HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Guide to
Preparation of a Site Master File for Breeder/Supplier/Users under Scientific Animal Protection Legislation

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CONTENTS

1 SCOPE

This guidance applies to all establishments involved in the breeding, supply and ~~scientific~~ use of animals regulated by Directive 2010/63/EU (the Directive) and S.I. No. 543 of 2012, as amended by S.I. No. 434 of 2013 and S.I. No. 174 of 2014 (hereafter referred to as the Regulations). The guidance is an addition to the HPRA 'Guide to Applications for Breeder/Supplier/Users under Scientific Animal Protection Legislation'.

The purpose of the site master file (SMF) is to provide the HPRA with ~~:~~
an introduction to the breeder/supplier/~~user~~ user establishment ~~-~~and its activities.

- ~~an indication that appropriate animal care and welfare monitoring systems are in place~~
- ~~an indication that the principles of the 3Rs (replacement, reduction and refinement) are being applied~~
- ~~an indication that an appropriate quality management system is present~~
- ~~information about the breeder/supplier/user's record of compliance.~~

2 INTRODUCTION

A site master file (SMF) is a document that the HPRA requests the holder of ~~an~~ a breeder/supplier/user establishment authorisation that is regulated by scientific animal protection legislation, or an applicant for a new authorisation, to provide. It is a legal requirement in accordance with Regulation 36(2~~)()~~(h) of the Regulations.

The SMF provides information concerning the:

- organisational structure, including the lines of responsibility,
- establishment locations, premises and buildings where breeding, supplying or using takes place
- species of animals bred, supplied or used and the activities and principal areas of~~le~~ scientific research, educational or regulatory studies conducted,
- animal care and welfare monitoring systems in place,
- application of the 3R principles (replacement, refinement and reduction) ~~of animal testing)~~,
- quality management system employed,
- provision of training and supervision of competence of personnel at the breeder/supplier/user establishment.

The SMF is needed whether or not the breeder/supplier/user actively operates an animal facility, or is simply the initiator or coordinator of studies on animals which are regulated under the legislation and which are conducted on its behalf, under an authorisation pertaining to the breeder/supplier/user whether for profit or not. Given the heterogeneity of breeders/suppliers/users ~~establishments~~, there will be aspects of this guide that are more relevant to some applicants than others. However, applicants should endeavour to complete all sections in as much detail as possible.

The SMF belongs to the quality management system of the establishment and must be kept updated accordingly.

3 FORMAT OF SITE MASTER FILE

The SMF should contain adequate information in an easily-readable format when printed. Simple plans, outline drawings or schematic layouts should be used where possible instead of narratives.

Where a single SMF is common between two or more establishment locations that share the same animal welfare body and quality management system, site-specific details of each establishment location should be provided separately to easily allow the identification of:

- the species of animal bred/supplied/used at each establishment location,
- the buildings and facilities at each establishment location,
- the activities conducted at each establishment location,
- the identities of those persons designated under Regulation 44-48 of the Regulations and other key personnel as appropriate at each establishment location.

Where an application for a breeder/supplier/user authorisation is in respect of wild animals or for farms not owned or managed on behalf of the breeder/supplier/user, the SMF will be necessarily succinct but should still address the main points set out in section 4 below.

There should be version control of the SMF and it should contain information on both effective and review dates. It should be subject to regular review to ensure that it is up-to-date and representative of current activities. Each appendix can have an individual effective date, allowing for independent updating of the appendices.

The following section provides information on the content and key areas for the SMF.

4 CONTENT OF SITE MASTER FILE

It should be noted that the content is not limited to the items indicated and described in this section but is inclusive of all relevant details related to the ~~management of the~~ breeder/supplier/user.

4.1 Title page

This page should display the name of the breeder/supplier/user authorisation holder. The address, telephone number and key contact details should be included.

The title page should also indicate the name of the author(s), the date of issue, the version number and the date on which revision is due.

4.2 Copy of any current breeder/supplier/user authorisation(s)

If the breeder/supplier/user already holds an authorisation ~~or registration~~ for any of the establishment locations, details of this should be provided. This section may be relevant for ~~in~~ cases where an additional establishment location is proposed for use by a breeder/supplier/user ~~who~~ that ~~is~~ already authorised by the HPRA.

4.3 Details of animals and activities

Details of the species of animals kept, or proposed to be kept, at each establishment location should be provided. This information should include the approximate numbers of animals of each species, as well as information on whether the animals are bred on site or imported.

Where the animals have been supplied to a breeder/supplier/user from a source within the EU, details of the authorisation of the supplier by the relevant member state competent authority should also be provided. Where the animals have been sourced from outside the EU, information should be provided confirming that the animals have been sourced from an authorised breeder in the country of origin and have been transported to Ireland in accordance with national and EU legislation.

Information should be provided on how the requirement is met that animals belonging to the species listed in Annex I of Directive 2010/63/EU are specifically bred for use in procedures.

Where a breeder/supplier/user does not have an animal facility itself but acts as a coordinator for projects undertaken at farm level or involving wild animals at additional locations that are not authorised, information on the species and numbers of animals proposed for use should be provided.

An estimate of the number of ~~new~~ active project authorisations~~s~~ and~~or~~ overall number of animals used in procedures ~~undertaken~~ annually at the establishment should be provided in the SMF.

The nature of the activities carried out should be outlined in a general way, so as to provide an understanding of the operations and procedures being undertaken.

4.4 Establishment locations

A detailed description of all the establishment locations of the breeder/supplier/user where animals are bred and/or supplied and/or used should be provided. This should include a map from the nearest national primary route. If an~~d~~ establishment location is within a university campus or other institutional site, details of the exact location within the grounds should be given. If an establishment location is within an industrial development, an access map should be provided. This information must be provided for every establishment location for which authorisation is sought.

Where a breeder/supplier/user does not have an animal facility itself but acts as a coordinator for projects undertaken at farm level or involving wild animals at additional locations that do not have their own breeder/supplier/user authorisation, the SMF should detail from where operations are initiated and managed, and where records are kept. A map showing the route from the nearest national primary route should also be included here.

4.5 Access information

Details of any local access information or special precautions that might be relevant to the HPRA inspector should be identified. This includes information such as any Health and Safety Statement applying to personnel, as well as practical information e.g. visitor car parking, security requirements, relevant contact telephone numbers to organise the visit etc. Note that unannounced inspections may ~~will~~ also be conducted; information on how inspectors will be accommodated on arrival for an unannounced inspection should ~~also~~ be provided ~~here, to include~~including information on out-of-hours and weekend access by inspectors.

Information on how unauthorised access to animal units is prevented should also be provided.

4.6 History

A brief history of the breeder/supplier/user establishment should be provided. This should detail on when the breeder/supplier/user establishment was initially set up and provide a brief chronology of the various activities relating to the conduct of procedures on animals from commencement to the present day. Any new units or buildings or significant upgrades to facilities should be highlighted.

4.7 Site drawing and description

In this section, a basic schematic drawing or plan of the facilities at each establishment location covered by the breeder/supplier/user authorisation should be provided.

For example, in the case of a laboratory animal facility, the drawing should indicate (as relevant/not exhaustive):

- Animal breeding areas
- Animal receipt and holding rooms
- Animal procedure rooms, including surgery, imaging rooms or other rooms
- ~~Any rooms where specific pathogen-free animals are housed~~
- Facilities for gowning and showering for personnel/visitors
- Feed rooms, cleaning rooms and stores
- ~~Pass-through rooms~~
- Culling rooms
- Freezers
- ~~Dispatch areas~~
- Office and administrative areas
- ~~Quality control laboratories~~
- Facility maintenance rooms
- ~~Location where records related to the facility monitoring and procedural activities are kept~~
- Toilets and locker rooms
- ~~Laminar flow cabinets~~
- ~~Autoclaves~~
- Location of pest control baits or traps

Where the rooms are multipurpose and can accommodate animals of different species, the plan should refer to the species most commonly kept.

In the case of a facility housing farm animals, including bloodstock, the plan should indicate (as relevant and not exhaustive):

- Areas such as sheds/stables/~~Rooms or~~ paddocks where ~~in which~~ animals are kept~~housed~~
- Procedural areas~~re rooms~~
- Feed rooms~~, cleaning rooms~~ and stores
- Recovery areas~~rooms~~
- ~~Freezers~~
- Office and administrative areas
- ~~Quality control laboratories~~
- ~~Facility maintenance rooms~~
- ~~Location where records related to the facility monitoring and procedural activities are kept~~
- Toilets and locker rooms
- Location of pest control baits or traps

~~In the case of a breeder/supplier/user that does not have an animal facility itself but acts as a coordinator for projects undertaken at farm level or involving wild animals at locations that do not have their own breeder/supplier/user authorisation, the plan should detail the location where records relating to the conduct and management of procedures are kept. In this case, a~~

~~description of the type of activities being conducted and the locations where they are undertaken should be provided.~~

4.8 Personnel

An organogram outlining the organisational structure should be provided. Job titles should be included, along with the names of individuals involved in the management of the breeder/supplier/user establishment and ~~in the activities undertaken which require authorisation (i.e.~~ the responsible persons, ~~-~~as defined in the legislation, outlined in the application form~~)~~. It may be necessary to include more than one organogram in order to capture all the relevant levels and departments of the organisation, or to capture the organisation structure of all establishment locations.

In the case of a breeder/supplier/user that does not have an animal facility itself but acts as a coordinator for projects undertaken at farm level, or involving wild animals at locations that do not have their own breeder/supplier/user authorisation, it is necessary to give the names, titles and contact details of key personnel involved in the conduct of the project management, procedures or euthanasia. ~~Copies of contracts with any third party contractors that set out their particular responsibilities are also requested here.~~

An indication of the number of employees engaged in caring for animals, project management, performing procedures (including staff or students if relevant) and~~or~~ performing euthanasia should be provided.

4.9 Responsibilities

Details of how the responsibilities of the following persons are exercised are required:

(i) Compliance officer(s): the person(s) responsible for compliance of the establishment with the provisions of Article 20(2) of the Directive and Regulation 44 of the Regulations

(ii) Animal care and welfare officer(s): the person(s) responsible for overseeing the welfare and care of the animals at the establishment and ensuring that the staff dealing with animals have access to information specific to the species housed in the establishment (Article 24(1)(a) and (b) of the Directive and Regulation 45 of the Regulations)

(iii) Training officer(s): the person(s) responsible for ensuring that the staff are adequately educated, competent and continuously trained and that they are supervised until they have demonstrated the requisite competence (Article 24(1)(c) of the Directive and Regulation 46 of the Regulations)

(iv) The designated veterinarian or suitably qualified expert in accordance with Article 25 of the Directive and Regulation 48 of the Regulations.

The list of responsible persons is not exhaustive. If other key members of staff are involved, their role and responsibilities should also be documented. In respect of each individual identified, the reporting lines for ensuring compliance with the legislation and for ensuring any corrective actions are taken should be made explicit. The responsibility for follow-up

actions advised by the animal welfare body and those listed above and/or otherwise responsible in the breeder/supplier/user establishment should be outlined.

In some smaller breeder/supplier/user establishments, several responsibilities may be undertaken by the same person.

In the case of establishment locations that are linked together as part of the same breeder/supplier/user authorisation, even if geographically distant from each other, the requirements outlined in this section apply. Thus, it is possible that the persons listed in points (ii) to (iv) above might differ between establishment locations within the same overall breeder/supplier/user authorisation. If so, the local arrangements for the responsibilities exercised should be documented in full and may be included as a separate appendix for each establishment location or in a secondary SMF.

In the case of a breeder/supplier/user that does not have an animal facility itself but acts as a coordinator for projects undertaken at farm level or involving wild animals at locations that do not have their own breeder/supplier/user authorisation, information on how the responsibilities are delineated as per the Regulations is still required.

~~Information on the qualifications of the designated veterinarian or suitably qualified expert should be provided. This should include information on his/her expertise in respect of the species of animals kept in the facility in accordance with Regulation 48 of the Regulations.~~

~~4.9~~4.10 Animal welfare body

The terms of reference and i~~I~~nformation on the composition and terms of appointment of members of the animal welfare body should ~~also~~ be provided here. It should ~~be~~ confirm~~ed~~ ~~clarified~~ that the members of the animal welfare body include at least one person responsible for the welfare and care of the animals, and in the case of a user, a scientific member.

How the animal welfare body performs the tasks required of it in Regulation 50 should be outlined. In addition,~~The~~ the means by which the animal welfare body receives input from the designated veterinarian or suitably qualified expert should be outlined.

An outline of the meeting schedule ~~(frequency and duration of meetings)~~ should be provided. The procedure for capturing the output of the animal welfare body and for acting on its advice should be documented.

Where the animal welfare body is a subgroup of an in-house ethics committee, clear information should be provided on the relationship between the two bodies and ~~outline~~ how the legal functions of the animal welfare body are met in practice.

In the case of breeder/supplier/user establishment locations that are linked together as part of the same breeder/supplier/user authorisation, even if geographically distant from each other, it is permissible for a single animal welfare body to serve all the establishment locations. In this case, it would be expected that members of the animal welfare body will have visited the establishment locations in question sufficiently often to be familiar with the well-being and care of the animals involved in projects being undertaken at those establishment locations. It is preferable that each establishment location would have at least one person serving on the animal welfare body.

In the case of a breeder/supplier/user that does not have an animal facility itself but acts as a coordinator for projects undertaken at farm level or involving wild animals at locations that do not have their own breeder/supplier/user authorisation, the animal welfare body remains a legal requirement and evidence that it operates in accordance with the legislation is mandatory. Persons serving on such a body are expected to be familiar with how animals are to be handled and cared for, as well as the 3R principles.

~~4.10~~4.11 Ethics committees

Although there is no legal requirement to have an ethics committee, if a breeder/supplier/user has its own ethics committee then a brief summary should be provided. The terms of reference of the ethics committee and information on meeting schedules as well as the composition, expertise and terms of appointment of the ethics committee should be given. The HPRA Guide to Ethics Committee Assessment of Project Applications under Scientific Animal Protection Legislation includes guidance on what ~~the HPRA expects~~is expected from an ethics committee.

~~4.11 Responsibilities~~

~~Details of how the responsibilities of the following persons are exercised are required:~~

~~(i) Compliance officer(s): the person(s) responsible for compliance of the establishment with the provisions of Article 20(2) of the Directive and Regulation 44 of the Regulations~~

~~(ii) Animal care and welfare officer(s): the person(s) responsible for overseeing the welfare and care of the animals at the establishment (Article 24(1)(a) of the Directive and Regulation 45 of the Regulations)~~

~~(iii) Training officer(s): the person(s) responsible for ensuring that the staff are adequately educated, competent and continuously trained and that they are supervised until they have demonstrated the requisite competence (Article 24(1)(c) of the Directive and Regulation 46 of the Regulations)~~

~~(iv) The designated veterinarian or suitably qualified expert in accordance with Article 25 of the Directive and Regulation 48 of the Regulations.~~

~~The list of responsible persons is not exhaustive. If other key members of staff are involved, their role and responsibilities should also be documented. In respect of each individual identified, the reporting lines for ensuring compliance with the 3R principles and for ensuring any corrective actions are taken should be made explicit. In the case of compliance officer(s), it should be clarified whether or not that individual(s) has budgetary authority to initiate improvements to animal procedures or facilities or to undertake remedial actions identified by the animal welfare body. The responsibility for follow-up actions advised by the animal welfare body and those listed above and/or otherwise responsible in the breeder/supplier/user establishment should be outlined.~~

~~In some smaller breeder/supplier/user establishments, several responsibilities may be undertaken by the same person.~~
~~In the case of establishment locations that are linked together as part of the same breeder/supplier/user authorisation, even if geographically distant from each other, the requirements outlined in this section apply. Thus, it is possible that the persons listed in points (ii) to (iv) above might differ between establishment locations within the same overall breeder/supplier/user authorisation. If so, the local arrangements for the responsibilities exercised should be documented in full and may be included as a separate appendix for each establishment location or in a secondary SMF.~~

~~In the case of a breeder/supplier/user that does not have an animal facility itself but acts as a coordinator for projects undertaken at farm level or involving wild animals at locations that do not have their own breeder/supplier/user authorisation, information on how the responsibilities are delineated as per the Regulations is still required.~~

~~In the case of universities or higher-level institutions that operate an animal research facility, the lines of responsibility for ensuring that students and users undertaking procedures are properly trained in the conduct and execution of the procedures should be outlined. The description should include information on how the users exercise appropriate actions in accordance with the 3Rs and follow the standard operating procedures in place in the establishment. The relationship between management, senior researchers/principal investigators responsible for the supervision of projects and designated veterinarian in the institution should also be outlined clearly.~~

4.12 Animal health and welfare system

The system for monitoring the health and welfare of animals at the breeder/supplier/user establishment should be outlined.

Information on the following should be provided:

- The routine health checks performed on animals on a daily basis
- Any preventative health programme in place, as well as any routine screening conducted on the animals

- ~~Any p~~Policies in place for out-of-hours animal care (evenings, weekends, and public holidays)
- The system in place for communicating with the designated veterinarian and how the advice of the DV is disseminated and recorded.
- ~~Arrangements for the removal of deceased animals and the treatment of sick animals, inncluding whether this task is carried out by staff, students or other persons and how any concerns are escalated to the designated veterinarian or suitably qualified expert.~~
- How any unexpected adverse events or increase in the level of severity encountered during the conduct of a procedure or project is escalated to the designated veterinarian and animal welfare body
- ~~How the development and outcome of projects is monitored~~
- How the 3R principles (~~Rr~~Replacement, ~~Rr~~Reduction and R~~R~~refinement) are applied – this should be evidenced by relevant examples
- ~~Any~~ The enrichment ~~practices~~ programme implemented and details on how this is reviewed to ensure best practice~~used in the housing of animals held~~
- ~~Breeder/supplier/user p~~Policies on good surgical practice and asepsis (if relevant)
- ~~Any policies~~Policies regarding the ~~choice~~ receipt, storage and usage of anaesthetics, ~~and~~ analgesics, and veterinary medicines (if relevant)
- The methods of euthanasia employed ~~used~~ and details on carcass disposal ~~H~~how any animals that have been culled are disposed of, the methods of euthanasia of animals (if any) whether animals are culled out of the sight of other animals. The system for animal disposal.
- ~~How animal remedies, anaesthetics and analgesics are received, stored, used and disposed of.~~
- ~~Breeder/supplier/user policies~~Policies on re-use of animals ~~and how they operate should be outlined~~ (if applicable)
- ~~Breeder/supplier/user policies~~Policies on re-homing and setting free of animals (if relevant) ~~and how they operate~~
- The supply of feed, how supplies are maintained in the face of adverse weather conditions, and any special treatments for feed (e.g. irradiation)~~.~~
- The water system used, how the system is tested and maintained, if relevant~~.~~
- ~~The system for creating and maintaining animal records (in accordance with the requirements of Regulation 63)~~
- How animal health and well-being is ensured where an application for a~~n~~ breeder/supplier/user authorisation is in respect of wild animals, or for farms not owned or managed on behalf of the breeder/supplier/user (short description).

4.13 Facility control and maintenance

Information on how the security of all establishment locations is maintained, including how access to unauthorised persons is prevented, should be provided.

Information about how environmental parameters (air changes, temperature, relative humidity, noise, lighting, etc.) are controlled ~~operate~~ and how they are ~~logged~~recorded

should be provided (if relevant). Information on how the lighting is adjusted for albino animals and the policy for filter changing should be provided (if relevant). ~~Air intake and extract positions should be outlined in a plan (if relevant).~~

In the case of aquatic animals kept in a tank, information on maintenance of water quality should be provided.

It should be clarified whether all ~~the~~ cages, pens or animal containment facilities are in accordance with the requirements of Annex III of the Directive (i.e. size and stocking density).

It should be indicated how any bio-security measures in place, including rodent, fly and pest control, are implemented ~~maintained~~.

Specific information on facility hygiene, including the cleaning of cages or rooms should be provided.

Details of periodic tests undertaken to demonstrate that systems are running effectively, including alarms to indicate system failure, should be provided. System back-up measures in place to ensure site functioning during times of electricity outages etc, should be described. Information on crisis/disaster planning and management should be provided.

4.14 Quality management system

This section should describe the elements of the quality management system in place at the breeder/supplier/user establishment. This should include details on the general organisation of the documentation system, including version control of documents, as well as training documents and standard operating procedures (SOPs).

Details on how project documentation is managed (~~to include~~including records of procedures performed) ~~is managed~~ should be provided. Information should also be provided on how project deviations are handled. The system for dealing with non-compliances with the legislation should also be described. The information ~~documentation~~ on the quality management system should ~~also~~ include a description of the processes in place which ensure that users are aware of the conditions attached to project and individual authorisations and how it is ensured that users comply with those conditions.

It is expected that there will be ~~in place~~ written processes (SOPs ~~standard operating procedures~~) for the care of animals and for the conduct of ~~projects and~~ procedures and euthanasia in place.
~~(including training in procedures).~~

Information should be provided on how reports from any internal audits ~~or external audits~~ conducted as well as any advice given by the designated veterinarian or suitably qualified expert and the animal welfare body ~~is~~ are collated.

Records should be provided of any ~~previous HPRA inspections or~~ other audits or inspections (e.g. good laboratory practice) related to the operations at the breeder/supplier/user within the previous three years as well as any remedial measures undertaken (if any) arising from such inspections.

~~The system for creating and maintaining animal records (in accordance with the requirements of Regulation 63)~~

A record should also be appended on any inspection conducted within the last three years by the Department of Agriculture, Food and the Marine, or local authority or other governmental organisation in relation to animal breeding, animal transport, animal welfare, controlled drug use, records of animal remedies etc.~~..~~

If there is a 'whistle blowers charter' in place, this system should be described.

A key part of the quality management system relates to training; this is described separately below.

4.15 Training

It is necessary to provide details of how the designated training officer(s) for the breeder/supplier/user exercises that responsibility in accordance with Regulation 46 of the Regulations.

Details of how training is undertaken and recorded at ~~the~~ organisational level should be provided. The system for ensuring that competency in the conduct of procedures and euthanasia should be clearly outlined. A detailed description should be provided of the system for ensuring that new personnel have the necessary education and theoretical training and are subsequently trained and assessed as~~to be~~ competent in any procedures, euthanasia or care of animals before they are approved to do so unsupervised.

The system for recording that personnel have been trained and judged to have achieved competence in procedures conducted, euthanasia and in animal care should be outlined, ~~to include~~including where training records are held and how they are kept up-to-date~~. Information on how updates or amendments to the conduct of a procedure are implemented and re-training provided should be given.~~ Information should also be provided in relation to how staff undergo continuous training and education in order to maintain competence (e.g. CPD).

~~The SMF should address under separate headings the conduct of education and training of the following functions (as relevant):~~

~~1 The design of procedures and projects involving animals~~
~~2 Carrying out procedures on animals~~
~~3 Taking care of animals~~
~~4 Euthanasia~~

~~The system for ensuring that personnel have been trained and supervised in the respect of any gowning processes to ensure that bioburden is reduced before entering a specific pathogen-free zone or surgical suite should be documented.~~

4.16 Records management

The following ~~records~~ information should be provided:

- ~~Which~~ How animal records are generated and maintained ~~a~~(in accordance with ~~the requirements of~~ Regulation 63)~~.nd how they are generated and maintained.~~
- How individual authorisation records and project authorisation records are kept.
- How the breeder/supplier/user ensures compliance with any specific conditions relating to the authorisations in place.

- How the breeder/supplier/user ensures compliance with any standard operating procedures for the conduct of procedures and/or euthanasia in animals.
- How ~~animal statistics on the use of animals in procedures and on~~ the actual severity of the procedures ~~are~~ is recorded in preparation for annual statistical reporting ~~generated and returned to the HPRA on an annual basis~~ (in accordance with Regulation 68). ~~This information is mandatory.~~

~~How records of project outcomes are made available for the purposes of collation of animal statistical returns.~~

5 MAINTAINING THE SITE MASTER FILE

Details should be provided on how the breeder/supplier/user establishment[2] plans to ensure the SMF is revised and updated on a periodic basis (at least once annually). ~~The breeder/supplier/user should include information on any amendments to the breeder/supplier/user authorisation and the subsequent changes will be integrated into the SMF.~~