 **DOKUZ EYLUL UNIVERSITY**

**IZMIR INTERNATIONAL BIOMEDICINE AND GENOME INSTITUTE**

**LOCAL ETHICAL COMITTEE ON ANIMAL EXPERIMENATION**

**APPLICATION FORM**

FORM NO 1 Issue Date: Date Of Update:

**Protocol Number:**

**Date of Approval:**

**1.PROJECT PERSONNEL**

|  |
| --- |
| **Project Coordinator** |
| Title |  |
| Name |  |
| Surname |  |
| Faculty |  |
| Department |  |
| Office Phone  |  |
| Signature |  |
| e-mail address |  |
| **Other Project Personnel** |
| **Name Surname** | **Title**  | **Institution/Faculty**  | **Department** | **Task in the project (Explain in details)** | **Signature** |
|  |  |  |  |  |  |
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**2.** **GENERAL INFORMATION ON THE PROJECT**

|  |
| --- |
| **Project Title:** |
| **The Institutions supporting the Project** [ ]  TUBITAK [ ]  BAP [ ]  DPT [ ]  Company [ ]  Reimburse Ourselves[ ]  Other (Please Specify) |
|  None:Supported by FUA Scientific Research Project Office Application date: |
| Supported by TUBITAK | Application date:  |
| Not yet applied for project support |  |
| Other (please specify): |  |
| A.  | Application date:  |
| B.  | Application date:  |
| **Duration of the project** : …….. months |
| **Type of project** |
|  [ ]  Thesis for Specialty in Medicine  |
|  [ ]  Doctoral (PhD) Thesis |
|  [ ]  Master’s Thesis |
|  [ ]  Research Project |
|  [ ]  Education |
|  [ ]  Other (please specify): |
| **Animal species used in experiment** |
|  [ ]  Rat |
|  [ ]  Mouse |
|  [ ]  Guinea Pig |
|  [ ]  Rabbit |
|  [ ]  Other (please specify) |
| **Nature of Work** |
|  [ ]  Acute |  [ ]  Chronic |

**3. VALID REASONS FOR THE SELECTIVE USE OF LABORATORY ANIMALS**

 **3.1. Using experimental animals is necessary for this research because... (You can choose more than one option)**

|  |  |
| --- | --- |
|  | [ ]  a. The complexity of the examination process makes it impossible to create or establish models in simpler systems.  |
|  | [ ]  b. There is lack of adequate knowledge in imitating the system to be researhed on non-living models. |
|  | [ ]  c. It is mandatory to test on experiment animals before human trials in preclinical studies. |
|  | [ ]  d. Other (please specify): |

 **3.2. This animal species has been selected because (you can choose more than one option):**

|  |  |
| --- | --- |
|  | [ ]  a. There is vast database that makes it possible to make comparisons with previously obtained data. |
|  | [ ]  b. With its anatomical and physiological characteristics described below, it is the only suitable model for this study. Please specify: … |
|  | [ ]  c. The proposed species is the lowest phylogenetic species with the suitable size, anatomy and tissue type for this study.  |
|  | [ ]  d. The proposed species constitutes a very suitable physiological model, which simulates the conditions in humans.  |
|  | [ ]  e. It has also been used in the previous studies that this research is based on. |
|  | [ ]  f. The characteristics of this species given below are the most suitable choice for study: |
|  | [ ]  g. Other : Please specify:… |

**4. INFORMATION ON ANIMAL SUPPLY AND HOUSING**

***4.1. Source of laboratory animals:***

|  |  |
| --- | --- |
|  | [ ]  a. Supplied from Dokuz Eylul University IBG Laboratory Animal Facility. [ ]  b. Supplied by another legal supplier. Please specify :[ ]  c. Derived from another study. Please specify: [ ]  d. Wild animal, isolated from its natural environment.[ ]  e. Received as donation. |
|  | [ ]  f. Other. Please specify: … |

**4.2. Experimental animal housing:**

|  |  |
| --- | --- |
|  | [ ]  a. Dokuz Eylul/ IBG Laboratory Animal Facility  |
|  | [ ]  b. Animals will be placed outside the IBG Laboratory Animal Facility |
| a. No      b. Yes      (If the answer is yes, please answer the following questions)[ ]  1. All animals will be transported to the laboratory stated below.Address: …[ ]  2. The approximate period of time that the experimental animal will be kept alive in the lab : [ ]  3. Is the necessary permission taken from the host laboratory unit responsible  |
|  | [ ]  c. Other. Please specify: … |

**4.3. Special housing, conditioning, diet and other requirements**

|  |  |
| --- | --- |
|  | [ ]  a. No special conditions will be applied. |
|  | [ ]  b. In the experiments, the below applications will be performed. (Please choose all that fits) |
|  | 1. Exposure to high / low temperatures for long periods       |
|  | 2. Exposure to nonstandard humidity/dryness for long periods       |
|  | 3. Exposure to nonstandard athmospheric pressure for long periods       |
|  | 4. Exposure to nonstandard athmosphere for long periods       |
|  | 5. Housing in nonstandard cages       |
|  | 6. Exposure to nonstandard light/darkness cycle for long periods       |
|  | 7. Leaving thirsty more than 12 hours       |
|  | 8. Leaving thirsty more than 24 hours (48 hours for ruminants)      9. Other. Please Specify:       |
|  |  |

**5. DETAILS ABOUT THE PROJECT**

## 5.1. Project Description

|  |
| --- |
| **Please summarize the objectives of the project in such a way that they can be understood by those who are not experts on the subject:** **SUMMARY:****INTRODUCTION:****OBJECTIVE(S):** |
|  |
| **Experimental procedures (describe the operations applied to animals):** |
| **MATERIALS AND METHODS:**- **Evaluation Methods:**- **Qualities To Bring To The Literature:**- **Statistical Analyses:**- **References:** |

## 5.2. Experimental animal groups and numbers

|  |  |
| --- | --- |
| Experimental and Control groups | Animal numbers per group |
|  |  |
|  |  |
|  |  |
|  |  |
|  |  |
|  |  |
| Total number of animals used |  |

**6.** **ANESTHESIA and ANALGESIA**

**6.1. Preanesthetic-analgesic or sedative drugs**

|  |  |  |  |
| --- | --- | --- | --- |
| Reagent | Dose | [Application](http://tureng.com/tr/turkce-ingilizce/route%20of%20administration) way  | Effect Time |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |

## 6.2. Anesthetic drugs

|  |  |  |  |
| --- | --- | --- | --- |
| Reagent | Dose | [Application](http://tureng.com/tr/turkce-ingilizce/route%20of%20administration) way  | Time under anesthesia |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |

## 6.3. Monitoring the depth of anesthesia (Please mark all that apply)

|  |  |
| --- | --- |
|  | [ ]  a. Application of the protocol is not appropriate  |
|  | [ ]  b. Responses after pinching the skin and the finger |
|  | [ ]  c. Palpebral or corneal reflex (not suitable for rodents) |
|  | [ ]  d. Monitoring of the jaw or skeletal muscle tone |
|  | [ ]  e. Monitoring physiological response |
|  | [ ]  f. Other. Please specify : … |

**6.4. Analgesic and tranquilizing drugs applied after the procedure (post-op)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Reagent | Dose | Application frequency | [Application](http://tureng.com/tr/turkce-ingilizce/route%20of%20administration) way  | Treatment time |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |

**Is there a post-op care responsible?**

|  |
| --- |
| [ ]  Yes [ ]  No |
| If yes, please specify : … |
| Name- Surname |  Telephone number in case of emergency: |

**7. COMPLETION OF THE EXPERIMENTAL (HOW TO END THE ANIMAL EXPERIMENT)**

|  |  |
| --- | --- |
|  | [ ]  a. Euthenasia will not be performed at the end of the experiment. |
|  | [ ]  b. Euthanasia will be performed before the implementation of any test or treatment. |
|  | [ ]  c. Euthanasia will be performed after living for a certain period of time (hour/day/month) |
|  | [ ]  d. Euthanasia will be performed after the application of the experimental protocol. |
|  | [ ]  e. The animal will be euthanized after losing more than 15% of its weight. |
|  | [ ]  f. Euthanasia will be performed if the general situation of the animal gets worse. Define:       |
|  | [ ]  g. After the experimental procedures, the animals may die. Please explain possible causes:       |

**Severity classification of procedures\* Please mark the appropriate box**.

      non-recovery       mild       moderate       severe

\*All procedures are classified as ‘non-recovery’, ‘mild’, ‘moderate’, or ‘severe’ on a case- by-case basis using the assignment criteria set out in Annex 1.

**8. EUTHANASIA please indicate**

|  |  |
| --- | --- |
|  | [ ]  a. Euthenasia will not be performed |
|  | [ ]  b. High doses of anesthetic |
|  | [ ]  c. Decapitation under Anesthesia / tranquilizer  |
|  | [ ]  d. Cervical Dislocation under Anesthesia / tranquilizer  |
|  | [ ]  e. Exsanguination during surgery (dilution) |
|  | [ ]  f. Carbon dioxide asphyxiation  |
|  | [ ]  g. Other. Please explain:  |

## 9. BIOLOGICAL AND ENVIRONMENTAL RISK FACTORS THAT MAY EMERGE DURING OR AFTER THE EXPERIMENTATION

|  |  |
| --- | --- |
|  | [ ]  a. Microbiological contamination risk. Define:     |
|  | [ ]  b.Carcinogens. Define type and risk-degree:  |
|  | [ ]  c. Radioisotopes. Define type and risk-degree:  |
|  | [ ]  d. Biological toxins. Define type and risk-degree:  |
|  | [ ]  e. Anti-neoplastic / cytotoxic agents. Define type and risk-degree:  |
|  | [ ]  f. Other reagents: … |
|  | [ ]  g. Other risk factors: … |
|  | [ ]  h. None |

## 10. POTENTIAL HEALTH PARAMETERS MONITORED ON THE EXPERIMENTAL ANIMALS

If it is not possible to apply the protocol, please explain:

Otherwise indicate below:

10.1. Possible changes to be monitored

|  |  |
| --- | --- |
|  | [ ]  a. % Body-weight loss  |
|  | [ ]  b. Death |
|  | [ ]  c. Behavioral changes. Please explain: … |
|  | [ ]  d. Reduced food and water intake |  | [ ]  n. Dyspnea |
|  | [ ]  e. Infection |  | [ ]  o. Hypothermia |
|  | [ ]  f. Abscess |  | [ ]  p. Hyperthermia |
|  | [ ]  g. Dehydration |  | [ ]  r. Skin changes |
|  | [ ]  h. Malnutrition |  | [ ]  s. Paresis / paralysis |
|  | [ ]  i. General weakness |  | [ ]  t. Ataxia |
|  | [ ]  j. Diarrhea |  | [ ]  u. Incontinence |
|  | [ ]  k. Constipation or ileus |  | [ ]  v. Diuresis |
|  | [ ]  l. Convulsion |  | [ ]  y. Other. Explain:  |
|  | [ ]  m. Coma |  | [ ]  z. None |

**10.2. Methods to monitor health changes (please indicate)**

|  |  |
| --- | --- |
|  | [ ]  a. Weighing. Specify the frequency:… |
|  | [ ]  b. Behavior, activity and posture control |
|  | [ ]  c. Observation regarding local pain or discomfort  |
|  | [ ]  d. Monitoring the operated parts for adhesions, rashes, flix or swellings |
|  | [ ]  e. Decrease in the animal’s mobility |
|  | [ ]  f. Monitoring the daily food and water consumption |
|  | [ ]  g. Other. Define: … |

**10.3. Frequency of observations to detect changes in the animal health (select only one)**

|  |  |  |  |
| --- | --- | --- | --- |
|  | [ ] a. Once a day |  | [ ] e. Once a week |
|  | [ ] b. Twice a day |  | [ ] f. Other. Define:       |
|  | [ ] c. Every other day |  | [ ] g. It is not possible to apply the protocol. |
|  | [ ] d. Twice a week |  |  |

**10.4. Elimination Criteria of the animals from the experimental protocol (please select all appropriate options)**

|  |  |
| --- | --- |
|  | [ ]  a. Approval of the veterinarian (humanitarian reasons) |
|  | [ ]  b. More than 15 % of body weight loss |
|  | [ ]  c. Inability to walk properly |
|  | [ ]  d. Inability to drink or eat properly |
|  | [ ]  e. Significantly decreased responsiveness to stimuli |
|  | [ ]  f. Other. Define:       |

## 10.5. The fate of animals after elimination from the experimental protocol

|  |  |
| --- | --- |
|  | [ ]  a. Euthanasia |
|  | [ ]  b. Other. Define:       |

**11. 3 full-text literature articles (supporting the experimental methodology)**

**12. 1 CD that contains project description text and project application form**

**TO THE ATTENTION OF THE APPLICANTS:**

**DEU employees will be given priority to work in the experimenatl animal facility after the Experimental Animal Ethics Committee approval.**

I have read the application form. As the project leader, I accept to observe the related regulations and Animal Protection Act no. 5199 with the date 24.06.2004 that was published and became effective in the Official Gazette on 01.07.2004. I take the moral responsibilities of this work. I declare that the study is open to all the inspections of the ethics committee and all laboratory animals will be handled as affirmed by the ethics committee.

|  |
| --- |
| **Project Coordinator** |
| Name/Surname |  Signature |  Date |

**CHECK LIST FOR THE LOCAL ETHICAL COMITTEE ON ANIMAL EXPERIMENTATION**

|  |  |  |  |
| --- | --- | --- | --- |
| **Project control box (please select check boxes, after completing your application files. Omissions on this list would delay the project review)** |  Application form (1 original and 2 copies) | Yes [ ]  | No [ ]  |
|  Project description (1 original and 2 copies ) | Yes [ ]  | No [ ]  |
|  Animal Experimentation Certificate (3 photocopies) | Yes [ ]  | No [ ]  |
|  Signed Statement (1 original 2 copies) | Yes [ ]  | No [ ]  |
|  CD with project description and application form | Yes [ ]  | No [ ]  |
|  3 full-text literature articles | Yes [ ]  | No [ ]  |
| If the Project has an ethical commitee approval before, please attach related documents  | Yes [ ]  | No [ ]  |
| If the Project has an ethical commitee refusal before, please attach related documents  | Yes [ ]  | No [ ]  |

**ANNEX 1**

**SEVERITY CLASSIFICATION OF PROCEDURES**

The severity of a procedure shall be determined by the degree of pain, suffering, distress or lasting harm expected to be experienced by an individual animal during the course of the procedure.

**Section I: Severity categories**

**Non-recovery**:

Procedures which are performed entirely under general anesthesia from which the animal shall not recover consciousness shall be classified as ‘non-recovery’.

**Mild:**

Procedures on animals as a result of which the animals are likely to experience short-term mild pain, suffering or distress, as well as procedures with no significant impairment of the well-being or general condition of the animals shall be classified as ‘mild’.

**Moderate:**

Procedures on animals as a result of which the animals are likely to experience short-term moderate pain, suffering or distress, or long-lasting mild pain, suffering or distress as well as procedures that are likely to cause moderate impairment of the well-being or general condition of the animals shall be classified as ‘moderate’.

**Severe:**

Procedures on animals as a result of which the animals are likely to experience severe pain, suffering or distress, or long- lasting moderate pain, suffering or distress as well as procedures, that are likely to cause severe impairment of the well- being or general condition of the animals shall be classified as ‘severe’.

**Section II: Assignment criteria**

The assignment of the severity category shall take into account any intervention or manipulation of an animal within a defined procedure. It shall be based on the most severe effects likely to be experienced by an individual animal after applying all appropriate refinement techniques.

When assigning a procedure to a particular category, the type of procedure and a number of other factors shall be taken into account. All these factors shall be considered on a case-by-case basis.

The factors related to the procedure shall include:

— type of manipulation, handling,

— nature of pain, suffering, distress or lasting harm caused by (all elements of) the procedure, and its intensity, the duration, frequency and multiplicity of techniques employed,

— cumulative suffering within a procedure,

— prevention from expressing natural behaviour including restrictions on the housing, husbandry and care standards.

Examples are given in Section III of procedures assigned to each of the severity categories on the basis of factors related to the type of the procedure alone. They shall provide the first indication as to what classification would be the most appropriate for a certain type of procedure.

However, for the purposes of the final severity classification of the procedure, the following additional factors, assessed on a case-by-case basis, shall also be taken into account:

— type of species and genotype,

— maturity, age and gender of the animal,

— training experience of the animal with respect to the procedure,

— if the animal is to be reused, the actual severity of the previous procedures,

— the methods used to reduce or eliminate pain, suffering and distress, including refinement of housing, husbandry and care conditions,

— humane end-points.

**Section III:**

Examples of different types of procedure assigned to each of the severity categories on the basis of factors related to the type of the procedure

1. Mild:

(a) administration of anaesthesia except for the sole purpose of killing;

(b) pharmacokinetic study where a single dose is administered and a limited number of blood samples are taken (totalling < 10 % of circulating volume) and the substance is not expected to cause any detectable adverse effect;

(c) non-invasive imaging of animals (e.g. MRI) with appropriate sedation or anaesthesia;

(d) superficial procedures, e.g. ear and tail biopsies, non-surgical subcutaneous implantation of mini-pumps and transponders;

(e) application of external telemetry devices that cause only minor impairment to the animals or minor interference with normal activity and behaviour;

(f) administration of substances by subcutaneous, intramuscular, intraperitoneal routes, gavage and intravenously via superficial blood vessels, where the substance has no more than mild impact on the animal, and the volumes are within appropriate limits for the size and species of the animal;

(g) induction of tumours, or spontaneous tumours, that cause no detectable clinical adverse effects (e.g. small, subcutaneous, non-invasive nodules);

(h) breeding of genetically altered animals, which is expected to result in a phenotype with mild effects;

(i) feeding of modified diets, that do not meet all of the animals’ nutritional needs and are expected to cause mild clinical abnormality within the time-scale of the study;

(j) short-term (< 24h) restraint in metabolic cages;

(k) studies involving short-term deprivation of social partners, short-term solitary caging of adult rats or mice of sociable strains;

(l) models which expose animals to noxious stimuli which are briefly associated with mild pain, suffering or distress, and which the animals can successfully avoid;

(m) a combination or accumulation of the following examples may result in classification as ‘mild’:

(i) assessing body composition by non-invasive measures and with minimal restraint;

(ii) monitoring ECG with non-invasive techniques with minimal or no restraint of habituated animals;

(iii) application of external telemetry devices that are expected to cause no impairment to socially adapted animals and do not interfere with normal activity and behaviour;

(iv) breeding genetically altered animals which are expected to have no clinically detectable adverse phenotype;

(v) adding inert markers in the diet to follow passage of digesta;

(vi) withdrawal of food for < 24h in adult rats;

(vii) open field testing.

2. Moderate:

(a) frequent application of test substances which produce moderate clinical effects, and withdrawal of blood samples (> 10 % of circulating volume) in a conscious animal within a few days without volume replacement;

(b) acute dose-range finding studies, chronic toxicity/carcinogenicity tests, with non-lethal end-points;

(c) surgery under general anaesthesia and appropriate analgesia, associated with post surgical pain, suffering or impairment of general condition. Examples include: thoracotomy, craniotomy, laparotomy, orchidectomy, lymphadenectomy, thyroidectomy, orthopaedic surgery with effective stabilisation and wound management, organ transplantation with effective management of rejection, surgical implantation of catheters, or biomedical devices (e.g. telemetry transmitters, minipumps etc.);

(d) models of induction of tumours, or spontaneous tumours, that are expected to cause moderate pain or distress or moderate interference with normal behaviour;

(e) irradiation or chemotherapy with a sublethal dose, or with an otherwise lethal dose but with reconstitution of the immune system. Adverse effects would be expected to be mild or moderate and would be short-lived (< 5 days);

(f) breeding of genetically altered animals which are expected to result in a phenotype with moderate effects;

(g) creation of genetically altered animals through surgical procedures;

(h) use of metabolic cages involving moderate restriction of movement over a prolonged period (up to 5 days);

(i) studies with modified diets that do not meet all of the animals’ nutritional needs and are expected to cause moderate clinical abnormality within the time-scale of the study;

(j) withdrawal of food for 48 hours in adult rats;

(k) evoking escape and avoidance reactions where the animal is unable to escape or avoid the stimulus, and are expected to result in moderate distress.

3. Severe:

(a) toxicity testing where death is the end-point, or fatalities are to be expected and severe pathophysiological states are induced. For example, single dose acute toxicity testing (see OECD testing guidelines);

(b) testing of device where failure may cause severe pain, distress or death of the animal (e.g. cardiac assist devices);

(c) vaccine potency testing characterised by persistent impairment of the animal’s condition, progressive disease leading to death, associated with long-lasting moderate pain, distress or suffering;

(d) irradiation or chemotherapy with a lethal dose without reconstitution of the immune system, or reconstitution with production of graft versus host disease;

(e) models with induction of tumours, or with spontaneous tumours, that are expected to cause progressive lethal disease associated with long-lasting moderate pain, distress or suffering. For example tumours causing cachexia, invasive bone tumours, tumours resulting in metastatic spread, and tumours that are allowed to ulcerate;

(f) surgical and other interventions in animals under general anaesthesia which are expected to result in severe or persistent moderate postoperative pain, suffering or distress or severe and persistent impairment of the general condition of the animals. Production of unstable fractures, thoracotomy without adequate analgesia, or trauma to produce multiple organ failure;

(g) organ transplantation where organ rejection is likely to lead to severe distress or impairment of the general condition of the animals (e.g. xenotransplantation);

(h) breeding animals with genetic disorders that are expected to experience severe and persistent impairment of general condition, for example Huntington’s disease, Muscular dystrophy, chronic relapsing neuritis models;

(i) use of metabolic cages involving severe restriction of movement over a prolonged period;

(j) inescapable electric shock (e.g. to produce learned helplessness);

(k) complete isolation for prolonged periods of social species e.g. dogs and non-human primates;

(l) immobilisation stress to induce gastric ulcers or cardiac failure in rats;

(m) forced swim or exercise tests with exhaustion as the end-point.