The University of Hong Kong
Centre for Comparative Medicine Research

Advice to New Animal Users

1. Government Legislation and Codes of Practice

All experiments involving the use of living vertebrate animals must fulfill all relevant legislation and Codes of Practice in Hong Kong including, but not limited to, the following:

1.1 Animals (Control of Experiments) Ordinance (Cap. 340)

1.1.1 The performance of experiments on living vertebrate animals in Hong Kong is subject to the provisions of the Cap. 340 Animals (Control of Experiments) Ordinance and Regulations. Please apply for a licence from the Director of Health (DH) if you want to carry out experiments on living vertebrates. Additional authorization is required for (i) experiments to attain manual skill (endorsement); (ii) experiments to illustrate lectures (teaching permit) and (iii) experiments not performed under anaesthesia and recovery experiments (endorsement). In this Ordinance, experiment means any experiment performed on an animal and calculated to give pain. The DH has advised that the following information should be provided in the application: (i) how the experiments advance scientific knowledge and benefit mankind and animals, and (ii) measures to minimise suffering of animals. For teaching experiments, the DH issues a "bloc licence" to cover a group of named students who perform experiments(s) under the supervision of a licensed staff with the relevant teaching permit. A new licence is required if there is a change in the type of animals to be used or a change in the experimental procedures to be performed on the animals.

1.1.2 The application form for Cap. 340 licence/permit/endorsement and guidelines for applications can be downloaded from the website of Department of Health (DH) http://www.dh.gov.hk/english/useful/useful_alo/useful_alo.html . DH's contact details are as follows:

Mailing address:	Special Health Service Department of Health Room 79, 21/F, Wu Chung House 213 Queen's Road East, Wan Chai, Hong Kong
Telephone No.:	2961 8975
Fax no.:	2127 7329
Email:	ro_al@dh.gov.hk
Website:	http://www.dh.gov.hk/english/useful/useful_alo/useful_alo.html

1.1.3 Every licensee is required under Cap. 340 to keep an up-to-date record of the particulars of their experiments in the form set out as "Form 6" in the Schedule of the Animals (Control of Experiments) Regulations http://www.dh.gov.hk/english/useful/useful_forms/files/AL_Form_6_eng.pdf Please refer to details at (http://www.dh.gov.hk/english/useful/useful_forms/useful_forms_ani.html). The licensee is also required to submit a return to the Department of Health on or before the first of January each year in the form set out as "Form 7 - Return of Experiments" in the Ordinance of all experiments performed (including information on the kinds and number of animals used, i.e. those animals which have been euthanased after completion of the experiments) during the preceding twelve months. Please note that "Nil Return" is required by the Department of Health. The CCMR issues an annual report in mid-December each year to individual researchers/ teachers listing the quantity of animals supplied by the Unit during the year to facilitate their submission of annual returns to the government. Department of Health officials may enter/inspect premises where licensed experiments are performed and carry out on-site inspection of "Form 6" records of licences with/without prior notice.

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1.2 Prevention of Cruelty to Animals Ordinance (Cap. 169)

1.2.1 The purpose of this Ordinance is to prohibit and punish cruelty (viz unnecessary suffering) to animals.

1.2.2 Unnecessary suffering includes any form of ill-treatment of animals by beating; failure to supply sufficient food and fresh water; failure to convey the animals in suitable containers; use of animals that are diseased or injured; or allowing to be kept under one's control, any animal in any way which may cause it suffering which could have been avoided.

1.3 Dangerous Drugs Ordinance (Cap. 134)

1.3.1 A person in charge of a laboratory which is used for the purposes of research and attached to a university is authorized under the Dangerous Drugs Ordinance to be in possession of and to supply dangerous drugs [(e.g. ketamine, buprenorphine (Temgesic®), midazolam (Dormicum®), fentanyl citrate/fluanisone (Hypnorm®)]. Dangerous drugs can be obtained from the Laboratory Animal Unit, subject to the approval of the Head of Unit, for use in CULATR (Committee on the Use of Live Animals in Teaching and Research) approved experiments only.

1.3.2 The aforesaid persons and researchers who use dangerous/scheduled drugs are required to comply with the storage and record keeping provisions of the Dangerous Drugs Ordinance as follows:

a. Storage:

Dangerous drugs should be kept in a locked receptacle which can only be opened by the person authorized under the Dangerous Drugs Ordinance to possess them.

b. Record-keeping

(i) The authorized person in possession of dangerous drugs must keep a "Dangerous Drugs Register" in which all transactions of dangerous drugs must be recorded. The format of this Register is fixed by the Ordinance.

(ii) A separate Dangerous Drugs Register, or a different page of the same Register, should be used for each dangerous drug. The name of the dangerous drug preparation and (where applicable) the strength or concentration of the preparation should be written at the head of each page of the Register.

(iii) Every receipt or supply of a dangerous drug must be recorded, in indelible ink, on the day of the transaction or, if this is not practicable, on the following day. No cancellation or alteration of any record is permitted, corrections must be made by means of a marginal note or footnote and must be dated.

(iv) All used registers must be kept in the laboratory for two years from the date on which the last entry was made. It is advisable that all supporting documents such as invoices should also be kept for two years.

1.4 Other related government legislation and Codes of Practice in Hong Kong

a. Antibiotics Ordinance, Cap. 137
b. Pharmacy and Poisons Ordinance, Cap. 138
Note:
Under Regulation 36B (the regulation) of the Pharmacy and Poisons Regulations, a "Certificate for Clinical Trial/Medicinal Test" (the certificate) is required for the purpose of conducting a 'clinical trial on human beings' or a 'medicinal test on animals'. The regulation only applies to pharmaceutical products.

"Pharmaceutical product" means any substance or combination of substances -

(a) presented as having properties for treating or preventing disease in human beings or animals; or
(b) that may be used in, or administered to, human beings or animals, either with a view to -

(i) restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action; or

(ii) making a medical diagnosis.

If you have an animal experiment which falls within the scope of the aforesaid regulation, you should apply for a "Certificate for Clinical Trial/Medicinal Test" from the Department of Health (DH). For details, please refer to the information posted at http://www.drugoffice.gov.hk/eps/do/en/pharmaceutical_trade/guidelines_forms/clinicalTrial.html of the DH website.

c. Public Health (Animals and Birds) Ordinance, Cap. 139
d. Animals and Plants (Protection of Endangered Species) Ordinance, Cap. 187
e. Radiation Ordinance, Cap. 303
f. Occupational Safety and Health Ordinance, Cap. 509
g. "Code of Practice for Care and Use of Animals for Experimental Purposes (2004)" which can be downloaded at:
English version
Chinese version

h. Code of Practice for the Welfare of Food Animals (by Food and Environmental Hygiene Department).

For more information on the individual legislation, please refer to http://www.legislation.gov.hk/eng/index.htm

2. Committee on the Use of Live Animals in Teaching and Research (CULATR)

2.1 The CULATR was established in 1980 by the University to advise teaching and research staff on matters concerning animal experimentation. The Committee has prepared guidelines for the use of experimental animals within the University. Currently it has a co-opted member from the Society for the Prevention of Cruelty to Animals. CULATR holds meeting at least twice a year and conducts bi-annual visits to all animal holding/breeding facilities and experimental animal research laboratories in the University.

2.2 Protocols for all teaching and research experiments using live animals have to be scrutinised by the Committee beforehand. CULATR application form, guidelines, Frequently Asked Questions and Protocol Vetting Procedures are available from CULATR link: http://www.med.hku.hk/research/research-ethics/animal-ethics-culatr (Enquiry Tel: 39179147). All applications for CULATR approval should be typed/printed and prepared in the format of the application form designed by the Committee. Applicants should follow the Committee guidelines and provide answers to all the questions listed in the application form. This will facilitate the processing of their applications and minimize any unnecessary delay.

2.3 The CCMR has been requested by the CULATR to exercise tighter control on the supply of animals to its users. Therefore, the Unit will only supply animals to those licensees who have submitted their "Form 7" (http://www.dh.gov.hk/english/useful/useful_forms/files/AL_Form_7_eng.pdf) to the Director of Health. All applicants for CCMR animals are required to forward a photocopy or scanned copy of their submitted Annual Returns to the Unit (Email: compmed@hku.hk, Fax No.: 28727598) before the end of January each year, failing which their animal orders will be rejected.

2.4 The CULATR is aware that some researchers may carry out collaborative projects involving live animals in other institutions/countries. Whilst CULATR, like its overseas counterparts, has no jurisdiction over a staff who chooses to do collaborative research in other institutions/countries, the researcher is required to inform the Committee that approval has been sought from the animal ethics committee of the visiting/collaborating institutions before commencement of the animal experiments.

3. CCMR Services

The services provided by the CCMR are as follows:

3.1 Supply of animals, diets, bedding/nesting materials (local sawdust/woodchip, local/overseas corn-cob/corn-husk, overseas Aspen woodchip and nesting strips), drugs and other consumables;

3.2 Centralised animal holding and surgical facilities;

3.3 Advisory/veterinary service on matters related to laboratory animals, this comprises clinical examination and disease investigation/treatment/prevention/control (disease investigation service includes post-mortems and follow-up bacteriological, mycological, parasitological, serological and histo-pathological examinations);

3.4 Cage washing/disinfection service and diet/bedding/cage autoclaving service;

3.5 Training for laboratory animal users;

3.6 Others: Importation/exportation of animals; issue of veterinary health certificates; full-profile serological screening, PCR tests and genetic monitoring by overseas laboratories; purchase/short-term loan of cage equipment and delivery service.

4. Animal Orders

4.1 Before you start your experiments, please discuss your animal requirements with the CCMR first. All orders for animals have to be processed via CCMR On-line System. All orders should be placed at least two working days before the requested date of delivery/collection of ordered items and they reach our General Office by 11:00 a.m. on Monday to Friday. The Unit will try its best to process every order but cannot guarantee issue/delivery of ordered animals in case of unforeseeable circumstances like fluctuating reproductive performance of breeding colonies and inclement weather.

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4.2 If you require a regular supply of a particular strain of animals for a defined period of time, please place a *"standing order"* with us by stating the animal specifications and delivery schedule on your order. Standing orders are encouraged as stocks will be set aside in the CCMR to assure continuous availability once the Unit have confirmed acceptance of your order.

4.3 The Unit's SPF (specific-pathogen-free) Breeding Area on 2/F of the CCMR Building maintains only limited surplus stock of its central breeding colonies to minimise unnecessary wastage. Please ensure that orders for large quantities of animals (in particular those orders with narrow specifications like single sex, restrictive weight/age range and orders for time-mated/pregnant animals) are submitted well in advance because it takes time to set up breeders to meet these difficult/bulk orders (refer "Waiting Time for Bulk Animal Orders" table).

4.4 Orders for time-mated animals can be problematic particularly if inbred animals (with poor reproduction performance) are requested. Please note that the CCMR cannot guarantee the outcome of the mating even though the presence of vaginal plugs may serve as an indicator of mating and abdominal palpation can be used to estimate the stage of pregnancy.

4.5 Birth dates of production animals are not recorded. Mice and rats are maintained in age cohorts relative to the week in which the animal is weaned (note: weaning is normally done on Thursdays). If exact age is required, the Unit will need to set up a supplementary colony at the applicant's own cost for the specific order.

4.6 The CCMR accepts that orders may have to be cancelled but the Unit will not accept a cancellation immediately prior to delivery or if animals have been specifically held or bred for the order. If an order is cancelled under these circumstances, the applicant will be required to pay for the ordered animals. In case of enquiries about availability of large quantities of animals or animals with narrow specifications, a service charge will be levied if an enquirer fails to submit a firm order after the Unit staff have spent a significant amount of time to handle the enquiry and confirmed availability of the requested animals.

4.7 For disease control reasons, the Unit will not accept the return of animals after dispatch as they cannot be returned to the SPF Breeding Area.

4.8 Please contact our General Office at 28168510 or email us at compmed@hku.hk if you have any problems with or queries on animal orders.

5. Experimental Holding

5.1 The CCMR provides "minimal disease" and "conventional" holding facilities for keeping experimental mice, rats, hamsters, gerbils, guinea-pigs, chickens and rabbits, and conventional holding facilities for keeping experimental pigs and goats.

5.2 If you want to carry out your experiments in the CCMR, please pay a visit to the Unit and discuss the experimental protocol, holding space and other requirements (e.g. cage items and surgical facilities) with us first. You have to submit a duly completed Experimental Animal Holding Accommodation Application Form https://intraweb.hku.hk/local/CCMRnit/content/holding/experiment_holding.pdf for the Head of Unit's approval before commencement of your experiment.

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5.3 Please observe strictly all CCMR rules and procedures when you are working in the Unit. These rules and procedures aim primarily at protecting the health status and welfare of all valuable experimental and breeding animal colonies kept under our care. Failure to do so can result in introduction of pathogens to the Unit and unnecessary animal suffering. The research and teaching experiments of colleagues in the University will also be affected because the follow-up measures required to eliminate an unwanted infection (e.g. by treatment, re-derivation or colony replacement) from the experimental and central breeding areas of the Unit are often very costly and time-consuming.

6. Animal Importation Procedures

The CCMR can import animals from overseas suppliers/institutions for researchers. If you would like to use this service, please complete the Animal Importation Application Form and submit it to our General Office.

A service charge at https://intraweb.hku.hk/local/CCMRnit/charges.html will be levied. The normal procedures for importation of laboratory animals are as follows:

6.1 Seek quotation and full health report (including serological, bacteriological, mycological, parasitological and pathological test results) from the supplier, the animals' health status must be acceptable to the CCMR if they are to be held in the experimental areas of the Unit.

6.2 Apply for a Special Import Permit from the Agriculture, Fisheries & Conservation Department (AFCD) [Note: The strain nomenclature, coat colour, sex and number of animals to be imported are required for this purpose. The AFCD also requires that the applicant is licensed under Cap. 340 and has obtained prior CULATR (Committee on the Use of Live Animals in Teaching and Research) approval in using the imported animals]. Send a copy of the permit to the supplier when it is available.

6.3 Ensure that the supplier's veterinary health certificate complies fully with the import permit requirements. It is advisable to send a copy of the veterinary health certificate to AFCD for their comment before shipping the animals to avoid hiccups during collection at the airport.

6.4 Request the supplier to schedule the shipment so that the animals can arrive Hong Kong during the daytime and in the earlier part of the week to facilitate collection and observation of the animals after their arrival.

6.5 The CCMR or an assigned courier agent can collect the animals from the air-port on behalf of the researcher/teacher.

6.6 If researchers want to handle the importation procedures themselves and hold the imported animals in the CCMR, prior approval (at least 5 working days advance notice) from the Unit is required in order to provide sufficient time to the CCMR staff for checking the availability of holding space and the health status of the imported animals. In this case, it is still necessary to complete the relevant sections of the Animal Importation Application Form and return it to the CCMR for vetting/approval at least 5 working days before the shipment date.

6.7 CCMR Quarantine and Animal Health Screening Procedures

(a) If the imported animals are to be held in the Minimal Disease Experimental Holding Area of our Unit (i.e. MDA on 1/F, CCMR Building and EG/F, Dexter H.C. Man Building) and they come from *approved suppliers* (i.e. Charles River Lab., Harlan, Jackson Lab. and Taconic), the animals upon arrival have to undergo *one round of CCMR Quarantine* in Individually Ventilated Cages [IVCs] in the "MDA Quarantine Room" on ELG2/F, Dexter H.C. Man Building (note: jump-start breeding of the rederived animals is allowed during the quarantine period subject to availability of holding space). The imported animals also have to undergo *one round of "Surveillance Plus PCR Rodent Infectious Agents (PRIA) animal health screening" on the 4th days after arrival* by an overseas laboratory. The PRIA animal health screening will take about 4 weeks to complete. The imported animals cannot be introduced to MDA on 1/F, CCMR Building and EG/F, Dexter H.C. Man Building unless the health screening results are acceptable to the CCMR. Therefore, the quarantine and animal health screening procedures will take a total period of about 4 weeks. Researchers have to bear the costs of the animal health screening tests.

(b) If the imported animals are to be held in the MDA and there is uncertainty about their health status (i.e. they come from *non-approved suppliers*), either <u>one</u> of the two procedures listed below has to be followed:

(i) <u>Rederivation by blastocyst transfer</u>

The imported animals can be rederived for holding in MDA by blastocyst transfer. The Transgenic Core Facility of the Li Ka Shing Faculty of Medicine provides embryo rederivation service for researchers. Foster mothers for blastocyst transfers are available from the CCMR. The rederived animals have to undergo *one round of CCMR Quarantine* in IVCs in the "MDA Quarantine Room" on ELG2/F, Dexter H.C. Man Building (note: jump-start breeding of the rederived animals is allowed during the quarantine period subject to availability of holding space). *One round of "Full-profile animal health screening"* has to be performed on at least one rederived animal or on the foster mother. The *"Full-profile animal health screening"* includes post-mortem examination by the Unit Laboratory (covering pathological, bacteriological, mycological and parasitological examinations) and contracted-out serological screening / Mouse Hepatitis Virus PCR tests by an overseas laboratory. The total duration of quarantine (including a 3-week gestation period of the transferred blastocyst and full-profile animal health screening) is about 9 weeks. OR

(ii) <u>Direct relocation of imported animals</u>

If the user wants to hold the "originally imported animals" in MDA rather than rederiving them by blastocyst transfer, the animals have to undergo a *"first round of CCMR Quarantine"* in IVCs in the "Quarantine Room EG01" on G/F of Dexter H.C. Man Building upon arrival (note: jump-start breeding of the imported animals is allowed during the quarantine period subject to availability of holding space). This includes a *"first round of Surveillance Plus PRIA animal health screening" on the 4th days after arrival* = by an overseas laboratory. The first round of PRIA animal health screening will take about 4 weeks to complete. If the "first round" animal health screening results are acceptable, the imported animals can be *relocated directly* to MDA for a *"second round of CCMR Quarantine"* in IVCs inside the "MDA Quarantine Room" on ELG2/F, Dexter H.C. Man Building. A "Second round of animal health screening (i.e. a *"FELASA Complete Annual PRIA animal health screening")* will be performed *on the 4th days after arrival* in MDA. The second round of PRIA animal health screening will also take about 4 weeks to complete. Therefore, the total duration of two rounds of quarantine and two rounds of animal health screening procedures is about 8 weeks.

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The imported/rederived animals cannot be introduced to MDA on 1/F, CCMR Building and EG/F, Dexter H.C. Man Building unless all the health screening results are acceptable to the CCMR. Users have to bear the costs of the animal health screening.

Details of the Quarantine and Animal Health Screening Procedures for Imported Animals are available at https://intraweb.hku.hk/local/CCMRnit/content/procedures/Imported_Animals.pdf

(c) If the imported animals are to be held in the Conventional Area (i.e. CA on G/F, CCMR Building, EG/F, Dexter H.C. Man Building and R/F, Laboratory Block, Li Ka Shing Faculty of Medicine), the CCMR Quarantine and Animal Health Screening procedures mentioned in para. 6.7(a) and 6.7(b) above will not apply irrespective of whether the animals are purchased from "*approved"* or *"non-approved suppliers"*.

7. Animal Exportation Procedures

The CCMR can export animals to overseas organisations/institutions for researchers. If you would like to use this service, please complete the Animal Exportation Application Form and submit it to our General Office. A service charge https://intraweb.hku.hk/local/CCMRnit/charges.html will be levied. The normal procedures for exportation of laboratory animals are as follows:

7.1 Obtain information from the receiving organization/institution regarding animal health status and documentation (e.g. veterinary certificate and animal health monitoring report) requirements.

7.2 CCMR will issue a veterinary certificate and have it endorsed by the local authority (viz The Agriculture, Fisheries and Conservation Department).

7.3 Appoint a mutually acceptable courier agent which can provide "door-to-door" delivery service. [Note: CCMR has an appointed agent to handle door-to-door delivery service.]

7.4 Liaise with the airline company and the courier agent regarding the choice of delivery boxes and a convenient shipment schedule for the animals (note: different airline companies may have different requirements).

8. Environmental, Equipment, Health and Genetic Monitoring

8.1 Environmental Monitoring

8.1.1 Supply air is checked every six months for bacterial and fungal counts by the University Safety Office. Water is sampled on alternate month for bacterial and parasitic counts by the Unit Laboratory and once a year for parasitological examination by the government veterinary laboratory. The University Estates Office submits water samples once a year to (i) an outside laboratory for bacteriological (coliforms, *E. coli* and plate counts), turbidity, pH value, conductivity, color and iron content examination and (ii) the government veterinary laboratory for parasitological examination.

8.1.2 The performance of autoclaves are monitored 3 times a week using spore ampoules "*3M Attest 1292E Rapid Readout Biological Indicator*®" in the CCMR Building (viz Specific Pathogen Free Breeding Area [SPFBA] and Minimal Disease Area [MDA]) and weekly in the Dexter H.C. Man Building/CCMR Extension (viz Conventional Area [CA] and Unit Laboratory). In addition, each autoclave load is monitored using a chemical indicator strip "*Getinge Steam Sterilization Integrator*®" in SPFBA & CA and an "*Interster ISP Steam Emulating Indicator*®" in MDA & Unit Laboratory

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8.1.3 Cabinet/Tunnel/Bottle Washers are monitored every six months by the Unit Laboratory by taking swabs from washed cages for bacterial counts and daily for washer temperature using *Pharmacal "Tri-Temp Strips®"*).

8.2 Health Monitoring

8.2.1 Specific Pathogen Free Breeding Area and Minimal Disease Experimental Holding Area

8.2.1.1 Half-yearly in-house post-mortem examination of sentinel animals (using soiled bedding exposure method) including gross-pathological (and histo-pathological if necessary), bacteriological, mycological and parasitological examinations by the Unit Laboratory.

8.2.1.2 Three-monthly serological screening of sentinel animals (using soiled bedding exposure method):- performed by Harlan, UK or Charles River Laboratories USA.

8.2.1.3 Monthly serological screening on Mouse Hepatitis Virus and pinworm screening of sentinel animals (using soiled bedding exposure method) in MDA:- performed by Microbiology Laboratory, Queen Mary Hospital & Unit Laboratory respectively.

8.2.2 Conventional Experimental Holding Area

Annual serological screening of sentinel animals (using soiled bedding exposure method):- performed by Harlan, UK or Charles River Laboratories USA.

8.3 Genetic & IgG Level Monitoring

8.3.1 Ear/tail samples taken from inbred strains maintained in the SPF Central Breeding Area & NOD SCID mice in the Minimal Disease Experimental Holding Area for genetic monitoring. In addition, serum samples taken from immuno-deficient animals for IgG level testing. Samples are sent to Envigo UK / Charles River Laboratories USA annually for genetic & IgG level monitoring.

9. Enquiries

If you have any questions, please feel free to send in your enquiries to compmed@hku.hk. You can also contact our General Office at 3910 2042 or our senior technical staff at 3910 2040.

Centre for Comparative Medicine Research
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