

Providing animal
technicians with the latest
news from the NC3Rs

Tech3Rs

Welcome to the latest edition of Tech3Rs. In each issue, we share updates on recent advances in the 3Rs and highlight new resources, research and events.

This newsletter is for animal technicians working in research establishments to help identify opportunities to embed the 3Rs in practice and ensure high standards of animal welfare. If you have any ideas for future issues or are working on a 3Rs approach you would like us to feature, please get in touch – we would love to hear from you! You can email us at tech3rs@nc3rs.org.uk.

In this issue we introduce our new online *Evaluating environmental enrichment* resource, look at new technologies that facilitate social housing of animals during drug development, and speak to two 3Rs champions about the refinements they have introduced in their facilities. We also highlight further resources from the NC3Rs and other organisations.



Don't miss the
next issue!

Tech3Rs is currently published online only – read all our past issues at www.nc3rs.org.uk/tech3rs.

You can stay up-to-date on the latest issue of Tech3Rs and more via the NC3Rs e-newsletter. Visit www.nc3rs.org.uk/register to subscribe to our monthly updates.



Evaluating environmental enrichment

A new online resource to support animal technicians carrying out enrichment studies.

In collaboration with the RSPCA and IAT, the NC3Rs has created a new online resource for animal technicians carrying out evaluations of environmental enrichment. Covering the process of evaluating enrichment from start to finish, the resource includes guidance on what to consider before you begin, the different approaches that can be taken, and the steps following on from data collection.

There are many options for enriching the environment of captive animals. These include making structural changes within enclosures and engaging the senses or cognitive capabilities of animals in a variety of different ways. Whatever the type of enrichment, it is important that it improves animal welfare in some manner. Not all animal species have the same needs, and even animals of different ages or strains within the same species can have different requirements or preferences. As providing enrichment can be costly in terms of both time and money, it is important to ensure you are using the most beneficial enrichment for the animals in question.

The resource was created after discussions with animal technicians (www.nc3rs.org.uk/EEEblogpost)

highlighted that many were enthusiastic about conducting studies to assess the effects of enrichment on animal welfare, but found it challenging to carry out more formal evaluations of enrichment. This informed the development of the resource, which contains tips for overcoming constraints in your facility as well as advice on improving the scientific quality of your study. This is particularly important if you plan to publish your results.

The study protocols, practical support and examples within the resource make reference to commonly used species, such as mice, rats and zebrafish. However, the resources we provide are intended to be tailored to your own project, and whatever species you work with. If you have specific examples of protocols that you have followed to evaluate enrichment, would like to share successful evaluations with us, or have any feedback on the new online resource, please do get in touch at tech3rs@nc3rs.org.uk.

To learn more about evaluating environmental enrichment for research animals, visit the resource at www.nc3rs.org.uk/EEE.

3Rs papers of interest

Each issue we feature recent 3Rs publications, providing summaries and links to the full articles for further reading. This issue we look at technological advances that allow social housing of animals during drug development.



Social housing in regulatory studies

A key part of the drug development process is getting the approval of regulatory authorities (e.g. the MHRA or FDA) to test in humans, based on safety and efficacy data generated in *in vivo*, *in vitro* and *in silico* tests. *In vivo* safety and efficacy studies are performed in rodents (mice or rats) and non-rodents (minipigs, dogs or non-human primates) and can involve individually housing animals during aspects of data collection. However, housing social species individually can significantly impact their welfare. Directive 2010/63/EU specifies that single housing should only be used in exceptional circumstances and for limited time periods (e.g. four hours for dogs). In addition to the negative effects of separation from cagemates, the introduction or reintroduction of animals to established pairs or groups can lead to aggression, which also impacts animal welfare (catch up on our recent webinar at www.nc3rs.org.uk/aggressionwebinar to learn more). Therefore, social housing should be the norm in regulatory studies and there is increasing evidence that this can be done without affecting the quality of the data collected.

Safety pharmacology and toxicology telemetry studies

Safety evaluation of most new drugs includes telemetry studies, which use implanted or wearable recording devices to assess drug effects on blood pressure, heart rate and electrocardiogram. It has been common practice to house animals separately during telemetry studies in order to avoid data contamination, i.e. interference between signals emitted

from different telemetry devices.

Rats are often used as the rodent species in early investigative telemetry studies and an NC3Rs-led survey of industry experts in 2017 showed that almost half of rats (46%) were single housed during telemetry recordings. Skinner *et al.* (2019) looked at telemetry recordings in pair-housed rats, both in standard individually ventilated cages (IVCs) and double-decker IVCs (taller cages with bigger vertical space allowing rats to perform natural behaviours, such as full upright posture – find out more at www.nc3rs.org.uk/labratbehaviour).

The study showed that the quality of data collected from pair-housed rats in standard and double-decker IVCs was comparable to previously published data from rats single housed in standard IVCs, demonstrating that recording from pair-housed rats in both types of caging can be used to accurately assess drug-induced cardiovascular changes.

The majority of non-rodent species used in regulatory telemetry studies are also single housed during recording days (Prior *et al.* 2016). However, social housing allows the expression of natural behaviours and reduces stress, which is reflected in lower heart rates. In fact, the quality of data in telemetry studies performed in socially-housed minipigs, dogs and non-human primates is actually the same or better than that from single-housed animals (Prior *et al.* 2016).

Prior and Holbrook published a new paper in early 2021 addressing the concerns around data quality and potential cross-contamination between socially housed animals. The paper highlights an increase in the adoption of social housing for cardiovascular telemetry studies in non-rodents and shares information and

experience from industry to encourage wider uptake internationally.

ADME studies with metabolism cages

Absorption, distribution, metabolism and excretion (ADME) studies of new drugs are an integral part of drug development, typically involving collection of urine and faeces from animals housed individually in metabolism cages, in order to examine how much of the administered drug has been absorbed by the body and how much has been excreted.

Covance Laboratories Ltd. and Novo Nordisk A/S collaborated to investigate whether dogs could be pair-housed during ADME studies (Kendrick *et al.* 2020). Pair housing was achieved by modifying and joining together two metabolism cages, providing sufficient space per dog and allowing co-housing and socialisation. The authors found that the amount of drug that was excreted in urine and faeces by single- and pair-housed dogs was comparable between the two groups. Dogs also appeared calmer and barked less when pair-housed. This finding supports the idea that metabolism studies can be refined through the use of pair-housing while still producing data suitable for regulatory submission.

The same collaboration led to the design of a novel metabolism cage that can allow group housing of cynomolgus macaques during ADME studies (Stow *et al.* 2021). As with dogs, group housing the macaques did not affect data quality. The new cage provides more living space and allows the animals to express species-typical behaviours and socialise in a more stimulating environment,

alleviating stress and boredom. As a result, group-housed animals showed increased play and grooming, and an absence of stereotypic behaviour such as rocking and pacing compared with single-housed animals.

Raising awareness and sharing experience

Despite growing evidence that social housing can be used in regulatory studies, single housing is still the preferred way of housing animals in many facilities, especially in non-European countries that are not covered by Directive 2010/63/EU. Communication between different facilities and sharing of practical advice within the community can help social housing become the new standard in regulatory studies and increase animal welfare without affecting the quality of data produced.

Kendrick J et al. (2020). A novel welfare and scientific approach to conducting dog metabolism studies allowing dogs to be pair housed. *Laboratory Animals* 54(6): 588–598.
doi: [10.1177/0023677220905330](https://doi.org/10.1177/0023677220905330)

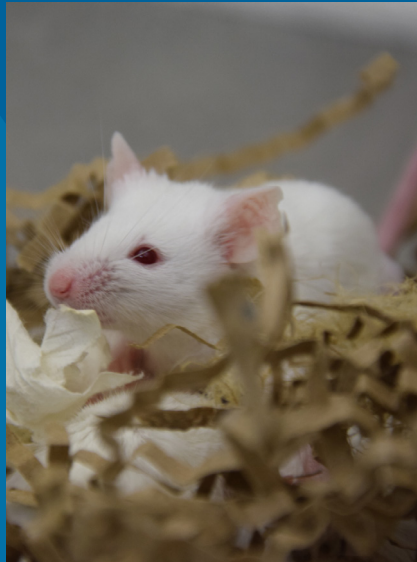
Prior H et al. (2016). Social housing of non-rodents during cardiovascular recordings in safety pharmacology and toxicology studies. *Journal of Pharmacological and Toxicological Methods* 81: 75–87.
doi: [10.1016/j.vascn.2016.03.004](https://doi.org/10.1016/j.vascn.2016.03.004)

Prior H and Holbrook M (2021). Strategies to encourage the adoption of social housing during cardiovascular telemetry recordings in non-rodents. *Journal of Pharmacological and Toxicological Methods* 108: 106959.
doi: [10.1016/j.vascn.2021.106959](https://doi.org/10.1016/j.vascn.2021.106959)

Skinner M et al. (2019). Social-housing and use of double-decker cages in rat telemetry studies. *Journal of Pharmacological and Toxicological Methods* 96: 87–94.
doi: [10.1016/j.vascn.2019.02.005](https://doi.org/10.1016/j.vascn.2019.02.005)

Stow R et al. (2021). A new group housing approach for non-human primate metabolism studies. *Journal of Pharmacological and Toxicological Methods* 107: 106947.
doi: [10.1016/j.vascn.2020.106947](https://doi.org/10.1016/j.vascn.2020.106947)

Highlights from the NC3Rs website



Single use of needles: how AWERBs can support refinements in practice

In a new blog post Dr Sally Robinson, Director of Animal Sciences and Technologies at AstraZeneca, explores the role of Animal Welfare and Ethical Review Bodies (AWERBs) and other oversight bodies in ensuring refinements, such as single use of needles, are put into practice. She shares how AstraZeneca's AWERB has helped to support the single use of needles as standard across the company and its global sites.

To read Sally's blog post, visit www.nc3rs.org.uk/needlesblogpost.

To find more resources to help you implement single use of needles at your facility, visit www.nc3rs.org.uk/needlereuse.



New resources: ferret and gerbil housing and husbandry

The NC3Rs website contains resources on the housing and husbandry of different species used in research. Through collaboration with expert reviewers, these resources have now been expanded to include two new dedicated pages for ferrets and gerbils.

These new pages contain recommendations on how to provide high-welfare environments, with a summary of the key features of good housing and husbandry for each species. Information is included on how to spot and prevent welfare issues associated with captivity, and on taking the sensory capabilities of the animals into account. For example, ferrets have poor eyesight and will nip at close objects – like fingers! As for gerbils, they communicate using ultrasonic vocalisations, which can be disrupted by some lab equipment.

To learn more about ferrets, visit www.nc3rs.org.uk/ferretcare.

To learn more about gerbils, visit www.nc3rs.org.uk/gerbilcare.

3Rs champions

We want to help you share your ideas for putting the 3Rs into practice. In every issue of Tech3Rs we feature technicians who are championing the 3Rs at their establishments.

Joe Peploe is an Animal Technician at the University of Cambridge. He spoke to us about using recycled materials to create environmental enrichment for rhesus macaques.

What 3Rs idea have you developed?

When looking for environmental enrichment for our rhesus macaques, we found that few commercially available enrichment items were designed specifically with monkeys in mind. As a result, we would often purchase devices designed for other species, such as parrots or dogs (e.g. Kongs®). We decided to have a go at making our own environmental enrichment out of waste materials we already had in the facility, such as plastic and cardboard containers.

It became evident early on that the monkeys were most interested in food-based enrichment. In response to this, we created different 'toys' and filled them with a variety of foods (e.g. nuts, dried fruit, forage mix), which are used to supplement their standard scatter-fed diet. Since making our own enrichment devices, our monkeys have been spending more of their time actively interacting with enrichment throughout the day and they are visibly (and audibly!) more excited at feeding time. We have also found that providing a range of food-containing items within the enclosure means that food is shared more evenly across the group. While the dominant animals are busy foraging from their favourite enrichment items, the lower-ranking monkeys can obtain treats from other items within the cage.

How did you develop your idea?

Together with my colleagues Chris Macaulay and Damian Quigley, we looked online for inspiration and began transforming old packaging materials into enrichment devices for our monkeys. Making enrichment is a fun job that we do on quieter days. Part of the process is ensuring that what

we create will be safe for the animals. We thoroughly disinfect plastics, file down any sharp edges and consult our NACWO if we are unsure of the safety of any particular type of material.

We quickly learned that variety is key for engaging all the monkeys in the group. Some of the macaques will patiently work on solving a puzzle, whereas others will only engage with the enrichment that allows them to access treats quickly and easily. To reflect the differences in skills and motivation between monkeys, a mixture of simple and more complex enrichment items is essential.

What are your future plans?

We will use what we have learned from the monkeys to continue providing the kinds of enrichment that they find most engaging. We will also carry on thinking of new ideas for providing a range of 'toys', although we have come up with so many that we might have exhausted all our ideas for now!

Joe, Chris and Damian have shared their ideas with other NHP facilities via the NC3Rs, as well as presenting at the 2021 IAT Congress. You can view some of their creations at www.nc3rs.org.uk/peploeposter.



A rhesus macaque tackles a puzzle created from recycled materials.

Sarah Taylor is also an animal technician at the University of Cambridge. She won the 2019 Janet Wood Innovation award for the 'rat scratcher' environmental enrichment device. Sarah spoke to us about habituating rats to transport boxes.

What 3Rs idea have you developed?

I have developed a method to habituate rats to transport boxes in order to reduce stress during transit around our facility. Before habituation, the rats were distressed by travelling short distances. After taking my new approach, the researchers who work with the rats have reported that the animals are notably calmer. They will now enter the transport boxes voluntarily – sometimes they are even too eager to do this and will jump into the box before I have had a chance to weigh them!

How did you develop your idea?

A researcher brought to my attention that the rats seemed stressed after being transported, even just one floor down. They asked if there was something I could do to address this. I had noticed that when the rats were in their playpen (a 'kiddy pool' filled with different objects for the rats to interact with), they would jump right into empty cardboard glove boxes and even curl up and sleep inside them. I decided to use the playpen to introduce the rats to the transport boxes so they would begin to associate the boxes with a positive experience. After this initial introduction (30 minutes in the playpen) I spent a week exposing the rats to the box within their home enclosure.

What are your future plans?

I would like to develop my approach into a proper study. I have the continued support of my manager Jenny Watson and NACWO Sarah Stone to do this and have started reading around the topic. My aim is to use behavioural observations and non-invasive sampling (e.g. faeces or saliva) to measure and compare the stress levels of rats that

have undergone habituation to those that have not. This way, I could scientifically validate my approach as an effective method for improving rat welfare.

I'm hoping that in-person events will resume next year as I enjoy talking to people about my work face-to-face. I plan on presenting my findings at the 2022 IAT Congress.

We have connected Sarah with a researcher to help her design and perform a study to evaluate the benefits of her habituation approach. If you would like advice from the NC3Rs on conducting 3Rs-focused work, please get in touch at tech3rs@nc3rs.org.uk.

Sarah works with rats, but her approach can be adapted to improve the welfare of other species, as being confined

and transported can be stressful for any animal. By habituating animals to transport containers, the fear and apprehension caused by the containers themselves is reduced (Swallow *et al.*, 2005; Jennings and Prescott, 2009).

Swallow J *et al.* (2005). Guidance on the transport of laboratory animals. *Laboratory Animals* 39(1): 1-39. doi: [10.1258/la.2008.007143](https://doi.org/10.1258/la.2008.007143)

Jennings M and Prescott MJ (eds) (2009). Refinements in husbandry, care and common procedures for non-human primates. *Laboratory Animals* 43(S1): 1-47. doi: [10.1258/la.2008.007143](https://doi.org/10.1258/la.2008.007143)

Would you like to be featured in Tech3Rs, or find out more about the refinements featured above? Please email tech3rs@nc3rs.org.uk.



Sarah's approach helps habituate rats to transport boxes by placing them in the rats' home enclosures (top) or playpens (bottom).

Highlights from beyond the NC3Rs

The IAT journal: *Animal Technology and Welfare*

Animal Technology and Welfare is a journal produced by the IAT, which is published three times a year and aims to be a platform for animal technicians to communicate good practice.

The journal contains peer-reviewed research, technical details on refinements, posters that have been presented at international meetings and other articles with relevance to laboratory animal use and care.

The most recent issue of *Animal Technology and Welfare* features research on mouse behaviour in response to alcohol-based hand sanitiser and a summary of the 2020 RSPCA/UFAW rodent and rabbit welfare meeting. It also takes a look at the emotional challenges of working with laboratory animals and the self-care tools that can be used to address these.

For a full list of contents and to read past issues of *Animal Technology and Welfare*, visit www.atwjournal.com.

RSPCA: Focus on severe suffering

Severe suffering can be caused by a single scientific procedure, but it can also be the result of many less severe negative experiences that add up over the lifetime of an animal. How animals are housed, bred, handled, monitored and transported all contribute to their lifetime experience, and these are all factors to consider when aiming to improve overall welfare.

Whatever your role in working with laboratory animals, it is important to consider how you can help reduce or avoid severe suffering. The RSPCA Lab Animal team has created a *Focus on Severe Suffering* website to provide practical advice on this topic. Guidance is provided on identifying sources of pain, suffering and distress along with practical examples of how to implement refinements to improve animal welfare.

To learn more about reducing and avoiding severe suffering, visit www.focusonseveresuffering.co.uk.

NAR3sC: Rodent health surveillance

From both a scientific and welfare perspective, it is important to ensure that rodent colonies are free from infectious diseases. Typically this requires the use of 'sentinel' animals, which are obtained and maintained for the purpose of monitoring whether infectious diseases are present within a colony.

The North American 3Rs Collaborative (NA3RsC) has created an online resource focusing on environmental monitoring as a means of replacing the need for sentinel mice, thus reducing the number of animals required for research. Other benefits of environmental monitoring include reducing the labour and costs associated with maintaining additional animals and increased accuracy of results. This webpage provides practical advice and addresses common concerns and questions around environmental monitoring for rodent health surveillance.

If you want to learn more about alternative techniques for monitoring environmental pathogens, visit www.na3rsc.org/health-monitoring.

Upcoming virtual events



LASA/UFAW 3Rs Section Meeting – “Enrichment and Science: A match made in Heaven?”

Thursday 9 September, 1pm – 3pm

The theme of this year's LASA 3Rs Section Meeting is the provision of environmental enrichment to research animals and how it may impact on science. The programme includes speakers from all sectors across the UK, EU, the USA and Canada and includes presentations validating the need for enrichment, how appropriate enrichment can be implemented, and how it affects data variability.

Dr Khia Dobbins (NC3Rs) will be introducing the *Evaluating environmental enrichment* online resource that was created by the NC3Rs in collaboration with the RSPCA and IAT to help animal technicians make informed decisions about the suitability of environmental enrichment items.

Register for the meeting and see the full programme at www.lasa.co.uk/lasameetings. Attendees will receive three LASA CPD credits.



NC3Rs/IAT Animal Technicians' Symposium 2021

Monday 11 and Tuesday 12 October

The NC3Rs and IAT are hosting an online symposium over two half-days, aimed primarily at junior technicians. This event will showcase the latest approaches to improving the welfare of laboratory animals and opportunities to refine their care and use.

The programme includes a range of talks on mouse, zebrafish and amphibian welfare from researchers and animal technicians. Topics will include handling, breeding and genotyping. The symposium will also feature a panel discussion led by experts in animal technology with a track record in promoting animal welfare and the 3Rs. You will be able to ask questions or just listen in for advice on your future career development.

Reserve your place now at www.nc3rs.org.uk/ATS2021. Registration closes on Sunday 10 October. Attendees will receive three IAT CPD credits for each day attended.

Enter this year's Andrew Blake Tribute Award

The Andrew Blake Tribute Award (ABTA) 2022 is now open for submissions. This award is presented annually to an animal technician who has made a significant contribution to improving laboratory animal welfare. Previous winners of the ABTA include John Waters and Stephen Woodley, who spoke about their careers and commitments to the 3Rs in previous issues of Tech3Rs (see www.nc3rs.org.uk/johnwaters and www.nc3rs.org.uk/stephenwoodley).

If you are an animal technician and you or your team have improved animal care and welfare in your facility during the last twelve months, make sure you submit your application before **Thursday 30 September**.

To learn more about how to apply, visit www.iat.org.uk/abta.



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