

Ethical Considerations in Research

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Good v Bad

Doing the Right Thing

ETHICS

ards

Values

Fairness

to

A model for ethical reasoning.

- Whether the proposed experiment is admissible or inadmissible from an ethical point of view???
- Ethical reasoning may also be the object of assessment with respect to its quality.
- Good reasoning should be valid.

Ethical Reasoning (Review)



Components in Ethical Review

- 1. Scientific value and validity
- 2. Fair selection of participants
- 3. Respect to the participants (Informed consent)
- 4. Sponsoring
- 5. Vulnerability
- 6. Risk benefit assessment
- 7. Community based study
- 8. Clinical Trials

Scientific Value of a Research



Scientific value of a Research

(Mainly evaluate technical issues)

- Whether the selected study will be able to improve human/animal wellbeing or increase knowledge ???

Eg: Sri Lankan grown Galangal (*Alpinia galanga*) or Maha araththa against *Staphylococcus aureus* and confirm possible toxicity for safe use.

Staphylococcus aureus is pathogenic to humans as well as to animals

Scientific value Continued..

- Whether the selected study is previously carried out locally or internationally (replication)
- If so - valid justification is needed
- Does the **literature review** provide adequate information to support the study??
- Are there any **conflict of interest** or undue inducement by giving finances
- Is there provision to **disseminate** the **new knowledge** after completion of the research

Scientific validity of a Research

Are the objectives clearly stated in the project proposal ???

Are specific objectives clearly stated ??

End of the research we should be able to achieve our objectives and specific objectives

Scientific validity Continued..

Study Design

We have to see whether study design is appropriate to achieve stated objectives in the project proposal

Is it clear ??

Whether it is Human or Animal

Is the study design using accepted principles/methods or practices??

Can the intervention/research be practically implemented

Scientific validity Continued..

Sample **size** is adequate??

Sampling techniques appropriate to produce reliable results using the smallest number of research participants/ animals

Do the **sample size** and **statistical technique** have adequate power to produce reliable and valid results??

Scientific validity Continued..

Is the **inclusion** and **exclusion** criteria in the selected appropriate to achieve the said objectives??

Are the **facilities** at the **site adequate**

Qualifications, competent, and **experiences** of the investigators are adequate

Fair Participants Selection

- If it is a human research, fair subject selection is very important.
- Study population should be determined primarily based on scientific goals of the study
(but not - convenience, ethnicity, age, gender, literacy, culture or economic status)

Fair Participants Selection coati..

- Is the selection of participants (Inclusion and exclusion criteria) appropriate so that **risks** are **minimized** and the **burden of research equitably distributed**
- Is the selection criteria based on science and not on convenience
- Does selection of participants **favor** or **stigmatize** any group
- If biological samples are collected, what is the fate of the samples

Fair Participant Selection Continued..

- In your opinion risk involved is **minimal, minor** or **major**

Respect to the participants (Informed consent)

- Is the process of obtained **informed consent** is appropriate (written/verbal) –adequate, complete, understandable?
- Are the participant **competent enough** to consent ?
- Is the justification for the insertion of **include individuals** who **can not consent** adequate?
- Are the arrangements for obtaining **proxy consent** is adequate??
- Will **descent** be **respected**?
- Are incentive provided, if so do you approve them?
- Is there provision to **ask questions** about the research?
- Will fresh inform consent be obtained if the procedures are changed??

Confidentiality

- Will the researcher collect minimum information or sample required to fulfill the study
- Is the **privacy** of the research participants safe guarded
- Is the place for data collection appropriate
- Are data/samples storage and disposal procedure adequate

Respect to the participants (Rights of the participants)

- Is there an opportunity for the participants to **ask questions** regarding the research
- Is there provision for participants to ask questions and **register a complaint**
- Is there **provision** for the participants to be informed about **newly discovered risk** or benefit during study

Externally sponsored Research

- There **should be a local collaborator**
- Has the research project been approved by the sponsoring country
- Is the research also being carried out in the sponsoring country
- Is the research related to Sri Lanka

Externally sponsored Research

- Does selection of subjects favor any group
- Is the initial contact and recruitment appropriate
- Are relevant local laws/regulations/guidelines of each country adequate
- Is the research responsive to cultural/social differences
- Is the research carried out in vulnerable group

Externally sponsored Research

- Are there provision for intellectual property right
- Is the data or biological samples are to be transferred
- Is there adequate provision to safeguard the interest of the participants and protect intellectual property rights
- Is there provision for results to be conveyed to the relevant authorities in Sri Lanka
- Are any conflict of interest resolved
- Is there written agreement between the collaborator

Vulnerability

- Can the research be equally well carried out in another **less vulnerable** group
- Will the study result in new knowledge relevant to health need of this population
- Is the **medical** and **psychological** support adequate
- Will the benefit of the research be made reasonably available for this group

Risk benefit assessment

- Is the involvement of human participants needed to obtain necessary information
- Are the researchers qualifications adequate for safe conduct of the study
- How safe the interventions to be used in research
- Are there any predictable risk and inconvenience weighted against the anticipated benefits

Risk benefit assessment

- Are there any plans to withdraw or withhold any standard treatment??
- If so, is it justified??
- Is the standard care best available locally
- Is the site include support staff, facilities and emergency procedure
- Is there adequate provisions been made dealing with participants any reporting adverse effect

Risk benefit assessment

- Have adequate provision been made for safety monitoring and termination of the research project
- Is there a possibility of an intervention being available to the participants if found effective

Community based /observational /qualitative research

- Are the impact and relevance of the research on the community in which it is to be carried out acceptable
- Has community concern obtained
- Has individual concern obtained
- Has privacy safeguarded
- If intervention is beneficial, is it available for the community
- Are there any conflict of interest

Clinical Trials

- Is it a multicentre trial and all the centre are following the same protocol
- Is the clinical trial is registered with the **clinical trial registry**
- Does the control group receive the standard therapy
- Are all the participants treated equally

Clinical Trials

- Is there provision for dealing with adverse effect
- Is the procedure for dealing with adverse event adequate
- Will the sponsoring agency provide the drug/device to the patient till it is marketed
- Are there the termination of trial given in details
- Is there provision for insurance of trial participants
- **HAS ADEQUATE ANIMAL TOXICITY AND TERATOGENICITY TRIAL BEEN CARRIED OUT??**

Animal Ethics.

There are three ethical concepts.

1. Deontological approach:

Animals have no value and we can use them the way we want.

2. Animal rights view:

Animals have same rights as human beings.

3. Utilitarian view:

One can use and manipulate animals for the benefit of human welfare with minimum violation of animal welfare.

Pain



Animals and Pain

- Animals feel pain same as human beings.
- But they do not always show their sign of pain by vocal sounds (e.g. birds).
- Some times an animal is in severe pain will not make any sound.
- Vocal expression in pain is not always a reliable method to assess animal's pain.
- Any procedure that cause pain or distress in human may be assume to cause pain in animals.

Pain scoring system

- It usually scores the parameters that demonstrate changes in normal behavior of the animals.
- Each species require its own pain scoring system.

General pain scoring system

- **Activity** : activity levels generally decrease with pain.
- **Appearance**: Animals may be hunched or have a rough hair coat and have discharge around eyes and nose.
(Porphyrin staining in rats may indicate pain or distress).

Porphyrin staining in rats in pain



General pain scoring system continued.....

- **Temperament** :Animals may be aggressive.
- **Vocalization** : Animals in pain make auditory noises (teeth grinding) when undisturbed in cage.
- **Feeding behavior** : water and food intake is often decrease when an animal is in pain.
reduction in body weights, hydration, urine or feces may be measured

General pain scoring system continued....

- **Physiological changes:**

respiratory rate and pattern, blood pressure, pulse, heart rate, skin color or body temperature can be changed.

- **Appearance in the surgery site :**

If an animal has undergone a surgery for an experiment, erythema or swelling in the tissues around the incision is indication of pain.

Assessment of pain.

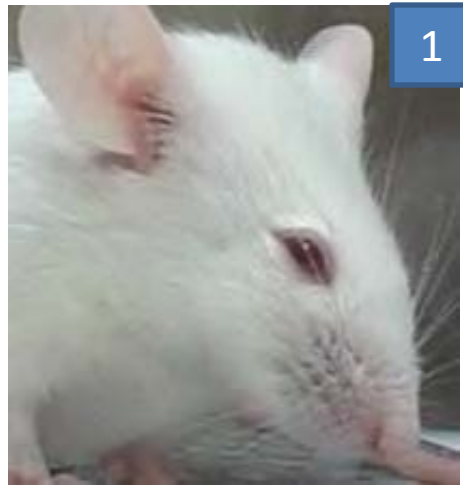
- This pain scoring system must be used to guide researchers in determining whether analgesic therapy or euthanasia is indicated

GRIMACE scale is a useful tool to identify the intensity of pain in laboratory animals

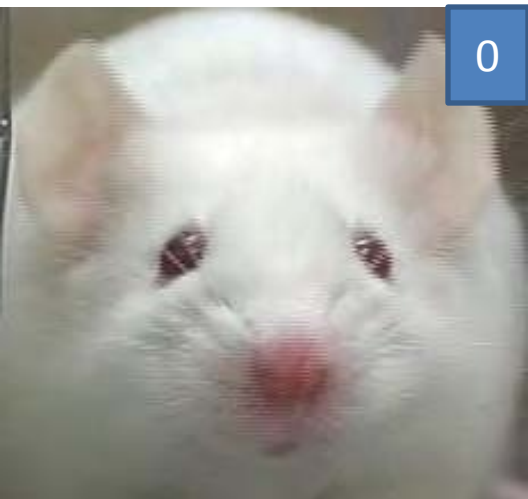
- Orbital tightening
- Ear position
- Nose bulge
- Whisker change
- Cheek bulge



EAR
POSITIONING



WHISKER
CHANGE



0



1

OTRBITAL TIGHTNING



2

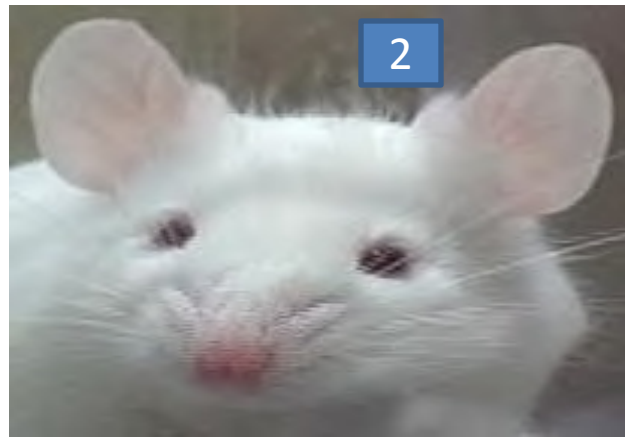


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1

NOSE BULGE



2



0



1

CHEEK BULGE



2

Euthanasia

- **It is a part of ethical approval protocol.**
- **It may be included as an end point of the experiment or as a legal requirement.**
- **In selecting a method it is important to take into account the purpose for which animal is being euthanized.**

Criteria for euthanasia

- Euthanasia of animal is expected if animal demonstrate condition listed below.
- It will do in order to minimize pain and distress.
 - 1) Weight loss by 20%-25%.
 - 2) In appetence or complete anorexia for 24 hrs in small rodents.
 - 3) Weakness or inability to obtain food or water.
 - 4) Moribund stage- weak attempt to get up.
 - 5) Infections- Not responding to antibiotics.
 - 6) Signs of organ dysfunction.

Five freedom in animal welfare

The Five Freedoms

for animals

Freedom to express
normal behaviour

Freedom from
hunger and thirst

Freedom from
discomfort

Freedom from
pain,
injury or disease

Freedom from
fear and distress



Don't
bark
at
it!

Barbican

Best welfare

- 12 hrs light dark cycle.
- Optimum relative humidity.
- Balanced feed formulas according to their nutritional requirements.
- Optimum condition for breeding.
- Clean and comfortable cages.
- Free from unnecessary disturbances.
- Environmental enrichment to enhance their natural behavior.

How bad welfare affects the results of the experiment

- In an animal experiment there can not be any other variables except the experimental variable.
- Animals in bad environment will induce stress hormones and it will affect the experimental results.
- Animals in dirty cages are susceptible to infections and it will affect the results of the experiments.
- Animals in pain give negative feedback on the experiment.

3 R concept

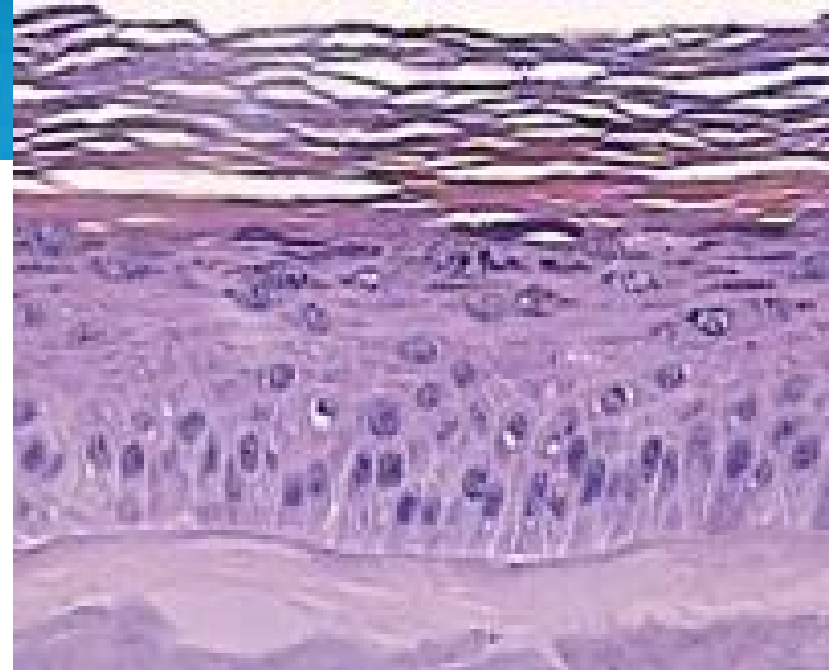
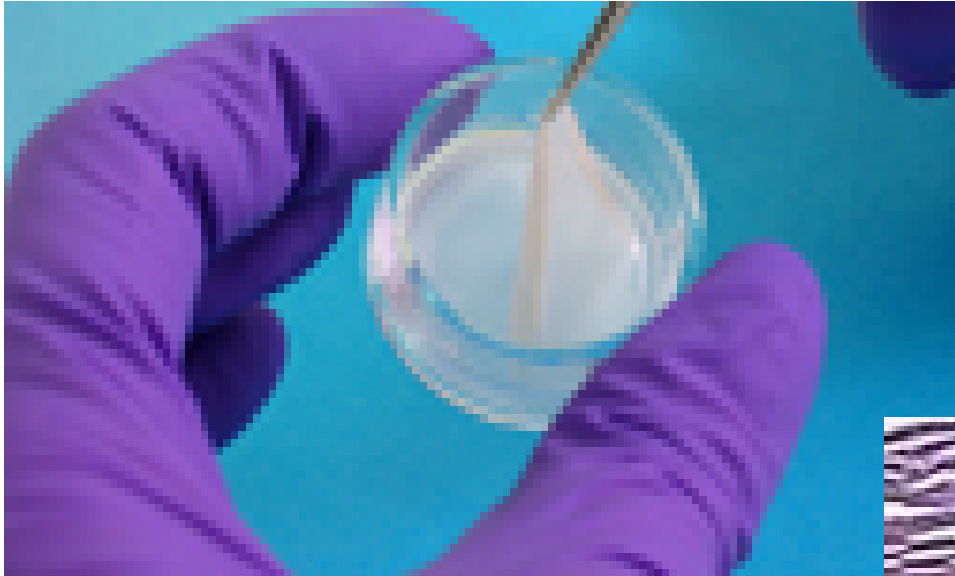


- Three R concepts were introduced by British Scientists, Russell and Burch in 1959; defined by the term
- Reduction
- Refinement
- Replacement

Before starting an animal experiment

- Encourage research students to do adequate literature survey before commencing the animal experiment
- Encourage them to find out suitable alternative technology
- If we can introduce these modern technologies and methodologies practiced in other countries; we can minimize the use of animals for experiments

Alternatives to Animal Testing



Alternative Methods in Animal Experiments.

- **Methods that enhance three R concept is define as an alternative method.**
 - Invitro*** : techniques such as tissue culture.
 - Lower species** : reduce the required number of vertebrate animals.

E.g. bacteria, fungus, insects, mollusks.
 - Immunological techniques:** Their application is useful in diagnostic test, vaccine quality control, fundamental immunological research.

Alternative Methods in Animal Experiment continued...

d) **Physical –chemical method:**

e.g. High Pressure Liquid Chromatography (HPLC).

In the past, potency testing of products such as insulin, calcitonin, oxytocine required animal model. Now it has been replaced by HPLC.

e) **Mathematical model and computer modeling**

e.g.: screening of series of related compounds.

Alternative Methods in Animal Experiment continued...

f) **Human method:** Human or their tissues can justifiably be used as test subject.

e.g. human blood is used to screen pyrogens.

g) **Telemetry:**

Telemetry permits the continuous measurement of several parameters of freely moving animals.

E.g.: body temperature, blood pressure, heart rate, electro cardiogram etc by using miniaturized transmitters.

Animal Ethics Committees.



Animal Ethics Committees

- **Category A: Veterinarian-** A degree in veterinary science with experience relevant to the species use in
- **Category B: Researcher/Teacher-** Member must demonstrate appropriate recent research or teaching experience.
(usually with higher degrees)

Composition of Animal Ethics Committees continued...

- **Category C : Animal welfare person.**

- *That person should have a demonstrable commitment and experience in animal welfare.

- *do not have any involvement with the institution.

- *Should not have any current involvement with care, supply or use of animals in research or training.

Composition of Animal Ethics Committees continued....

- **Category D: Independent person**
- who does not currently or has not previously conducted scientific research or teaching activities using animals.
- That member should bring '**independence of thinking**' to the committee.

Composition of Animal Ethics Committees continued....

Other members:

Additional members may be included into the AEC outside the above category.

The appropriate employees such as animal welfare officers, animal house managers, farm managers or other animal care staff who are responsible for day to day care of animals.

- The use of Laboratory Animals for teaching and research is a fundamental necessity.
- It is necessary for continuous progress of **Bio Medical Sciences.**
- Use of animals constitute a special privilege to scientific community.
- Therefore it is incumbent upon each investigator and every member of their staff to full fill all ethical and legal responsibilities.
- It will enhance the continues medical progress for the betterment of the animals as well as for mankind.

References

- Guideline for ethics review - Sri Lanka Medical association
- Guideline for ethics review- Medical Research Institute, Colombo 8.

THANK YOU