

The impact of closure of specialised mouse research facilities

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Sanger Institute animal research facility to close

Genomics institute to close world-leading animal facility

Sanger's decision prompts questions among some scientists, who fear the UK centre could fall behind.

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e Wellcome Sanger Institute, said the the next few years.



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Two prominent mouse centres in the UK closing/under review within six months.

Should we be celebrating?

UK's leading mouse genetics centre faces closure

Plan to halt academic work at Harwell Institute threatens research including on diabetes



A Harwell's Mammalian Genetics Unit studies gene function and how diseases and disorders arise when genes go awry. Photograph: Getty Images

Britain's leading centre for mouse genetics is facing closure in a move that critics say will undermine crucial research on serious diseases and threaten the standing of UK science.

The Medical Research Council has told staff at its Harwell Institute in Oxfordshire that an internal strategy board recommended the closure of all academic work at the site, threatening research on diabetes, neurodegenerative disease, child deafness and other conditions.



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Overbreeding is a GM issue



Source: Understanding Animal Research



- Overbreeding creates 'surplus' animals who are bred to be culled
- No scientific 'benefit'
- Waste of animal lives, time and money
- This 'surplus' equates to ~50% of animals recorded under UK statistics and has done for the past 7 years
- This is a total of
 27,487,033 animals



UK Home Office data from ASPA annual reports



Possible cause(s) of overbreeding

- Inefficient practices to generate mutant animals*
- Wild type animals bred and not required*
- Wrong mutation/errors in phenotyping*
- Tick-over breeding (e.g. possible publication need)
- 'Just in case' breeding (e.g. possible need of mutants for future projects)

*could be addressed with specialised centres



Solving the overbreeding problem

- Directive 2010/63 has the ultimate aim of **Replacement**, but requires dedicated efforts for **Reduction** and **Refinement** till we reach that point
- This indicates a role for established centres of excellence for animal breeding and welfare (Refine and Reduce)
- Genetic modification and breeding are a particular concern for mice, who are small, cheap, most frequently used and most frequently genetically modified
- Potentially huge impacts on animal numbers (Reduction) and welfare (Refinement)





Solving the overbreeding problem

What specialised centres offer that most research establishments lack:

- Centralised expertise
- Reduction of over-breeding (centralised cryopreservation facility; standardised protocols with improved efficiency)
- Evolving/enhancing welfare standards (e.g. Moshers CRACKIT challenge)
- A resource for all mouse users (mutation database, specific care requirements)
- A resource for prospective mouse users (provision of mutants, training sessions)





In-house breeding is the norm (Refine)

Year	GM animals/mice acquired in house (% total GM)	HM animals/mice acquired in house (% total HM)
2006	91.8	77.7
	96.3	87.4
2007	91.8	78.1
	97.3	85.8
2008	88.3	71.2
	97.2	88.0
2009	90.3	80.4
	96.7	88.5
2010	89.8	79.5
	96.4	90.6
2011	89.1	77.5
	96.1	87.1
2012	88.9	80.6
	97.1	89.9
2013	96.9	91.0
	96.8	89.0





But do we want to improve this practice? (Refine/Reduce)

UK GM Breeding Framework... yet every establishment is likely to have

- **Different** practices
- Different resources
- **Different** experiences

More impact on animals if specialised breeding centres are used rather than requiring everyone to follow the same rules for breeding

 \rightarrow Provide less support for in-house breeding at each establishment via project/licence approval process



Efficient Breeding of Genetically Altered Animals

Assessment Framework

Introduction

This assessment framework is intended to assist establishments to consider the efficiency with which they breed genetically altered (GA) animals. ASPA requires licencees to apply the 3Rs at all times, including in the context of the production and use of GA animals. This framework is intended to help with the assessment of establishments' success in this regard.

The framework was created in consultation with breeding experts and establishments, and provides background information, lines of enguiny 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. This assessment framework is designed around the breeding of GA mice, although the principles will apply to many species.

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 framework 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 framework useful to assist them with their statutory duty to advise on the application of the 3Rs within their establishments. Project Licence holders and Animal Unit Managers may also find it useful for self-assessment. Inspectors will use this assessment framework when considering how establishments apply the 3Rs to their GA breeding programmes.

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Not just overbreeding: also welfare implications (Refine)





Short-term solution (Reduce/Refine)

Whilst animals are bred and used for scientific purposes, we should maintain hubs of expertise and require their use to address the overbreeding problem

- Incentivise use of cryopreservation services to reduce colony tick-over and culling
- Advise reduce most harmful category
- Continue to refine breeding practices
- Better adherence to 3Rs





Shift the research paradigm (Replace)



Recognise failing preclinical models and stop authorizing Discontinue funding for animal models



Redirect funding to humanpredictive microphysiological and computational models



(Re)train scientists in nonanimal research designModify/redesign universitycurricula



Resolve to phasing out animal use in science, with defined timetable and metrics

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