

Faculty of Health Sciences Ethics Office for Research, Training and Support

[health-sciences.ac.za/healthethics](http://www.nwu.ac.za/healthethics)

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| North-West University Animal Care, Health and Safety Research Ethics Committee**NWU-AnimCareREC***registered as Animal Research Ethics Committee (AREC) with the South African National Health Research Ethics Council (NHREC) of the National Dept. of Health,* ***Reg. no. AREC-130913-01*****Ethics Amendment Application Form** to apply for the **amendments** to **approved** studies using animal vertebrates or higher invertebrates for research, education/training or repetitive testing purposes**AnimCare 03-02a, Version 5.10 (Aug 2019)** |
| **CONFIDENTIAL!** This document contains confidential information that is intended strictly and exclusively for the applicant and the NWU-AnimCareREC. Should this document or parts thereof erroneously come in your possession, you are requested to destroy it or to return it to Ethics-AnimCare@nwu.ac.zawithout delay. Unauthorised possession, reading, studying, copying or distribution of this material, or any other form of abuse, is illegal and prosecutable. |

**Please note!**

* You may use ***only a cover letter*** *(i.e. not this form)*, particularly for minor amendments/experienced researchers. Please ensure that you explain all aspects of the amendment in this letter (see the latest version of the **SOP for monitoring and amendment of approved research studies, SOP-Ethics\_1.6**, as available on the website of the Ethics Office - <http://health-sciences.nwu.ac.za/healthethics/sops>) and attach all required supporting documents (see § Checklist and attachments below). Alternatively, you may use ***this application form*** *(optional)* to ***guide & facilitate*** your application for the ethical approval of an amendment, so that you do not miss anything important.
* Refer to ***Addendum A: Applicant’s Instructions*** and ***Addendum B: Study Proposal Requirements*** for more information on how to complete this ethics application form and for requirements for the research proposal document. Also familiarise yourself with ***Addendum C: Moral Declaration*** and ***Addendum D: Severity Categories***.

|  |  |
| --- | --- |
| **Research Ethics Number** | **NWU-?????-??-??** |
| **Campus** | Click here to enter text. |
| **Faculty** | Click here to enter text. |
| **Research Entity** | Click here to enter text. |
| **Discipline** | Click here to enter text. |
| **Principle Investigator/ Researcher/ Study Supervisor** | Click here to enter text. |
| **Student** *(name & surname)* | Click here to enter text. |
| **Study Title** | Click here to enter text. |

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**Tip!** Jump-link to appropriate sections: Ctrl + mouse-click on page number.

As you are completing the application form, you have to update page numbers with the F9 keyboard function.

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| Section 1: General Study Identification |

Provide the necessary descriptions below to identify this study application:

* 1. **Ethics number *(issued upon 1st submission)***

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| Click or tap here to enter text. |

* 1. **Full, descriptive title of the study**

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| Click or tap here to enter text. |

* 1. **Name of the responsible researcher or study leader**

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| ***More information****In case of research studies this refers to the person who takes final* ***responsibility****, or in case of training courses to the Lecturer. In the case of postgraduate studies, also provide the details of the postgraduate student and select the postgraduate level of the study from the dropdown list. The extended study team is described in Section 1: Changes to the Study Team, Collaborators and Professional Supervisors.* |

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| **Role** | **Name** *(title, first name and surname)* | **NWU staff/student no.** |
| PI | Click here to enter title, first name and surname. | Click here to enter number. |
| Student | Click here to enter title, first name and surname. | Click here to enter number. |
| Level of the study | Choose an item. |

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| Section 2: Nature of the Amendment & Required Processes |

* 1. **Motivation for the amendment & brief description of changes**

Briefly describe why this amendment became necessary, and briefly what the changes entail.

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| ***More information******The need for change(s):*** *Many matters can require changes to an approved study. These could, for example, include the* ***addition/withdrawal of team members****, a* ***serious adverse event*** *or* ***observations*** *that requires change in animal procedures or welfare monitoring,* ***new insights*** *gained from literature, congress lectures or discussions with experts,* ***results*** *that require change in the study design, methodologies, animal procedures or welfare monitoring, etc.****Brief description of change(s):*** *Briefly describe* ***specifics*** *of* ***what will change****, as compared to the currently approved study, thereby to address the needs (in a nutshell). These could, for example, include how many members change, how many additional animals, changes to the experimental design (e.g. new test groups) or new/amended animal procedures, how animal welfare monitoring will be changed, etc.* |

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| Click or tap here to enter text. |

* 1. **Extent of change for the amendment being applied for**

Is this an application for a **minor amendment** or a **major amendment** to an approved study? Select the option from the dropdown list below (see “[Choose an item]” below) that best describes this application.

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| ***More information****A* ***minor amendment*** *typically entails small changes, such as a change in the animal age, weight or line, or to add/replace a small number of animals within the same experimental design, etc. A minor amendment will NEVER change the category of the study (i.e. impact on animal wellbeing). Minor amendments are handled via an expedited process (faster feedback in between ethics committee meetings).**A* ***major amendment*** *typically entails significant changes that affect the study objectives, study design, methodology such as any new invasive or risky/harmful procedures, etc. A major amendment may change the category of the study (i.e. impact on animal wellbeing), which should be clearly indicated and justified, and accompanied with a revised harm-benefit analysis. Major amendments should be submitted by the agenda closing date for the upcoming ethics committee meeting, when the amendment will require approval by the full ethics committee.* |

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| Choose an item. |

* 1. **Severity category of the study**

Please indicate the appropriate severity category (compare **Addendum D: Severity Categories**) applicable to this study as a whole. This can be completed here only when considering the cumulative severity category as indicated in **question 4.2** below, towards the end of this application form.

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| ***More information****This estimation should be done after you have described your study in full.****Please note!*** *The selected category will be evaluated and may be changed by NWU-AnimCareREC.* |

|  |  |
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| **Severity category for the study as already approved:** | **Choose an item.** |
| **Severity category for the study after the amendment:** | **Choose an item.** |

**Motivation and/or any comments:**

Briefly motivate your selection of the category as indicated above, with reference to question 4.2.

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| Click or tap here to enter text. |

* 1. **Type of approved study to be amended**

Is the approved study to be amended a *single*or a *larger study, affiliated study, educational (training) course or repetitive testing intervention in animals*? Select the option from the dropdown list below *(see “[Choose an item]” below)* that best describes this application.

|  |
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| ***More information******Please note!*** *“Single” study refers to a study consisting of one or more researchers not intending to involve Master’s or doctoral students, or for the purpose of a single Master’s or doctoral study, whereas a “larger” study refers to a study planning to involve several Master’s and doctoral students and that includes the full methodology, as well as clearly identifies the objectives per student. For more elaborate definitions and explanations of “single” and “larger” studies you are referred to the latest version of the SOP for the research ethics approval application process, SOP-Ethics\_1.4), as available on the website of the Ethics Office (*[*http://health-sciences.nwu.ac.za/healthethics/sops*](http://health-sciences.nwu.ac.za/healthethics/sops)*).* |

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| Choose an item. |

**Please note!** To amend a **sub-study** under a larger project, you need to either (1) indicate that the amended sub-project still fits exactly under what is already approved in the larger study, or (2) apply for approval of an amendment to the large project, whereafter you can apply for approval of amendment to the sub-project *(i.e. you cannot apply for amendment of the larger and sub projects simultaneously)*. For amendment of a **sub-study** *(not necessary for a single study)* it is therefore necessary clarify below how the amended sub-study still fits exactly under what is already approved in the larger study.

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| Click or tap here to enter text. |

* 1. **Any NEW animals to be used** *(not for already approved animals)*

Give a full description of all **additional** animals that you will use in the amendment *(i.e. not accounted for in the currently approved project)*.

|  |  |  |  |
| --- | --- | --- | --- |
| **Animal species** | **Number** | **Gender** | **Age/Mass** |

|  |  |  |  |
| --- | --- | --- | --- |
| Click or tap here to enter text. | 00 | Choose | Type here. |

*Type only one animal species per row, or type “none” if there are no animals.
To add for more rows, click in the last (very right) cell and press the [Tab] key on your keyboard.*

* 1. **Evaluation and approval by a formal scientific committee** *(for major amendments)*

In case of a **major amendment**, provide proof that this amendment has already been evaluated and approved by a **scientific committee** *(not necessary for minor amendments)*.

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| ***More information****The Scientific Committee is also sometimes referred to as a committee for higher degrees, research committee, etc. In case of education/training, the official study/training guide will suffice.****Please note!*** *A letter confirming approval of the* ***major amendment*** *by the scientific committee* ***MUST BE ATTACHED*** *and submitted to* *Ethics-AnimCare@nwu.ac.za**, together with this application (****not necessary for minor amendments****). This letter should be printed on a formal letterhead and signed by the chairperson of the scientific committee, as well as state the approved study title, name of the primary investigator, the date of approval, names of committee members who approved the study proposal, plus suggest (estimate) and motivate the severity category 0 to 5 of the study.****Please note!*** *Whenever the Chairperson of the Scientific Committee is a team member for this application, he/she should step down to avoid conflict of interest and the vice-chairperson or another authorised signatory should sign.* |

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| **Confirm** | **Details** |
| **Yes**[ ]  | Name of the NWU scientific committee | Click or tap here to enter text. |
| Members of scientific committee present | Click or tap here to enter text. |
| Date of approval | Click or tap to enter a date. |
| **No**[ ]  | **Please note** that the study proposal **MUST** be approved by a formal scientific committee (compulsory) for all research studies **BEFORE** it will be reviewed by NWU-AnimCareREC. |
| **n/a**[ ]  | This is an education/training course |

**Any comments:**

|  |
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| Click or tap here to enter text. |

* 1. **Track record of submission dates and version numbers**

Indicate the date of submission of the first application of this amendment and of any subsequent revisions (based on feedback from NWU-AnimCareREC) until the current version.

|  |
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| ***More information****Provide a track record of the submissions and versions of this application, from the first submission, subsequent revisions until the current version. The 1st submission will be version no. 1, and thereafter, the 1st corrections based on comments from the Ethics Committee will be version no. 2, etc.). Complete the date until the current version, and leave the dates for the remainder unselected.****Please note!*** *The latest version will always be used as the current version for the purpose of any passive or active monitoring, or audit. The dates and version no. (based on previous submissions, corrections and/or amendments) may automatically be calculated by an electronic submission platform (once implemented).* |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Select date. |  | Select date. |  | Select date. |
|  | Select date. |  | Select date. |  | Select date. |
|  | Select date. |  | Select date. |  | Select date. |

* 1. **Envisaged implementation date of the amendment and completion date of the study**

Anticipated dates, once ethics approval has been granted.

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| ***More information******Please note!*** *Approval for a maximum of one year will be granted. Thereafter an annual monitoring report will serve as mechanism for notification of completion, or to obtain permission for continuation of the study.* |

|  |  |
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| **EnvisagedImplementation Date** | **EnvisagedCompletion Date** |
| Click or tap to enter a date. | Click or tap to enter a date. |

* 1. **Reviews by other Animal Research Ethics Committees (ARECs)**

*(Select the appropriate option from each dropdown list below)*

|  |  |
| --- | --- |
| **Type** | **Response** |
| This study is currently/has been evaluated by ***another AREC*** (e.g. multi-institutional studies)? | Choose an item. |

If so, provide full details of all other Animal Research Ethics Committees (ARECs) evaluating the study.

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| **Other Animal Research Ethics Committee** *(if applicable)* |
| **Name of the AREC** | Click to type name. |
| **Name of the institution** | Click to type name. | **Country of institution** | Click to type name. |
| **Approval date** | Click to enter date. | **Expiry date** | Click to enter date. |
| **Ethics approval no.** | Click to type number. |

*Please note! Type the information for only one AREC per table, or type “none” if there are no other committees. For more ARECs, fill in the relevant details (as in the table above) in the text box below.*

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| Click or tap here to enter text. |

* 1. **Checklist and attachments**

Indicate the number of each type of attachment below, together with the document names of all the attachments. Document names, as explained below, should follow a systematic order.

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| ***More information****More information on required attachments is available at the end of this document in* ***Addendum A: Applicant’s Instructions****:** *Remember to start* ***document names*** *as per prescribed format (see “****Addendum A: Applicant’s Instructions****”), i.e. starting with the* ***designated numbering****, for example**[****1) Cover letter****], [****2) Research proposal****],etc.)*
* *Where there are two or more documents per category (i.e. line number in the table below), provide the* ***names*** *of both* ***documents****, again using the designated* ***numbering*** *before the descriptive name, for example [****5.1) SOP for waste removal****] and [****5.2) SOP for euthanasia****], etc.).*

***Please note!*** *Please keep the* ***names brief****, because long names will not save properly in the complex folder systems sometimes required for official archiving.* |

|  |  |  |
| --- | --- | --- |
| **Document(s)** | **No**  | **Name(s) of documents** |
| 1. Cover letter for the amendment application
 | **00** | Click or tap here to enter document name(s). |
| 1. Amended research study proposal *(as approved)* or study guide for training, indicating changes with a yellow highlighter.
 | **00** | Click or tap here to enter document name(s). |
| 1. Approval letter from the Scientific Committee for this amendment *(major amendments only)*
 | **00** | Click or tap here to enter document name(s). |
| 1. Amended ethics application form, indicating changes in **red** text
 | **00** | Click or tap here to enter document name(s). |
| **…below only for NEW matters, as applicable** |
| 1. Any NEW approved SOPs to be used in the study *(copies of animal intervention SOPs)*
 | **00** | Click or tap here to enter document name(s). |
| 1. Any NEW animal welfare monitoring sheets *(general and project specific)*
 | **00** | Click or tap here to enter document name(s). |
| 1. Proof of ethics training (<3 yrs) for each NEW team member
 | **00** | Click or tap here to enter document name(s). |
| 1. Training certificates for animal handling for each NEW team member to handle animals
 | **00** | Click or tap here to enter document name(s). |
| 1. SAVC authorisation for each NEW team member to handle animals
 | **00** | Click or tap here to enter document name(s). |
| 1. Proof of SAVC registration of any NEW animal facility (*when applicable)*
 | **00** | Click or tap here to enter document name(s). |
| 1. Signed NWU code of conduct for each NEW team member
 | **00** | Click or tap here to enter document name(s). |
| 1. Narrative curriculum vitae of each NEW team member
 | **00** | Click or tap here to enter document name(s). |
| 1. Contract(s) *(signed copies of any and all NEW contracts when applicable)*
 | **00** | Click or tap here to enter document name(s). |
| 1. Permits(s) *(copies of any and all NEW* *permits when applicable)*
 | **00** | Click or tap here to enter document name(s). |
| 1. Any NEW informed consent(s) *(when applicable)*
 | **00** | Click or tap here to enter document name(s). |
| 1. Any NEW goodwill permission(s) *(when applicable)*
 | **00** | Click or tap here to enter document name(s). |
| 1. Any NEW legal authorisation(s) *(when applicable)*
 | **00** | Click or tap here to enter document name(s). |
| 1. Any NEW approval letters from any other AREC *(when applicable)*
 | **00** | Click or tap here to enter document name(s). |
| 1. Other documents not mentioned above *(when applicable)*
 | **00** | Click or tap here to enter document name(s). |
| 1. **Signed new declarations** by the:
	1. PI / Researcher / Study Supervisor (**MUST**)
	2. Director
	3. Supervising Veterinarian
	4. Biosafety Officer
	5. Animal Facility Manager
	6. Statistician
	7. Supervising Pharmacist
	8. Laboratory Animal Technician (LAT)
	9. Radiation Protection Officer
	10. Any other professional supervisor not mentioned above
 | Included **in this form** below,  and only when new,to be completed and signed electronically  *(only if not possible, print, complete & sign,  scan and attach the declaration page)* |

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| Section 3: Changes to the Study Team, Collaborators and Integrity & Legal Matters |

* 1. **New or Resigning Study Team Members, Professional Supervisors or Collaborators of the Study Team *(where and as applicable)***

Names, qualifications and associations of any:

* + - NEW or RESIGNING **team members** (e.g. researchers, students) who respectively were not previously on the study team, or will not continue to be involved in the study.
		- NEW or RESIGNING **supervisory professional persons** (e.g. veterinary surgeon, pharmacist, veterinary nurse, qualified scientist, etc.) who respectively were not previously on the study team, or will not continue to be involved in the study.
		- NEW or RESIGNING **collaborators** who respectively were not previously on the study team, or will not continue to be involved in the study.

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| ***More information******Team members:*** *These include researchers and postgraduate students in the case of a research study, or lecturers in the case of education/training, and assistants/field workers who form part of the study team.****Professional Supervisors:*** *Being a professional supervisor implies that the individual is an independent monitor involved during data gathering of the study and acts as an advocate for the animal subjects.****Collaborators:*** *Your local team may collaborate with a team from a different institution in South Africa or internationally, thereby, for example, to incorporate and benefit from their expertise and/or facilities. Typically, in such cases, you take responsibility for a certain part of the study and the collaborator for a different part. These responsibilities and agreements must be fully described and declared here.****Please note!**** *For each* ***NEW*** *team member and professional supervisor involved in the study,* ***ATTACH*** *a two-page narrative curriculum vitae (CV). If this* ***NEW*** *team member will handle animals, also* ***ATTACH*** *evidence of appropriate training plus the applicable proof of SAVC authorisation or SACNASP registration.*
	+ *In the table below “Functions and Responsibilities” relates to the role of the individual within the study, which can refer to study design, processing and/or archiving of data, reporting and/or writing of article, study guidance, training, performing certain procedure on animals, etc.*
	+ *In the table below “Competency Certification” refers to the requirement that all team members should provide copies of valid certificates for ethics training (within the last 3 years), and that those researchers or students who will be handling animals should also have undergone training in animal handling and have obtained SAVC authorisation/SACNASP registration to do so (not applicable when NOT handling animals or if registered as a professional with the SAVC).* ***ATTACH*** *copies for new members only.*
* *For each* ***NEW*** *professional supervisor involved in the study,* ***ATTACH*** *a two-page narrative curriculum vitae (CV). The professional supervisor(s) may NOT be part of the study team!*
* *For larger studies involving multiple postgraduate students over multiple years,* ***you MUST apply for a sub-study under the large study for each new student when joining the research team****.*
* *For any* ***NEW*** *collaborations with non-NWU parties, refer to §****Error! Reference source not found.*** *below and* ***ATTACH*** *a copy of the contractual agreement, as approved by the NWU Legal Office.*
* *For any* ***NEW*** *conflict of interest, declare this in full in §2.1.*
 |

Complete the answer to the question below:

|  |  |  |
| --- | --- | --- |
| **Question** | **Yes** | **No** |
| Are there any changes to the Study Team Members, Professional Supervisors or Collaborators? | [ ]  | [ ]  |

**Please note!** If “**Yes**”, complete the table on the next page, providing the applicable information of the new or resigning individuals. If “**No**”, you may skip this table.

|  |
| --- |
| **Table for Details of Any New or Resigning Study Team, Collaborators and Professional Supervisors** |
| **Role** | **New / Resign** | **Name and NWU number** *(if applicable)* | **Functions and responsibilities** | **Qualifications and professional registration** | **Competency certification** |
| Choose an item. | Choose an item. | Type name and no., or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. |
| Choose an item. | Choose an item. | Type name and no., or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. |
| Choose an item. | Choose an item. | Type name and no., or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. |
| Choose an item. | Choose an item. | Type name and no., or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. |
| Choose an item. | Choose an item. | Type name and no., or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. |
| Choose an item. | Choose an item. | Type name and no., or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. |
| Choose an item. | Choose an item. | Type name and no., or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. |
| Choose an item. | Choose an item. | Type name and no., or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. |
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| Choose an item. | Choose an item. | Type name and no., or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. |
| Choose an item. | Choose an item. | Type name and no., or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. |
| Choose an item. | Choose an item. | Type name and no., or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. |
| Choose an item. | Choose an item. | Type name and no., or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. |
| Choose an item. | Choose an item. | Type name and no., or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. |

*Please note! Type the information for only one individual per row.*

* 1. **Conflict of Interest and Sponsorship**

Declare with full details any conflict of interests of any one member of the study team or professional supervisor,
 AND/OR
Give full details of all sponsors of the study (name, address, affiliation with the study and the nature and extent of each sponsor’s contribution).
 AND/OR
Declare with full details all contractual agreements (e.g. with team members, collaborators or sponsors) on the study. This is particularly important for multi-institutional collaborations (i.e. bilateral of multilateral cooperation agreements), when a contractual agreement is required.

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| ***More information****Examples of conflict of interest: financial, non-financial: intellectual, bias, overly optimistic promises of potential benefits, role of the researcher(s), desire of professional advancement, desire to make a scientific breakthrough, relationship with participants. Clearly explain the type of conflict and how this will be managed or resolved.* |

Complete the answer to the question below:

|  |  |  |
| --- | --- | --- |
| **Question** | **Yes** | **No** |
| Are there any changes that related to conflict of interest or sponsorship or contractual agreements? | [ ]  | [ ]  |

**Please note!** If “**Yes**”, complete the table on the next page, providing the applicable information of the new or resigning individuals. If “**No**”, you may skip this table.

|  |
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| **Table for Details of Any New Conflict of Interest** |
| **Role** | **Name**  | **Full declaration and description** | **How will this be managed?** |
| Choose an item. | Type name, or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. |
| Choose an item. | Type name, or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. |
| Choose an item. | Type name, or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. |
| Choose an item. | Type name, or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. |
| Choose an item. | Type name, or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. |

*Please note! Type the information for only one individual per row.*

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| **Table for any New Sponsors** |
| **Name of sponsor** | **Contact details** | **Affiliation and contribution** | **Conflict of interest** | **How will this be managed?** | **Association of any researcher with the sponsor?** | **Any remuneration or benefits to the researcher?** |
| Type name, or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. |
| Type name, or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. |
| Type name, or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. | Type details or “not applicable”. |

*Please note! Type the information for only one sponsor per row.*

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| **Table for Details of Any New Contractual Agreements** |
| **Name of Contractor** | **Full Declaration and Description** |
| Type name, or “not applicable”. | Type details or “not applicable”. |
| Type name, or “not applicable”. | Type details or “not applicable”. |

*Please note! Type the information for only one contractor per row.*

* 1. **Any other changes**

Are there any other **changes** regarding the animal facility, transportation of animals, requirements of permits (e.g. environmental studies), registration/authorisation at SACNASP or SAVC, informed consent from owners, goodwill permission, insurance requirements or any other matter that you need to declare?

|  |  |  |  |
| --- | --- | --- | --- |
| **Yes** | **No** |  | **Details** |
| [ ]  | [ ]  |  | Type details here. |

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| Section 4: Specific Ethical Implications of Amendment |

* 1. **Ethics category and 4Rs**

Explain how the changes to the protocol will affect the project’s ethics category, how it affects the 4Rs (specific reference to impact on animal well-being, probable animal experience, animal number, replacements, refinements & responsibility).

|  |
| --- |
| Click or tap here to enter text. |

* 1. **Any newly introduced procedures, risks and safety measures**

Describe any newly introduced procedure(s) and/or risks, and the corresponding safety measures, as applicable to this amendment request.

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| Click or tap here to enter text. |

* 1. **Detailed identification of ALL requested changes to the protocol**

Describe in detail any and all changes to the protocol, animal number, etc. Also indicate exactly where *(pages, paragraphs, line numbers, etc.)* and how these changes are reflected in the new amended protocol attached. Describe changes in such a way that it will be easy for reviewers to find them.

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| Click or tap here to enter text. |

* 1. **Is there any significant, newly introduced bearing of this study on any endangered or protected species or significant impact on the environment?**

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| Select | If yes, click or tap here to provide details. |

**Please note!** If yes, please provide details on the risk level, identify risk factors and associated precautionary/mitigating measures, AND complete the form on “Estimated Environmental Impact Category” (form no. NS Ethics 01-01a).

* 1. **Any additional comments from the Project Head**

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| Section 5: Amended Harm-Benefit Analysis |

* 1. **Any NEW interventions and associated harm**

[Refer to and consider **Addendum D: Severity Categories**, as well as **General Study Identification, question (g)**, as well as **questions** Error! Reference source not found.**,** Error! Reference source not found.**,** Error! Reference source not found.**,** Error! Reference source not found. **& 4.1** above]. Identify all key interventions on live animals in the study (i.e. withholdings, handling, exposure, procedures, methods, procedures, tests, etc.)*.* Then consider associated animal experience, stressors, risks and justification of these interventions:
**Please note!** Whereas for human studies we estimate risk-benefit, or for projects we estimate cost-benefit, in animal studies we estimate harm-benefit. Benefit should outweigh the harm, for a study to be approved.

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| ***More information****Discuss all key interventions on animals one by one, each in a separate table indicating animals/harm/benefit/outcome #1, #2, etc. Keep in mind that we want to honour the Five Freedoms[[1]](#footnote-1) for animals, namely (1) freedom from hunger and thirst, (2) freedom from discomfort, (3) freedom from pain, injury and disease, (4) freedom to express normal behaviour and (5) freedom from fear and distress. For each table (intervention), provide the following as indicated in the table:** *Indicate and describe the particular intervention to be analysed:*
* *Give a brief description of which intervention you are referring to. This may include, but is not limited to, animal handling, drug administration (e.g. injections or oral gavage), device implantation, surgery or other invasive procedures, infliction of pain or discomfort, exposure to stress or fear, social isolation, withholding of food, water and/or normal husbandry, behavioural testing, euthanasia, etc.*
* *Indicate which animal species, number of animals and experimental test group(s) (as reflected in the study layout) are involved in this specific intervention.*
* *Indicate and describe the specific harm**[[2]](#footnote-2) associated with this particular intervention:*
* *Give a brief description of what the specific harm (from the withholding/intervention/procedure) you are referring to.*
* *Indicate the context of the harm, i.e. whether is physical (including sensory, physiological) or psychosocial (including anxiety), and whether it is repetitive or of long duration (typically >30 minutes).*
* *Describe what the probable experience of the animal will be?*
* *Indicate the severity category of the harm (i.e. impact on animal wellbeing, considering the degree of discomfort or suffering, as specified by the categories officially adopted by NWU-AnimCareREC – see descriptions of these categories in* ***Addendum D: Severity Categories*** *below).*
* *How can this intervention be justified (i.e. why is it necessary)?*
* *What are the aggravating factors (i.e. cause and nature of the harm, or factors making it worse)?*
* *What are the mitigating factors (i.e. precautionary measures in place to minimise this, and to optimise wellbeing? This could include the use of painkillers, anaesthetic, intra-operative and post-operative care and/or euthanasia at the end of the experiment, proper training, and even how you implemented the 3Rs.)*
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| **Inter-vention #1** | **Description of intervention** | Type details here. |
| **Which species, test group?** | Type details here. |
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| **Harm #1** | **Description of harm (what?)** | Type details here. |
| **Context (i.e. nature of the harm) … choose one or more options** | **Number of animals** | **00** | **Physical** | [ ]  | **Psycho-social** | [ ]  | **Environ-mental** | [ ]  |
| **Acute** | [ ]  | **Chronic (lasting)** | [ ]  | **Repetitive** | [ ]  | **Long duration** | [ ]  |
| **Animal experience** | Type details here. |
| **Severity category** | **0** | [ ]  | **1** | [ ]  | **2** | [ ]  | **3** | [ ]  | **4** | [ ]  | **5** | [ ]  |
| **Justification (necessity?)** | Type details here. |
| **Aggravating factors** | Type details here. |
| **Mitigating factors** | Type details here. |

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| **Inter-vention #2** | **Description of intervention** | Type details here. |
| **Which species, test group?** | Type details here. |
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| **Harm #2** | **Description of harm (what?)** | Type details here. |
| **Context (i.e. nature of the harm) … choose one or more options** | **Number of animals** | **00** | **Physical** | [ ]  | **Psycho-social** | [ ]  | **Environ-mental** | [ ]  |
| **Acute** | [ ]  | **Chronic (lasting)** | [ ]  | **Repetitive** | [ ]  | **Long duration** | [ ]  |
| **Animal experience** | Type details here. |
| **Severity category** | **0** | [ ]  | **1** | [ ]  | **2** | [ ]  | **3** | [ ]  | **4** | [ ]  | **5** | [ ]  |
| **Justification (necessity?)** | Type details here. |
| **Aggravating factors** | Type details here. |
| **Mitigating factors** | Type details here. |

Paragraph mark 🡺

*Copy the table #2 + paragraph mark above, click at the beginning of this line (before the word “Copy”) and paste consecutive tables*

*Please note! Type one intervention plus associated harm per table. To add for more tables, copy the whole table #2 plus its paragraph mark below (to view, unhide non-printing symbols), and paste a third, fourth, etc. table beneath, indicated with #3, #4, etc.*

* 1. **Any NEW benefit, scientific integrity and translatability of the study**

Reflect on the likely **benefit** from this study *(by referring to and considering your* ***Research Proposal*** *(i.a. the problem statement, hypotheses & expected outcomes)*, the matters related to **research integrity** *(discussed in* ***Section 3: Specific Ethical Implications of*** *)*, as well as the **translatability** of the study results and findings to real-life practice *(for example the human condition or treatment in the case of pre-clinical studies, or environmental sustainability in the case of environmental studies, or food production in the case of agricultural studies)*:
**Please note!** Benefit (and the robustness thereof), should withstand the “So what?” question on relevance, and will be used to ensure that benefit outweigh the harm, for a study to be approved.

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| ***More information****The SANS 10386 discusses “governing principles in the care and use of animals for scientific purposes”, and then explains what can be seen as the “justification of the use of animals” for this purpose. It then states that (in brief summarised here) there should be evidence to support a case to use animals by demonstrating scientific merit, with the potential to benefit humans, animals or the environment. It also explains that projects using animals may be undertaken only when it is essential to obtain and establish such information, maintain and improve human and/or animal health and welfare, improve animal management or production, understand, maintain or improve the natural environment, achieve educational outcomes.* |

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* 1. **Amended overall harm-benefit analysis**

[Refer to and consider **question 4.1** above]. This question describes the overall outcome of the respective harm analyses of all individual particular interventions in the previous question, as compared to the overall benefit analysis.

**Please note!** Benefit should outweigh harm for any study to be approved.

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| ***More information******Harm-benefit analysis:***1. ***Indicate and describe the overall harm****2 associated with this study:*
	1. *Indicate the cumulative severity category plus degree of overall harm2 associated with this study, considering all of the specific harm in the previous question. The cumulative severity category refers to the overall experience of the animal resulting from all interventions. This should be estimated/deduced/projected, either from the most severe intervention, or when multiple consecutive (combination of) interventions per animal would cumulatively aggravate the experience of the animal, it may be higher than the category for the most sever single interventions.*
	2. *Indicate the degree of overall harm2 associated with this study on a scale from 0 to 5.*
2. ***Indicate and describe the overall benefit****2 associated with this study:*
	1. *Give a brief description the specific benefit (theoretical or practical value) associated with this particular intervention*
	2. *Indicate the domain of the benefit (i.e. who or what will benefit), e.g. social benefits (including human health from a better understanding of a particular phenomenon or treatment, animals directly when the animals in the experiment will benefit from, for example, a treatment, animals indirectly when the representative species will benefit, but not the animals being used themselves, or the environment) socio-economic benefits, scientific benefits, educational benefits or enhancement of safety and efficacy.*
	3. *Indicate the degree of overall benefit2 associated with this study on a scale from 0 to 5.*
3. ***Indicate the final outcome of your analysis****, as applicable to this study:*
	1. *Consider from the cumulative severity factor, overall harm2 and overall benefit2 of the study, whether overall the benefit2 of the study outweighs the overall harm2 of the study. Add a brief motivation and comments to support your final analysis.*
	2. ***Please note!*** *It is particularly important to clearly motivate your analysis outcome. As an example, in a case of “extreme harm = 5”, with “very high” benefit, it may still be that the benefit outweighs harm when benefit is in multiple domains and/or of extreme/critical significance and/or with critically important impact. Even more so in such cases a clear motivation becomes of paramount importance for ethical approval of the study.*
	3. ***Please note!*** *Keep the motivation concise and to the point.*
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| **Overall Harm** | **Cumulative severity category (overall degree of harm)** | **0****Negli-gible** | [ ]  | **1****Low** | [ ]  | **2****Mild** | [ ]  | **3****Mode-rate** | [ ]  | **4****High** | [ ]  | **5****Ex-treme** | [ ]  |
|  |  |  |
| **Overall Benefit** | **Description of the benefit (what?)** | Type details here. |
| **Domain (who/what will benefit?) … choose one or more options** | **Humans (e.g. health)** | [ ]  | **Animals (direct)** | [ ]  | **Animals (indirect)** | [ ]  | **Environ-ment** | [ ]  |
| **Socio-economic** | [ ]  | **Scientific** | [ ]  | **Educational** | [ ]  | **Safety and efficacy** | [ ]  |
| **Overall degree of benefit** | **Negli-gible** | [ ]  | **Low** | [ ]  | **Mild** | [ ]  | **Mode-rate** | [ ]  | **High** | [ ]  | **Very high** | [ ]  |
|  |  |  |
| **Analysis outcome** | **Benefit outweighing the harm?** | **Yes** | [ ]  | **Equal**  | [ ]  | **Unclear** | [ ]  | **No** | [ ]  |
| **Motivation and comments** | Type details here. |

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| Section 6: Declarations |

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| * 1. **Declaration by the Sub-Study’s PI / Researcher / Supervisor**
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I, the undersigned, hereby apply for approval of this study using vertebrate or higher invertebrate animals, as described in the scientific study proposal, and hereby declare that:

1. I have familiarised myself thoroughly as to the content of NWU-AnimCareREC’s rules and procedures, and the latest South African National Standards and regulations for the use of animals in research and training, and I will keep to these guidelines and the details described in the scientific proposal as and when ethically approved.
2. The current study and its experimental design is scientifically justifiable and affordable (i.e. it can be finished once the use of animals will have commenced). Accordingly I:
	1. will ensure sound scientific integrity and research ethics in the planning, execution, data handling and work-up and scientific reporting of the current study,
	2. will ensure that all raw data is stored safely and remains in the possession of the North-West University,
	3. undertake to respect intellectual property rights throughout and to avoid any form of plagiarism.
3. The use of animals can be justified for the current study, no unnecessary repetition of previously done work is included and due consideration has been given to implementation of the 3Rs (replace, reduce and refine, which I am familiar with) and the principle of due responsibility. I therefore also confirm that:
	1. the study objectives cannot be achieved meaningfully through replacement of animal subjects (e.g. lower order animals without consciousness/feeling or tissue or other models),
	2. the experimental design is such that the minimum number of animal subjects is used, no animals are wasted unnecessarily and the optimal quantity of data is obtained from the studies with the number of animals used,
	3. any discomfort/suffering for animal subjects is kept to the minimum and no unnecessary suffering is caused,
	4. the potential predominant benefit arising from the study exceeds the harm to the animal subjects.
4. I will always value the wellbeing of the animal subjects above the interest to continue with or complete an experiment or the study, and the humane handling and treatment of animals and immediate relief of any undue discomfort, pain or distress will remain the highest priority of all team members,
5. I will ensure that the study is managed ethically justifiably from start to finish. This imply that I will:
	1. oversee the study,
	2. ensure that all team members (e.g. myself, co-workers/assistants/technicians) are appropriately trained, experienced, qualified, authorised, registered and otherwise legally competent to implement the approved studies/procedures/interventions,
	3. where applicable and necessary, always ensure that I have the necessary permits at my disposal before the relevant actions are carried out,
	4. confirm that the facilities where animals are housed and procedures performed is appropriately maintained and registered, and that all instruments and apparatus are appropriate for the animals, well maintained and calibrated as required,
	5. confirm that all required and appropriate safety measures are in place and that appropriate monitoring and response measures are in place,
6. I have familiarised myself with the processes and form for unscheduled incidents and adverse events, and will ensure that all team members (including students) working with the animals will be properly informed and trained in emergency procedures as well as provided with the report guidelines and forms.
7. The information provided in this application is, to the best of my knowledge, correct and that no ethical codes will be violated by the study.
8. I will not deviate from the approved proposal, or if required I will formally apply for approval of any amendments, and I understand that the study may be suspended or terminated if I deviate from the proposal without the approval of the Ethics Committee, which may also lead to disciplinary action.
9. I will report to NWU-AnimCareREC:
	1. without delay, as prescribed by the unscheduled incident and adverse event report, any such unscheduled incidents or adverse events experienced during the course of the study,
	2. annually to the Ethics Committee (or as determined by the Ethics Committee) on the prescribed monitoring report form concerning any and all progress and ethical aspects of the study,
	3. concerning any and all progress and ethical aspects of the study once the study is completed.

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| **Name** *(title, full names and surname)* |  |
| Click or tap here to enter text. |
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| **Date** |
| Click or tap to enter a date. | **Signature** |
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| **Any comments (optional)**Click or tap here to enter text. |

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| Addendum A: Applicant’s Instructions |

More detailed information are available in the latest version of the **SOP for monitoring and amendment of approved research studies, SOP-Ethics\_1.6**, as available on the website of the Ethics Office (<http://health-sciences.nwu.ac.za/healthethics/sops>).

1. **General instructions**
	1. **Important!** Always ensure that you have the latest version of the application form, downloadable from <http://health-sciences.nwu.ac.za/healthethics>. Previous versions will not be accepted.
	2. All major amendments research study proposals MUST be approved by an appropriate Scientific Committee BEFORE submitting this application for an amendment *(not necessary for minor amendments)*.
	3. All applications and supporting documentation must be in English only, and only electronic versions submitted via e-mail will be accepted.
	4. Complete this application form and attach all supporting documentation (e.g. NEW certificates, authorisation documents to verify sound sources of animal tissue/fluids and disposal).
	5. You are advised to convert final versions of documents to PDF (i.e. “save as PDF”) before submitting them via e-mail.
2. **Documents and attachments to be submitted**

The following schema and descriptions below explain all documents to be submitted
*(compare with the check list under §3.5 above)*:



Figure 1: Flow diagram of all documents to be submitted with the ethics application, where SOP = standard operating procedure; SAVC = South African Veterinary Council; CV = curriculum vitae. More details follow below.

1. ***Cover letter:*** Prepare a brief cover letter indicating that this is an application to amend an approved study, the title of the study and ethics approval number, principal investigator and student *(if applicable)*, nature of the amendment and other information that will provide context. Give this document a name starting with [1) ###].
2. ***Amended research study proposal:*** The amended study proposal MUST be attached (see Addendum B: Study Proposal Requirements below), which must be Scientific Committee-approved for all research studies and with all changes marked with a yellow highlighter. Give this document a name starting with [2) ###].
3. ***Letter of approval:*** Only in case of major amendments *(not necessary for minor amendments)*, attach the letter of approval of the amendment by the Scientific Committee if this application relates to a research study. This letter should be printed on a formal letterhead and signed by the chair of the Scientific Committee *(or other authorised signatory if there is a conflict of interest)*, as well as state the approved study title, name of the principle investigator, the date of approval, names of committee members who approved the study proposal and recommendation for the severity category. Give this document a name starting with [3) ###].
4. ***The amended original ethics application form plus this amendment application form:*** All changes to the application form MUST indicate all changes with **RED text**. Give each of these documents a name starting with [4.1) Amended Ethics Application Form.docx; 4.2) Amendment Application form].
5. ***Any NEW SOPs:*** Attach a copy of all new SOPs that you refer to in the study proposal and/or ethics application form. Please remember that, when you refer to a SOP in the study proposal and/or ethics application form, you need to indicate which section of the SOP is applicable, and also provide a brief description of the procedure as applicable in the study proposal and/or ethics application form. Give each of these documents a name starting with [5.1) ###]; [5.2) ###], etc.
6. ***Any NEW monitoring sheets:*** All new study-specific monitoring sheets to observe any undue pain and suffering, and to manage (alleviate) pain and suffering when humane endpoints are reached) MUST be attached. Give each of these documents a name starting with [6.1) ###]; [6.2) ###], etc.
7. ***Any NEW proof of ethics training:*** Proof of ethics training (preferably followed by assessment) in the last 3 years for each member of the team. Give each of these documents a name starting with [7.1) ###]; [7.2) ###], etc.
8. ***Any NEW training on animal handling:*** Provide proof of an appropriate animal handling course for each new member of the team that will handle animals. Give each of these documents a name starting with [8.1) ###]; [8.2) ###], etc.
9. ***Any NEW SAVC authorisations or SACNASP authorisations:*** Provide applicable proof of authorisation by the South African Veterinary Council (SAVC) or registration at the South African Council for Natural Scientific Professions (SACNASP) for each new member of the team that will handle animals. SAVC authorisation is typically required for any veterinary of para-veterinary intervention, usually in animal holding facilities, whereas SACNASP registration is typically required for zoological/environmental studies, usually during field work. If you need ethics approval before council authorisation will be granted, conditional ethics approval will be issued, whereafter will to need to provide the proof of authorisation before final ethic approval will be issued. Give each of these documents a name starting with [9.1) ###]; [9.2) ###], etc.
10. ***Any NEW facility registration:*** If applicable, attach the appropriate SAVC registration certificate for all animal holding facilities. Give this document a name starting with [10) ###]
11. ***Any NEW Codes of Conduct:*** Ensure that a signed NWU Code of Conduct for Researchers is attached for each new member of the study team *(study head, supervisor, researchers, students, co-workers, technicians, assistants, etc.).*  Give each of these documents a name starting with [11.1) ###]; [11.2) ###], etc.
12. ***Any NEW Narrative CVs:*** Ensure that a 2-page narrative CV is attached for each new member of the study team *(study head, supervisor, researchers, students, co-workers, technicians, assistants, etc.)* and professional supervisors that are involved in the study (demonstrating qualifications, professional registrations, publications over the last 4 years, other publications related to the study, research expertise and other relevant competencies). Give each of these documents a name starting with [12.1) ###]; [12.2) ###], etc.
13. ***Contracts:*** If applicable attach a copy of all new signed contracts or other agreements, as approved by the NWU legal office. Give each of these documents a name starting with [13.1) ###]; [13.2) ###], etc.
14. ***Permits:*** If applicable attach a copy of all new permits as required. If you need ethics approval before the permit will be issued, conditional ethics approval will be issued, whereafter will to need to provide the permit before final ethic approval will be issued. Give each of these documents a name starting with [14.1) ###]; [14.2) ###], etc.
15. ***Informed consent:*** If applicable, attach the copy of any new informed consent form to be used in English plus translated in all other languages as necessary. Take note of the NWU template to guide you in formulating the informed consent. Give each of these documents a name starting with [15.1) ###]; [15.2) ###], etc.
16. ***Goodwill permission:*** If applicable, attach the copy of any new goodwill permission form to be used in English plus translated in all other languages as necessary. Give each of these documents a name starting with [16.1) ###]; [16.2) ###], etc.
17. ***Legal authorisation:*** If applicable, attach the copy of any new legal authorisations obtained. Give each of these documents a name starting with [17.1) ###]; [17.2) ###], etc.
18. ***Approval letters from other ARECs:*** If applicable, attach the new ethical approval letters of any other animal research ethics committee (AREC) that reviewed the amendment. Give each of these documents a name starting with [18.1) ###]; [18.2) ###], etc.
19. ***Declaration signed by the Responsible Researcher or Study Leader (in this document):*** The Responsible Researcher or Study Leader MUST sign the declaration included in this ethics application form (above). This should preferably be signed electronically. However, if a hard copy is signed, attach
20. ***Signed declaration by the director of the research entity:*** NOT applicable to amendment applications.
21. ***Signed professional supervisor letter by the veterinarian:*** Only when animal procedures change, or new procedures are introduced that may affect animal wellbeing, must the supervising veterinarian complete and sign the applicable declaration form. Give this document a name starting with [21) ###]
22. ***Signed declaration by die statistician:*** Only when the study layout and animal numbers will change, to affect statistical analyses, must the consulted statistician complete and sign the applicable declaration form. Give this document a name starting with [22) ###]
23. ***Signed declarations by other supervisors:*** Only when new procedures would require new declarations, must signed Supervisor Declaration Forms from relevant professional supervisors (e.g. pharmacist, radiation officer, biological safety officer, facility head) be attached. *(****Please note!*** *The application MUST be discussed timeously with ALL professional supervisors, any resulting corrections or amendments made and then returned to be signed off in time for submission. Professional supervisors may not be unduly pressured to sign off to meet deadlines, so that applicants should plan for this.)* Give each of these documents a name starting with [23.1) ###]; [23.2) ###], etc.
24. ***Other documents:*** Any other supporting documents not mentioned above. Give each of these documents a name starting with [24.1) ###]; [24.2) ###], etc.

**Please note!** Keep document names brief, because long names will not save properly in the complex folder systems sometimes required for archiving.

1. **Final submission steps for this application**

The following process must be followed to submit amendment applications *(until the implementation of Info-Ed, whereafter online submissions will apply)*:

* 1. Submit via e-mail the completed Amendment Application Form (with the attached documentation as discussed above) to the Faculty of Health Sciences Ethics Office for Research, Training and Support (Ethics-AnimCare@nwu.ac.za).

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| Addendum B: Study Proposal Requirements |

The study proposal (or training study guide) forms the pivotal document of any ethics application, and must discuss the scientific/educational validity or the study, as well as address ethical considerations and implications, and scientific integrity of the application. Consult also the latest version of the SOP for the research ethics approval application process, SOP-Ethics\_1.4), as available on the website of the Ethics Office (<http://health-sciences.nwu.ac.za/healthethics/sops>).

For amendments you should add the original study proposal document as previously submitted, with all changes indicated with a yellow highlighter. Indicate in this amendment form §3.3 exactly where (i.e. which document, page & paragraph) the applicable changes, as marked with the highlighter, can be found.

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| Addendum C: Moral Declaration |

NWU-AnimCareREC adopted the following moral values as ethical point of departure regarding the care and use of animals in research:

1. It is recognised that non-human animals are valuable beings, **worthy of dignity and respect that** should be protected. In this regard it also recognises the **moral dilemma** of using sentient animals with sensations and emotions for experimentation. At the same time, it is accepted that experimentation with animals is **essential** to advance biomedical sciences, ultimately reducing suffering and enhancing life and wellbeing:
	1. In all instances sound **motivation** and **justification** for the use of animals and procedures must be provided.
	2. The **repetition** of previously performed research experiments with animals will not be considered, unless it can be motivated to be necessary and shown to contribute to new knowledge.
	3. Animal should be **protected from exploitation** via their use in research for trivial, irrational, unjustified or inappropriate reasons.
	4. Animals should **receive optimal care** to promote thriving, manage any disease and avoid unnecessary suffering.
2. The principle of the **4Rs** will be applied to promote humaneness:
	1. ***Replace:*** to replace animals (in absolute, relative or partial terms), where possible, with non-animal alternatives, tissue and fluids of already euthanised animals or less sentient animals
	2. ***Reduce:*** to reduce the number of animals used to the minimal to answer the research question(s), without compromising statistical validity or increasing animal suffering
	3. ***Refine:*** to refine experimental design, animal interventions/procedures and/or the animal model(s) employed to promote thriving of animals *(welfare)*, minimise discomfort and/or suffering *(harm)* and to optimise scientific value *(benefit)*.
	4. ***Responsibility:*** to promote responsible care and use of animals by ensuring competence of all who work with animals, to fostering a culture of compassion and care, to establish clear communication channels for unscheduled adverse events, and to establish clear responsibilities and accountability.
3. Ethical reflection will consider human / experimenter safety, animal wellbeing and environmental integrity. In this regard, the **wellbeing of animals will remain of utmost importance**, firstly by ensuring humane treatment of animals at all times, and by recognising undue stress, pain or discomfort and making relief thereof a priority above the interest of scientific / experimental interest.
4. All keeping, handling, and experimentation with animals must be done according to well-designed experimental protocols and with appropriate safety measures in place, in appropriate, approved, maintained and monitored **facilities** and by appropriately qualified, trained and competent **researchers** and **technicians**, under supervision of appropriately qualified and registered **professionals**.
5. All projects utilising animals for research or training purposes at the North-West University will stand the test of **scientific integrity** and **must be approved by AnimCare** or another appropriate Animal Research Ethics Committee (AREC) of the NWU. In all studies sound scientific integrity shall be evaluated to ensure trustworthy, repeatable results and to provide maximum benefit from the study. In particular, when health-of health-related studies are performed in animals, there is an additional responsibility to ensure that studies are truly translatable and able to advise follow-up animal studies and clinical studies in humans as accurately and comprehensively as possible.

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| Addendum D: Severity Categories |

The following severity categories for animal interventions (i.e. classification of pain, discomfort or stress) have been adopted by the NWU-AnimCareREC. These categories are applicable to selections under **General Study Identification, question (g)** and to **question 4.3** above.

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| ***More information****All vertebrate or higher invertebrate animal procedures and interventions must be classified according to the estimated experience of the animal (discomfort, stress and distress) as below, also adhering to national legislation, the National Code for the handling and use of animals and the North-West University’s (NWU) regulations in this regard. Ethics approval is required for use of vertebrate or higher invertebrate animals, whereas for all other animals the Ethics Committee must only be notified (see Category 0). Categories of impact on animal wellbeing (in the laboratory, wild, farm or domestic) are as below, from which you need to make your selection according to the most severe intervention in your application.****Please note!*** *The six severity categories here (0, 1, 2, 3, 4 & 5) are comparable with the corresponding “informative” six category examples (A1, A2, B, C, D & E) in the SANS 10386:2018, 2nd ed.* |

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| **Category** | **Description of Severity & Examples** |
| **0** | **None**, e.g. use of dead vertebrate or higher invertebrate animals (already euthanized legally and ethically for another purpose and not for this study) or tissue or biological fluids thereof, or using any live lower invertebrate. Also, archived animal specimens from the laboratory, museum, private or any other collections. Non-invasive behavioural studies, e.g. observation of wild animals *in situ* (natural environment) without interference, including minimal disturbance to other biota. Domestic or farm animals on their home property, where procedures are occurring as normally part of the routine management or professional (e.g. veterinary) care. |
| **1** | **Mild**, e.g. keeping of animals in captive conditions (including all animals housed in registered animal holding facilities), or animals collected domestically, from the farm, in the field or other environment, confined and/or transported for subsequent observation. Handling animals or applying minimally invasive examinations, depriving animals of food/water for a few hours (no longer than experienced in nature) or anaesthetising animals that will not regain consciousness (non-recovery). |
| **2** | **Medium**, defined as induced stress of short duration, not requiring anaesthesia or tranquilisation, e.g. parenteral administrations, small subcutaneous implants, exercise or low-stress behavioural testing. Collection of tissue from animals after non-anaesthetic euthanasia for research purposes. Open field testing. Depriving animals of food or water for periods longer than experienced in nature, but without becoming distressful or causing permanent harm. |
| **3** | **Severe**, defined as induced stress of short duration, requiring anaesthesia or tranquilisation, e.g. surgical procedures (including larger implants), multiple injection sites or high-stress fluid/tissue sampling, e.g. cardiac puncture. Procedures that include known disease or severe stress-inducing agents/interventions (e.g. known genetic manipulations, pathogens, toxicity studies or toxic agents, nutrition and trauma, such as perceived unescapable predator exposure), provided the study is terminated (i.e. endpoint) at the onset of relevant symptoms (e.g. lowest observed effect concentration). Restriction of movement over a prolonged periods of time, e.g. metabolic cages or keeping large animals in bomas. |
| **4** | **Very severe**, defined as induced stress of long duration, e.g. prolonged stress (>30 minutes) without anaesthesia or tranquilisation, anaesthesia of long duration (>30 minutes), procedures producing defects or long-term feeding (> 2 days) of deficient or special diets. Forced swim or exercise tests with exhaustion as the end-point. Cancer models and new genetic manipulation. |
| **5** | **Excessively stressful**, where exceptional motivations and justification are needed for approval, e.g. application of noxious stimuli to conscious animals from which the animal cannot escape or any experiments in which total distress is the likely outcome. Toxicity/virulent studies where the endpoint is the moribund state or death. Extended social isolation of sociable animals (e.g. social isolation rearing of rats). Real, staged predator exposure which may lead to attack with harm or kill. |

1. More information on the origins of the universal Five Freedoms can be accessed at the National Archived of the Farm Animal Welfare Council, [http://webarchive.nationalarchives.gov.uk/20121010012427/http://www.fawc.org.uk/freedoms.htm](http://webarchive.nationalarchives.gov.uk/20121010012427/http%3A//www.fawc.org.uk/freedoms.htm), with a 1st press release at [http://webarchive.nationalarchives.gov.uk/20121010012428/http://www.fawc.org.uk/pdf/fivefreedoms1979.pdf](http://webarchive.nationalarchives.gov.uk/20121010012428/http%3A//www.fawc.org.uk/pdf/fivefreedoms1979.pdf). [↑](#footnote-ref-1)
2. More information on harm-benefit analysis can be found in Laber et al. (2016) Recommendations for Addressing harm-benefit analysis and implementation in ethical evaluation – report from the AALAS-FELASA working group in Harm-benefit analysis – Part 2. Laboratory animals, 50(1S):21-42. DOI 10.1177/0023677216642397. [↑](#footnote-ref-2)