Matters concerning safety assurance and safety management related to animal experiments, experimental animals, facilities, etc.

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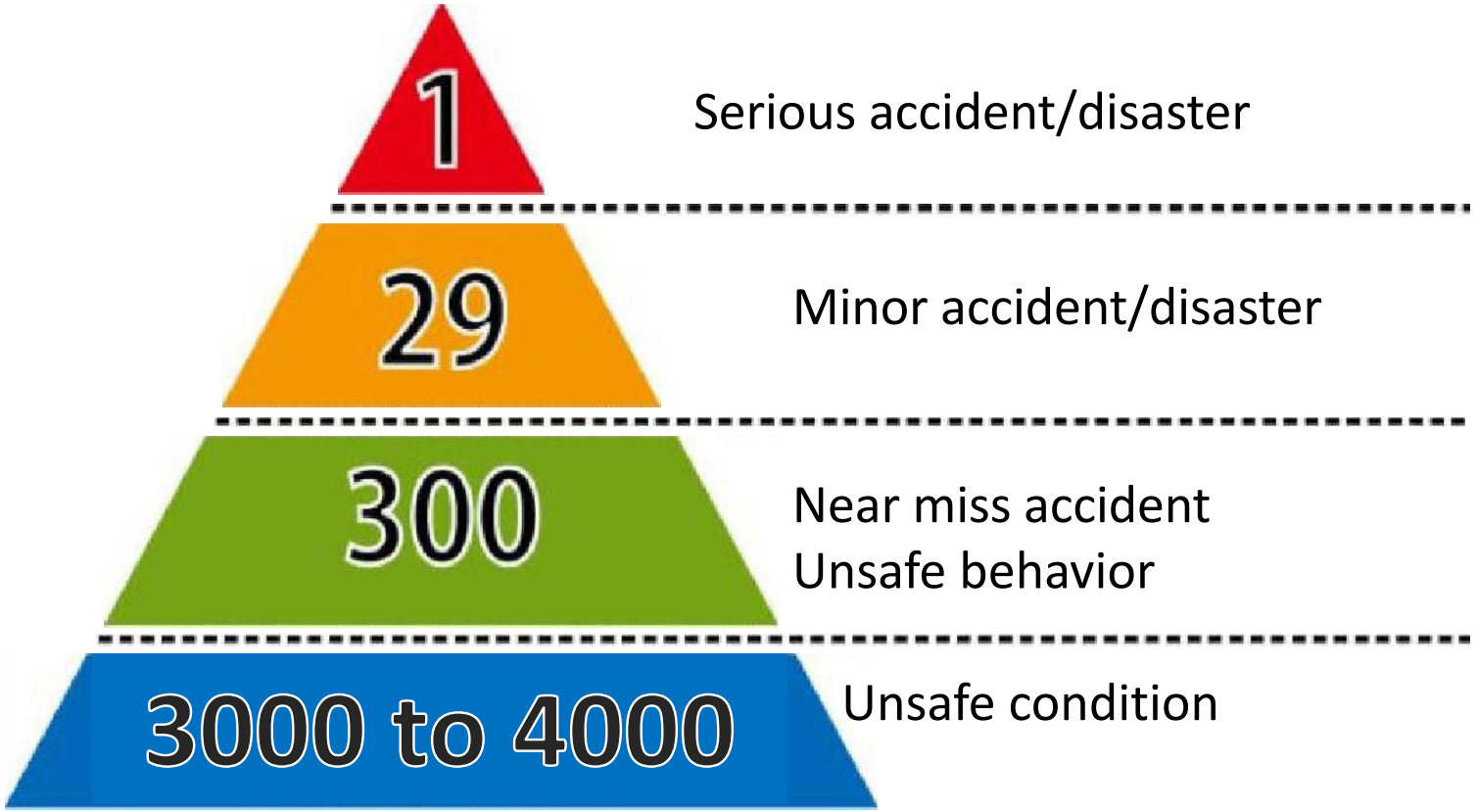
Accidents and injuries that are likely to occur in experimental animal facilities

Situation	Major cause
Animal bites/scratches	Inappropriate/unreliable restraint, lack of understanding of animal habits, and mentally unstable condition of animals
Needle prick/cut	Injection needle injection, puncture wounds during cap removal, scalpel, glassware, belt entanglement during gage cleaning, injection needle, scalpel, and dissecting instrument (scissors) found in bags containing animal carcasses
Fall/slip	A fall on a disinfectant-wet floor. stumbling in a rat return
Burns, harmful gas	Not wearing protective equipment when handling autoclaves and cage washersExposure to formaldehyde gas, hydrogen peroxide gas, hydrogen peracetic acid gas, etc.
Low back pain, tenosynovitis, eye conjunctivitis	Low back pain due to heavy lifting, repetitive work, and unnatural posture work, wrist tendonitis due to repetitive work, ocular conjunctivitis due to germicidal lamps
Hearing loss (noise)	Barking dogs, noise from cage washers, large autoclave sterilizers, etc.
Dust/allergy	Laboratory animal allergy, latex rubber allergy
Infection	Infection from infected animals, zoonotic diseases
Fall	Inappropriate use of step stools, excessively stacked tops (lids)
Natural disasters	Overturning of facilities and breeding equipment due to earthquakes, wind and flood damage, etc.

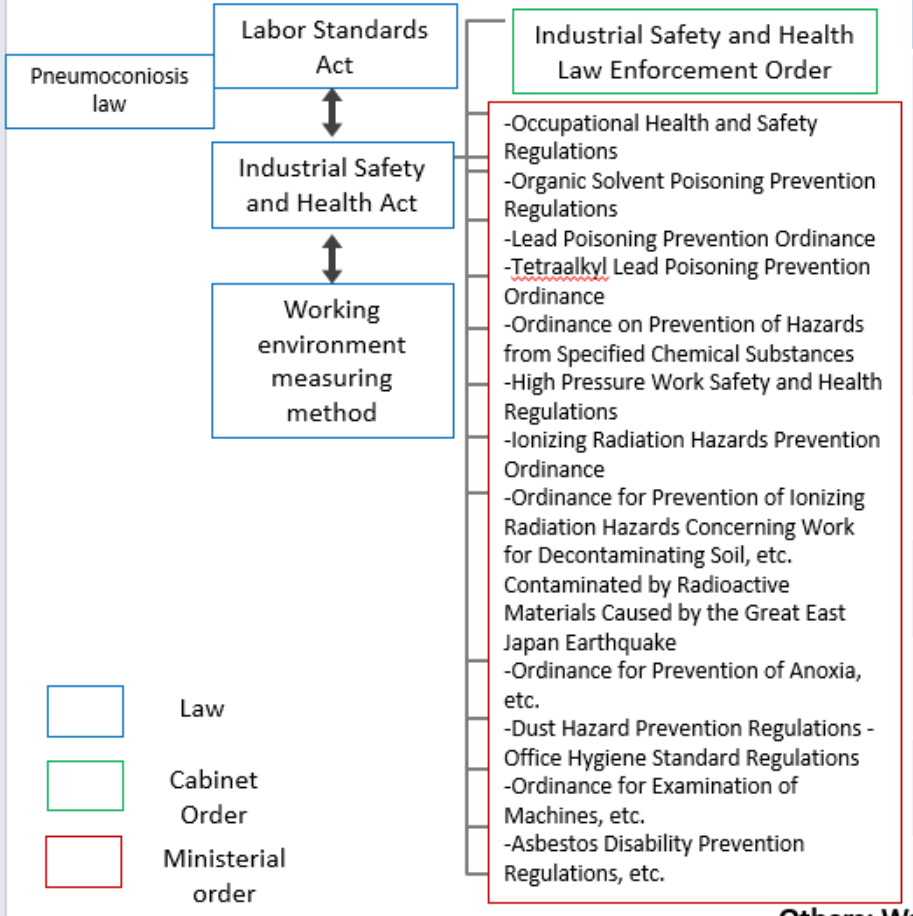
Rule of thumb in occupational accidents (Heinrich's law)）



In order to prevent serious accidents and disasters, we routinely identify these problems at the stage of near-miss incidents that cause accidents and disasters, and always take measures to predict danger. Efforts to minimize the number of near misses are important and necessary to prevent major accidents.

Major laws and regulations related to occupational safety and health, animal experiments, and facility management

Occupational safety and health



Related to animal experiments and experimental animal facilities

Subject	Related laws and regulations
Experiments using genetically modified organisms, etc.	・Act on the Conservation and Sustainable Use of Biological Diversity through Regulations on the Use of Living Modified Organisms (Cartagena Act)・Points to consider regarding the use of organisms obtained through the use of genome editing technology at the research stage (Notice)
Animal experiments using radioisotopes and radiation generators	Law Concerning Regulation of Radioisotopes, Etc. (RI Regulation Law), Ionizing Radiation Ordinance
Experiments using poisonous and deleterious substances	Poisonous and Deleterious Substances Control Law
Experiments with psychotropic drugs	Narcotics and Psychotropics Control Law
Experiments with chemicals	Organic rule, special rule
Experiments using pathogens	Infectious disease law, family law

Others: Waste Disposal Law (medical waste (injection needles, blood deposits, etc.), infectious waste)

Standards for care and storage of experimental animals and alleviation of suffering

(2006 Ministry of the Environment Notification No. 88, Revised 2013 Ministry of the Environment Notification No. 84)

3rd. Common Criteria

1. Maintaining animal health and safety
   - (1)Feeding and storage method
   - (2)Facility structure, etc.
   - (3)Education and training, etc.
2. Conservation of living environment
3. Prevention of harm, etc.
   - (1)Method of breeding and storage and the structure of the facility
   - (2)Raising and keeping poisonous animals
   - (3)Response to escape
   - (4)Emergency response
4. Acquisition of knowledge related to common infectious diseases between humans and animals
5. Appropriate record management of laboratory animals
6. Handling during transportation

Standards for care and storage of experimental animals and alleviation of suffering

(2006 Ministry of the Environment Notification No. 88, Revised 2013 Ministry of the Environment Notification No. 84)

3rd. Common Criteria

3. Prevention of harm, etc.

The structure of the facility and the method of breeding and storage

(a) The manager shall maintain facilities with a structure and strength that will not allow experimental animals to escape.

(b) Managers shall implement necessary health management to prevent laboratory animal managers, experimenters, and caretakers from contracting diseases derived from laboratory animals.

(c) Managers and laboratory animal managers should ensure that experimenters and animal caretakers can work without risk, and that the structure of the facility and methods of rearing and storage are in place.

(d) The Laboratory Animal Manager should ensure that the number and condition of the Laboratory Animals being reared or kept are confirmed through daily management and maintenance inspections of the facility and periodic patrols.

(e) Experimental animal managers, experimenters, and caretakers shall endeavor to provide each other with the information necessary to prevent the occurrence of harm from experimental animals in accordance with the following.

(i) The Experimental Animal Manager shall provide the experimenter with information on how to handle the experimental animal and provide the caretaker with necessary guidance on the care and storage of the animal.

(ii)The experimenter shall provide the laboratory animal manager with information on the laboratory animals used in the experiment, etc., and give necessary instructions to the caretakers regarding their care and storage.

(iii)The caretaker shall report the condition of the experimental animal to the experimental animal manager and experimenter.

(f) Managers, etc. shall take necessary measures to prevent persons unrelated to the care and storage of Experimental Animals and experiments, etc. from coming into contact with Experimental Animals.

Standards for care and storage of experimental animals and alleviation of suffering

(2006 Ministry of the Environment Notification No. 88, Revised 2013 Ministry of the Environment Notification No. 84)

3rd. Common Criteria(continuation)

3. Prevention of harm, etc.

(2)Raising and keeping poisonous animals

When raising or keeping poisonous animals such as poisonous snakes, to stocking emergency medicines such as antitoxin serum, establish a system that allows doctors to provide prompt emergency treatment in the event of an accident, and strive to prevent the occurrence of harm to humans by laboratory animals

(3)Response to escape

Managers, etc. shall take necessary measures to prevent experimental animals from escaping from storage facilities, etc. In addition, the manager shall determine in advance the measures to be taken in the event that a laboratory animal escapes, and endeavors to prevent harm to humans and the occurrence of environmental conservation problems when the animal escapes, as well as inflicting harm on humans. In the event that an experimental animal that is at risk of escaping from the facility, immediately contact the relevant organizations.

(4)Emergency response

In cooperation with relevant administrative agencies, the administrator shall prepare in advance a plan concerning measures to be taken in the event of an emergency such as an earthquake or fire while ensuring consistency with the local disaster prevention plan. In the event of an accident, immediately endeavor to protect laboratory animals and prevent harm to humans and environmental conservation problems due to escape of laboratory animals.

4. Acquisition of knowledge related to common infectious diseases between humans and animals

In addition, the manager, laboratory animal manager, and experimenter should establish a communication system with public health institutions, etc., so that necessary measures can be taken promptly in the event of an outbreak of a common infectious disease between humans and animals. Strive for maintenance.

Guidelines for Proper Conduct of Animal Experiments

Science Council of Japan June 1, 2006

9th. Safety management

The heads of institutions, etc., shall endeavor to ensure safety and health in operations at facilities, etc. in accordance with relevant laws and regulations. In addition, in order to prevent from contracting diseases derived from experimental animals, the laboratory animal manager, animal experimenter, and breeder will prepare the necessary equipment and manage health. In animal experiments, etc. that handle physically or chemically dangerous materials or pathogenic microorganisms (hereinafter referred to as risk factors), and animal experiments that use genetically modified organisms, safety and health of humans and experimental animals, ecosystems, etc. It must be ensured that the reliability of the experimental results is not lowered due to adverse effects on the animal, damage to the experimental animals, etc. In addition, necessary measures must be taken to prevent hindrances to public health, the living environment, and conservation of the ecosystem for those conducting animal experiments and surrounding facilities.

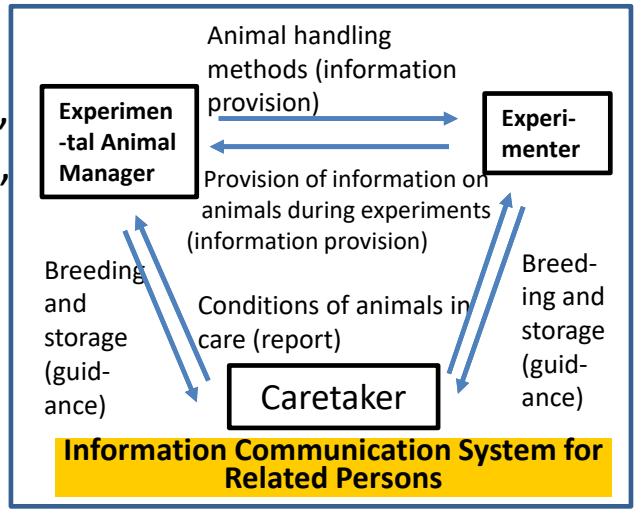
1) Understanding and handling risk factors

Grasping of occupational health and safety risk factors (chief engineer/manager), Providing information necessary for the danger of risk factors, handling methods, disaster prevention, etc.

2) Prevention of harm caused by experimental animals

To prevent , bites and scratches,zoonotic diseases,andallergies from animals

Mutual sharing of information on how to handle experimental animals to prevent harm



Guidelines for Proper Conduct of Animal Experiments

Science Council of Japan June 1, 2006

9th Safety management

3) What to do when experimental animals run away

Managers, etc., take necessary measures to prevent laboratory animals from escaping from storage facilities, etc. When not working, keep the lid of the cage housing the laboratory animal properly, or lock the door of the cage.

- Keep the door of the breeding room closed at all times. Immediately contact the relevant organizations.

4) Emergency response

In cooperation with relevant administrative agencies, the manager prepares in advance a plan regarding measures to be taken in the event of an emergency such as an earthquake or fire, while ensuring consistency with the local disaster prevention plan. 。

- In the event of an emergency, promptly strive to protect experimental animals and prevent the occurrence of environmental conservation problems, such as harm to humans due to escape.
- Established an emergency contact system by developing a contact network for holidays, nights and emergencies.

5) Conservation of living environment

Occupational health and safety hazards

- Biological factor

  Zoonotic diseases, toxic animal species, toxins, cells, allergens

  Poisonous animals: Venomous snakes (pit vipers, habu, sea snakes), fish (pufferfish, stonefish), reptiles/amphibians (gila, poisonous frog), birds (black shrike), cnidarians (jellyfish, sea anemones)

- Chemical factor

  Drugs (carcinogens, mutagenic substances), reagents, anesthetics, disinfectants

- Physical factor

  Heavy objects, falling objects, noise, high temperature, high pressure, low temperature, injection needles, knives

- Radiation factor

  Ionizing radiation, non-ionizing radiation, sealed source, unsealed source

  (X-rays, gamma rays, etc.) (Visible light, infrared rays, etc.)

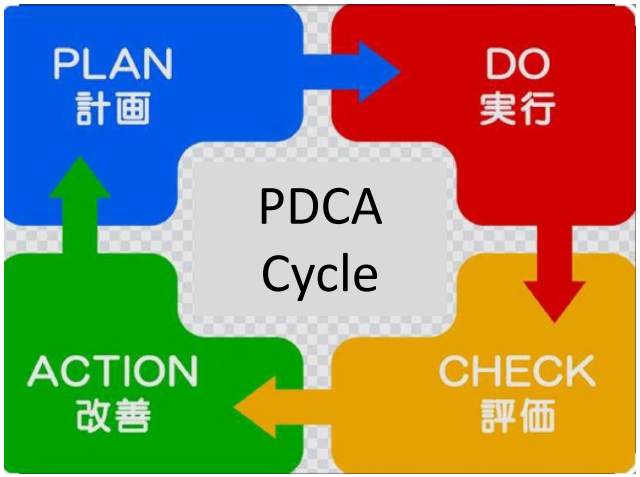
- Psychosocial factors

  Harassment/mental stress

Japanese Society for Laboratory Animal Science
Quoted from the text of the laboratory animal manager workshop

Occupational health and safety in laboratory animal facilities

- Extraction and analysis of potential risk factors associated with experimental animal breeding and animal experiments
- Understanding risk factors and their locations (parts) and estimating risks
- Consider risk reduction measures for each risk factor and implement measures according to priority
- Formulation and operation of an occupational safety and health plan for experimental animal facilities (breeding, experiments, etc.) based on institutional policies and regulations
  - ・Operating procedures
  - ・Record
  - ・Report (near-miss incident report)
  - ・Regular inspection of equipment
- Regular education and training (overall/individual level)
  Be especially careful during pregnancy, illness, and immunosuppression.
- Periodic evaluation and review of occupational health and safety plans
  Occupational Health and Safety Management System: PDCA



Quoted from the Japanese Society for Laboratory Animal Science, Laboratory Animal Manager Workshop Textbook

Risk factors in the working environment of laboratory animal facilities

- Breeding room
  - ・Experimental animals (bites, scratches, etc.)
  - ・Breeding management work (falling, back pain, etc.)
- Laboratory (animal laboratory)
  - ・Experimental animals (bites, scratches, needle sticks)
  - ・Drugs and chemicals
  - ・Research equipment (injuries, burns, frostbite, pinched fingers)
- Corridor
  - ・Transportation of heavy equipment (back pain/collision)
- Washing room

  Poor work environment
  - ・High temperature/humidity
  - ・Wet floor (falling over)
  - ・noise
  - ・Dust (allergy)
  - ・Large equipment, heat generating equipment (injuries, burns, pinched fingers)

Japanese Society for Laboratory Animal Science

Quoted from the text of the laboratory animal manager workshop

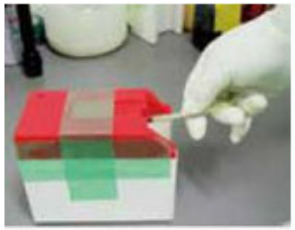
Chemical factor

・Formalin ➡ Protective equipment, local exhaust,

・Isoflurane ➡ measures for surplus gas (Use of adsorbent)

Physical factor

・Needlestick injury (syringe needle, scalpel blade) ➡ Prohibition of recapping



・Allergy to experimental animals

・ As part of labor management, ascertain the experimenter's and breeder's allergies to laboratory animals.
In serious cases, take measures such as changing the work department.

・ Thorough use of personal protective equipment.
(latex, rubber) gloves allergy

Animal Allergy! You are the one to pay attention!

Beware of bites and needlesticks!

Animal bites and needle sticks can be fatal!
May cause anaphylaxis.

Who should be careful!

1. person with allergies
   (Hay fever, atopic dermatitis, food allergy, etc.)
2. People who have been bitten by an animal in the past or who have had a needlestick injury.

If an accident occurs, the next five minutes are very important.

1. If the bite or needle prick site swells, or if you feel it is difficult to breathe, leave the breeding room immediately and talk to someone nearby.
2. If you have an EpiPen, inject it immediately.
3. Run to a nearby hospital or call an ambulance immediately.

Things to keep in mind for people with allergies

1. Do not enter the breeding room alone!
2. Ask your doctor to prescribe a fast-acting anti-anaphylaxis drug (e.g. EpiPen)!
3. Finish the work when the hospital is open (9:30 to 16:00)!

*Even latex gloves can cause anaphylaxis!

Japanese Society for Laboratory Animal Science
Animal Allergy Study Working Group

Partially quoted from the Japanese Society for Laboratory Animal Science, Laboratory Animal Manager Workshop Textbook

Personal protective equipment
（PPE：Personal protection Equipment）

- ●Head/face： Hats,Helmets,Face shields
- ● Ear: Earplugs,Earmuffs
- ●Eye： Dust-proof glasses,Goggles(protective glasses)
- ●Respiratory system：Masks,Dust-proof masks,Gas masks
- ●Hand： Protective gloves(infection prevention/heat resistant/chemical resistant/bite prevention),Arm cover,Long waterproof gloves
- ●Legs： Shoes(work shoes,safety shoes,boots)
- ●Others： Protective clothing(dedicated workcolothing,aprons,etc.)

Obligation to wear personal protective equipment

●Employers must have workers use protective equipment in certain work and environments.

● Workers must comply with the measures and instructions implemented by the employer.

Japanese Society for Laboratory Animal Science

Partially quoted from the text of the workshop for laboratory animal managers

Items to be considered and implemented by institutions and facilities

- Change or replacement of duties
- Burn protection (coating of high temperature parts, etc.): steam and hot water supply pipes
- Ventilation, etc. of breeding rooms, washing rooms, laboratories, operating rooms, etc.: temperature, humidity, illuminance
- Change to a safer method (sterilizer/sterilization method)
- Weight reduction, downsizing, and mechanization of transportation equipment and goods
- Securing sufficient work space
- Introduction of dedicated work equipment (local exhaust system, clean booth, safety cabinet)
- Separation of waste and introduction of dedicated containers (infectious, medical, syringes, hypodermic needles)
- Equipment inspection (statutory inspection, etc.)
- (Gas, etc.) Introduction of alarm devices
- Occupational safety and health plan and manual development as a facility
- Develop and post accident response (flowchart, emergency contact information)
- Preparation of first-aid kits (first-aid medicines) (when handling poisonous animals: antiserum effective against poison, including preparation of 5% tannic acid)
- Education and training (lectures, technical guidance)
- Support for acquisition of qualifications (experimental animal technician, various work chief licenses, etc.)

Partially quoted from the Japanese Society for Laboratory Animal Science, Laboratory Animal Manager Workshop Textbook

Consideration and implementation of risk reduction measures

Implementation of matters stipulated by laws and regulations
(if there are applicable matters)

1 Measures in the design and planning stages

Abolishment or change of dangerous work, substitution of materials with less danger or toxicity, change to safer construction methods, etc.

2 Engineering measures

Guards, interlocks, safety devices, local exhaust ventilation systems, etc.

3 Management measures

Development of manuals, prohibition of entry, exposure control, education and training, etc.

4 Using personal protective equipment

Even if the above measures 1 to 3 are taken, it is limited to those that are implemented for the risks that could not be eliminated or reduced.

High

Priority of risk reduction measures

Low

Quoted from Guidelines for Investigation of Danger or Harm
(Ministry of Health, Labor and Welfare)

Implementation of risk reduction measures

1.Substances with high hazards changed to substances with low hazards

2. Installation of local exhaust ventilation

3. Install partitions (partitions, vinyl curtains, etc.) to prevent diffusion in the work area.

4. Implementing education to change work procedures to those with less divergence, work procedure manuals, and to protect off-limits areas, etc.

5. Use gas masks and dust masks (pay attention to expiry dates (breakthrough*, etc.) and storage methods)

※ Breakthrough refers to a state in which the detoxification capacity of the canister is limited and the permeating toxic gas concentration exceeds the maximum allowable permeation concentration of the canister.

Notification of risk assessment results to worker

1.Well-known matter

- Name of target substance, content of target work
- Risk assessment results (identified hazards or hazards, estimated risks)
- Details of risk reduction measures to be implemented

2. Well-known method

Either posted at the workplace at all times, issued in writing, or confirmed by computer terminal at the workplace

3. Education at the time of hiring, education at the time of work change

Partially quoted from the Japanese Society for Laboratory Animal Science, Laboratory Animal Manager Workshop Textbook

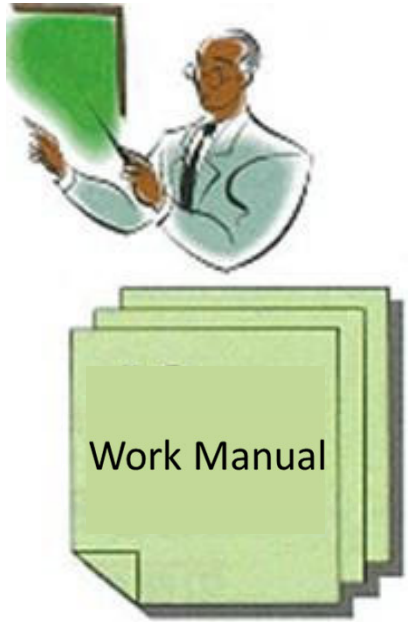
How to implement safety assurance and safety management?

Health checkup

Basic items 10 Items according to work

(Work that requires additional inspection: handling of specific chemical substances/organic solvents, ionizing radiation work, etc.)

Education and training



■ Need for occupational health and safety
- ・Laws, etc.
- ・Ensuring safety
- ・ Near miss reports and records

■ Perception of risk factors

■ Preparation of work manual and dissemination
- ・Handling heavy objects
- ・Handling of chemical substances
- ・Handling of experimental animals
- ・Prohibition of needle recapping
- ・Handling, inspection and maintenance of equipment (for research, transportation, etc.)

■ Necessity and wearing of personal protective equipment

Partially quoted from the Japanese Society for Laboratory Animal Science, Laboratory Animal Manager Workshop Textbook

Conclusion

In order to prevent serious accidents and disasters, we routinely identify these problems at the stage of near-miss incidents that cause accidents and disasters, and always implement risk prediction measures to reduce the number of near-miss incidents. It is important to make efforts to reduce accidents as much as possible in order to prevent serious accidents.