Technion – Israel Institute of Technology

Procedures, guidelines and instructions for the use of animals in experiments at the Technion

This booklet constitutes the Technion Code for Experimentation on Animals

Submitted to the National Council for Animal Experimentation

May 1997

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Technion Code for Experimentation on Animals

General

Animal experiments are conducted at the Technion in order to advance knowledge in the life sciences and medicine through basic and applied research and for instructional purposes in teaching medicine and life science.

The responsibility of researchers and the institution in all matters related to animal experimentation is defined in the Prevention of Cruelty to Animals Law (Experiments on Animals), 1994-5754, see **Annex A**. Pursuant to the Law, any Technion researcher who intends to conduct an experiment or instructional demonstration on animals (vertebrates) must submit a work plan for approval by the Technion Committee for Supervising Implementation of the Technion Code for Animal Experimentation (hereinafter: the "Animal Ethics Committee"), pursuant to the Code's provisions. In order to do so, the researcher must hold an academic position (regular or clinical track) at the Technion.

Any external entity interested in using the services of the Technion's Experimental Surgery Unit will submit a detailed work plan for approval by the Animal Ethics Committee. The Chief Investigator of that entity will serve as its senior scientist while all other participants will be considered as secondary researchers. Additionally, a representative of the Experimental Surgery Unit, a veterinarian, will be listed in the application as a secondary researcher. He will serve as the Technion's representative in accompanying and overseeing the entire experiment, from the application stage through to its completion.

Any laboratory used for experimentation in association with Technion personnel will remain open to visits by members of the Animal Ethics Committee. In addition, all animal holding facilities in the laboratory and all animal suppliers must be approved by the Committee.

When performing an experiment on animals, researchers must weigh the following considerations: ensure that the animals are always treated in the best possible way, and that all resultant suffering (if any) is as minimal as possible. Properly holding laboratory animals, minimizing pain and treating them humanely demand professional and scientific judgment founded on an understanding of needs – both species-specific and unique to the particular study or demonstration. It is the researchers who are responsible for correctly treating their experimental animals.

Do not conduct an experiment on laboratory animals without considering the scientific value the experiment is intended to yield. No animal experimentation should be performed if similar results can be achieved in alternative ways. If animal

experimentation cannot be avoided, use the smallest quantity of animals as possible that are as low as possible on the phylogenetic scale. (For the purpose of this document, an 'experimental animal' consists of any vertebrate separated from its natural environment in order to serve for research or instructional purposes).

Suitable buildings and properly working equipment are important for holding laboratory animals suitably. More important, however, are the considered judgment and sincere concern for the animals among those who come into contact with them.

In order to fulfill the above norms and in order to meet legal requirements and conditions for obtaining research funds, all users of animals are obliged to read and confirm these procedures and guidelines, and undertake to act accordingly, by signing the Experiment Approval form.

Animal research – procedures and control

Principles

A. No experiments shall be conducted on animals unless they satisfy the provisions of this Code.

B. Performing animal experiments is conditional on prior approval by the Animal Ethics Committee.

C. The Chief Investigator shall be responsible for upholding procedures during the course of the experiment. He must ensure that the research and technicians working with the animals have received suitable training for doing so. He must also be accountable to the Animal Ethics Committee and must uphold all procedures.

D. All employees taking part in animal research will enroll in a special course conducted twice a year at the Faculty of Medicine. New employees will register for the first course that takes place after beginning work.

E. All experiments and treatments will be under the supervision of an authorized veterinarian. The veterinarian will be available for consultation and guidance and will attend to the health and welfare of the animals.

F. Use of animals for teaching purposes will be permitted solely after approval is obtained from the Animal Ethics Committee.

G. Experiments on animals are liable to cause pain, suffering, or discomfort. Therefore operations of all types will be performed under general or local anesthetic or other suitable anesthetic in accordance with accepted veterinary methods (see Annex B).

H. Performing a painful experiment using central or peripheral muscle relaxation is prohibited unless accompanied by general anesthesia.

I. Animals in the process of recovering from an operation must receive preventive treatment for pain in consultation with the authorized veterinarian.

J. Use of restraint accessories shall be for as short a time as possible, this after all other less distressful means have been rejected or proven to be inefficient.

K. Small blood samples may be taken for diagnostic purposes, without the need for anesthesia. In the event of massive blood samples (up to 10% of total blood capacity, no more frequently than once every eight weeks) or terminal bleeding, anaesthetize the animal prior to the bleeding.

L. Animals suffering chronic pain, sustained discomfort, or an irreparable deformity shall be euthanized.

M. Euthanizing animals must be done by a skilled employee, in the least painful and swiftest manner possible and according to an accepted method. For partial details on methods – see Work procedures with Laboratory Animals.

N. Euthanizing animals after an experiment using general anesthesia will be done (as best as possible) prior to them regaining consciousness.

O. At the end of such an experiment, the researcher must arrange for euthanizing the animal, collecting the body in a plastic bag, and bringing it to a specially designated location. Animal corpses will be will be freeze-stored in designated refrigerators of the Animal Dept. and be removed as needed by an authorized body with the appropriate government license. Corpses and radioactive waste will be stored in separate refrigerators with standard markings for radioactive materials and be removed as needed under the responsibility of the Technion Radiation Risk Supervisor.

P. Transferring information concerning the use of experimental animals including the principles, policy, rules, guidelines, and practical instructions as well as the actual use of animals at the Technion will be done in coordination with the Chair of the Animal Ethics Committee and the Technion veterinarian or spokesperson.

Q. Animal experiments are subject to provisions of Israeli law; all Technion principles, general policy and practical instructions pertaining to performance of experiments shall not negate or derogate from any legal provisions. Awareness of pertinent laws is incumbent on all users and involved parties. The institution, its managers, office holders and/or employees shall not bear responsibility for users' lack of knowledge pertaining to such provisions (enclosed is the text of the Prevention of Cruelty to Animals Law (Experiments on Animals 1994-5754, see **Annex A**.)

Supplemental: Based on requirements of the National Council for Animal Experimentation, in its letter dated October 6, 1998.

R. Decisions of the National Council including updates published on the Animal Ethics Committee website:
http://md.technion.ac.il/committees/committee_desc.asp?committeeID=15&contentC
and on the National Council website:
http://www.health.gov.il/pages/default.asp?maincat=92&catId=906&PageId=4689 and updates appearing in Annex I of the Technion Code shall constitute the basis for the Technion Code for Experimentation on Animals.

Fate of animals no longer used for experimentation

A. Animals that are unhealthy or those that have undergone treatment that poses possible danger to their surroundings shall be euthanized.

B. Healthy animals that no longer serve for experimental purposes:

1. Mice and rats shall be euthanized unless it is possible to transfer them to zoos while observing provisions of the Prevention of Cruelty to Animals Law.
2. Cats and dogs – Efforts will be made to find an adopting body within a reasonable space of time, otherwise they shall be euthanized.
3. Primates – It is mandatory for the Internal Committee to contact the Israel Nature and Parks Authority in order to check whether it can transfer the primate to a suitable framework. Otherwise, primates shall be euthanized.
4. Other animals: Based on Sections A, B, and C respectively.

The Technion Ethics Committee for the Use of Laboratory Animals

All experiments involving the use of animals, including in teaching laboratories, must be approved by the Animal Ethics Committee. The Committee is responsible for the application of the Prevention of Cruelty to Animals Law – Animal Experimentation in all Technion activity, including the holding and treatment of animals.

The Committee's authority includes formulating guidelines for holding, treating, utilizing and euthanizing animals; inspecting animal holding facilities at the Technion; and issuing permits for conducting animal experiments for research and teaching purposes at the University.

The Committee operates according to rules of the National Council as well as those of the American NIH – National Institutes of Health.

Specifically, the Committee's roles include:

A. Representing the Technion before the National Council for Animal Experimentation (hereinafter: "the Council") as well as government entities relevant to animal experimentation.

B. Ensuring the implementation of procedures for the correct use of animals at the Technion.

C. Inspecting facilities used for holding and experimenting on animals.

D. Approving applications for using animals.

E. Contact with the public for all matters concerning the use of animals at the Technion – via the Technion spokesperson.

F. Issuing periodic reports to the Council on behalf of the Technion on all approved applications – as required by law.

G. Offering a course in working methods for animal experimentation and granting permits to employees after being trained pursuant to guidelines of the National Council (see **Annex C**).

H. Reviewing faculty/Technion plans for utilizing animals including plans for altering or building holding facilities or working with laboratory animals.

Composition of the Committee

The Animal Ethics Committee will include representatives (one or more) of all units that conduct animal experiments. Additionally, the Committee will include the Technion veterinarian, a member of the Technion staff not involved in animal experimentation, and one member who has no employer-employee relationship with the Technion. The Committee will consist of no less than six members (including the Chair). The Executive

Vice President for Research, the Technion's supreme authority in matters of holding and utilizing animals at the Technion, will appoint the Committee Chair and its members based on recommendations of the deans of the relevant faculties.

The Committee will convene at least four times a year. Membership will be terminated for members who do not participate in three consecutive meetings; they shall be replaced by another member, based on the Dean's recommendation to the Executive Vice President for Research. If a Committee member leaves for a sabbatical year, the Executive Vice President for Research will appoint another member in his place, in consultation with the faculty Dean.

Submitting applications to conduct experiments on animals

All applications for using animals in experiments or for teaching purposes shall be submitted to the Animal Ethics Committee on the appropriate forms (see **Annex D).** Applications will include all of the following information:

A. Name of the research
B. Name and address of the Chief Investigator and all partners in the project involving in working with animals
C. Rationale for using animals (including quantity of animals)
D. Declaration of the necessity for using animals in the project including failure to discover suitable alternatives
E. Type and number of animals to be used
F. Detailed description of the intended work with animals including full names of medications and anesthetic substances to be used, with specific reference to steps taken in order to minimize pain and suffering to the animals
G. Chief Investigator's declaration the project's suitability to Technion and national requirements pertaining to the use of animals.

In order to draft such applications, the Committee Chair will appoint an ad hoc committee of three members of the Animal Ethics Committee, at least one of whom is not affiliated with the requesting unit, as well as the Technion veterinarian.

Committee members examining the application may approve or reject it, request clarifications, corrections or completions. Any reservations concerning the application on the part of one or more members will lead to the rejection of the application, including suitable notification to the researcher.

Upon the application's approval by all three members of the ad hoc committee, by signing an evaluation form, copies of the application will be sent to all members of the Animal Ethics Committee. Members of the Committee who have reservations concerning the decision must submit their reservations within two weeks of the date on the copies they have received. **The final decision will be determined by the Chair of the Committee, based on a majority vote in the Committee – with absence of reservations by a member considered as a positive answer.** In the event of a decision in favor of the application, the Chair of the Committee will sign the approval form for the project and the researchers may begin work.

Appeals on decisions of the ad hoc committee will be made by submitting a letter of explanation to the Committee Chair, who will present the application for discussion at the Committee's next plenum meeting. Approval or rejection of the application in that meeting shall be based on a majority vote, with each participant having one vote. Such a meeting may be convened only with the participation of at least six members. The decision of the plenum meeting of the Committee is final.

Project proposals shall be approved for a period of no more than four years.

Application submission procedure: The application will be submitted electronically, directly to the website of the National Council for Animal Experimentation**.** Instructions for accessing the website can be found in **Annex E.** An original copy, signed by the Chief Investigator must be sent to the secretary of the Committee prior to processing the application. In addition the Technion Annex to the application on the Committee's website must be filled out (**Annex F)**.

Changes in the protocol:

All changes to the protocol (changes of experiment, addition of animals, changes in animals, supplementary time) require the submission of a request via the National Council website. The Committee will treat the request as a change if it is so indicated on the application form. The request must be approved by a member of the Committee as well as the Chair.

<u>Numbering of approval forms</u>

Approval forms issued to researchers by the Animal Ethics Committee (see **Annex G***)* will include an approval number. The number will begin with the prefix IL (symbol of Israel) and continue with a serial number (based on order of receipt at the faculty), the month, and year submitted, as follows:
IL-XX-MO-YEAR.

Procedures for ordering, holding, and working with animals

1. Ordering animals

The researcher will send the order for animals to the Animal Department (Faculty of Medicine) or to a member of the Animal Ethics Committee (for other faculties). The order must be submitted on an animal order form that includes the Committee's approval number. The order will contain all necessary details and will receive budget approval from the appropriate parties. Orders must arrive to the Animal Department at least seven working days prior to the desired delivery date.

A researcher who wishes to bring in animals from outside entities shall do so solely after coordinating with the director of the Animal Dept. All animal purchases, whether in Israel or abroad, will be executed only after obtaining approval from the director of the Animal Dept.

Procedure for bringing animals to the Animal Dept.:

A. Receive the appropriate health report from the animal supplier prior to the animals' arrival, and send it to the director of the Animal Dept. Only after the director's authorization is received can the process begin for bringing in the animals.

B. Submit an order for animals and fill out the purchase order form.

C. The Animal Dept. will ensure the receipt of the animals from the supplier, delivery of animals to the Animal Dept. and their introduction to the appropriate unit.

D. Order surgical and other services and tissues in advance using the 'Animals and Services Order Form'. The researcher and Animal Dept. will coordinate in processing the order.

2. Holding animals

During an experiment, animals will be kept solely in the Animal Dept. or in other authorized areas. All efforts should be made to conduct experiments in rooms belonging to the Animal Dept. If this is not possible, the animals will be removed from the Animal Dept. with the sole authorization of the Department director.. Animals removed from the Animal Dept. will not be returned unless special authorization is received from the director. After treating an animal, the researcher or technician must make certain that the cage contains sufficient water and food.

Rodent young up to the age of three weeks scheduled to be held for more than 24 hours must be supplied with a nursing female and not remain alone (one nursing female for every 10 rodent young).

3. Certifying employees for work with laboratory animals

Entry to and work in the Animal Dept. will be permitted solely to authorized personnel or with their accompaniment. Holding facilities for animals exist in the following units:

1) Faculty of Medicine (Rappaport Building)
   Detailed instructions appear in **Annex H.**
2) Faculty of Biology and the Faculty of Food Engineering and Biotechnology (on the Technion Neve Shaanan campus). The parties responsible for the facilities will consist of representatives of those units on the Animal Ethics Committee in addition to the Technion veterinarian.
   All additional animal holding facilities must be approved by the Animal Ethics Committee, after having been inspected by the Committee Chair and the Technion veterinarian, and following notification to the National Council for Animal Experimentation.
   Members of the Supervisory Committee for Animal Experimentation will visit the Technion's animal holding facilities once a year.
   The entrance to facilities shall have signs posted indicating the names and phone numbers of responsible parties.
   Rooms will be locked during all times that employees are not on the premises.
   Those in charges of the facilities will set suitable procedures for ordering animals, removing corpses and other actions.

Training employees for animal experimentation

Any person who is involved in, or shall be involved in, animal experimentation must be suitably trained to work with animals. In order to ensure that they are adequately skilled, each employee who intends to work with animals must pass a suitable training – under the auspices and responsibility of the institution – and receive written authorization for working with animals. In the event that the institution considers that a specific individual is already sufficiently skilled to work with animals, it can issue a permit without the individual taking the course. That said, the National Council for Animal Experimentation (hereinafter: "the Council") recommends that each person, even if highly experienced in animal experimentation, take this course.

Written confirmation of a person's reliability to conduct experiments on animals will be issued by the institution authorized for animal experimentation and under its

responsibility. Such confirmation will be held by the institution and available for presentation to the Council or a representative on its behalf. If the institution has an internal committee certified by the Council as being a responsible body for animal experimentation at the institution, the confirmation for working with animals must be signed by the Committee Chair and by the institution's authorized veterinarian. If the approved institution has no internal committee, the confirmation will be signed by the institution's general director (or proxy) and the institution's authorized veterinarian.

A person who conducts animal experiments without the above confirmation will be found in violation of the Prevention of Cruelty to Animals Law (Experiments on Animals), 1994-5754 and be subject to penalty under the Law.

Confirmation for performing animal experiments for a brief period – up to six months

A person who is not an authorized researcher and makes a request to conduct animal experiments for a brief and limited period up to six months will be authorized to do so by the institution's internal committee if he meets one of the following conditions:

1. He has successfully completed the full training course mentioned above.
2. He has successfully completed a special training session by the authorized researcher in coordination with a veterinarian authorized by the institution. The training will include:
    a. An explanation concerning correct treatment of experimental animals, the use of alternatives, and minimizing pain.
    b. Practical demonstration of the specific experiment to be performed.
    c. Trial run of at least two experiments by the authorized researcher in coordination with the veterinarian.

The internal committee of the institution at which the experiments are performed will grant authorization solely for the specific requested animal experiment and for a limited period of up to six months. This will be accompanied by a written commitment on the part of the authorized researcher that all animal experimentation performed by the requesting individual will be under the researcher's supervision and responsibility.

Work procedures with laboratory animals

See Annex B (anesthetics for common types of animals), Annex I (Work Code for the Faculty of Medicine Animal Dept.), and Rules for Working with Animals, adjusted to

rules appearing in: **Guide for the Care and Use of Laboratory Animals, National Research Council, National Academy Press, Washington DC, USA.**

Euthanizing animals

Euthanasia must be performed with the minimum of fear and pain to the animals and with maximum speed. Euthanasia must be adapted to the experiment and must satisfy safety restrictions for employees.

The preferred method for euthanasia is administering surplus anesthetic via inhalation or injection. Small rodents may be placed into a tank with CO_2. For animals that are anesthetized, KC1 may be injected into the vein. Researchers must confirm the death of the animal following the above actions. If deemed necessary from a scientific standpoint, beheading using a special guillotine (for rats or guinea pigs) or breaking the neck (for mice) will be approved.

It is prohibited to anesthetize animals **onsite** in the Faculty of Medicine's Animal Dept.

Annexes

Annex A from the Prevention of Cruelty to Animals Law – 1994

Presented below is the third section of the Prevention of Cruelty to Animals Law, Sections 8–12 under the heading 'Animal Experimentation'. The Law in its entirety shall be in the possession of each researcher.

8.
(a) No animal experiments shall be performed unless in accordance with this Law.

(b) The quantity of animals in an experiment shall be the minimum necessary for performing the experiment.

(c) Experiments on animals must ensure that minimum pain and suffering is caused to the animals.

(d) Animal experiments will be conducted as per the supplement.

9. No permit for an animal experiment will be issued if it is possible to accomplish the experimental goal in reasonable and alternative ways.

10. No experiments shall be performed for checking cosmetic products that are not for health purposes or for cleaning substances, unless such substances are permissible for experimentation by the Council plenum.

11.
(a) Animal experiments will be performed solely by an authorized researcher at an institution approved by the Council and in accordance with the rules it has established.

(b) When conducting an experiment not exclusively for teaching purposes, the researcher will maintain records pursuant to the procedure set by the Committee according to Section 13. At the end of the experiment he will report its results to the Committee.

(c)
(1) Notwithstanding that which is stated in subsection (a), students at educational institutions or institutions of higher learning are entitled to conduct experiments under the supervision and in the presence of an authorized researcher;

(2) In the matter of this Law – All educational institutions shall be considered as a single institutional entity under the management of the Director General of the Ministry of Education, Culture and Sport.

12. The Council will be authorized to permit animal experimentation at an institution that meets all of the following:

(1) The institution understands the written guidelines that are binding on its employees and that have been confirmed by the Council with respect to: holding animals, work arrangements at the institution, safety procedures, methods of anesthesia, care/treatment of animals, euthanasia methods and removal of animals under the law, all with attention devoted to avoiding harm to the quality of the environment and ensuring that employees have been suitably instructed.

(2) The institution employs a veterinarian who supervises the health and wellbeing of animals; administers medical treatment to them; is charged with preventing illness, reducing suffering before, during and after an experiment; euthanizing an animal if needed; and guiding the staff of employees in these subjects.

<u>Annex B</u> – Medications for anesthetizing common types of laboratory animals

(Additional details concerning dosage, manner of injection, and anesthetizing different types of animals in the relevant literature may be obtained from the Faculty of Medicine's Experimental Surgery Unit)

In mixtures of two substances, dosage is indicated according to the order of the substances' appearance, for example:

Ketamine + xylazine HCl	i.m., i.p.	100–200 + 5–16 mg per kg body weight.

The intention is:

Ketamine 100–200 mg per kg. body weight

Xylazine 5–16 mg per kg body weight

Mouse – *Mus musculus*

Substance	Administration	Dosage
Thiopental (Pentothal)	i.v., i.p.	25–50 mg / kg body weight
EMTU (Inactin)	i.p.	80 mg / kg body weight
Pentobarbital Na (Nembutal)	i.p.	40–60 mg / kg body weight
ketamine HCl	i.m., i.p., i.v.	80–100 mg / kg body weight
Ketamine + xylazine HCl	i.m., i.p.	100–200 + 5–16 mg / kg body weight
Fentanyl + fluanisone solution (Hypnorm)	i.p.	0.01–0.02 ml / kg body weight
Halothane	Inhalation	Until anesthetized
Isoflurane	Inhalation	Until anesthetized

Rat – *Rattus rattus*

Substance	Administration	Dosage
Thiopental (Pentothane)	i.v., i.p.	25–40 mg / kg body weight
EMTU (Inactin)	i.p.	80–100 mg / kg body weight
Pentobarbital Na	i.p.	40–60 mg / kg body weight

(Nembutal)		
ketamine HCl	i.m.	50–100 mg / kg body weight
Ketamine + xylazine HCl	i.m., i.p.	40–90 + 5–13 mg / kg body weight
Fentanyl + fluanisone solution (Hypnorm)	i.m., i.p.	0.4–0.5 ml / kg body weight
Halothane	Inhalation	Until anesthetized
Isoflurane	Inhalation	Until anesthetized

Guinea pigs – *Cavia poircellus*

Substance	Administration	Dosage
diazepam (Valium)	i.p.	2.5–5.0 mg / kg body weight
xylazine HCl	i.p.	5–40 mg / kg body weight
Pentobarbital Na (Nembutal)	i.p.	30 mg / kg body weight
ketamine HCl	i.m.	50 mg / kg body weight
Fentanyl + fluanisone solution (Hypnorm)	i.m., s.c.	0.2–1.50 ml / kg body weight

Hamster – *Mesocricetus auratus*

Substance	Administration	Dosage
Pentobarbital Na (Nembutal)	i.p.	30 mg / kg body weight
ketamine HCl	i.p.	50–100 mg / kg body weight
Halothane	Inhalation	Until anesthetized
Isoflurane	Inhalation	Until anesthetized

Rabbit – *Oryctolagus cuniculus*

Substance	Administration	Dosage
Pentobarbital Na	i.v.	30 mg / kg body weight

(Nembutal)		
ketamine HCl	i.m.	35–50 mg / kg body weight
Ketamine + xylazine HCl	i.m.	5–10 + 35–50 mg / kg body weight
Fentanyl + fluanisone solution (Hypnorm)	i.m., s.c.	0.2–0.6 ml / kg body weight
Halothane	Inhalation	Until anesthetized
Isoflurane	Inhalation	Until anesthetized

Dog – *Canis familiaris*

Substance	Administration	Dosage
Pentobarbital Na (Nembutal)	i.v.	30 mg / kg body weight
Thiopental (Pentothal)	i.v.	30 mg / kg body weight
Ketamine + xylazine HCl	i.v.	10 + 0.3 mg / kg body weight
Ketamine + diazepam (Valium)	i.v.	10 + 0.5 mg / kg body weight
Buprenorphine (Nopan)**	i.m.	0.005–0.02 mg
xylazine HCl***	i.m.	0.5 mg / kg body weight
Halothane	Inhalation	Until anesthetized
Isoflurane	Inhalation	Until anesthetized

Pig – *Sus scrafa*

Substance	Administration	Dosage
Ketamine + diazepam	i.m.	15.0 + 2.0 mg / kg body weight
Ketamine + acepromazine	i.m.	20–30 + 1.1 mg / kg body weight
Ketamine + xylazine HCl	i.m.	20 + 2.0 mg / kg body weight
pancuronium*	i.v.	0.02–0.15 mg / kg body weight

pentobarbital Na	i.v.	20–40 mg until animal is anesthetized
Thiopental	i.v.	10–25 mg until animal is anesthetized
buprenorphine**	i.m.	0.05–0.1 mg
Isoflurane	Inhalation	Until anesthetized
Halothane	Inhalation	Until anesthetized

Non-human primates

Substance	Administration	Dosage
Ketamine HCl	i.m.	10–20 mg / kg body weight
pentobarbital Na	i.v.	20–25 mg / kg body weight
Telazol	i.m.	4–30 mg / kg body weight
Halothane	Inhalation	Until anesthetized
Isoflurane	Inhalation	Until anesthetized

* Muscle relaxant – Limited for use on anesthetized animals (general anesthetic) only.

** Analgesic – pain killer

*** Tranquilizer

Literature:

Research Animal Anesthesia, Analgesia and Surgery, Eds. Alison C. Smith and Michael Swindle, 1994. Scientists' Center for Animal Welfare, Library of Congress 94-68123.

Annex C – Employee instruction confirmation form

_____ (institution)

_____ (employee)

_____(instructor / institution's veterinarian)

The employee has been instructed in the following:

- Entering the Animal Dept. in appropriate clothing
- Biology of rats and rabbits
- Safety instructions related to work with animals
- Animal Dept. procedures
- Methods of anesthetizing and euthanizing animals
- Holding, caring for and maintaining the wellbeing of experimental animals
- Holding and caring for animals after experiments
- Equipment for working with animals

In signing this form, the employee declares that he has read and understood Animal Dept. procedures and has read and understood the Prevention of Cruelty to Animals Law (Experiments on Animals), 1994-5754.

Employee's signature _____

Instructor's signature _____ Date: _____

Annex D – National Council form

Application to perform animal experimentation

(Name of institution) _____

Approval number: _____

A. Explanation for applicant

A. The Prevention of Cruelty to Animals Law (Experiments on Animals), 1994-5754 regulates the matter of animal experimentation. The Law's implementation is supervised by the Ministry of Health via the National Council for Animal Experimentation.

B. Animal experimentation in Israel is permitted solely according to the Law.

C. You are hereby requested to read the Law and confirm you have done so in writing.

D. The Law states that no animal experiments may be performed if such experiments have suitable alternatives. Please confirm with your signature that there are no alternatives to the proposed experiment.

E. If the experiment involves the use of hazardous materials (biological, chemical or physical) you must obtain the approval of the institution's Safety Committee.

F. You are hereby requested to state your commitment to conduct the experiment(s) solely in facilities that have been approved by your institution's Animal Experimentation Committee.

G. Upon signing the form you are undertaking to act in accordance with the Law and conduct the experiment(s) solely in facilities approved by your institution's animal experimentation committee and in accordance with Council guidelines.

B. The research study

1.	Research topic in Hebrew		
2.	Research topic in English		
3.	New study Continuing study	☐ ☐	If this is a continuing study, indicate the previous approval number:

4.	Approval term		-select- years	

C. Chief Investigator

1.	ID card no.		Passport no.	
2.	Surname / Hebrew		First name / Hebrew	
3.	Surname / English		First name / English	
4.	Department		Faculty	
5.	Phone		Additional phone	
6.	Mobile phone		Fax	
7.	Email			

D. Partners

	Surname	First name	ID / passport no.	Relationship with researcher
1.				-select-
2.				-select-
3.				-select-
4.				-select-
5.				-select-
6.				-select-

Professional training

Please specify the professional training received by each research partner in the study (including Chief Investigator) authorized to engage in the experiment:

	Surname and first name	Certificate no.	Certifying institution	Other	Type of animal
1.			-select-		-select-
2.			-select-		-select-

3.			-select-		-select-
4.			-select-		-select-
5.			-select-		-select-
6.			-select-		-select-

1. The experiment
General

1.	Primary goal	Advancing health, medicine and prevention of suffering.	☐
		Advancing scientific research	☐
		Inspection or production of materials or objects	☐
		Education and teaching	☐
2.	Secondary goal	Examinations performed according to legal requirements.	☐
		Examinations for the wellbeing of the animals	☐
		Observing behavior	☐
		Animal nutrition	☐
		Other – specify:	☐
3.	Abstract of the study and goal of using animals in the study / in English /		
4.	Give reasons for the use of animals for the purpose of the study		

2. Animals required for the study

	Animal	Number
1.		
2.		
3.		
4.		
5.		
6.		

Details of each animal and experiment

Group 1

General information on animals in the study

Animal	**Variety (compulsory for mice and rats)**	**Gender**	**Age**	**Weight**	**Number**
		-select-	-select-	-select-	
Source of animal				Has undergone genetic change: Y/N	-select-
		-select-	-select-	-select-	
Source of animal				Undergone genetic change: Y/N	-select-

Reasons for selecting the animals and description of the course of the experiment

1.	Rationale for selecting type and variety of animal.	
2.	Rationale for number of animals	
3.	Description of the animal	

	experiment and treatment of animals (if anesthetic substance and painkillers are used, please indicate dosages and method of administration).		
4.	Anesthetic substances		
5.	If the use of anesthetic substances and/or painkillers is not suited to the experiment, explain why.		
6.	Level of pain and suffering during and after the experiment	Collection of organs from animals that have not undergone experimentation and have been euthanized using accepted methods for this purpose	☐
		Experiments that cause no (or minimal) temporary discomfort or distress.	☐
		Experiments that cause mild distress or short-term pain. Experiments at this level are prohibited from causing significant changes in the animal's appearance and in physiological parameters such as: heart/respiratory rate or social behavior. During or after experiments in this category, the animals will not exhibit signs of self-harm, anoxia, dehydration, hyperactivity, aberrant posture in laying down, emitting loud sounds, particularly aggressive behavior or isolation.	☐
		Experiments that cause medium to severe pain or distress, treated with painkillers.	☐
		Experiments that cause considerable and sustained pain or suffering and that do not administer painkillers to the	☐

		animals for metastatic cancerous growths, or experiments that cause death (such as: use of poisons). Give scientific justification for why painkillers will not be used.	
7.	Methods and substances for reducing pain		
8.	Conditions for terminating a specific animal's participation in the experiment.		
9.	Have the animals in this application been experimented upon previously?		
10.	If so, indicate the number of the previous experiment (with permit attached).		
11.	Fate of animals upon the end of the experiment	-select-	
12.	Euthanasia method	-select-	

Group 2

General information on animals in the experiment

Animal	**Variety (compulsory for mice and rats)**	**Gender**	**Age**	**Weight**	**Number**
		-select-	-select-	-select-	
Source of animal				Undergone genetic change: Y/N	-select-
		-select-	-select-	-select-	
Source of animal				Undergone genetic change: Y/N	-select-

Reasons for selecting the animals and description of the course of the experiment

13.	Rationale for selecting type and variety of animal.		
14.	Rationale for number of animals		
15.	Description of the animal experiment and treatment of animals (if anesthetic substance and painkillers are used, please indicate dosages and method of administration).		
16.	Anesthetic substances		
17.	If the use of anesthetic substances and/or painkillers is not suited to the experiment, explain why.		
18.	Level of pain and suffering during and after the experiment	Collection of organs from animals that have not undergone experimentation and have been euthanized using accepted methods for this purpose	☐
		Experiments that cause no (or minimal) temporary discomfort or distress.	☐
		Experiments that cause mild distress or short-term pain. Experiments at this level are prohibited from causing significant changes in the animal's appearance and in physiological parameters such as: heart/respiratory rate or social behavior. During or after experiments in this category, the animals will not exhibit signs of	☐

		self-harm, anoxia, dehydration, hyperactivity, aberrant posture in laying down, emitting loud sounds, particularly aggressive behavior or isolation.	
		Experiments that cause medium to severe pain or distress, treated with painkillers.	☐
		Experiments that cause considerable and sustained pain or suffering and that do not administer painkillers to the animals for metastatic cancerous growths, or experiments that cause death (such as: use of poisons). Give scientific justification for why painkillers will not be used.	☐
19.	Methods and substances for reducing pain		
20.	Conditions for terminating a specific animal's participation in the experiment.		
21.	Have the animals in this application been experimented upon previously?		
22.	If so, indicate the number of the previous experiment (with permit attached).		
23.	Fate of animals upon the end of the experiment	-select-	
24.	Euthanasia method	-select-	

Group 3

General information on animals in the experiment

Animal	Variety (compulsory for mice and rats)	Gender	Age	Weight	Number
		-select-	-select-	-select-	
Source of animal				Undergone genetic change: Y/N	-select-
		-select-	-select-	-select-	
Source of animal				Undergone genetic change: Y/N	-select-

Reasons for selecting the animals and description of the course of the experiment

25.	Rationale for selecting type and variety of animal.		
26.	Rationale for number of animals		
27.	Description of the animal experiment and treatment of animals (if anesthetic substance and painkillers are used, please indicate dosages and method of administration).		
28.	Anesthetic substances		
29.	If the use of anesthetic substances and/or painkillers is not suited to the experiment, explain why.		
30.	Level of pain and suffering during and after the experiment	Collection of organs from animals that have not undergone experimentation and have been euthanized using accepted methods for this purpose	☐

		Experiments that cause no (or minimal) temporary discomfort or distress.	☐
		Experiments that cause mild distress or short-term pain. Experiments at this level are prohibited from causing significant changes in the animal's appearance and in physiological parameters such as: heart/respiratory rate or social behavior. During or after experiments in this category, the animals will not exhibit signs of self-harm, anoxia, dehydration, hyperactivity, aberrant posture in laying down, emitting loud sounds, particularly aggressive behavior or seclusion.	☐
		Experiments that cause medium to severe pain or distress, treated with painkillers.	☐
		Experiments that cause considerable and sustained pain or suffering and that do not administer painkillers to the animals for metastatic cancerous growths, or experiments that cause death (such as: use of poisons). Give scientific justification for why painkillers will not be used.	☐
31.	Methods and substances for reducing pain		
32.	Conditions for terminating a specific animal's participation in the experiment.		
33.	Have the animals in this application been experimented upon previously?		
34.	If so, indicate the number of the		

	previous experiment (with permit attached).		
35.	Fate of animals upon the end of the experiment	-select-	
36.	Euthanasia method	-select-	

Chief Investigator's declaration

I have read the Law and hereby undertake to use the animals specified in this application according to the Law and the institution's animal experimentation code.

I undertake to conduct the experiment solely in facilities approved by the institution's Animal Experimentation Committee.

I undertake contact the Committee in order to obtain its approval for any change in the promised conditions of this document.

I have read the institution's guidelines concerning animal experimentation and undertake to act accordingly and as per the Council guidelines.

I declare that no alternative exists for the requested experiment.

I have undergone training in animal experimentation and in minimizing pain caused to animals.

All partners in this study have undergone, or will undergo, such training prior taking part in the experiment (pursuant to paragraph D)

_____ _____

Signature Date

Decision of the institutional Committee

☐ The experiment proposal as been examined and approved. The Committee is convinced that it is not possible to achieve the goals of the experiment using reasonable alternatives.
Approval valid until:

☐ The experiment proposal has not been approved.

Remarks:

Annex E – Instructions for entering the website and accessing/submitting the National Council form

Submitting applications via the National Council website

Website of Ministry of Health

http://www.health.gov.il/pages/default.asp?maincat=60&catId=424&PageId=2851

Click 'application form'

Enter the Connectra security system

See browser settings

Enter using Technion code	Technion
Technion code	lz4zm9m
Sign in	
Press	Connect
Click	Animals
Click	Open

Press 'Work with form'

Select name of institutional committee – select 'Technion'

Enter system – select the 'researcher' window

Existing form – press 'no' to request new form

Press 'OK'

Fill in all applicant's details

Choose a personal code name for the application

Fill in all sections of the application.

It is advisable to fill in the windows by copying and pasting from an existing document.

Save the form frequently.

Only after pressing on 'send form to committee' will the form be sent to

the Committee – to be processed after receiving a signed copy that includes the Technion Annex.

Annex F – Appendix to application for animal experimentation at the Technion

*** <u>Application heading:</u>**

*** <u>Application number:</u>**

***<u>Company/department:</u>**

<u>Address:</u>

Phone number:

Email:

* **<u>Contact person</u>:**
* **<u>Type of animal requested</u>**
* **<u>Number of animals requested</u>**

1. **<u>Lay summary</u>**
   Summary for a non-professional, in two or three sentences (avoid the use of professional terms).
2. **Specify experience and training in animal experimentation of each participant in the study**
   - I hereby declare that students listed in the application who have not been trained will take a training course during the first year. The students will not perform animal experimentation without the supervision of a suitably trained participant.
3. **<u>Specify the role of each participant in the proposed experiment:</u>**
4. **<u>Specify where the experiment will be conducted:</u>**
   Faculty of Medicine _____ researcher's laboratory _____
   Faculty of Biology _____ Faculty of Food Engineering _____
   Faculty of Biomedical Engineering _____
5. **<u>Follow-up experiments</u>**
   Indicate the number(s) of the previous application _____
   Explain why the projects needs to be followed up:
6. **<u>Does the experiment affect the environment?</u>** Yes__ No__

Use hazardous materials? Yes___ No___
Use biological/polluting substances? Yes___ No___
If so, please specify:
*Radiation Yes___ No___ (sent to Radiation Hazard Supervisor)
* Use viral vectors Yes___ No___
If you have answered 'yes' to one of the questions, please give details:
_____
Specify the steps to be taken in order to avoid harming the animals and employees in the Animal Department:

7. **<u>For applications from companies or for any experiment using animals larger than a rabbit:</u>**
   Obtain the signature of the veterinarian of the Experimental Surgery Unit attesting that he has read the application and found it to be suitable for submission to the Committee.
   Name of veterinarian of the Experimental Surgery Unit _____

   Signature _____ Date: _____

<u>Send this appendix by email to Ora Lapidot at ora@tx.technion.ac.il</u>

<u>Annex G</u> – Approval of the institution's committee

Technion Israel Institute of Technology
The Committee for the Supervision of Animal Experiments

Approval number IL-XXX-MO-YEAR

Date:

<u>For:</u>

<u>Approval period</u>: from _____ until _____

<u>The Committee has examined your application under the heading of</u>:

and found it to be suitable and in compliance with requirements of the Prevention of Cruelty to Animals Law (Experiments on Animals), 1994-5754

Type of animal:

Approved number of animals:

Any change from the approved procedure must be brought for the Committee's approval prior to implementation.

Chair of the Committee for the Supervision of Animal Experiments

Email:

<u>Annex H</u> – Code for working with animals

The Animal Dept. has been renovated in order to upgrade research conditions at the Faculty of Medicine and to satisfy requirements of the Prevention of Cruelty to Animals Law (Experiments on Animals), 1994-5754 as well as GLP (Good Laboratory Practice) regulations.

Bear in mind that these rules are meant of preserved the health and wellbeing of the animals and ensure successful research.

In order to meet these standards, observe all rules upon entering the Animal Dept. rodent wing and in your work habits.

The researcher is requested to read these rules carefully and sign at the bottom of the form –

A. <u>Entrance procedures</u>:

1. Each researcher / employee / student will receive a personal entrance card for entering the Animal Dept. and the rooms in which he will be working.
   The entrance card is personal and may not be transferred.
2. Do not bring any accompanying individual without an entrance card to the Dept. without prior approval from the Animal Dept. administration.
3. No employee / researcher / student will enter the sterile rodent wing if he has been in one of the other wings of the Dept. on that same day.
4. Entry to the rodent wing, operating rooms, and rabbit room is conditional on wearing suitable clothing (robe, shoe coverings, mask, head covering and gloves).
5. Do not bring in equipment (unless via the fumigation or autoclave room) to the sterile rodent area.
6. Make certain that <u>each door</u> remains shut after passing through it. Do not open two doors in rodent rooms at the same time (dirty and clean sides).

B. <u>Work procedures:</u>

7. Three separate cleanliness levels for holding rodents –
    1. Sterile 'clean' rooms.
    2. Quarantine rooms (for clean rodents)
    3. Regular 'dirty' holding rooms.

8. Work in rodent rooms / operating rooms is conditional on understanding and maintaining the chain of actions for ensuring implementation of sterile conditions for the animal and/or operating area.
9. Animals that have been removed from the sterile wing may not be returned to the wing unless it is to the non-sterile rodent wing.
10. Animals taken for surgery in the work room of the sterile rodent wing will be returned solely to a quarantine room.
11. An employee / researcher / student holding rodents in the non-sterile 'dirty' wing shall not enter the sterile rodent wing.

Passage from a dirty area to a clean area is prohibited.

12. Do not remove IVC cages from the rodent wing. Simple plastic cages are available for transferring rodents to laboratories.
13. **It is the researcher's responsibility to record the ethics number on the cards attached to the cages**. (Animals in cages without an ethics number will be destroyed).

C. <u>Conclusion of work</u>

14. Dirty cages will be removed by pushing them with the feet into the dirty corridor.
15. Make certain to clean the work surface, operating table and other areas from debris upon finishing work.
16. Rodents to be destroyed will be removed via the dirty corridor (removal of cage into the corridor). Made certain the cage is equipped with food and water sufficient for 24 hours.
17. Do not remove corpses or animals scheduled to be destroyed from laboratories after 14:30 (after that time, leave animals scheduled to be destroyed in the laboratory with enough food and water to last until the following day).
18. Researchers may not pass through the area of the service rooms.
19. Make certain that doors remain shut at all times. Do not open doors on the dirty and clean sides at the same time.

20. Researchers / employees / students must be certified to work with animals. Certification must be received within three semesters from the date of acceptance for work in the study.

I have read these instructions and undertake to comply with them.

_____

Confirmation number of certification for work with animals.

_____	_____
Signature of researcher / employee / student	Date

Annex I – Resolutions of the Committee for the Supervision of Animal Experiments

LD50 experiments

Resolution of the Committee in the matter of conducting experiments for the purpose of determining LD50 values.

To:

Responsible veterinarian at the institution approved for animal experimentation.

The National Council for Animal Experimentation, in its meeting of June 15, 2003, resolved the following:

Resolved:

"The Council had decided to prohibit the use of LD50".

"Only in exceptional cases will the Council in plenum session approve an LD50 experiment."

We ask that you conduct yourselves accordingly.

Provision of permits for animal experimentation for up to four years.

Council resolution concerning the possibility of granting approval for experimentation for four years was passed at its meeting of April 1, 2003:

Resolved:

"The maximum term of approved experimentation has been changed from three years to four years in order to solve the problem of research funds."

Council member attorney Benny Rubin called attention to the need to check and prepare this amendment in the Council's regulations.

Granting of permits for education and teaching purposes

Council resolution concerning animal experimentation for education and teaching purposes, passed at its meeting on October 23, 2007:

Resolved:

"In seeking to adapt animal experimentation for education and teaching purpose to the Prevention of Cruelty to Animals Law, the Council has decided to allow animal experimentation as follows:

A. Courses meant for training researcher to perform experiments on animals. Each course will be brought for approval by the Council according to the rules it has determined.

B. Courses aimed at instruction/teaching

1. All courses that seek to use animals for teaching purposes must be brought for approval by the institution's Teaching Committee (just as any other course). The Committee will approve a course and its use of animals only if it is convinced that the use of animals is vital for accomplishing the course's goals and that no reasonable alternative to animal experimentation exists (as required by the Law).
2. After the course is approved by the Teaching Committee, an application for its experiments will be brought to the Committee for the Supervision of Animal Experiments. The application will be considered as any other application for conducting animal experimentation.
3. Approval for animal experimentation in a course is valid only for the applicable school year in the application.
4. Prior to the course's registration date, the institution will announce that the course involves compulsory experimentation on animals and that the experiments have been approved by institution's Teaching Committee in accordance with the Law.
5. The institutional Committee will report to the Council on applications for using animals for teaching purposes, similar to reports received by the Council for any other animal experimentation application.

   In view of the Resolution, all applications for approving animal experimentation for teaching purposes must reach the Committee for the Supervision of Animal Experiments accompanied by approval of the course by the Teaching Committee.

Note: Paragraph 9 of the Prevention of Cruelty to Animals Law (Experiments on Animals), 1994-5754 states that: "**No permit shall be given for conducting animal experiments if the experiment's goals can be accomplished through reasonable and alternative ways.**"