Efficient Breeding of Genetically Altered Animals

Assessment Tool

Introduction

This assessment tool is intended to assist duty holders to consider the efficiency with which genetically altered (GA) animals are bred in establishments. It was created in consultation with breeding experts and establishments, and provides background information, lines of enquiry and examples of acceptable findings, as well as the underlying performance standards and potential performance outcomes that establishments may wish to measure in order to track progress.

There is no such thing as a single "breeding management blueprint" that will work in every establishment. Establishment factors, scientific factors, species and strain factors and the resources available will all influence what an optimum breeding programme looks like in each establishment. However, even if the way they are achieved is different, core underlying performance standards are common to every establishment.

This assessment tool is designed around the breeding of GA mice, although the principles will apply to many species.

This assessment tool is not in itself mandatory and does not define mandatory or additional requirements. Some elements within it are, however, required by licence standard conditions or the Code of Practice. It is anticipated that AWERBs may find this assessment tool useful to assist them with their statutory duty to advise on the application of the 3Rs within their establishments. Inspectors will use this assessment tool when considering how establishments apply the 3Rs to their GA breeding programmes.

Contents

Background

This section provides background information for each focus area and explains the significance of the lines of enquiry.

EXAMPLES OF LINES OF ENQUIRY	EXAMPLES OF SATISFACTORY FINDINGS
Examples of questions that may be used for assessment of the focus area.	Examples of satisfactory findings.
	There may be several contrasting findings that would all be satisfactory if they met the underlying performance standard.
	Different establishments need and will have different practices and systems.
	The findings should be: a) demonstrable b) context- and/or establishment-specific
Not all of the possible lines of enquiry will be listed here.	Not all of the possible satisfactory findings will be listed here either.

Performance Outcomes

- These are measurements that establishments may wish to make in order to monitor performance within each focus area
- It is not mandatory that they are monitored or reported, although your inspector may make a special request for specific outcomes to be measured
- Target values may be set on an establishment-specific basis to assist with focused improvements where necessary

EXAMPLE FOLLOW-UP QUESTIONS Questions or lines of enquiry that may follow on from those above.

An efficient breeding establishment...
- The underlying performance standards for each focus area are listed in this box;
- The performance standards can also be found in a comprehensive list (see contents).

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Background

Archiving is the storage of cryopreserved sperm and/or embryos such that the particular strain can subsequently be rederived as required.

Archiving is a powerful safety device for ensuring valuable lines are not lost due to mutation or another unforeseen event. Archiving can also present an opportunity for efficiency benefits, particularly where a strain will not be required for experiments for some time.

However, archiving in itself can require large numbers of animals to produce the sperm/embryos to be preserved and to recover the lines. There can also be strain-specific variation in the ease of obtaining embryos for cryopreservation. There is therefore a balance to be struck between archiving an unused line too early or too late.

Some archiving services require that lines are made publicly available available after a certain period, and this can cause reluctance to archive due to protection of intellectual property.

EXAMPLES OF LINES OF ENQUIRY	EXAMPLES OF SATISFACTORY FINDINGS
Do you have arrangements in place so that scientists can archive lines if they wish to?	Yes, we perform that in house. Yes, scientists use a free archiving service as we do not have the facilities to do that ourselves here.
How do you decide whether or not it is appropriate to archive a line?	We discuss the likely “down time” before the colony will be needed again (in-house or by collaborators) and assess the relative cost of low-rate tick-over and archiving/rederivation. We also consider any strain-specific technical factors that may influence the number of animals required to complete the archiving/recovery process.
How do you manage tick-over colonies?	We reduce the number of breeding pairs to the minimum we can, striking a balance between the numbers required to assure continued genetic integrity and reduction.
Have you analysed whether or not there are any disincentives at work that inappropriately discourage scientists from archiving?	Yes, we have asked scientists about the barriers to archiving and have minimised these as far as possible.
What information do you keep with your archived lines?	We keep the mouse passports, as well as information about what has been cryopreserved, how it was done, and protocols for thawing and using the materials.

Performance Outcomes

- Proportion of lines that have been reviewed for archiving (i.e. whether or not archiving is appropriate) within last 6 months.

EXAMPLE FOLLOW-UP QUESTIONS Are your scientists generally happy to archive lines when it is appropriate to do so? Are you aware of the free archiving service provided by MRC Harwell and the Sanger Institute? Do you have technical difficulties rederiving the lines? Are you aware of the *Sharing and archiving of genetically modified mice: opportunities for reduction and refinement* booklet produced by the RSPCA Resource Sharing Working Group and endorsed by the BBSRC, CRUK, MRC and NC3Rs?

An efficient breeding establishment...

- Will have or make use of facilities to archive lines;
- Will have minimised as far as possible the barriers faced by scientists to archiving lines;
- Will have a policy and process in place to ensure that tick-over colonies are assessed to determine the point at which archiving would represent a reduction;
- Will have considered the optimum strategy for managing tick-over colonies to minimise the over-production of animals.

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Background

The AWERB should play a key role in advising the establishment licence holder on the application of the 3Rs at the establishment.

In addition, the AWERB should advise staff dealing with animals at the establishment on matters related to the welfare of animals, in relation to their acquisition, accommodation, care and use.

More generally, the AWERB should promote awareness of animal welfare and the 3Rs and help to promote a “culture of care” within the establishment.

Performance Outcomes

- Not applicable

EXAMPLES OF LINES OF ENQUIRY	EXAMPLES OF SATISFACTORY FINDINGS
Does your AWERB take an interest in the efficiency of your GA breeding?	Yes, the AWERB requests a report on our breeding programme every year, and the breeding manager defends this report in person at one of the AWERB meetings.

EXAMPLE FOLLOW-UP QUESTIONS Is there a member of your AWERB with particular expertise in GA breeding? Does the AWERB include questions about breeding and maintenance of GA lines when they are considering new project licence applications?

An efficient breeding establishment...
- Will have active oversight of the GA breeding programme by the AWERB.

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Background

Breeding establishments inevitably use a large number of GA animals. Small changes in efficiency can therefore have a large impact.

Efficient breeding aligns to both welfare and business goals, and there is therefore a strong incentive towards best practice.

These lines of enquiry are specifically tailored for breeding establishments, however they may equally apply to other establishments supplying GA animals to external organisations.

EXAMPLES OF LINES OF ENQUIRY	EXAMPLES OF SATISFACTORY FINDINGS
Do you keep a stock of popular GA lines "on the shelf" so that customer orders can be fulfilled at short notice?	Although we keep popular lines ticking over (this is more efficient than archiving/rederivation between orders) all GA lines require sufficient lead-in time with each order that we can vary our breeding according to demand.
How do you encourage your customers to give you as much notice as possible?	We have an early order discount and we charge for cancelled orders.
How do you discourage your customers from changing their minds?	As well as the cancellation charge we never breed animals unless there's a contract in place. Where the animals are going to be used in experiments, we require confirmation that necessary licence authorities are already granted and that funding is available.

Performance Outcomes

- Proportion of tick-over lines with no orders in the last six months
- Proportion of orders where rederivation of the line was required within six months of archiving
- Proportion of orders cancelled
- Number of animals bred but not used for a scientific purpose (not sold to user or used for breeding/research)

EXAMPLE FOLLOW-UP QUESTIONS How do you predict demand? Did you lose custom when you moved to a demand-led system (requiring the customer to give more notice)? Did this have any knock-on impact on animal welfare?

An efficient breeding establishment...
- Will have minimised the number of animals kept "on the shelf" and will, as far as possible, breed on demand;
- Will have considered incentives and disincentives to customers for appropriate timings of orders, and to minimise cancellations.

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Background

Matching the supply of animals with the scientific demand for them is an essential element of efficient breeding. Failure to do this may lead to under-powered studies (not enough animals available to produce statistically significant results) or overproduction of animals, contributing to avoidable surplus.

Active and informed colony management is essential for efficiency. The colony manager must be able to ascertain how many animals are in the programme, when they were paired, when the litters were born, the size of the litters and other basic information to facilitate good management.

EXAMPLES OF LINES OF ENQUIRY	EXAMPLES OF SATISFACTORY FINDINGS
How do you decide whether to set up and breed a new colony in-house versus buying in animals required for specific experiments?	We evaluate the scientific need and whether the number of animals required and the aniticipated timescales justify breeding in-house. Sometimes it is more efficient to buy in animals when required.
How do you match the production of animals to the demand for them?	We perform breeding calculations before we plan our experiments and only produce the numbers of animals that we need. (Demand led)
	We know in advance what experiments we want to run, but we finesse the details of the experiments based on how the particular strains breed. The scientists have to make a case that their experiment is the best use of the animals that we have. (Supply led)
	Animal production is consistent throughout the year. We plan our experiments based on this predictable “pipeline” of animals.
How do you keep track of how your colony is doing? For example, how many animals there are, how many matings, how many litters of what size, etc.	We have a database that tracks all this information and also gives me historical data. It is very easy to see how many animals there are in each colony, how frequently they are producing litters and the size of the litters. It is easy to see when the pairs need to be replaced.
	The technicians complete spreadsheets which are held on the shared drive so I can access it whenever I want.

Background

EXAMPLES OF LINES OF ENQUIRY	EXAMPLES OF SATISFACTORY FINDINGS
Who does the colony management for each group?	This depends on the skill and experience available in the group. About half of the PIs do their own colony management, but for new or inexperienced researchers the facility manager gives someone in the group very close guidance ("on the job training").
How do you identify people who need extra support with their colony management and/or whether colonies are being efficiently managed?	The breeding/unit manager liaises closely with the colony managers and the technicians so he/she picks up on situations where extra support is required.
	Every colony manager has a monthly meeting/ phone call with the breeding/unit manager to discuss how the colony is doing and any issues that have cropped up.
	The technicians have a list of requests or unusual situations that automatically flag the need for sign off from the breeding/unit manager (e.g. requests for second genotype sample, unusual pairings).
How frequently and by whom are breeding programmes reviewed?	The principles of management of breeding programmes are considered formally every year by the AWERB. Monthly check-ups are held with colony managers of all ongoing programmes. Colony managers are responsible for day-to-day monitoring of their programmes.
What indicators of good breeding performance do you use?	Litter frequency and size for each pair are compared against the strain norm.

Background

The controls that are the most convenient to generate are not necessarily the most scientifically robust. Controls are often required to be line-, gene-, breed-, and age-specific, therefore using previously-generated controls may not be scientifically valid and may represent a “false economy”.

EXAMPLES OF LINES OF ENQUIRY	EXAMPLES OF SATISFACTORY FINDINGS
How do you track the characteristics of each strain?	We have a mouse passport system but also a cage-side label that contains a very brief summary of what harmful phenotypes to look out for.
How do you approach breeding strains that are known to be “difficult breeders”?	We make very careful observations of the strain and analyse the core reason for the difficulty. This can then be directly addressed through husbandry interventions, or we adjust the expectations of the scientists with regards the productivity of the line. We also liaise with other groups/establishments where the same strain is being bred.
How do you control for your conditional knock-out lines?	We have a central database of frozen-down controls for conditional knock-outs available establishment-wide. This might save us having to generate new ones each time, although usually we find we need controls specific to our experiment and have to generate them from scratch.

Performance Outcomes

- Proportion of colony managers who have received formal training in colony management.
- Proportion of colony managers who complete annual CPD or training updates in colony management to keep key skills up to date.
- Proportion of colony managers who report that they have sufficient expert support in colony management available to them.
- Proportion of colony managers who feel their skills are up-to-date.
- Proportion of colony managers who report that they have easy access to the information they need to efficiently manage their colonies.
- Proportion of technicians reporting they feel confident to challenge or report any instructions or requests that are unusual or that they don’t understand.
- Proportion of colony managers who monitor strain-appropriate breeding performance indicators.
- Pre-weaning loss rate (by strain).
- Proportion of technicians/scientists who report that they can easily find phenotype information for familiar and unfamiliar strains.

EXAMPLE FOLLOW-UP QUESTIONS Who is involved in deciding whether to breed in-house or buy animals in? How do you assess whether a colony is being well managed? How quickly are any issues identified and dealt with? What training do you give new researchers in colony calculations? Is it convenient for colony managers to access the colony data? How often do you [colony manager] look at it? Is historical data easy to access? How do you determine if someone is sufficiently skilled at colony management? How does this change with multiple knock-out strains (complex genetics)? Where do you get information about the "strain norm"? Are you aware of the *GA passports: the key to consistent animal care* booklet by the RSPCA Passport Working Group and endorsed by the Wellcome Trust Sanger Institute? Where ticking over a colony is appropriate, how many pairs do you keep? Why have you settled on this number?

An efficient breeding establishment...

- Will have an individual identified as the primary colony manager for each colony;
- Will have regular reviews of colony performance and management at individual colony and establishment-wide levels;
- Will have colony managers who are skilled in matching supply and demand, so that sufficient animals are available to ensure high quality science, while minimising the avoidable production of surplus animals;
- Will provide training and support to colony managers to equip them with the skills they need, keep their skills up to date and assist them with challenging situations;
- Will have oversight of the relative strengths of their colony managers, and will understand situations where individuals may require extra support or training;
- Will have colony managers who are able to keep up to date with accurate information about their colonies;
- Will gather all the information required by colony managers to make sound breeding decisions;
- Will have technicians who are empowered to challenge colony managers directly or indirectly if unusual or unclear requests are made;
- Will have defined strain-appropriate breeding performance indicators for each colony, and be monitoring against them;
- Will have a methodology for assessing strain-specific tendencies, preferences and phenotypes and planning and providing optimum conditions for those strains;
- Will have considered the optimum strategy for maintenance of colonies, balancing genetic needs against practical constraints;
- Will have considered the optimum controls for conditional knock-outs and will have a system for making these available across research groups.

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Background

Tight finances have been cited as a major driver to minimising animal use, improving efficiency and minimising the animals that are bred but not used for a scientific purpose. However, inappropriate financial arrangements may hinder good science and discourage good breeding practices.

For commercial breeding organisations, breeding efficiency and business performance are closely aligned.

EXAMPLES OF LINES OF ENQUIRY

How have you ensured that financial arrangements encourage efficiency and disincentivise poor practices with respect to breeding GA lines, while supporting good science?

EXAMPLES OF SATISFACTORY FINDINGS

We have analysed the barriers to best practice experienced by colony managers and we are actively working to minimise as many of these barriers as possible. We are prioritising addressing the financial barriers because these are particularly strong drivers of behaviour. We are also investigating how financial incentives can be used to encourage desirable breeding practices at the same time as encouraging and supporting good science.

Performance Outcomes

- None applicable

EXAMPLE FOLLOW-UP QUESTIONS What are the financial pressures that your colony managers face? Do they encourage desirable practices while enabling good science?

An efficient breeding establishment...

- Will have analysed the barriers to efficient breeding and ensured that any influenceable barriers are minimised or removed, including financial barriers;
- Will have considered the design and use of financial structures that encourage desirable practices as well as encouraging and supporting good science.

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Background

Practices around genotyping can have a major impact on the number of animals bred but not used, and also the number of animals kept alive and any one moment. Inefficient, inaccurate or delayed genotyping can lead to avoidable surplus animals.

EXAMPLES OF LINES OF ENQUIRY	EXAMPLES OF SATISFACTORY FINDINGS
How do you avoid genotyping mistakes?	We have a set procedure for genotyping that is the same across the unit. That way the technicians do not have to change the way they work between colonies.
Do you outsource your genotyping or perform it in-house? Why?	We do our genotyping ourselves because it is the most efficient way of analysing the small number of lines that we hold.
	We outsource the genotyping because the external provider is far more efficient, fast and cost-effective than employing someone in our lab to do it. In addition, they can easily set up new PCRs for complex genetics and there is no downtime due to technical problems that we would inevitably have in our own small lab.
	We are a large facility and run a central genotyping service that caters for all the lines we hold.
How long does it take for animals to be genotyped?	It only takes a couple of days for the results to come back and we can do that prior to weaning.
How/when do you set up the genotyping method for new lines?	Genotyping for new lines is always planned in advance of the line being produced, so that we don't find ourselves in a position where there's a new line and we don't immediately have a way of genotyping it. We don't allow new lines to be brought into the facility until a satisfactory genotyping programme is in place and ready to be used.

EXAMPLES OF LINES OF ENQUIRY	EXAMPLES OF SATISFACTORY FINDINGS
Do you bank your samples?	Yes, we always bank samples in case we need to re-run an analysis.
How do you minimise downtime of equipment critical for genotyping (e.g. PCR)?	We have a proactive maintenance regime and robust emergency response plan, including the use of a back-up lab if needs be.

Performance Outcomes

- Genotyping error rate;
- Genotyping turnaround time (sample collection to results available);
- Genotyping service downtime.

EXAMPLE FOLLOW-UP QUESTIONS What is your quality control process for genotyping?

An efficient breeding establishment...

- Will have a quality control process for their genotyping;
- Will have assessed the relative merits of in-house versus outsourced genotyping;
- Will have minimised the time that elapses between taking the sample and receiving genotype data;
- Will prepare the genotyping process in advance of bringing in/producing new lines;
- Will have access to an archive or bank for samples;
- Will have maintenance, repair and contingency plans in place for critical equipment (e.g. PCR) to miminise downtime.

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Background

Quality assurance of lines requires that they are periodically rederived. In addition, lines may need rederivation in order to move from a low health status to a high health status facility, or to restore a line that has been cryopreserved.

This rederivation process requires the use of additional animals.

EXAMPLES OF LINES OF ENQUIRY	EXAMPLES OF SATISFACTORY FINDINGS
How do you decide whether/when a line requires rederivation?	We consider the research demands and strain demands (specifically in relation to health status) versus the animal cost of rederivation and come up with the most appropriate answers on a strain by strain basis.
What policy or oversight do you have to ensure that any rederivation on the grounds of biosecurity is proportionate to the biosecurity risk?	We consider each rederivation request on its merits, balancing a risk of a biosecurity breach and the consequence of such a breach against the welfare impact of the rederivation.
How do you monitor lines to ensure that their genotype does not drift in a manner detrimental to the scientific aims?	For each strain we monitor the number of inbred generations and the potential magnitude of any effect that genetic drift would have on the science. If the impact would be significant we refresh the line. This is commonly done every ten generations.
Where are new lines created? In house or at a supplying establishment?	We have the facilities to create new lines in house, but it is ultimately up to the researcher to decide what the best approach is, considering the complexity of the genetics and the resources available.
	We do not have the facilities or skills to create new lines in house, so we import them from a specialist supplying establishment.

Performance Outcomes

- None applicable

EXAMPLE FOLLOW-UP QUESTIONS How do you assess the impact, if any, of genetic drift on your science? What is your strategy for limiting the impact of genetic drift? How do you ensure your staff stay up to date and skilled in the techniques required to create new lines, particularly if they don't do it that often? Do you have any policies or procedures for vetting/approving rederivation requests?

An efficient breeding establishment...

- Will have a flexible, situation-led policy on rederivation that allows case by case consideration, rather than a “one size fits all” approach;
- Will have a risk based approach to biosecurity rather than a blanket requirement for lines to be rederived as they enter the facility;
- Will consider the risk of genetic drift on scientific outcomes and have procedures in place to prevent significant impact, through appropriate colony management;
- Will have considered the pros and cons of generating lines in-house versus importing custom-created lines from a specialist supplier.

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8. Sharing animals and minimising avoidable surplus

Background

Breeding of GA animals produces unavoidable and avoidable surplus animals. “Non-target” animals are created as a by-product of the creation of “target” animals.

Unavoidable surplus is caused by Mendelian genetics and the fact that technology for genetic manipulation is not 100% efficient. In addition, not all non-target animals produced can necessarily be used for a scientific purpose.

Avoidable surplus occurs if the non-target animals are not used for a scientific purpose (where this is possible), or where more of them are produced than the inevitable minimum. In addition, some researchers only use animals of one sex for their research, with the potential to waste the animals bred of the opposite sex.

Formal and/or informal systems can reduce the number of animals that are “bred but not used”.

EXAMPLES OF LINES OF ENQUIRY	EXAMPLES OF SATISFACTORY FINDINGS
Why do you use animals of only one sex in your research?	The model is of a disease that only occurs in males.
	There is a fundamentally different mechanism in males and females - we only wish to study one mechanism at this stage.
How do you ensure that animals that are bred are used, wherever possible, for a beneficial scientific purpose? What happens to unwanted animals (e.g. wrong genotype)?	We have a formal arrangement to share strains and/or tissues on our intranet.
	We are a small unit and informal communication with collaborators ensures that animals/tissues are shared as much as possible.
	All surplus animals are used for tissue harvest or teaching purposes.
How do you ensure that all researchers at your establishment are aware of the lines already being bred here?	We have a searchable database that all researchers can access. We also publicise new lines in our newsletter that goes out to users.

Performance Outcomes

- Number of animals bred but not used for a scientific purpose;
- Proportion of scientists who report that they have access to information about animals being bred at the establishment and sharing colonies and/or tissues.

EXAMPLE FOLLOW-UP QUESTIONS Why don’t you use age *and sex* matched controls? How do you track the number of animals that are “bred but not used”? How do you monitor how surplus animals are used? How do you ensure your database of lines being bred is up-to-date and complete? How do you manage researchers’ concerns regarding potential Intellectual Property issues in the context of sharing lines/tissues? Can you identify core colonies that could be centrally managed for all researchers?

An efficient breeding establishment...

- Will have systems in place to ensure that researchers know what lines are currently being bred at the establishment;
- Will have one or more systems in place, formal or informal, to ensure that researchers share the available animals or their tissues whenever possible;
- Will question the exclusive use of male or female animals in experiments and ensure the approach is scientifically necessary.

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Background

Successful breeding of GA animals relies on partnership between the scientists, unit managers and animal technicians.

EXAMPLES OF LINES OF ENQUIRY	EXAMPLES OF SATISFACTORY FINDINGS
How do you organise which technician works with which colonies?	There is a named technician attached to every group, so although every technician can do all the procedures for all groups, there is one person with an in-depth knowledge of the group's colonies.
How do you ensure that the technicians understand the scientific requirements of the programme?	We have regular meetings between the scientists and the technicians where the scientists explain the background and importance of the work that the technicians are facilitating.
What happens if the technician does not feel the instructions given by the colony manager are appropriate, or if he/she does not understand the instruction or the rationale behind it?	The technicians are empowered to challenge the colony managers directly in this situation. The technicians are able to use their professional judgement (e.g. if a requested pairing involves animals that don't look in the best clinical condition on the day).
Do the technicians have an alternative to direct communication with the colony manager if needs be?	The technicians have a route to challenge the colony managers which does not involve direct conversation with them if needs be (e.g. via a supportive unit manager).
How do the scientists regard the technicians?	The scientists feel supported by the technicians, and respect their skills. They work effectively together as a team.

Background

Successful strategy here will ensure that planned or unplanned absences of the colony's lead technician does not result in a drop in standards of animal welfare or colony management.

EXAMPLES OF LINES OF ENQUIRY	EXAMPLES OF SATISFACTORY FINDINGS
How do you ensure continuity of the colony manger-technician relationship (i.e. reduced rotation of technicians) while still maintaining strength and depth in the skills of the technical staff (e.g. to cover absence and maintain interest through variety)?	We balance the need for more than one technician to be knowledgable about each group's colonies against the need for continuity by slowly rotating technicians between groups. Although the colony managers would prefer that we never rotate, they also recognise the need for all our technicians to be sufficiently familiar with the strains that they can detect any issues at the weekends, for example.
How do you ensure that the phenotype of new or existing strains is recorded and made immediately available to technicians, scientists and people concerned with animal welfare, for example the NVS?	When the strain is imported or created we work out when the phenotype assessments need to take place, according to the known and unknown strain characteristics. We have a cage-side phenotype card which alerts people to the expected harmful phenotypes and also clearly indicates what is and is not permitted by the project licence. In addition, we create mouse passports that are held on a shared drive.

Performance Outcomes

- Proportion of strains that have cage-side basic phenotype information available.
- Proportion of strains that have phenotype information held in a mouse passport.

EXAMPLE FOLLOW-UP QUESTIONS If you were working at the weekend, would you easily be able to check the expected phenotype of an unfamiliar strain, permitted adverse effects and humane endpoints, and act appropriately?

An efficient breeding establishment...

- Will have scientists who regularly take time to explain the science behind the strains and the benefits of the work being done to the technicians;
- Will have technicians who are empowered to challenge colony managers directly or indirectly if unusual requests are made;
- Will have technicians who are skilled and confident enough to use their professional judgement when carrying out instructions given to them by colony managers if the instructions don't seem to be right for the animals in front of them, or if there may be a better alternative way of achieving the same end result;
- Will have an indirect route to raise concerns and/or resolve disagreements between the technicians and colony managers, for example via the unit manager;

An efficient breeding establishment... (continued)

- Will have constructive working relationships between the technicians and the colony managers, based on mutual respect;
- Will have a strategy for ensuring that the need for technicians to have an in-depth knowledge of a small number of colonies is balanced against the need for sufficient technicians to have enough knowledge of multiple colonies;
- Will have a strategy for assessing the phenotypes of newly created strains;
- Will have a strategy for capturing unexpected phenotypic traits of established strains;
- Will have a system for recording phenotype information, including making critical information available at cage-side.

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Background

Training and leadership can have a vital impact on skills and teamworking, and therefore animal welfare.

EXAMPLES OF LINES OF ENQUIRY	EXAMPLES OF SATISFACTORY FINDINGS
How do you ensure that your researchers and technicians have the required skills when they first start at your unit?	We have formal induction and training for new starters but also a mentor system. We also make sure we have frequent meetings between staff which breaks down barriers and makes everybody more approachable.
How do you ensure that your researchers and technical staff keep up to date with new skills and techniques?	Our staff have a CPD allowance and personal development goals set each year with their line manager.
What sources of expert advice do you recommend to your researchers and technical staff? How do you make sure that the advice is appropriate to the context of *this* establishment?	We have a breeding manager who is our in-house expert. He/she is available for advice on an informal basis or by appointment.
What proactive measures do you take to ensure that the people involved in breeding GA animals have enough support?	We have a staff survey every year which anonymously asks staff to assess the support to which they have access.
	Unit managers work on the floor regularly which provides informal routes for feedback.
Do you have a GA breeding lead at the establishment?	Yes, we have an in-house breeding expert.
	No, but we have established a relationship with a breeding expert at another establishment who can help us with any issues.
How often is the NVS in the unit? Does he/she take an active interest in GA breeding?	The NVS visits regularly and always checks the breeding colonies.

Performance Outcomes

- Proportion of staff inducted/trained on starting;
- Proportion of staff meeting CPD targets;
- Proportion of staff reporting that they feel adequately supported in their role through access to specialist assistance.

EXAMPLE FOLLOW-UP QUESTIONS How are good ideas propagated within the unit? Do staff have enough time and space to innovate, or even just share best practice?

An efficient breeding establishment...

- Will provide training and support to new staff to equip them with the skills they need, keep their skills up to date and assist them with challenging situations;
- Will have opportunities for formal and informal interactions between scientists and technicians;
- Will have ongoing training/CPD opportunities for staff, with hours tracked;
- Will monitor staff views of their working conditions and be responsive to any issues raised;
- Will have appropriate in-house or external expertise available to advise on breeding strategy and practices;
- Will have an NVS who is actively involved with the GA breeding programmes.

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Collated list of performance standards

An efficient breeding establishment...

1. Archiving
   - 1.1. Will have or make use of facilities to archive lines;
   - 1.2. Will have minimised as far as possible the barriers faced by scientists to archiving lines;
   - 1.3. Will have a policy and process in place to ensure that tick-over colonies are assessed to determine the point at which archiving would represent a reduction;
   - 1.4. Will have considered the optimum strategy for managing tick-over colonies to minimise the over-production of animals.

2. AWERB
   - 2.1. Will have active oversight of the GA breeding programme by the AWERB.

3. Breeding establishments
   - 3.1. Will have minimised the number of animals kept “on the shelf” and will, as far as possible, breed on demand;
   - 3.2. Will have considered incentives and disincentives to customers for appropriate timings of orders, and to minimise cancellations.

4. Colony management
   - 4.1. Will have an individual identified as the primary colony manager for each colony;
   - 4.2. Will have regular reviews of colony performance and management at individual colony and establishment-wide levels;
   - 4.3. Will have colony managers who are skilled in matching supply and demand, so that sufficient animals are available to ensure high quality science, while minimising the avoidable production of surplus animals;
   - 4.4. Will provide training and support to colony managers to equip them with the skills they need, keep their skills up to date and assist them with challenging situations;
   - 4.5. Will have oversight of the relative strengths of their colony managers, and will understand situations where individuals may require extra support or training;
   - 4.6. Will have colony managers who are able to keep up to date with accurate information about their colonies;
   - 4.7. Will gather all the information required by colony managers to make sound breeding decisions;
   - 4.8. Will have technicians who are empowered to challenge colony managers directly or indirectly if unusual or unclear requests are made;
   - 4.9. Will have defined strain-appropriate breeding performance indicators for each colony, and be monitoring against them;
   - 4.10. Will have a methodology for assessing strain-specific tendencies, preferences and phenotypes and planning and providing optimum conditions for those strains;
   - 4.11. Will have considered the optimum strategy for maintenance of colonies, balancing genetic needs against practical constraints;
   - 4.12. Will have considered the optimum controls for conditional knock-outs and will have a system for making these available across research groups.

5. Financial pressures
   - 5.1. Will have analysed the barriers to efficient breeding and ensured that any influenceable barriers are minimised or removed, including financial barriers;
   - 5.2. Will have considered the design and use of financial structures that encourage desirable practices as well as encouraging and supporting good science.

6. Genotyping
   - 6.1. Will have a quality control process for their genotyping;
   - 6.2. Will have assessed the relative merits of in-house versus outsourced genotyping;
   - 6.3. Will have minimised the time that elapses between taking the sample and receiving genotype data;
   - 6.4. Will prepare the genotyping process in advance of bringing in/producing new lines;
   - 6.5. Will have access to an archive or bank for samples;
   - 6.6. Will have maintenance, repair and contingency plans in place for critical equipment (e.g. PCR) to miminise downtime.

7. Rederivation
   - 7.1. Will have a flexible, situation-led policy on rederivation that allows case by case consideration, rather than a “one size fits all” approach;
   - 7.2. Will have a risk based approach to biosecurity rather than a blanket requirement for lines to be rederived as they enter the facility;
   - 7.3. Will consider the risk of genetic drift on scientific outcomes and have procedures in place to prevent significant impact, through appropriate colony management;
   - 7.4. Will have considered the pros and cons of generating lines in-house versus importing custom-created lines from a specialist supplier.

8. Sharing animals and minimising avoidable surplus
   - 8.1. Will have systems in place to ensure that researchers know what lines are currently being bred at the establishment;
   - 8.2. Will have one or more systems in place, formal or informal, to ensure that researchers share the available animals or their tissues whenever possible;
   - 8.3. Will question the exclusive use of male or female animals in experiments and ensure the approach is scientifically necessary.

9. Teamworking and cooperation
   - 9.1. Will have scientists who regularly take time to explain the science behind the strains and the benefits of the work being done to the technicians;
   - 9.2. Will have technicians who are empowered to challenge colony managers directly or indirectly if unusual requests are made;
   - 9.3. Will have technicians who are skilled and confident enough to use their professional judgement when carrying out instructions given to them by colony managers if the instructions don’t seem to be right for the animals in front of them, or if there may be a better alternative way of achieving the same end result;
   - 9.4. Will have an indirect route to raise concerns and/or resolve disagreements between the technicians and colony managers, for example via the unit manager;
   - 9.5. Will have constructive working relationships between the technicians and the colony managers, based on mutual respect;

9.6. Will have a strategy for ensuring that the need for technicians to have an in-depth knowledge of a small number of colonies is balanced against the need for sufficient technicians to have enough knowledge of multiple colonies;
9.7. Will have a strategy for assessing the phenotypes of newly created strains;
9.8. Will have a strategy for capturing unexpected phenotypic traits of established strains;
9.9. Will have a system for recording phenotype information, including making critical information available at cage-side.

10. Training and leadership

10.1. Will provide training and support to new staff to equip them with the skills they need, keep their skills up to date and assist them with challenging situations;
10.2. Will have opportunities for formal and informal interactions between scientists and technicians;
10.3. Will have ongoing training/CPD opportunities for staff, with hours tracked;
10.4. Will monitor staff views of their working conditions and be responsive to any issues raised;
10.5. Will have appropriate in-house or external expertise available to advise on breeding strategy and practices;
10.6. Will have an NVS who is actively involved with the GA breeding programmes.

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