

A quantitative approach to assessment of colony management practices using the ASRU GAA framework

PAUL CAIRNS, DEMI MINHINNETT and HEATHER CRAWFORD

Newcastle University

Correspondence: cbc.colony@newcastle.ac.uk

Introduction

Animals in Science Regulation Unit (ASRU) published the Genetically Altered Animal (GAA) framework in 2016¹ in consultation with breeding experts and establishments. This was intended to support establishments in assessing the efficiency with which they bred genetically altered (GA) animals. The framework outlines background information, lines of enquiry, examples of acceptable findings, performance standards and potential performance outcomes enabling establishments to track progress. Although this framework was designed for GA mice, the principles can apply to other species.

The framework is not mandatory and does not define requirements such as compulsory active tracking and analysis of defects, specific training requirements for colony managers or the need for a designated colony manager within an institute. However it does list relevant licence standard conditions, elements of the code of practice and is utilised during ASRU audits. It was anticipated that Animal Welfare and ethical review bodies (AWERBs) would find this framework useful in implementing the 3Rs within their establishments. Additionally, the framework provides unit managers and project licence holders (PPL) with a means of self-assessment of the efficiency of their breeding practices with GA animals.

The framework

The framework comprises ten key focus areas. Within each of these, there are performance indicators/standards that an efficient breeding establishment will do/have:

1. Archiving
2. AWERB
3. Breeding-only establishments
4. Colony management
5. Financial pressures
6. Genotyping
7. Oversight, leadership and training
8. Rederivation
9. Sharing animals and minimising avoidable surplus
10. Teamwork and cooperation

The assessment is designed as a qualitative framework that is useful for capturing the process and is essential for mapping what works, what has a positive impact and what has evolved. However it does little to quantify progress and overall impact.

Consequently, the objective of this study was to develop a method for visually and objectively quantifying progress and impact following the framework used by ASRU. This was achieved through the following aims:

- To assess and establish the current practices for the breeding and maintenance of GAAs.
- Establish a meaningful means of assessment that could be compared over the years with the same criteria.
- Attempt to make the qualitative sections of the assessment framework quantitative.
- Utilise the framework to guide projects to deliver refinement in GAA breeding.

Methods

Location:

Across all breeding sites for GAA rodents at Newcastle University, which included:

- Functional Genetics Unit (FGU) at the International Centre for Life: Between 2,000 to 4,000 mice over the recording period.
- Comparative Biology Centre (CBC) at the Medical School: Between 4,000 to 8,000 mice over the recording period.
- Keith Unit at the Campus of Ageing and Vitality: Approximately 800 mice over the recording period.

Ethics:

This project was undertaken, and the findings were reported to the AWERB periodically. It was not deemed to require institutional ethical approval as it specifically recorded practices with no animals used directly.

Quantifying the assessment and developing visual indicators of performance:

Performance was assessed in November 2018, 2022 and 2024 allowing for the evaluation of progress in performance. The initial 2018 assessment was conducted by the technical manager (TMO), who remained involved in subsequent assessments. In 2022, the assessment was conducted by the established colony manager (CM) and TMO. The most recent assessment conducted in 2024 involved the entire team (TMO, CM, and colony management procedural technician). In 2018, performance indicators/standards were collated against the assessment framework by providing bullet point examples of achievements or processes as asked by the assessment framework, e.g.:

Question: Does the establishment have an establishment-wide archiving policy?

Answer: No policy in place (Score as per below: 0).

Question: How are tick-over colonies managed?

Answer: Research groups manage and decide on maintenance for tick-over colonies, with no CBC staff or named person input or consultation. (Score as per below: 0.5).

These answers were then assigned numerical values based on the degree of performance:

Score	Definition
1	Achieved to high standard/complete answer.
0.5	Partial achievement/incomplete or full answer.
0	Not achieved/not started/unable to provide answer.

This allowed performance to be scored against the criteria, enabling the following benefits:

- Easy presentation of current position to enable proactive GAA management against the framework (e.g. for AWERB).
- Positive 3Rs impact (i.e. on animal health and welfare, reproducibility and reduction of wastage).
- Focussed project setting and staff drive.
- Positive financial impact.

Following the 2018 assessment, the scoring matrix for assessing framework performance was refined to better reflect smaller but significant developments in both 2022 and 2024. Numerical values were assigned on a scale from 1 to 10, where 10 equates to full achievement of a high standard or a fully complete process, decreasing incrementally to 1, where minimal progress or consideration is given to the question. Examples of this scoring on an individual criterion are shown below.

Archiving:

Criteria

As far as possible, barriers to archiving lines faced by the scientists have been minimised.

Scoring

Based on cost-effective access to onsite sperm and embryo cryopreservation.

Score distribution

20% (score 2) for cost-effectiveness and turnaround, 60% (Score 6) if from sperm, 20% score 2) for embryo access (includes genetic health and cryopreservation QC). Total score 10.

Oversight, leadership and training:

Criteria

Ongoing training/CPD opportunities for staff, including tracking training time.

Score distribution: 60% (score 6) for CBC staff and 40% (score 4) for scientists. Total score 10.

Rederivation:

Criteria

Proportion of colony managers considering genetic drift in their colony reviews.

Score distribution: 50% (score 5) for manager based in the facility management team, 50% (score 5) for a manager based in the research groups. Total score 10.

Sharing animals and minimising avoidable surplus

Criteria

One or more systems (formal or informal) are in place to ensure that researchers share the available animals or tissues whenever possible.

Score distribution

50% (score 5) if a formal system is in place, 40% (score 4) if tissue is effectively used and 10% (score 1) if the system is researcher driven. Total score 10.

Genotyping

Criteria

Quality control process for genotyping.

Score distribution

Awarded based on the % of groups where known quality control is used, e.g. 60% equals a score of score. Total score 10.

Results

Comparison and progress

Figure 1 and table 1 illustrate the scoring as a percentage of achievement, categorised by the year the assessment was conducted and the applicable criteria for the facility at Newcastle University. The progress

between 2018 and 2022 was delayed due to the COVID pandemic. The progress between 2022 and 2024 across all areas was greater than in the previous four years, which is attributed to momentum, focus and an increase in team membership. The value of researcher engagement across this period cannot be underestimated. Currently, the highest scoring criteria were:

- Financial pressures as the facility’s senior management team worked to deliver a robust charging model that encourages efficient breeding.
- AWERB who have been supportive, engaged and recognise the value of effective and efficient breeding on animal experience and reduction in numbers. They have played a key role in empowering the colony manager by requiring periodic reports and proactively ensuring the 3Rs are applied to our breeding practices. The latter being due to the establishment of breeding standards for defects, age and ear notching systems.

There remains significant work to be done in areas with additional criteria to be fulfilled, such as the sharing of tissue, archiving and genotyping. These can be difficult to influence due to in-house capabilities and some are scored to reflect engagement with initiatives such as external genotyping. Other areas such as colony management, continue to develop as the active change programme of proactive management of GAA colonies progresses and the team builds resources to support research colleagues and this is larger category with the total score being larger to achieve.

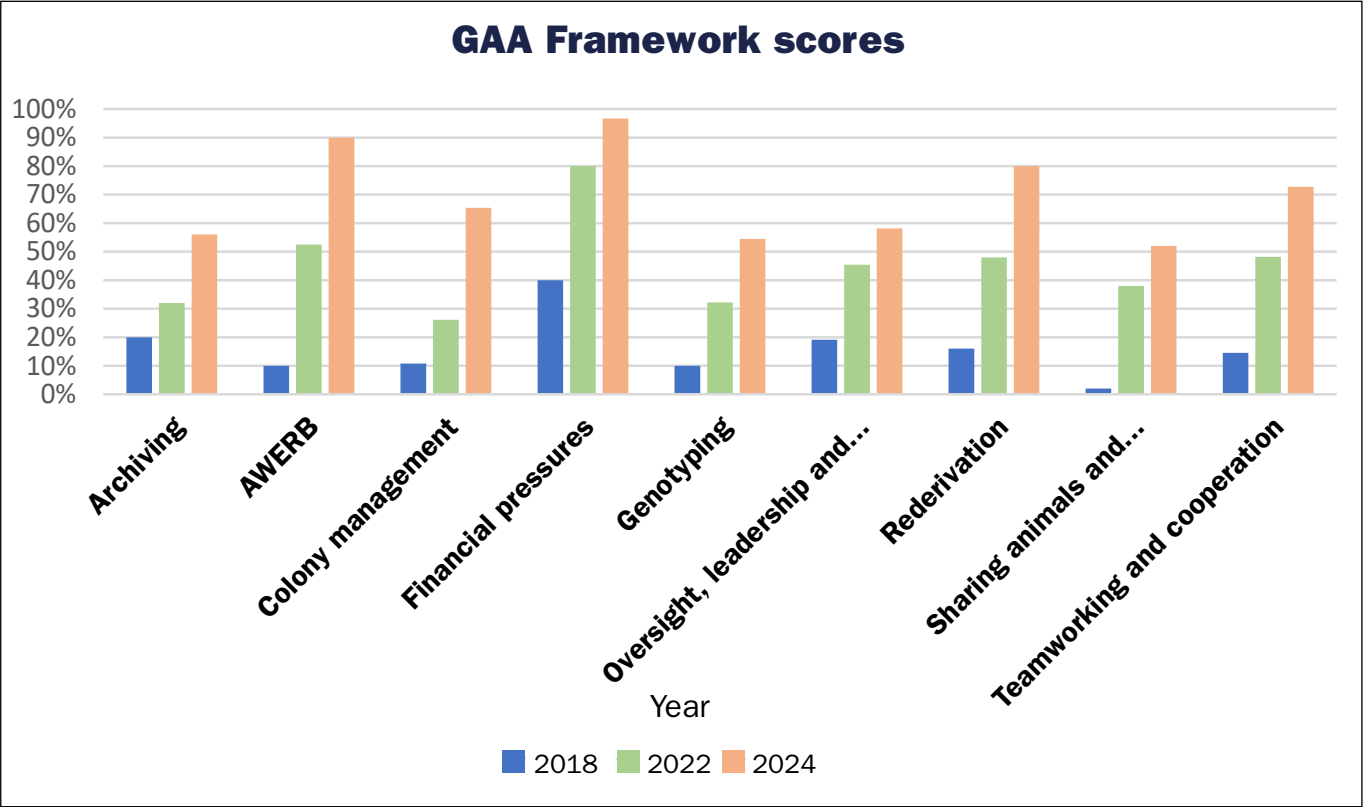


Figure 1. Percentage score against assessment focus areas from 2018 to 2024.

Focus area	Percentage score			Reasons for increase
	2018	2022	2024	
Archiving	20	32	56	<ul style="list-style-type: none"> • Routine confirmation of background at archiving via SNP analysis. • Guidelines for when to archive provided in line with <i>NC3Rs guidance</i>.² • Proactive archiving increasing at correct timepoints e.g. import and after backcross as <i>suggested by NC3Rs</i>.
AWERB	10	52.5	90	<ul style="list-style-type: none"> • Employment of a dedicated colony manager. • Annual CM report. • CM specific section included in 1, 3, 5-year reviews. • PPL pre-review involvement. • AWERB local standards/good practice as referred to by the <i>RSPCA in the guiding principles for AWERBs</i>.³ • Periodic updates.
Colony management	11	36	65.5	<ul style="list-style-type: none"> • Tracking of defects/environmental challenges. • Weekly reviews of defects and colony concerns. • Proactive flagging of potential breeding concerns. • CM Hub on internet for advice and training/CPD developed online. • Development of animal breeding champions (ABCs). • Development of two-way communication and confidence between CM team and technicians.
Financial pressures	40	80	96.5	<ul style="list-style-type: none"> • Introduction of breeding cage charges to encourage productive breeding. • Cryopreservation cost includes SNP analysis. • Support of timely tissue sampling for genotyping. • Annual review of costing model.
Genotyping	10	32	54	<ul style="list-style-type: none"> • AWERB standard regarding ear notching as refinement. • Increasing percentage of colleagues using external provider where human error is decreased significantly. • Starting to increase genotyping protocol established in passport before import.
Oversight, leadership and training	19	45	58	<ul style="list-style-type: none"> • Increase in T&C oversight including bespoke breeding modules and practical assessment • Development of animal breeding champions (ABCs) in the core technical rodent team. • Colony core team now has dedicated technical support and is led by the colony manager. • Protected time for researcher meetings starting to establish. • Protected time for ABCs to discuss items with core CM team.
Rederivation	16	48	80	<ul style="list-style-type: none"> • Proactive genetic health monitoring in place and guidance provided. • Abilities to create new lines in house but recognise the value of external creation and the QC that can provide. • Rederivation is case by case and joint decision with CM, NVS and researcher.
Sharing animals and minimising avoidable surplus	2	38	52	<ul style="list-style-type: none"> • Increased scrutiny of single sex projects with principles like those now published in the <i>Sex Inclusive Research Framework by Karp et al 2025</i>.⁴ • Tissue request system – CBC driven, needs more work to be proactively driven by the research community. • Increased scrutiny of required lines. • Requesting of passports at import.
Teamworking and cooperation	17	48	72	<ul style="list-style-type: none"> • Development of relationship between CM team, technicians and researchers continue with mutual respect. • Ability for technicians to raise concerns and challenge through various routes is well established. • Core technicians, deputy NACWOs and flexible technicians are well established to manage business need and specialised knowledge. • Recording of phenotypic presentation via the 'defect' reporting to CM mailbox and logging on strain management board. • Technicians empowered to challenge requests or breeding decisions. • Skilled and confident techs to use professional judgement.

Table 1.

Discussion

Impacts on the 3Rs

Over the period from 2018 to 2024, we have observed a Reduction in:

- Excess stock with limited or no purpose.
- Number of breeding animals on PPLs.
- Breeding of animals on PPLs that are commercially available e.g. immunocompromised models.
- Phenotypic defects from colonies through their removal from breeding stock, increasing Animal Welfare.
- Genetic drift.
- Birth difficulties and increased birth success due to reduced age limit for breeding stock.

We have also observed the refinement of:

Breeding processes, including business continuity planning.

Breeding performance increases, leading to:

- Fewer breeding animals being held.
- Increased number of offspring per breeding.
- Less time to achieve the desired n number.
- More cost-effective outputs achieved by the least number of animals being maintained to produce the n number for studies
- Understanding of strain backgrounds and breeding complexity to increase reproducibility.

Focussed project setting and staff drive

Utilising the framework has allowed the colony management team to ensure they are driving forward improvement projects in line with assessments from ASRU, including novel ideas supporting the 3Rs from colleagues (technicians, project licence holders, etc.) that ultimately increase compliance. Focus has been placed on areas needing further improvement through task and finish projects, charting progress using established tools within the CBC. For 2023/24, the areas we focussed on were:

Colony management

- Formally identifying people responsible for colony management within each research group so that colony management can provide more dedicated support for those individuals and build a strong working relationship.
- Focus on basic training to support and encourage annual continuing professional development (CPD) in breeding.
- Standard colony reviews to assess performance and management using defined strain-appropriate breeding performance indicators, including the introduction of the strain MOT. Further emphasis should be placed on breeding standards and establishing on-site breed characteristics to better manage any variation observed from strain to strain, allowing the development of a tailored approach to management.

- Defined breeding strategy resources for researchers to reference.
- Long-term development of standardised phenotyping procedures.
- Development of a colony management Hub (CM Hub) on the internal intranet to support staff and research colleagues with resources and reference materials to inform breeding decisions by making support/services and CPD opportunities available.

Teamwork and cooperation:

- Complete mouse passports for all research groups and strains.

Genotyping

- Establish methodologies for each strain or group through the mouse passport.

Management of GAA projects

Closer management of task and finish projects ensures progress. Each project is logged on a Trello⁵ board and labelled to reflect the GAA framework focus area (Figure 2). A team decision on a realistic completion date is established based on quarterly deliverables. Weekly meetings are scheduled in advance to enable progress updates or dedicated working time. Additionally, those projects deemed linked to far-reaching goals are logged to ensure they eventually move into being task and finish projects.



Figure 2. Project management.

Each task/card (Figure 3) is broken down into checklists (Figure 4) of activities that ensure small incremental progress is catalogued, building a clear picture of both the work undertaken to date, the progress made and the work that remains outstanding. This is essential and effective when several individuals work toward a single deliverable. This has supported staff drive, determination and development as team members all work towards an agreed upon goal representing a real team effort.



Figure 3. Project example.



Figure 4. Incremental step wise project breakdown.

Conclusions

The GAA framework is a useful qualitative tool that can be easily adapted to produce a quantitative output, allowing accurate comparisons to be made over time and between facilities. This enables the effective tracking of progress against an indicator framework. Additionally, as the framework's use increases and more supportive processes are implemented, it will be possible to tailor or add performance indicators or standards for each specific establishment. Elements (e.g. the sections on colony management, genotyping, etc.) can also be incorporated into the review of project licences that include GA breeding as part of an annual review of colonies and breeding or as dictated by the AWERB/facility.

Specifically, using the framework as a guidepost for developing colony management within a facility drives the breeding of animals directly in line with the 3Rs, good practices, compliance with ASPA and other leading GA breeding facilities. Ensuring an audit trail of proactive management of GA colonies allows the framework to guide and develop focus areas and projects.

The Comparative Biology Centre (CBC) has conducted periodic assessments of the management of GAA breeding colonies for over 7 years. The data generated by this quantitative approach to fulfilling the GAA framework have been key in driving change in the research community and in initiating a proactive approach to refining GA animal breeding and reproducibility. The CBC has experienced the following using this methodology:

- Increased fulfilment of GAA framework performance indicators.
- Increased uptake of refined breeding practices e.g. cryopreservation at the optimal time, best breeding strategy, etc.
- Improvement in animal genetic health, such as a reduction in undesirable traits and an understanding of background sub strains through proactive analysis.
- The reduction of animals generated and held in the facility for no purpose leads to more cost-efficient animal production and genotyping as well as increased staff satisfaction.

Acknowledgements

We want to acknowledge the wider CBC technical team for their support and hard work in ensuring we continue to improve Animal Welfare by increasing our expectations of those responsible for breeding animals, the NTCO team for supporting the CM team's development of resources and practical training for breeding selection and the AWERB for offering support and listening to the ambitions of the CM team.

References

- 1 https://assets.publishing.service.gov.uk/media/5c4b0998ed915d38a2f5e2b5/GAA_Framework_Oct_18.pdf
- 2 NC3Rs 3Rs Archiving best practice <https://nc3rs.org.uk/3rs-resources/breeding-and-colony-management/archiving-best-practice>
- 3 Guiding Principles on Good Practice for Animal Welfare and Ethical Review Bodies RSPCA 3rd Edition September 2015 <https://www.rspca.org.uk/documents/1494935/9042554/Guiding+principles+on+good+practice+for+Animal+Welfare+and+Ethical+Review+Bodies+%282015%29+%28PDF+1.76MB%29.pdf>
- 4 The Sex Inclusive Research Framework to Address Sex Bias in Preclinical Research Proposals Karp *et al.* Nature Communications 16, Article number: 3763 (2025) <https://rdcu.be/ejPRN>
- 5 <https://trello.com>