

Tech3Rs

Providing animal technicians with the latest news from the NC3Rs

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 at tech3rs@nc3rs.org.uk – we would love to hear from you!

In this issue, we share Stephen Woodley's career journey from junior animal technician to Director of Biological Services at King's College London and discuss non-invasive methods of oral administration in mice. We also highlight our new zebrafish welfare resources page and recently updated blood sampling pages.



Don't miss the next issue!

Tech3Rs is published online every quarter – download every issue 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.



Image from www.thepigsite.com

Aggression in laboratory animals

Strategies and tips for preventing and managing aggression.

Aggression can be a problem in a range of laboratory species, from mice and rats to dogs and non-human primates. As well as causing stress and painful injuries, it can lead to animals being culled or removed from studies and introduce variability into experimental results. Animals may be housed singly to protect them from injury, but this can also negatively affect their welfare. It is therefore crucial to detect aggressive behaviour as early as possible, understand its causes, and take steps to minimise it.

In March, the NC3Rs ran a virtual interactive workshop at the 2021 Institute of Animal Technology (IAT) Congress, exploring ways to reduce aggression in laboratory species. Animal technicians, Named Animal Care and Welfare Officers (NACWOs), facility directors and researchers in the UK and overseas

joined us to discuss the reasons why aggression may occur within the animal facility, how this can affect animal welfare and science, and strategies and tips for preventing and managing aggression.

If you missed the live workshop but are interested in learning more about managing aggression, a recording of the presentation is now available at www.nc3rs.org.uk/aggressionworkshop.

To read the results of our study on aggression in group-housed male mice, based on crowdsourced data from facilities around the world, visit www.nc3rs.org.uk/mouseaggression.

For information on creating optimal living conditions for different species, which can also help reduce aggression, visit our housing and husbandry pages at www.nc3rs.org.uk/housinghusbandry.

Tech Journeys

We speak to inspirational technicians who have demonstrated a long-term commitment to the 3Rs about their career paths. If you have an inspirational story, or know someone else who does, please get in touch via tech3Rs@nc3rs.org.uk.

This issue we are featuring Stephen Woodley, the Director of Biological Services at King's College London (KCL), who talks about how his passion for improving animal welfare and increasing the transparency of research using animals has shaped his career path. Stephen was awarded the AAALAC International Fellowship in 2016 and the IAT Andrew Blake Tribute Award in 2019 in recognition of his commitment to the 3Rs.

Working with animals was something I always wanted to do, so in 2002 I joined University College London (UCL) as a junior animal technician, embarking on my career in animal technology. In this role I gained experience working with a multitude of species and performed a range of husbandry-related duties. Over the years I gained more experience in colony management, research ethics

and law, and really enjoyed learning more about the fascinating research taking place in my unit.

Collaborating to develop new refinements

Since the early stages of my career, I have worked on ideas to improve animal welfare alongside researchers and animal technicians. One example is the development of a 3D printed anaesthesia face mask for mice, where the standard commercial models did not work. The new mask reduced the need for injectable anaesthesia, which has a longer recovery time and a higher risk of mortality compared to gaseous anaesthesia.

I have also performed a large amount of positive reinforcement training with macaques, to teach them to

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I would advise anyone working in animal technology to get involved in the various networking events and learn as much as you can.”

voluntarily cooperate with routine husbandry and scientific procedures, thereby reducing the negative effects of these procedures on their welfare. I believe animal technicians are in a great position to provide advice on refinements to research procedures and there have been some fantastic examples of this in recent years across the sector. For example, I have witnessed animal technicians lead on introducing non-aversive methods of picking up mice (see www.nc3rs.org.uk/mousehandling) and trialling different types of enrichment suitable for mice with headpost implants (see page 6 of the August 2019 issue of Tech3Rs, www.nc3rs.org.uk/tech3Rsissue4).

Advocating for animal welfare

I have always been willing to challenge people in their work, if I felt that their actions might compromise animal welfare. I believe that being confident when discussing welfare-related topics can help get your message across and lead to better engagement. However, I have also been mindful to listen to researchers' needs and work with them as part of a team to improve both animal welfare and science. Having an open mind and being willing to accept new ideas is key to success.



Stephen presenting at the 2019 FELASA Congress in Prague.



Stephen and Stuart receive the 2019 IAT Andrew Blake Tribute Award.

Another area I have focused my energy on is improving the transparency of research involving animals. This has led to me being elected as a Member of Council for organisations such as Understanding Animal Research.

As my career evolved I became facility manager at UCL, overseeing a multi-species unit with a fantastic team of seven personnel. In 2015 I took up a new and exciting role as deputy site manager at KCL's Guy's campus. After two months I was promoted into the role of site manager, overseeing approximately 40 staff.

An award-winning career

My commitment to the 3Rs was acknowledged in 2016 when I received a call to say that I had been awarded the AAALAC International Fellowship Award, given to UK registered animal technicians who make significant contributions to animal welfare. I was incredibly grateful to receive this award, which gave me the unique opportunity to visit several US facilities and attend the AALAS national conference.

In 2019 I was jointly awarded the Andrew Blake Tribute Award with Stuart Newman for a paper entitled "Time's up for tick-over colonies... Do we now need to maintain so many GA mouse lines?", published in the IAT journal *Animal Technology & Welfare*. The paper described the creation of a genome editing and embryology core within KCL Biological Services for rapid and

efficient archiving, which in turn has led to a substantial reduction in tick-over colonies. Between September 2015 and October 2017 various subsidy incentives were offered to research groups, resulting in over 350 lines being cryopreserved, with 97 removed as a live resource. This led to a significant reduction in animal use, preventing the breeding of an estimated 4,000 mice per year. Stuart Newman was a key person in establishing this programme, alongside all other BSU staff who liaised with researchers on this. Tolga Oralman now leads this programme and we are continually improving colony management through these methods.

We are currently working on creating an open source online platform, which we hope will allow researchers and animal technicians to improve colony management by using algorithms rather than manual calculations to calculate the number of breeding animals needed to create a line. In time we hope this system will be able to provide predictions on individual colonies and help further reduce animal wastage.

Taking on new challenges during the pandemic

In early 2020 I became Interim Director of Biological Services at KCL. Taking on such an important role during a pandemic was not something I could have predicted, but it provided an opportunity to condense many years of experience into just a few months. In recognition of my efforts during a very difficult time, I was appointed in

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Find someone to mentor you, take an interest in the incredible science that you are an important part of, and create a personal action plan to forge a rewarding career path for yourself.”

November 2020 as the permanent Director, making me responsible for more than 60 staff. I am also a Home Office project licence holder for the breeding, production and archiving of genetically altered mice at KCL.

COVID-19 has posed an extremely challenging year for everyone, but I have seen first-hand how animal technologists have shown a huge commitment to the welfare of animals. I would like to thank the KCL team for all their work ensuring animal welfare and research support are maintained to the highest standards.

Read Stephen and Stuart's Andrew Blake Tribute Award-winning paper in the December 2018 edition of *Animal Technology & Welfare*: journal.atwjournals.com/atwdecember2018



Stephen learning microinjection for genome editing.

3Rs papers of interest



A mouse voluntarily drinks from a micropipette following training (Scarborough *et al.*, 2020)

Each issue we feature recent 3Rs papers, providing summaries and links to the full articles for further reading. This issue we look at new non-invasive methods for oral administration of substances to mice.

Substances are commonly administered to mice orally in the course of studies – for example, when testing drugs. Gavage is often used to administer precise doses at specific times, but it is an invasive method that can lead to stress, especially if repeated. If performed incorrectly, gavage can also injure a mouse's oesophagus or stomach or result in aspiration.

It is possible to administer drugs non-invasively through mixing them in food or water. However, it can be difficult to determine how much of the drug each mouse has consumed and when, particularly for group-housed animals.

Micropipette-guided drug administration (MDA) is a new non-invasive method for precise oral administration, developed by Scarborough *et al.* (2020) at the University of Zurich using C57BL6/N mice. This method involves training mice over two consecutive days to voluntarily drink a solution of the drug mixed with a pleasant vehicle, such as sweetened condensed milk, from the tip of a micropipette. On the first day mice are restrained by the scruff and the pipette tip is offered to their mouth until they begin to drink. On the second day, mice are restrained only by the tail while placed on the metal grid of the food hopper, and the pipette tip is again positioned next to their mouth until they drink. Once the training is complete, the mice are no longer restrained and drink from the micropipette voluntarily.

MDA leads to a smaller acute stress response compared to gavage, as measured by plasma levels of the stress hormone corticosterone. However, MDA still requires scruff and tail restraint during the training period, and restraint stress can be made worse if the mice are also routinely picked up by the tail. A recent NC3Rs-funded study by Henderson *et al.* (2020) showed that the simple refinement of replacing tail with tunnel handling can substantially improve mouse welfare and the benefits persist even when the mice experience stressful procedures, including repeated scruff restraint.

We featured a similar method to the MDA in a previous issue of Tech3Rs, including some tips on how to encourage mice to voluntarily drink drug solution directly from a syringe (see page 2 of issue 7, www.nc3rs.org.uk/tech3rsissue7). For example, providing a small amount of the vehicle straight after dosing rinses out any remaining drug solution, preventing an unpleasant aftertaste, while administering a syringe of just the vehicle later in the day prevents mice from associating the vehicle with any adverse effects of the drug.

Another non-invasive method of oral administration that does not require restraint has recently been described by Teixeira-Santos *et al.* (2021) at the University of Porto. The method involves mice voluntarily consuming the drug mixed into a small quantity of strawberry

jam. Group-housed mice are placed individually into a separate cage for up to 20 minutes and habituated to the jam for three consecutive days before the drug is added. The authors found that, following training, mice consumed all of the jam within five minutes. This method ensures a precise dosage and time of dose, though care should be taken to transfer mice in a non-aversive manner (e.g. tunnel handling).

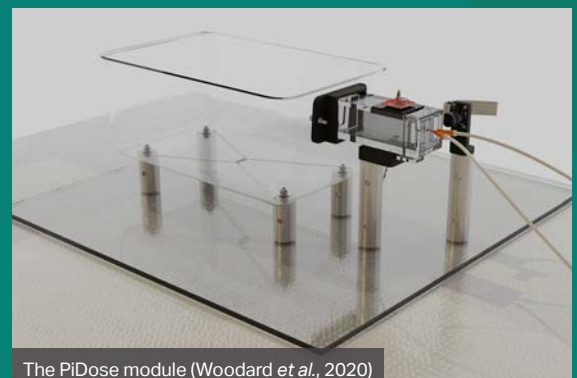
Finally, new technologies are enabling non-invasive oral administration to group-housed mice in their home cages. Woodard *et al.* (2020) at the University of British Columbia, developed PiDose, a low-cost device that weighs individual animals and administers an appropriate daily dosage of drug solution through their drinking water. Mice are identified through an implanted tag and receive both water and drug solution by licking a spout within the PiDose module. While this allows precise dosing and does not require moving the mice from their home cage, the time of administration cannot be controlled as mice can access the spout and drink freely at any time.

Each of these oral administration methods comes with advantages and disadvantages that need to be considered based on study requirements. However, it is important to re-visit commonly used procedures, such as oral dosing, and challenge how they can be improved and how to put refinements into practice.

Scarborough J *et al.* (2020). Preclinical validation of the micropipette-guided drug administration (MDA) method in the maternal immune activation model of neurodevelopmental disorders. *Brain, Behavior, and Immunity* 88: 461-470. doi: [10.1016/j.bbi.2020.04.015](https://doi.org/10.1016/j.bbi.2020.04.015)

Teixeira-Santos L *et al.* (2021). An alternative method for oral drug administration by voluntary intake in male and female mice. *Laboratory Animals* 55(1): 76-80. doi: [10.1177/0023677220950782](https://doi.org/10.1177/0023677220950782)

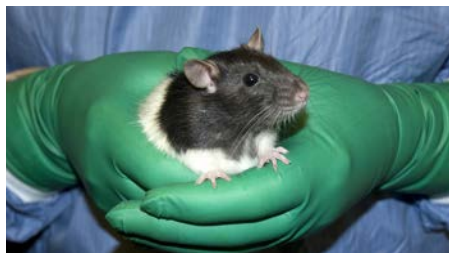
Woodard CL *et al.* (2020). PiDose: an open-source system for accurate and automated oral drug administration to group-housed mice. *Scientific Reports* 10: e11584. doi: [10.1038/s41598-020-68477-2](https://doi.org/10.1038/s41598-020-68477-2)



The PiDose module (Woodard *et al.*, 2020)

Spotlight on... NC3Rs webinars

The NC3Rs hosts regular webinars on different 3Rs topics, delivered by NC3Rs staff members, our grant holders and invited speakers. Below we highlight three recent webinar recordings available to watch online. To learn more about all our previous and upcoming webinars, visit www.nc3rs.org.uk/webinars.



Efficient management of genetically altered mouse colonies

In this joint webinar from the NC3Rs and the Mary Lyon Centre (MRC Harwell), Dr Sara Wells and Dr Michelle Stewart from the Mary Lyon Centre discussed key themes from the NC3Rs breeding and colony management resource (www.nc3rs.org.uk/colonymanagement), including strategies for maintaining colonies and breeding genetically altered strains for studies.

To watch the recording of this webinar, which is relevant to anyone who manages mouse colonies or provides training in breeding and colony management, visit www.nc3rs.org.uk/GAcolonywebinar.

Refining rodent stereotactic surgeries

Amanda Novak, Named Veterinary Surgeon at the University of Edinburgh, presented this NC3Rs webinar on refining rodent stereotactic surgery procedures. Amanda covered current advice on planning and preparing stereotactic surgeries, options for anaesthesia and analgesia, and good aseptic technique, with suggestions also applicable to other rodent surgeries.

The webinar recording is now available at www.nc3rs.org.uk/stereotacticwebinar. To learn more about aseptic technique, visit www.procedureswithcare.org.uk, or find further e-learning resources at www.nc3rs.org.uk/elearning.

Rat playpens for improved welfare

In this webinar, Dr Jessica Eddy from the NC3Rs presented an overview of rat playpens and tips for setting them up. This was followed by Kirsty Watson, a Senior Animal Technician at University College London, who shared how rat playpens were introduced at UCL's Institute of Ophthalmology and the positive results staff saw.

If you are involved in the care of laboratory rats, catch up on this webinar at www.nc3rs.org.uk/playpenwebinar. For more information on playpens, visit www.nc3rs.org.uk/playpenworkshop to read the report of our 2017 IAT Congress workshop on the topic.

Upcoming virtual events

UFAW conference: Recent advances in animal welfare science VIII

29-30 June 2021

This two-day Universities Federation for Animal Welfare (UFAW) conference will bring together cross-disciplinary research into a range of species, with the common goal of advancing animal welfare. It will feature talks and posters on topics including welfare assessment, humane killing and the impact of laboratory animal welfare on scientific validity. This free conference will be relevant for anybody interested in improving the welfare of laboratory, farm, zoo or companion animals.

To learn more and register, visit www.ufaw.org.uk/conf2021.

11th World Congress on Alternatives and Animal Use in the Life Sciences

23 August-2 September 2021

Originally due to take place in Maastricht in 2020, this event will now be held online. NC3Rs staff will be delivering talks on a range of 3Rs-related topics: from applying the 3Rs in regulatory drug development studies and minimising aggression in laboratory mice, to highlighting NC3Rs resources that can help you design and run more reproducible experiments.

Further details, including how to register for this year's event, can be found at www.wc11maastricht.org.

Highlights from the NC3Rs website



Visit our updated blood sampling pages

The NC3Rs website provides a wealth of tools to support animal technicians in applying the 3Rs. We regularly update these resources with information on contemporary best practice and opportunities to refine common procedures.

Most recently we have updated our blood sampling pages, with assistance from colleagues at the Laboratory Animal Veterinary Association. The pages feature in-depth information on refining blood sampling in a range of common laboratory animal species – from choice of technique and sample volume, through equipment and practical considerations, to the use of vascular catheters and microsampling.

Visit the updated pages at www.nc3rs.org.uk/bloodsampling.



New resource page on zebrafish welfare

To help you stay up to date with our zebrafish-related news, research and other online information, we have collated these resources on our website. This new page brings together NC3Rs-funded research projects, highlights potential refinements and links to external resources relevant to animal care staff working with zebrafish. Topics covered include refining DNA collection, welfare monitoring and anaesthesia.

Find our new resource page at www.nc3rs.org.uk/zebrafishwelfare.

Additional information on zebrafish welfare, housing and husbandry can be found on the North American 3Rs Collaborative (NA3RsC)'s website: www.na3rsc.org/zebrafish

Norecopa, the Norwegian 3Rs Centre, also maintains a page of resources on the use of zebrafish: norecopa.no/species/fish/zebrafish



Refining non-human primate vaccine studies in the age of COVID-19

Non-human primates are used to develop and test vaccines to combat human diseases. The COVID-19 pandemic has driven an increased demand for non-human primates globally, and it is vital to ensure their welfare remains a priority.

Experts from the NC3Rs and the Coalition for Epidemic Preparedness Innovations, a foundation that finances independent research projects to develop vaccines against emerging infectious diseases, have authored a review identifying features of contemporary good practice in vaccine and drug efficacy studies that use non-human primates. Recommendations focus on topics including animal selection, environmental enrichment, social housing, training for cooperation with husbandry and procedures, and the use of early humane endpoints.

Read more about this review and find links to other relevant resources at www.nc3rs.org.uk/nhpvaccines.