HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Guide to
Amendment and Renewal Applications for Projects under Scientific Animal Protection Legislation

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1 SCOPE

This guidance is intended to assist applicants in completing ~~the form~~a Health Products Regulatory Authority (HPRA) 'Application for an ~~amendment~~ Amendment and/or ~~renewal~~Renewal to a ~~project authorisation~~Project Authorisation under ~~scientific animal protection'.~~ Scientific Animal Protection Legislation'.

In accordance with Article 44 of Directive 2010/63/EU (the Directive) and Regulation 30 of S.I. 543 of 2012 ~~as amended~~ (hereafter known as the ~~S.I.),~~Regulations), a user or project manager shall not make a substantial change to a project unless granted an amendment or renewal of the relevant project authorisation by the HPRA. An amendment/renewal application must therefore be submitted and approved in order to proceed with a substantial change to a project involving the use of animals.

2 INTRODUCTION

A user or project manager shall not make a substantial change to a project unless granted an amendment or renewal of the relevant project authorisation by the HPRA. A substantial change in the project means any change to the project which would result in one or more of the following:

a) A failure to comply with the requirements of the ~~S.I.~~Regulations
b) A negative impact on animal welfare~~.~~

A project must be carried out in accordance with the terms and conditions of the relevant project authorisation. A change to a procedure that would potentially result in an increase in the level of pain, distress or suffering (whether ameliorated by treatment or not) or the addition of a new procedure to an existing project authorisation will require an application for an amendment of the project authorisation. An amendment to a project authorisation will not be required for changes that will improve the welfare of the animals involved, e.g. reducing the dose of a test substance being administered or improving the animal's environment.

It is important to note that if there is a significant change to the objectives or scope of the project, or in some circumstances the harm-benefit analysis as a result of the proposed changes, a new project authorisation ~~will likely~~may be required. ~~In addition, a new project authorisation may also be required if the proposed changes negatively impact on the original harm-benefit analysis. However, situations~~Situations in which a new project authorisation is required instead of a project amendment will be decided on a case-by-case basis. ~~Queries in respect~~Applicants who are unsure whether the magnitude of ~~this process can be emailed to~~any proposed changes necessitates a new project authorisation rather than an amended project authorisation should contact sap@hpra.ie.

An application for an amendment or renewal to a project authorisation can be made to the HPRA by the user (e.g. commercial entity, educational institution) or the project manager, on behalf of the user.

Note that an application for a project amendment or renewal must be made to the HPRA, whether or not the project amendment or renewal in question has been approved by the user's ethics committee or another regulatory body. The HPRA endeavours to complete the evaluation of project amendment applications and project renewal applications within 40 working days. This does not include any time taken by the applicant to respond to queries sent by the HPRA. In addition, the HPRA reserves the right to extend the time taken to make a decision regarding an application for project amendments to 55 working days, when justified by the complexity or the multi-disciplinary nature of the project concerned. However, the HPRA expects this to be a rare occurrence and will not make these decisions lightly. When such a situation arises, the HPRA will notify the applicant of the additional time required to evaluate the project amendment/-renewal application prior to the completion of the original timeline outlined by the HPRA upon receipt of the application.

~~Where a substantial change is required to a Department of Health project licence, it is necessary to apply to the HPRA for a new project authorisation. However, if personnel wish to join an existing project licence issued by the Department of Health, the HPRA requires that such individuals apply to the HPRA for an individual authorisation, and attach the existing licence for the relevant project along with a cover letter explaining that they wish to work on that licence. If personnel who already possess a HPRA individual authorisation, wish to join an existing Department of Health project licence, the existing project licence should be submitted along with a cover letter explaining that they wish to work on that licence. The cover letter should include the individual authorisation number issued by the HPRA, details of the Department of Health licence (i.e. project title, project manager and licence number) and the cover letter should be signed and dated by the compliance officer of the authorised user establishment (including a printed name).~~

3 DEFINITIONS

Please refer to Appendix I for relevant definitions relating to the application form.

4 APPLYING FOR AN AMENDMENT OR A RENEWAL OF A PROJECT AUTHORISATION

Please select the purpose of the application as '~~renewal' or '~~amendment' or 'renewal', provide the name of the project authorisation holder, the project authorisation number~~,~~ and the name of the user establishment ~~and complete the relevant section(s) of the form.~~. A brief narrative explaining the reason for the amendment or renewal is also required.

4.1 Renewal

A renewal of an existing project authorisation can be requested by providing the current expiry date, the time extension sought and the justification for the time extension. Where a project authorisation has a condition that retrospective assessment must be submitted at renewal, this should be submitted with the renewal application. The HPRA endeavours to complete the evaluation of project renewal applications within 40 working days, which is exclusive of time taken by applicants to respond to queries. Therefore, the HPRA recommends that applications for renewals are submitted at least three months prior to the expiration date of the project authorisation. It is a legislative requirement that projects are not authorised for any longer than five years. Beyond this time a new project authorisation will be required.

4.2 Amendments

If the application is for amendment(s), select all amendment types that apply in Section C and complete the relevant subsection(s) of the form.

4.2.1 Change to the project start date

The project must commence within one year of the date of authorisation. In order to extend the start date of the project, ~~justification must be provided~~the reason(s) why procedures on animals did not commence within one year of the issue date of the project authorisation must be provided along with information on how it is ensured that no alternative methods (e.g. *in vitro* methods) have become available since the project authorisation was first approved. In addition, assurance must be given that the work has not been carried out elsewhere since the project authorisation was first authorised.

4.2.2 Amendment or change to project manager/amendment to or addition of deputy project manager(s)

If the purpose of the application is to change the project manager, enter details of the proposed new project manager. The proposed new project manager should sign the declaration and undertaking in Section J of the form. The proposed project manager must hold a valid individual authorisation for the purpose of project management. If an individual authorisation has not yet been received, the date of application for an individual authorisation must be provided. The HPRA will be unable to grant an amendment for the project until the proposed new project manager has been issued with an individual authorisation. ~~If both the project manager and~~If the project authorisation holder ~~are~~is to be replaced, an 'Application for ~~transfer~~Transfer of a ~~project authorisation~~Project Authorisation under ~~scientific animal protection legislation'~~Scientific Animal Protection Legislation' must be submitted ~~simultaneously~~ to the HPRA.

~~4.2.3 Amendment to or addition of deputy project manager~~

If the application is to amend an ~~-~~existing deputy project manager(s) or add a new~~-~~/additional deputy project manager, this should be outlined clearly including the full name of the existing deputy project manager(s) to be replaced. The proposed deputy project manager(s) must hold a valid individual authorisation for the purpose of project management. If an individual authorisation has not yet been received, the date of application for an individual authorisation must be provided. The HPRA will be unable to grant an amendment to the project authorisation until the proposed deputy project manager(s) have been issued with an individual authorisation.

Multiple deputy project managers can be added by copying and pasting the table in Section ~~D3~~D2 as many times as required.

~~4.2.4 Addition of new personnel~~

~~Details of all new personnel who plan to perform procedures as part of the approved project authorisation must be provided. All personnel must hold a valid individual authorisation for the purpose of carrying out procedures. If an individual authorisation has not yet been received, the date of application for an individual authorisation must be provided. The HPRA will be unable to~~

~~grant an amendment to the project authorisation until all new personnel named within the amendment form have been issued with an individual authorisation.~~

~~4.2.5~~4.2.3 ~~Amendment / addition of~~ user establishment(s~~) /)~~/additional location(s)

Details of the additional user establishment(s~~) /)~~/location(s) where procedures are planned to be carried out must be provided. In the case of an additional location that is not an authorised user establishment; a justification as to why each additional location is required must be provided. In the case of the amendment or addition of a user establishment, the compliance officer at the new user establishment must also sign the project amendment application form in Section J.

~~4.2.6~~4.2.4 Amendments to procedure(s)

Provide details of the proposed procedure amendment(s). The procedures to be amended must be listed using the procedure number and the exact title of the procedure as per ~~Part 8~~the procedure table of the current HPRA project authorisation document. Clearly outline how each amendment proposed differs from the approved procedure(s) and the justification/relevance of the amendment to the procedure. ~~-~~If required, further guidance for the completion of this section of the form can be found within the 'Guide to ~~project applications under scientific animal protection legislation'.~~Project Applications under Scientific Animal Protection Legislation'.

It may become evident during the evaluation of a project amendment application that the proposed amendment(s) to existing procedures impacts negatively on the original harm-benefit analysis. A new project authorisation may be required in these situations, however this will be decided on a case-by-case basis and applicants will be notified by the HPRA as soon as possible.

For multiple procedure amendments, the table in Section E can be copied and pasted as many times as necessary.

When applying for an amendment to procedures, the following accompanying documentation must be provided:

1 The original project protocol with the proposed amendments highlighted in yellow or added as tracked changes.

~~2 The finalised version of the non-technical project summary approved during the evaluation of the authorised project, including the proposed amendments as track changes or highlighted in yellow.~~

~~3~~2 If the amendment has been approved by an ethics committee, please provide the ethics committee approval document, the completed ethics committee application form and the ethics committee report. If an ethics committee report is not available, correspondence to and from the ethics committee relating to the project in which queries have been raised and addressed should be submitted as an alternative. In addition, if a ~~biostatistician~~statistician has reviewed and approved the proposed amendment as part of the ethics committee review, a signed letter should be included from the ~~biostatistician~~statistician with ~~his / her~~their recommendation.

If, during the course of an authorised project, the severity classification of a procedure is found to be higher than that originally proposed and authorised, this should be reported to the animal welfare body (AWB) immediately and recorded as a project deviation. If the project is to be progressed with the increased severity classification, an application for a project amendment must be submitted to the HPRA without delay. Additionally, a letter of recommendation from the ~~animal welfare body~~AWB must accompany the documentation outlined above ~~(1-3 where relevant).~~

~~4.2.7~~4.2.5 Addition of new procedures

Details of the proposed new procedures should be provided, including a justification as to why the new procedures are necessary. ~~-~~If required, further guidance for the completion of this section of the form can be found within the 'Guide to ~~project applications~~Project Applications under ~~scientific animal protection legislation'~~Scientific Animal Protection Legislation'. It may become evident during the evaluation of a project amendment application that the new procedures proposed impact negatively on the original harm-benefit analysis and a new project authorisation may be required in these situations; however, this will be decided on a case-by-case basis.

For multiple new procedures, the table in Section ~~E~~F can be copied and pasted as many times as necessary.

When applying for an amendment to add new procedures, the following accompanying documentation must be provided:

1 The original project protocol with the proposed amendments highlighted in yellow or added as ~~track~~tracked changes.

~~2 The finalised version of the non-technical project summary approved during the evaluation of the authorised project, including the proposed amendments as track changes or highlighted in yellow.~~

~~3~~2 If the amendment has been approved by an ethics committee, please provide the ethics committee approval document, the completed ethics committee application form and the ethics committee report. If an ethics committee report is not available, correspondence to and from the ethics committee relating to the project in which queries have been raised and addressed should be submitted as an alternative. In addition, if a ~~biostatistician~~statistician has reviewed and approved the proposed amendment as part of the ethics committee review, a signed letter should be included from the ~~biostatistician~~statistician with his/her recommendation.

~~4.2.8~~4.2.6 Amendment to species/strains

If the amendment involves the inclusion of a new species or strain, the relevant fields should be completed in Section G.

~~4.2.9~~4.2.7 Increase in total animal numbers

If animal numbers have increased as a result of the amendment, all fields in Section H must be completed. Please note that if the increase in animal numbers relates to multiple species, a breakdown per species is required.

~~4.2.10~~4.2.8 The 3Rs

~~This section~~Section I must be completed if there have been amendments to procedures, addition of new procedures, and/or an increase in animal numbers~~.~~ or change to the experimental design. If required, further guidance for the completion of this section of the form can be found within the 'Guide to ~~project applications~~Project Applications under ~~scientific animal protection legislation~~'Scientific Animal Protection Legislation'.

~~4.2.11~~4.2.9 Update to non-technical project summary

~~When applying for a project amendment, this may trigger an update to the non-technical project summary, as outlined for certain amendment types above in sections 4.2.6 and 4.2.7. The situation may also arise where an update to the non-technical project summary only is requested, without an amendment to the project authorisation. When applying for an amendment of this type, please provide the finalised version of the non-technical project summary approved during the evaluation of the authorised project, including the amendments as track changes or highlighted in yellow.~~

There is no requirement to submit an updated non-technical project summary when applying for a project amendment. If an update is required, the project evaluator will ask for approval of the updated NTPS.

4.3 Declaration and undertaking

The declaration and undertaking section must be signed by the project authorisation holder, project manager (or the proposed project manager in the case of a new project manager being proposed~~)~~), and the establishment's compliance officer on behalf of the breeder~~ / /~~supplier~~ / /~~user. In the event of the project amendment or renewal being granted, by signing the declaration and undertaking ~~both~~all persons are assuming the responsibility for the overall implementation and compliance of the project with the legislation and with respect to fulfilment of the conditions and obligations as set out in the declaration and undertaking. They are also confirming they will comply with any conditions which may be imposed in the authorisation itself, in the event that it is granted.

5 MAKING AN APPLICATION

An application for an amendment or renewal of a project authorisation must consist of a completed project amendment/renewal application form. Signed copies of all application forms must be submitted to the HPRA. In addition, any relevant associated documentation must be included. The necessary documentation for each category of amendments is outlined in the relevant sections of this guide. A covering letter may also be provided, but this is not a requirement.

The HPRA requests that applications and their accompanying documents are named appropriately. Each document name should begin with the original project authorisation number. This should be followed by a further underscore and one of the following words~~ / /~~phrases:

- Amendment form: to be used for the application form when the purpose is for amendment(s) (where applicable)
- Renewal form: to be used for the application form when the purpose is for renewal (where applicable)
- PP: to be used for the updated project protocol (where applicable)
- ~~NTPS: to be used for the updated non-technical project summary (where applicable)~~
- ECR: Ethics committee approval document, ethics committee report and the completed ethics committee application form. Alternatively, where an ethics committee report cannot be provided, correspondence to and from the ethics committee relating to the project in which queries have been raised and addressed should be submitted. Also to be used for a signed letter from a ~~biostatistician~~statistician (where relevant~~).~~)
- Score sheet: to be used for the animal welfare score sheet (where applicable)
- Cover letter (where applicable~~).~~)

The following is an example of how the files should be named for a hypothetical project amendment application with the project authorisation number AE12345/P001. In this example the project manager is applying for the addition of a new deputy project manager, the addition of a new animal species to an existing procedure and the addition of a new procedure.

DOCUMENT	FILE NAME
Amendment form	AE12345_P001_Amendment form
Updated project protocol	AE12345_P001_PP
~~Updated non-technical project summary~~	~~AE12345_P001_NTPS~~
Cover letter	AE12345_P001_Cover letter
Ethics committee application form	AE12345_P001_ECR
Ethics committee approval document	AE12345_P001_ECR2
Ethics committee queries~~ / /~~correspondence	AE12345_P001_ECR3
Ethics committee ~~biostatistician~~statistician letter	AE12345_P001_ECR4

Any supporting documents included with the application should also be named appropriately. In the example given above, the supporting documentation from the ethics committee is numbered sequentially after the letters 'ECR'.

6 ADMINISTRATIVE DETAILS

Due to the potentially sensitive nature of information contained in amendment ~~/~~ /renewal applications, the HPRA provides a secure online system to enable submission of applications and data. This system is known as CESP, the Common European Submission Platform. Establishments that use CESP will have a nominated person who has registered with CESP, so applicants should liaise with the nominated person to arrange submission of their application. Nominated persons can contact cesp@hma.eu for further information.

Applications can also be submitted by standard e-mail to sapsubmit@hpra.ie.

~~If the application cannot be submitted electronically, applications will be accepted in hard copy by post. Send hard copy applications to:~~
~~Receipts and Validation Section~~
~~Health Products Regulatory Authority~~
~~Kevin O'Malley House~~
~~Earlsfort Centre~~
~~Earlsfort Terrace~~
~~Dublin 2~~

Applications that do not include the necessary information are not eligible for HPRA evaluation. If an application is incomplete, the applicant will be notified as quickly as possible via the e-mail address on the application form.

Queries in respect of application requirements or communications relating to applications submitted can be made by telephone~~, fax,~~ or e-mail ~~or by post to the address below:.~~
~~Scientific Animal Protection Section~~
~~Veterinary Sciences Department~~
~~Health Products Regulatory Authority~~
~~Kevin O'Malley House~~
~~Earlsfort Centre~~
~~Earlsfort Terrace~~
~~Dublin 2~~
Tel: ____+353 1 676 4971
~~Fax: +353 1 676 7836~~
~~E~~Queries e-mail: sap@hpra.ie
Communications relating to existing applications e-mail: sapsubmit@hpra.ie

Fees: Currently there are no fees for this application.

APPENDIX I DEFINITIONS

Compliance officer – the person indicated in Regulation 44 of the ~~S.I.~~Regulations. who is responsible for ensuring compliance with the provisions of the ~~S.I.~~Regulations.

Project manager – the person who holds a project manager authorisation pursuant to Part 8 of the ~~S.I.~~Regulations and is responsible for the overall implementation of the project and its compliance with the project authorisation. The project manager shall ensure that:

a) any unnecessary pain, suffering, distress or lasting harm that is being inflicted on an animal in the course of a procedure is stopped,
b) the project is carried out in accordance with the relevant project authorisation, and
c) in the event of non-compliance, the appropriate measures to rectify it are taken and recorded.

Premises – means any place (physical or virtual), ship or other vessel, aircraft, railway wagon or other vehicle or other mobile facility, and includes a container used to transport animals or relevant thing.

Additional location – an additional ~~premise~~premises, other than the authorised establishment, where procedures and~~/~~/or methods of euthanasia are conducted in accordance with the ~~S.I.~~Regulations, e.g. a commercial farm, wild life park or river basin (depending on the species involved). Procedures and~~/~~/or methods of euthanasia carried out at these locations must be conducted in association with the relevant authorised breeder/supplier/user establishment.

User – any natural or legal person using animals in procedures, whether for profit or not.

Breeder – any natural or legal person breeding animals referred to in Annex I of the Directive with a view to their use in procedures or for the use of their tissue or organs for scientific purposes, or breeding other animals primarily for those purposes, whether for profit or not.

Supplier –~~-~~ any natural or legal person, other than a breeder, supplying animals with a view to their use in procedures or for the use of their tissue or organs for scientific purposes, whether for profit or not.

Procedure –~~-~~ any use, invasive or non-invasive, of an animal for experimental or other scientific purposes, with known or unknown outcome, or educational purposes, which may cause the animal a level of pain, suffering, distress or lasting harm equivalent to, or higher than, that caused by the introduction of a needle in accordance with good veterinary practice.
This includes any course of action intended, or liable, to result in the birth or hatching of an animal or the creation and maintenance of a genetically modified animal line in any such condition, but excludes the killing of animals solely for the use of their organs or tissues.

Project – a programme of work having a defined scientific objective and involving one or more procedures.