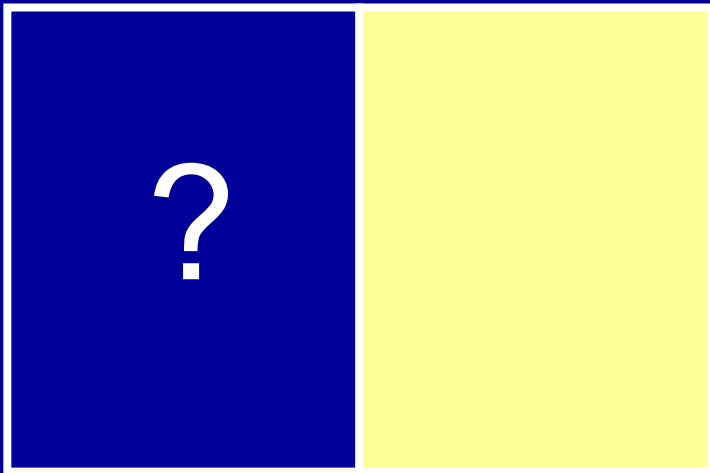
バイオセーフティー

Biosafety (current)

リスク
Risk

と

危険
Danger



Acknowledgement

We would like to thank all colleagues helped for this presentation, especially

Tokyo Metropolitan Fire Suppression Agency and
Dr. K. Nakajima (NIID)



月下美人

Thank you for
your attention!

ご静聴ありがとうございました

ご協力いただいた
国立感染症研究所
感染病理部の皆様、
厚生労働省中山様
富山衛研東山様に
感謝いたします。