UNIVERSITÉ LAVAL

CORE CURRICULUM

THEORY

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1. Ethics in Animal Experimentation

1.1 Generalities

"…the use of animals in research is accepted insofar as it serves to help better understand fundamental biological principals or to help gain knowledge that can reasonably be expected to benefit human beings or animals…"

The use of animals in research is the source of genuine social debates. That is why researchers, Animal Care Committees and all those involved in the use of animals in research must make sure that they use animals in a responsible and respectful way. As soon as the matter of animal experimentation is raised, ethical issues as well as animal rights must be given due consideration. Always keep in mind that the use of animals in research is a privilege.

The review of protocols regarding animals by an Animal Care Committee (ACC) constitutes the cornerstone of any program concerning the care and use of animals. ACCs must always remain focused on the goal of reconciling public expectations and experimentation needs. Therefore, committees must address ethical issues in the context of research projects that involve animal testing. Therefore, a review based on Marshall Hall's principles is beneficial:

- No experiment should be carried out if the information searched for can be obtained through simple observation;
- No experiment should be carried out without a clearly defined, achievable goal;
- Unnecessary repetition of the experiment should be avoided especially if a renowned physiologist was in charge during the first experiment conducted;
- All experimentation should be carried out with the least possible infliction of suffering on the animal;
- All physiology experiments should be witnessed by peers to diminish the need for repetition.

The implementation of Marshall Hall's principles as well as the Three Rs tenet ensures an ethical and responsible use of animals. Université Laval and all affiliated research centres are committed to complying with this line of conduct.

1.2 Canadian Council on Animal Care

The Canadian Council on Animal Care (CCAC) is a national organization that relies on peer review. It is responsible for establishing and maintaining standards regarding the care and use of experimental animals (i.e., in research, teaching and testing) throughout Canada.

To accomplish this task, the CCAC:

- Establishes guidelines regarding the use of animals in research;
- Inspects institutions every three years to make sure they conform to these guidelines;

- Reviews the work accomplished by the care committee of every institution.

The CCAC then presents institutions with an evaluation report, so they may take corrective action within a given time frame.

The mission of the CCAC is to ensure that animals used in science are given optimal care, both physically and psychologically in accordance with acceptable scientific standards. Another task of the CCAC is to promote a high level of knowledge and sensitivity regarding ethics. In order to reach these goals, the CCAC offers the following programs:

- Assessment and Certification Program;
- Guideline Program;
- Education, Training and Communications Program;
- Three Rs Program.

For further information, visit: http://www.ccac.ca/en_/

1.3 Animal Care Committee

The mandate of the Animal Care Committee (ACC) is to ensure that CCAC guidelines and policy are observed. To fulfill this task, the committee must:

- Review and approve authorization requests and the protocols submitted by researchers;
- Annually review every protocol and of any modification made to the protocols;
- Ensure that a training program meeting the standards of the CCAC is available to users;
- Ensure that no animal is obtained or any protocol initiated without its authorization;
- Inspect the institutions under its jurisdiction at least once a year.

***No protocol can be initiated or any modification introduced**

without prior approval of the ACC *

The ACC is made up of:

- A president;
- Scientists and /or teachers whose research involves the use of animals;
- Veterinarian(s) having relevant experience in animal care and use;
- An institutional member whose regular activities do not involve the use of animals;
- At least one person representing public interest and concerns who is not involved with the institution or the use of animals in research, teaching or testing;
- A member of the technical staff involved in the care and use of animals;
- A student representative of the institution;
- The manager(s) of the animal supply facility;
- The coordinator of the ACC.

There are 2 ACC at Université Laval:

- Comité de protection des animaux de l'Université Laval (CPAUL) (animal care committee of Université Laval) that receives requests from researchers working for the following institutions:
    - University campus
    - Centre de recherche de l'institut universitaire de cardiologie et de pneumologie de Québec (CRIUCPQ)
    - Centre de recherche de l'institut universitaire en santé mentale de Québec (CRIUSMQ)
    - Laboratoire d'organogénèse expérimentale (LOEX)
    - Laboratoire de recherche en sciences aquatiques (LARSA)
- Comité de protection des animaux du CHUQ (CPAC) (animal care committee of the CHUQ) that receives requests from researchers working at:
    - Centre de recherche du CHUQ (CRCHUQ)

When a researcher issues an authorization request, it must meet the following criteria:

- Clearly identify the objective of the project;
- Justify the need for use of animals;
- Justify the number of animals used;
- Provide a detailed description of the manipulations carried out on animals and of anticipated effects;
- Describe measures taken to minimize the discomfort experienced by animals and describe limit humane endpoints.

Requests will be transferred to the ACC and reviewed during a committee meeting.

The ACC must ensure the following:

- The scientific merit of the project has been demonstrated previously through an independent peer review;
- Qualified personnel will be responsible for managing the animal supply facility and for the handling and care given to the animals;
- The animals will receive appropriate veterinary care;
- The chosen methods of euthanasia comply with CCAC standards;
- The Three Rs tenet is observed;
- The objective and procedures are thoroughly detailed.

Throughout the course of any research, the ACC is entitled, if necessary, to take the following actions:

- Put a term to any reprehensible procedure if unnecessary suffering or distress is found to be inflicted on an animal;
- Put a term to any procedure not authorized within the framework of the protocol;
- Have an animal euthanized if it is impossible to relieve the pain or distress experienced.

Personnel of the animal facility as well as users of animals must report any problem related to the care and use of animals to the veterinarian, who must contact the researcher when necessary or discuss the issue with team members.

Researcher and users of animals must comply with protocols, University policies and standard operating procedures at all time. In case of non-compliance, actions will be taken and may lead, after 3 offenses, to a suspension of funds and animal facility access.

1.4 Legislation and regulation

Different reference documents (*Legislative jurisdiction over animal used in research, teaching and testing*, 1998 and *The Protection of Animals Used for the Purpose of Xenotransplantation in Canada*, 2000) conclude that under the *Constitution Act 1867*, the federal government does not have jurisdiction to legislate in the animal experimentation field, which is subject to provincial jurisdiction. However, laws that were established by the government within three other fields can apply to animal experimentation:

- Sections 446 and 447 of the Criminal Code protect animals against cruelty, abuse and neglect;
- The Health of Animals Act protects livestock against infectious diseases that could be a threat to humans, other animals and Canadian international trade;
- The federal government has the jurisdiction—which is not strictly speaking legislative in nature—to award grants subject to various conditions. Therefore, grants awarded by the Canadian Institutes of Health Research (CIHR) or the Natural Sciences and Engineering Research Council (NSERC) are conditional to compliance by the institution with the CCAC policy. The CCAC establishes standards regarding the care and use of experimental animals in research, teaching and testing throughout Canada.

All Canadian provinces have legislated in the field of animal welfare, and in absence of more specific laws, animal welfare laws are to be observed when using animals in science. The following provinces have specifically legislated on the use of animals in research, teaching and testing: Alberta, Manitoba, Saskatchewan, Ontario, New Brunswick, Nova Scotia and Prince Edward Island.

1.5 The Three Rs tenet

The Three Rs tenet (replacement, reduction and refinement) serves as a guide for an ethical use of research animals. Université Laval has added a fourth R, which stands for **R**espect of the animal.

Numerous methods have been developed to progressively reduce the number of animals used in research. Nevertheless, these methods have limitations. Animals can be used when it has been determined that no replacement alternative is suitable to reach the objectives of a research project with previously established scientific merit.

Replacement: Using alternative methods such as computer programs, videos or dummies instead of experimenting on animals. It can also refer to the use of cells and tissues maintained in culture, invertebrates, or species more suitable for experimentation.

Reduction: Using the minimal number of animals required to obtain statistically valid experimental data without losing useful information.

Refinement: Modifying at least one aspect of the experimental procedure or the husbandry to minimize pain, distress or stress experienced by animals or to enhance their general welfare.

When presenting an authorization request for the use of live animals, researchers must demonstrate how they plan to respect and apply the Three Rs tenet.

Finally, at Université Laval, one guiding principle must be observed at all times. A fourth R was developed: **R**espect of the animal. In order to apply this principle, animal users must display compassion, sensitivity and empathy toward the animal, as well as concern for its physical and psychological welfare.

Above all, the researcher must demonstrate that his scientific objective cannot be achieved using alternative methods. There are many alternative methods, and they must be considered before opting for the use of animals.

Here are some useful links to inquire about available alternatives:

CCAC

Center for Alternatives to Animal Testing (CAAT)

Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM)

The National Centre for the Replacement, Refinement and Reduction of Animals in Research

Before starting any experiment, the researcher must complete an authorization request for review by the ACC. In this request, among other things the researcher must present his research objective, the protocol to be followed, how he intends to apply the Three Rs tenet and the products to be used, as well as their dosage. No animal can be ordered priori to having obtained final approval of the protocol by the ACC. The number of animals ordered must be the same as the number indicated in the authorization request.

1.6 Standards and Procedures

Standard Operation Procedures (SOP) describes the procedure carried out on laboratory animals. They must be consulted prior to any intervention performed on animals and must be

followed to the letter. If the procedure has to be modified, the modifications must be justified in the protocol and approved by the ACC.

When developing a protocol, researchers must consult pre-existing standards and policies. The SOP may be consulted on the web page of the Direction des services vétérinaires.

1.7 Confidentiality

Users of the animal supply facility as well as members of ACCs are subject to the CCAC confidentiality policy.

It is also forbidden to use cameras or video cameras in animal facilities without prior authorization from the ACC and the manager of the animal facility, and without first tabling a request in the authorization request for the use of live animals.

2. Prevention – occupational health and safety

2.1 Regulation

There are many laws and regulations concerning occupational safety and health (OHS):

- An Act Respecting Occupational Health and Safety → enforces and provides rules on prevention;
- An Act respecting industrial accidents and occupational diseases → indemnifies workers;
- Regulation respecting occupational health and safety → defines rules governing the work environment: workplace layout, protective personal equipment, storage, hazardous material, WHMIS, etc.;
- The civil code → deals with relations between people;
- Bill C-21 → deals with some rules of penal law concerning serious behavioural problems;
- The board of directors of the Université Laval (Resolution 2011-17) → enforces and structures the role of managers.

2.2 An Act Respecting Occupational Health and Safety

An Act Respecting Occupational Health and Safety entails some responsibilities for the employer and the worker. Among those responsibilities, the employer must ensure that management is adapted and provide appropriate methods and techniques. The employer must also monitor the work environment and provide information to workers on risks inherent in their job. As well, sufficient safety training for employees to work safely and minimal supervision are mandatory.

The worker also has responsibilities regarding health and safety at work: some measures should be taken by the worker to ensure safe work conditions for the worker as well as for the others. The worker must also take part in the accident risk evaluation process to help mitigate risks and

submit to requisite medical examinations. It is necessary to collaborate with the health and safety committee.

2.3 Board of Directors of Université Laval resolution 2011-17

The obligations of Université Laval are the following:

- Providing a safe environment by removing, when possible, risks to health or safety;
- Promoting health, safety and the improvement of the work environment by observing laws, regulations, policies and procedures concerning these three themes;
- Establishing a means of communication to enable consultation between managers, employees and their union or association in order to identify job-associated risks and take measures to eliminate these risks;
- Defining the responsibilities of the authorities and various third parties.

2.4 Regulation respecting occupational health and safety: recommendations

2.4.1 Physical risks

Handling sharp objects

Sharp objects are used frequently in a protocol involving animals, such as needles used for injection or surgical tools. In such case, it is important to follow these rules:

- Do not replace the cap on a used needle; if you need to do so, hold it against a surface then use only one hand to replace the cap;
- Do not leave a needle without protection;
- Dispose of needles with used syringes in biohazard containers right after use;
- Sweep up broken glass and dispose of it in a container for breakable objects;
- Dispose of, or send for repair, slightly cracked glass or glass with a broken extremity.

Noise exposure

Exposure to noise should not exceed 85 adjusted decibels (dBA) during an 8-hour work shift for a 40-hour week.

Electricity

Accidents related to electric current may happen anywhere. In the presence of water and electricity exercise caution. Help prevent potential accidents by maintaining equipment, declaring deficiencies or equipment breakdown and following a safe work method.

Installing or repairing equipment must be done by a professional.

Radiation

There are two types of radiation:

- Ultraviolet radiation, which may cause burns; protection glasses are needed.
- Ionizing radiation (X-ray, computed tomography) must be controlled according to the standards issued by the local Radiation Protection Committee.

Using radiation requires a certificate issued by a Radiation Protection Committee.

The manager must be informed as soon as possible of any pregnancies among female staff.

Lasers

The use of lasers and others dangerous optical sources is supervised by the Comité de sécurité dans l'utilisation des lasers et des sources optiques dangereuses. The role of the latter is to counsel operators of lasers or apparatus working with lasers on safety aspects. Depending on the classification of the laser, operators must have received training and an eye examination, and the classification must be posted at the entrance of the laboratory.

2.4.2 Ergonomic risks

Carrying objects or heavy loads, handling carriages or cage pallets, repeated movements and repetitive movements are risks factors. A course on ergonomics at work and adapted tools may be offered.

When storing, there should be a sufficient space to move around and place objects or heavy boxes. Items should be stored efficiently as the material arrives in order to avoid overcrowding of the work environment.

2.4.3 Chemical risks

During experimental protocols, detergents/disinfectants, pesticides, anaesthetic gas and chemical products to preserve tissues are used during experimental protocols.

Each product used should have a data sheet visible in the work place. These data sheets are kept in a designated location and should be available at all times.

An Act Respecting Occupational Health and Safety states that all employers must provide WHMIS (Workplace Hazardous Materials Information System) training if workers must work with chemical products: training is **mandatory**.

Each product is labelled with a pictogram indicating the WHMIS category. Here are the main categories:

2.4.4 Bio-hazard

The use of experimental pathogens is legislated by *Laboratory Biosafety Guidelines* issued by Health Canada and the *Containment Standards for Veterinary Facilities* published by Agriculture and Agri-Food Canada, Appendix A. When research involves a bio-hazard, the candidates must receive a certificate from the Comité de gestion des risques biologiques de l'Université Laval to attest that containment requirements meet the safety standards corresponding to the containment level required by the project, or the research program.

The first rule for infection prevention is to maintain excellent personal hygiene. Washing the hands is to be performed before and after handling products or animals even if handling with gloves. Doing so helps to reduce the risks of contamination for both the researcher and the surrounding environment.

The main exposure channels to infectious agents are the following:

- Aerosols;
- Ingestion;
- Absorption by the skin, mucosa or wounds;
- Injection (accidentally during the research).

Protection requirements consider these channels of exposition; it is extremely important to respect these requirements.

Infectious agents are grouped in four levels of bio-safety depending of their contagion degree and the severity of the infection. Each level of bio-safety corresponds to a level of containment which should be respected for health reasons.

The Public Health Agency of Canada published pathogen safety date sheets (PSDS) which describes the characteristics of the pathogenic agents and also includes recommendations for working with these substances in the laboratory.

http://www.phac-aspc.gc.ca/lab-bio/res/psds-ftss/index-eng.php

2.4.5 Self-protection

Self-protection equipment

Some experiments require the use of personal protective equipment (PPE) which includes:

- Safety glasses;
- Frock;
- Gloves;
- Overshoes;
- Hat;
- Respiratory protection.

These measures must be posted at the entrance to offices, laboratories or any place where needed. Wearing sandals or open shoes is prohibited.

Even when wearing personal protective equipment, it is important to keep in mind that there are still risks. The material has to be maintained and used according to rules. Cleaning the workspace is also important and must be done frequently.

Laboratory hood and biological safety cabinet:

- **The fume hood:** Protects the handler when manipulating chemicals like paraformaldehyde. The fume hood MUST not be used when manipulating infectious agents.
- **Laminar flow positive pressure cabinet:** Air is filtered out of a HEPA (High Efficiency Particulate Air Filter) that removes fumes from the work space channelling them outside the hood. The material is protected, but the handler is not.
- **Biological safety cabinet:** The biological safety cabinet, when well maintained and used according to safety rules, makes primary containment efficient and is adapted to the handling of human pathogenic agents. The Laboratory Biosafety Guidelines are the reference to distinguish the different types of biological safety cabinet.

2.4.6 First aid

Event declaration: accident/incident

It is most important to notify the manager or another person in charge before leaving, if it is not possible, it should be done as soon as possible.

Spatter of chemical products

In the case of spatter, call the emergency number of the establishment and rinse with water for 15 minutes. Thereafter, the person must go to the hospital and bring the data sheet when possible. Eyewash fountains or eyewash bottles are located near the sinks. Do not put any product on the surface of the eyes or put any fat substance on the burns.

Bite or abrasion

In the case of bite, abrasion or contact with the fluids of an animal, immediately bleed the wound, clean with water and soft soap for 15 minutes then rinse with water. If the eyes or mucosa are involved in the accident, rinse with tepid water for 15 minutes. After, go to the hospital with the protocol explanation sheet. Any accident or incident involving contact with an animal or its excretions must be reported. There is a specific procedure for injuries involving a primate.

2.4.7 Vaccination

Vaccination, when available, helps reduce the risk involved in handling infectious agents. An evaluation prior to hiring determines which employees are more likely to get infected and provides the information on adequate preventive vaccination according to the handling the employee will be involved in and depending on the availability of the vaccines.

According to the protocols, an additional vaccination may be offered later.

2.4.8 Zoonosis

Zoonosis is a disease transmitted from animals to humans or from humans to animals. There are different types of zoonosis for each species. When the animal comes from a recognized supplier that certifies the health status of the animal, it is rare that the animal is infected with this type of disease.

Since there are risks that cannot be completely eliminated, it is essential for health concerns to:

- Respect the dress code established according to the species;
- Report any accident or incident involving contact with an animal or its excretions;
- Receive the necessary vaccines according to the species the handler is exposed to;
- Quarantine animals recently arrived.

If primates are used, there is a specific procedure in case of accident or incident since the risk of zoonosis is higher with primates.

In order to learn more about existing zoonosis, read Appendix VII in the Guide to the Care and Use of Experimental Animals of the CCAC:

http://www.ccac.ca/Documents/Standards/Guidelines/Experimental_Animals_Vol1.pdf

2.4.9 Allergies

Developing allergies as a result of handling laboratory animals is an increasingly frequent phenomenon.

Most common allergens are:

- Rat urine and saliva;
- Mouse urine;
- Rabbit hair;
- Saliva, skin and hair of cats and dogs;
- Latex gloves.

Personal protective equipment helps prevent the development of allergies. Proper wearing of gloves, respiratory protection and compliance with the dress code help to manage the risk.

2.4.10 Psychosocial risks

Every individual may experience personal or professional problems and require support. A confidential professional counselling service is offered when someone has problems that may affect health, personal life or the ability to work.

http://www.santepsy.ulaval.ca/webdav/site/cspt/shared/pdf/Depliant_PAP_06-2010.pdf

References

CCPA (CCAC)

http://3rs.ccac.ca/en/

Centre for Alternatives to Animal Testing (CAAT)

http://caat.jhsph.edu/

Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM)

http://iccvam.niehs.nih.gov/

The National Centre for the Replacement, Refinement and Reduction of Animals in Research

http://www.nc3rs.org.uk/