Imperial College London

www.imperial.ac.uk/animal-research

ANIMAL RESEARCH ANNUAL REPORT 2014

On the cover: This rat has been taken out of its cage so that scientists can study its movement and behaviour. The rat is used to humans and is naturally curious. This research is part of a study to improve our understanding of how problems with the immune system affect the brain and spinal cord in patients with multiple sclerosis.

Table of contents

Imperial's policy on the use of animals is available at
www.imperial.ac.uk/animal-research/policy

“2014 was a year of significant positive change for Imperial.

We have carried out a major restructure of the way we govern and support our animal research work at the College, and reviewed the culture of care for our animals. The benefits of these changes are already being seen and I am certain that we will make substantial further progress in 2015.”

— PROFESSOR JAMES STIRLING, PROVOST AND ESTABLISHMENT LICENCE HOLDER

Imperial researchers studying flu work with ferrets, as they are susceptible to human influenza viruses and develop some of the same symptoms as we do. This cage houses two animals, and contains cardboard tunnels and a hammock to provide a more stimulating environment.

FOREWORD
ANIMAL RESEARCH AT IMPERIAL

This is Imperial's first animal research annual report. It details our progress in implementing the changes we announced in the *Action Plan for world class animal research* in January 2014, and offers insight into how and why we carry out this important work.

We have reformed our ethical and welfare review process, introduced a new governance structure and created stronger links between different parts of our animal research community. We have also strengthened our approaches to finding replacements for animal research, to reducing the number of animals used in experiments and to refining methods to minimise suffering – a set of principles often referred to as the 3Rs.

Change on this scale requires the dedication and commitment of many people. It does not happen overnight. The advances you read about here represent significant first steps in a programme to improve the culture of care for animals at Imperial over the years ahead.

Many staff across the College are working hard to create the culture and the environment that leads to best practice in animal research. Many collaborators, research funders and policy organisations have also given generously of their time to help us move forward in the last year, while a positive relationship with the statutory regulatory authorities has also been a great help. I thank everyone who contributed in 2014.

As a gauge of our positive approach I am delighted that Imperial launched a series of Awards for Excellence in Animal Research this year. These are designed to recognise staff in categories including application of the 3Rs, commitment to enhancing communications, and a lifetime achievement award.

In our Action Plan we committed to strengthening support for the animal research community. I am delighted we have been able to do this, and have welcomed a number of highly capable team members over the last year, all of whom are already making a significant contribution to our work. One commitment we are still working on is the appointment of a Director of Bioservices. This was proposed as part of the broader review of strategic leadership we carried out while strengthening the governance framework and is now being considered in more detail in the light of the many changes that have taken place in the last year.

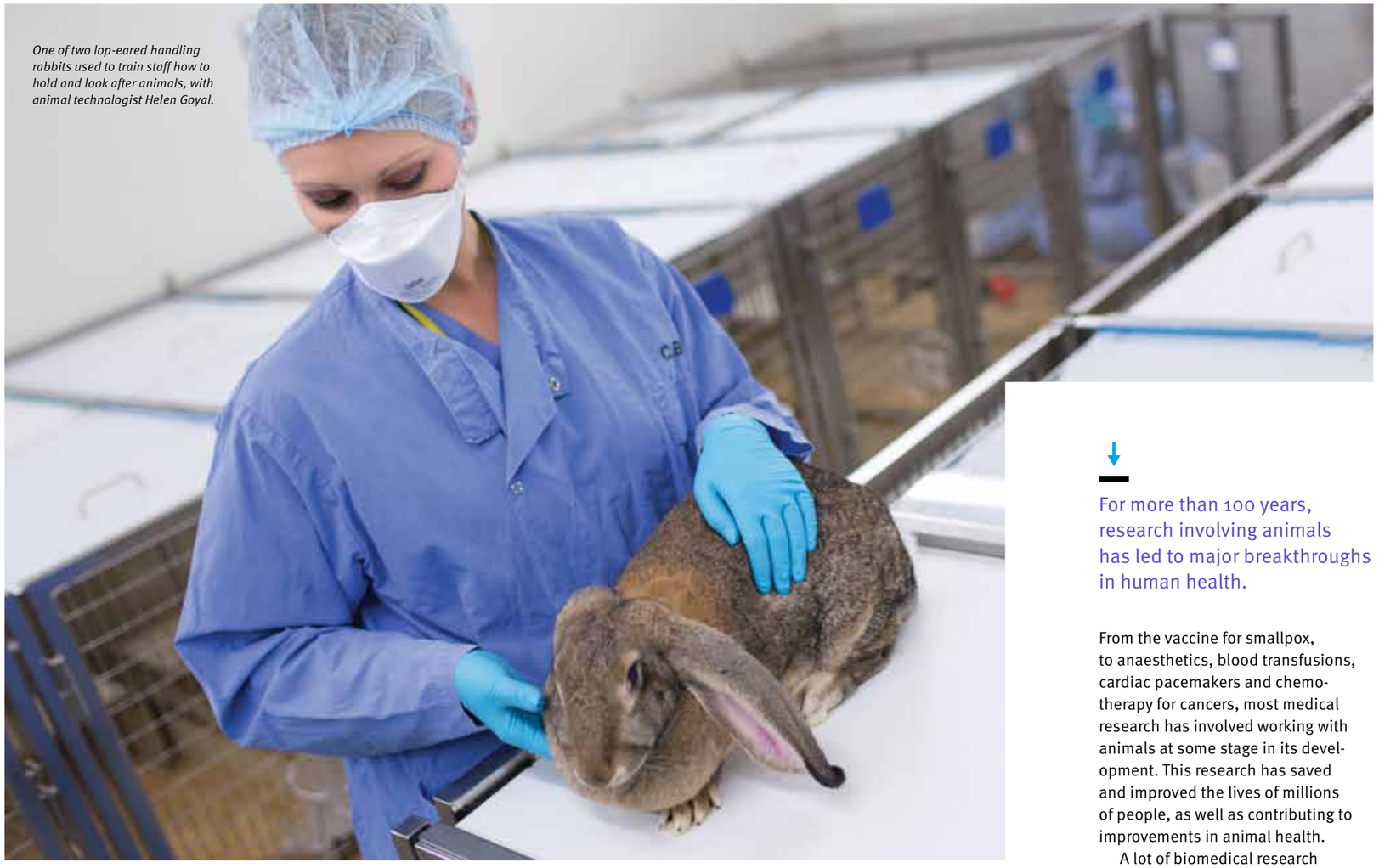
Since taking up the reins as the College's Establishment Licence Holder in July 2014, I have experienced a steep learning curve about animal research, as it is so far removed from my career as a physicist, and I firmly believe that producing great science requires excellence in all that we do. This applies to the way we care for our animals as much as anything else, and for us to achieve our mission means treating our animals with great consideration and compassion at every moment. Therefore I have been particularly impressed with the dedication of our staff to the welfare of the animals in their care. I look forward to supporting them to refine the ways we apply the 3Rs, to embed ethical and welfare considerations at the heart of everything we do and to communicate widely about our work.

In the Action Plan we pledged to communicate more effectively and in May 2014 we signed up to the UK's *Concordat on Openness on Animal Research*. Together, these have provided us with the impetus to adopt more proactive ways of communicating about our animal research and engaging more thoroughly with public audiences, our staff and students.

This report is just one example of our renewed emphasis on openness and transparency. We hope you will use it not only to review our progress on implementing our Action Plan, but also to understand why we believe this work is necessary, how seriously we take its regulation and how much we care for our animals. Please share it widely with colleagues, friends and family.

W. James Stirling

Professor James Stirling,
Provost and Establishment Licence Holder
January 2015



One of two lop-eared handling rabbits used to train staff how to hold and look after animals, with animal technologist Helen Goyal.

WHY DO WE NEED TO CARRY OUT ANIMAL RESEARCH?

For more than 100 years, research involving animals has led to major breakthroughs in human health.

From the vaccine for smallpox, to anaesthetics, blood transfusions, cardiac pacemakers and chemotherapy for cancers, most medical research has involved working with animals at some stage in its development. This research has saved and improved the lives of millions of people, as well as contributing to improvements in animal health.

A lot of biomedical research at Imperial is carried out using non-animal methods and we continue to work on alternative experimental techniques to use in preference to animals. Despite this, many vital questions in medical science can still only be addressed by studies with animals. The part of Imperial's research that does involve animals is only carried out where there are no alternatives. Animal research is strictly regulated under EU and UK law.

Animal research at Imperial

Research involving animals at the College is improving our fundamental knowledge of biological systems and helping to find new treatments for a wide range of human and animal diseases. We work in areas that include:

- Animal health
- Brain sciences
- Cancer
- Cardiovascular disease
- Diabetes and obesity
- Genetics and genomic medicine
- Infectious diseases
- Immunology and inflammation
- Organ transplantation
- Respiratory diseases
- Clinical trials

Each year we provide the Home Office with data on the number and type of animals we work with, which we publish at **www.imperial.ac.uk/animal-research/numbers**. The vast majority of our animals are mice (90% in 2013), with other animals including rats, amphibians, fish, birds, guinea pigs, rabbits and ferrets.

Alternatives to animals in research

Imperial is developing and using new ways to replace, reduce and refine the use of animals for scientific purposes wherever possible. This approach, known as the 3Rs, is defined as follows:

- ***Replacement:*** the preferred use of non-animal methods over animal methods whenever it is possible to achieve the same scientific aim
- ***Reduction:*** methods that enable researchers to obtain comparable levels of information from fewer animals, or to obtain more information from the same number of animals
- ***Refinement:*** methods that alleviate or minimize potential pain, suffering or distress, and enhance animal welfare for the animals used.

In the last decade, Imperial has been awarded grants and awards from the National Centre for the Replacement, Refinement & Reduction of Animals in Research (NC3Rs) totalling £3.38 million, demonstrating the College's scientific rigour and commitment to decreasing reliance on animals wherever possible. You can read more about Imperial's work in the 3Rs on page 24.

Non-animal biomedical research at Imperial includes in vitro *bacterial cultures (above), and human brain tissue samples (below).*

Recent findings from animal research at Imperial

Imperial research involving animals has improved our understanding of many aspects of life. Here are a few examples.

> “Our aim remains to deliver world class research for the benefit of humans and animals, whilst treating all our animals with full respect and the highest standards of care.”
>
> — *Professor Dermot Kelleher, Vice President (Health)*

TACKLING MALARIA

Imperial researchers have modified the mosquitoes that carry malaria so that they produce only male offspring. If this could be replicated in the wild, then local mosquito populations could be eliminated, which would in turn reduce the transmission of a disease that affects around 200 million people each year.

Researchers have identified a molecular mechanism that could explain why the common cold can bring on life-threatening attacks in asthma patients. By simulating asthma in mice and infecting them with the rhinovirus that often causes the cold, scientists have identified a new molecular target for possible treatment to reduce attacks.

UNDERSTANDING MORE ABOUT THE CAUSES OF ASTHMA

SAVING AMPHIBIANS FROM EXTINCTION

A skin-eating fungus has wiped out thousands of frog, toad and salamander populations across the world. Research with amphibian species in the laboratory and the field has identified water-borne microorganisms that consume the fungal spores that spread the disease and could be used to protect populations at risk.

Scientists have discovered a new target for drugs to treat inflammatory diseases such as arthritis by studying the large network of genes involved in controlling the production of infection-fighting cells called macrophages. Treating mice with drugs that focus on this target has alleviated arthritis symptoms by preventing bone erosion and inflammation.

NEW DRUG TARGETS FOR TREATING PATIENTS WITH ARTHRITIS

POTENTIAL TREATMENT FOR PATIENTS WITH MULTIPLE MYELOMA

Scientists are planning to start clinical trials of a new cancer drug in patients with multiple myeloma, following promising results in mice. The drug has been shown to kill myeloma cells in mice by blocking a key process that enables cancer cells to multiply, with none of the side effects of existing treatments.

A new technique using CT scanning technology has enabled researchers to visualise the complex manoeuvres of the bluebottle fly and understand how one of nature’s most complex flying machines uses its muscles in flight. The results could inform the design of micromechanical devices and miniature unmanned aerial vehicles.

BETTER FLYING MACHINES

GENE THERAPY FOR HEART FAILURE

A gene therapy for heart failure is being trialled in patients for the first time thanks to earlier studies on rats. The therapy was developed to increase the levels of a protein called SERCA2a in patients’ heart muscles. Research suggested that SERCA2a plays an important role in heart muscle contraction.

Scientists have identified how high-fat foods could be contributing to digestive diseases such as irritable bowel syndrome. Studies in zebrafish and mice have revealed that cholesterol irritates the lining of the gut, slowing down the movement of food through the body — a common symptom of human gastro-intestinal disorders.

INSIGHTS INTO DIGESTIVE DISEASES

ANIMAL WELFARE: HOW WE LOOK AFTER OUR ANIMALS

The health and welfare of research animals are of paramount importance to Imperial. The College employs more than 60 members of staff to care for animals.

World-class facilities

Imperial is committed to investing in world-class facilities for all its research, and its work with animals is no exception. Modern, well-equipped facilities increase the welfare of our animals and provide the best possible working environment for staff. Both are vital to ensure the highest quality research.

The design of our most recent purpose-built animal facility takes advantage of the latest technologies to keep the animals that live there healthy.

Once a week, staff move the mice to clean cages by hand, and then send the soiled cages for washing using a robot production line. With around 500 cages in each room, automation of such labour-intensive jobs ensures a consistently high standard of care, and frees up staff time to focus on other aspects of animal care and welfare.

The cages are wheeled into the cleaning area where robots rapidly empty the bedding from a large group of cages at a time. They send the cages through an industrial washer, dry them and refill them with clean bedding.

A similar robotic process occurs with the water bottles, which are emptied, cleaned and refilled with purified water.

The animal facilities are equipped with air filtering technology to trap pollutants and particles and prevent them from entering the facility. The filtered air is ducted into the holding rooms where the animals are kept in individually ventilated cages (IVCs). Air is filtered for a second time before entering the cages. The air is filtered once more as it is extracted before being vented directly out of the building.

Some of our smaller facilities, which have been operating for many years, do not yet have this same level of automation in the cage wash area, although an ongoing project to upgrade those facilities is a priority.

"In addition to world-class facilities, we are also committed to providing round the clock care for all our animals, with at least one veterinarian and five senior animal care staff on call 24/7", says Mandy Thorpe, Director of Central Biomedical Services (CBS). "We also monitor the animals' environment night and day, and if conditions fall outside of the Home Office Code of Practice, we will be notified by text and email alerts. In order to provide the best post-operative care, we also have a long-standing practice not to carry out surgery on Fridays, weekends, bank holidays or College closure days."

Animal technologist Wendy Steel transfers mice to a clean cage. Cages are cleaned once a week and mice are moved with some of their existing bedding so that the new cage retains some of their scent and feels familiar to them. The mice in this room are helping researchers to understand respiratory diseases such as asthma.

International accreditation

All animal research facilities in the UK have to abide by Home Office regulations. In addition, an international accreditation programme is offered by the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) – a private, non-profit, organisation that promotes the humane treatment of animals in science. AAALAC accreditation provides an internationally respected validation for standards of animal welfare, facilities, training and competency assessments. Accreditation also demonstrates an institution's accountability and its efforts to promote sound, ethical practices.

Imperial is seeking accreditation and has appointed a dedicated AAALAC project manager to support the process. He has more than 20 years' experience in animal care and has previously helped commercial organisations gain accreditation. Imperial is the first university in the UK to seek AAALAC accreditation.

The aim of the AAALAC accreditation programme is to review, update and document our current animal care programme and to meet with the required AAALAC standards.

Gaining accreditation is a lengthy process and the benefits of working towards it include continuity and standardisation across all campuses.

Streamlined training and record keeping

Imperial has made several new appointments to strengthen the culture towards training and establish a centralised record-keeping system.

These include a dedicated Named Training and Competency Officer (NTCO) to ensure that everyone working with animals is adequately educated, trained and supervised. The NTCO also helps staff maintain relevant expertise by creating and delivering tailored training courses where required.

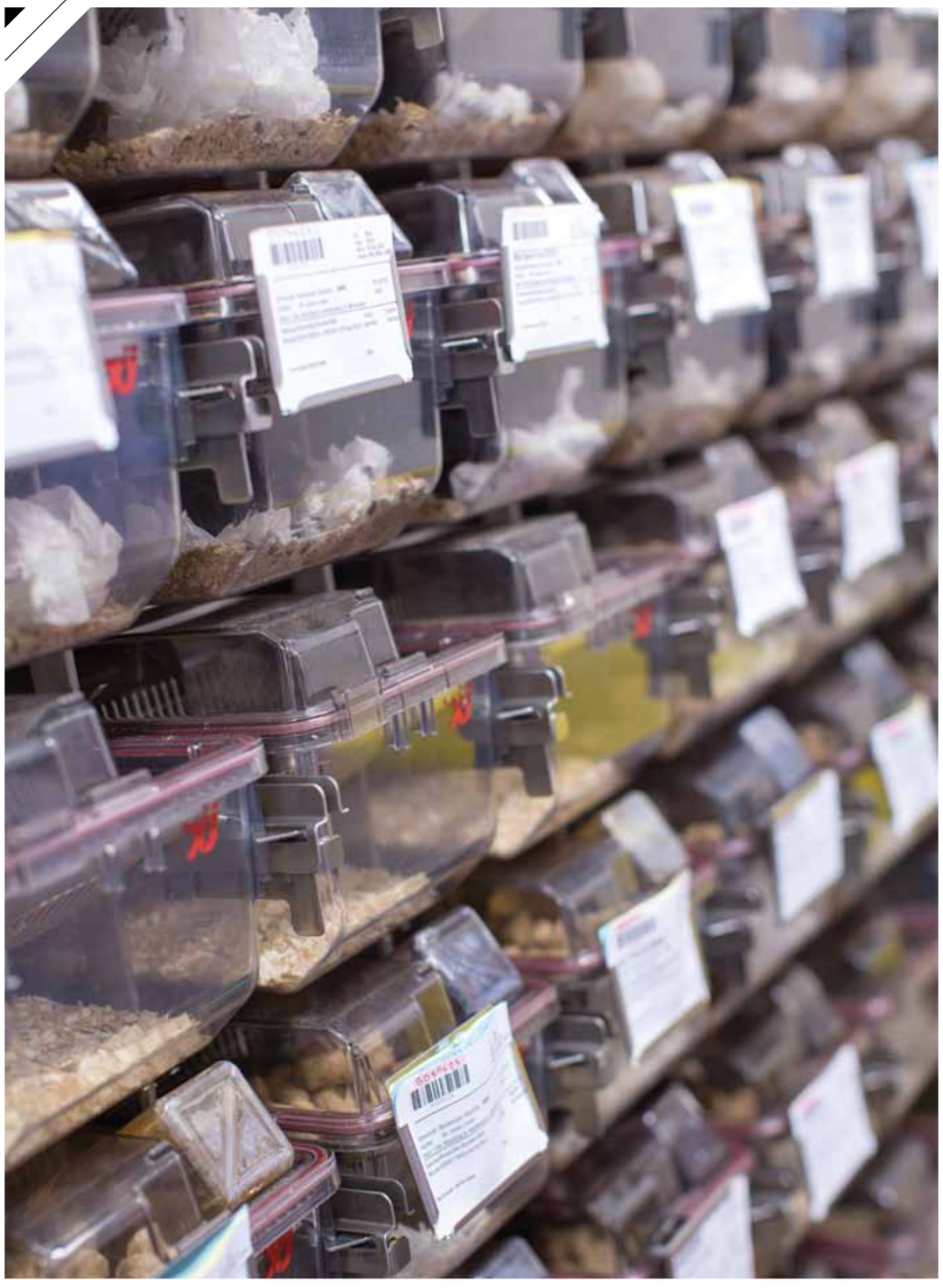
Alongside this, we have invested in a secure, online system for recording training and competency for staff who work with animals. The system, known as a-tune, maintains effective centralised records.

A culture of care

Finding ways to help our staff feel part of a single community across all our campuses is one of our biggest challenges. Creating a shared culture and promoting stronger links between our researchers and our animal technologists play a critical part in maintaining high standards of care for our animals.

In the past year we have put in place a number of ways to keep people connected. Changes include workshops for researchers and animal technologists, new approaches to training, and a programme of lunchtime seminars that are filmed and available for viewing online for those who are unable to attend in person.

We have also launched a monthly newsletter for the College's animal research community to celebrate good practice and build better connections (see page 28).



REFLECTIONS OF A HOME OFFICE INSPECTOR

The Home Office employs a team of inspectors to make sure that all animal research is carried out according to the terms of its licence. Inspectors are all qualified vets or doctors. In addition to assessing licence applications, they visit research establishments regularly, and as appropriate, usually unannounced.

People often assume that the role of an inspector is to 'catch an organisation out' for any licence failings. While ensuring compliance with the law is paramount, here Imperial's inspector explains that his role is far more complex and nuanced than a simple checklist.

"When I'm on site I'm not just looking for non-compliance or trying to catch people out. My starting point is much more neutral. It often surprises people that I don't just work with a checklist, but that's because I'm inspecting at a whole range of levels. By walking round, without saying a word, I can take in all sorts of information and much of it is environmental.

How tidy is the unit? Do staff seem calm and in control or are they running around, looking stressed? Are the cages clean? Do all the animals have adequate food and water supplies? I will look at temperature charts as well as the appearance and behaviour of the animals. This gives me an overall sense of how good the animals' welfare is.

My role is a mix of statutory and non-statutory functions — the latter are aimed at encouraging good practice. The more I see of an organisation's daily work, the more I see what's being done well and can identify opportunities to share it, and also provide advice on how things could be done even better.

The scale and complexity of animal research at Imperial is greater than the activity of a large pharmaceutical or small academic or contract research organisation. The biggest challenge for a large academic institution is its culture. It can be challenging to move towards a unified culture where there is a standard approach to animal welfare and continuous improvement across all facilities.

As an inspector, you are constantly nudging organisations towards an improved culture of care and continuous improvement. Despite all the things that can be done at an organisational level — having an active Animal Welfare and Ethical Review Body, known as an AWERB, or implementing a comprehensive training programme — ultimately, it is about the attitude and working practices of each individual involved in the research. Their mind-set has a direct effect on the welfare of the animals.

The Animals (Scientific Procedures) Act [the legislation that regulates the use of animals used for research in the UK] is about ensuring the best welfare for the animals. But it is also about having a good, robust model so that the scientific results carry more weight. If an animal has a sub-clinical infection, you'll get variation in the results between animals A and B. That's exactly the kind of thing you need to minimise if you want to get the most robust data. As an inspector, I can give advice on standardising approaches and getting consistent results. This helps provide assurances that good quality science is being carried out and wider benefits are being achieved.

Often, welfare or compliance-related incidents are caused by things that are unexpected rather than being down to carelessness. Of course, if an incident gives us cause for concern, we will need to investigate it appropriately.
All research establishments are obliged to self-report any incidents that they come across, even when they seem fairly minor. One of the benefits of this is that the establishment can look for patterns and this may help to make local systems more robust. This all leads to better welfare for the animals."

GOVERNANCE: HOW WE UNDERTAKE ANIMAL RESEARCH

In January 2014, Imperial published its Action Plan for world class animal research, putting in place a robust governance model to manage and deliver our research, and making new commitments to reform our ethical and welfare review processes, address the 3Rs, and strengthen our communications.

The governance model combines decision-making, advisory and oversight functions to assure regulatory compliance, promote leadership in animal research, and improve the way that decisions by AWERB translate into management and operational improvements.

The new structure reflects the 3Rs commitments set out in the Action Plan and has been designed so that the College can continue to deliver world class research, whilst treating all animals with full respect and providing the highest standards of care.

The model has clear reporting procedures across all processes linked with animal research, with overall accountability resting with the College's senior management. It includes operational groups for each facility, as well as expert Advisory Groups for the 3Rs, Quality Assurance and Designated Rooms.

Governance Board for Animal Research

The governance model is overseen by the Governance Board for Animal Research, which was established in July 2014 to provide strategic oversight and assurance to the College. Chaired by Professor Dermot Kelleher, Vice President (Health), the Board met twice last year.

Central and Local AWERBs

The existence of an AWERB is a statutory requirement for all organisations working with animals. AWERB's primary role is to ensure we only use animals in research when it is the only legitimate way for us to answer research questions. A new structure at Imperial has been implemented with the creation of two local AWERBs to serve different campuses, in addition to a central body. All researchers applying for a licence to work with animals need to present their proposal to an AWERB meeting. The new chair of the central AWERB, Professor Maggie Dallman, takes part in a Q&A on page 18 to explain the review process in more detail.

The 3Rs Advisory Group

Imperial has a strong track record for its work to replace, refine and reduce the use of animals in research. The Action Plan created a new 3Rs Advisory Group so that everyone who works with animals at Imperial – whether as a technician, researcher or in another capacity – has the fullest possible engagement with the principles and application of the 3Rs. The Group, chaired by Professor Richard Reynolds, is encouraging innovative approaches by staff for exploring new and effective ways to implement the 3Rs across College. You can read more about his work and that of some of our researchers working in the 3Rs on page 24.

Quality Assurance Advisory Group

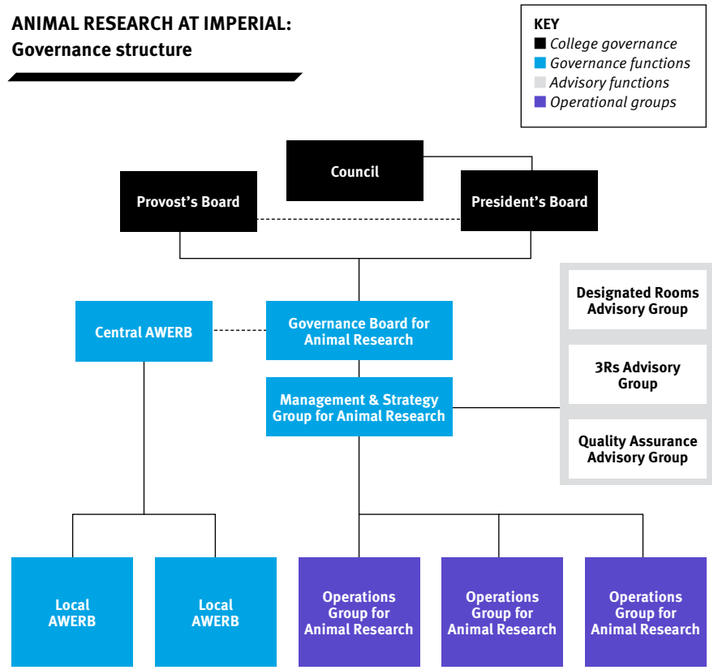
Following publication of the Action Plan, the remit of the College's pre-existing Quality Assurance Group widened to include the provision of advice on how world class animal research developments can be integrated into operational management of research facilities. The Group, chaired by Professor Marina Botto, Director of the Centre for Complement and Inflammation Research, organises meetings for project licence holders to share best practice and oversees the process for gaining the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) accreditation.

Designated Rooms Advisory Group

All animal research must, by law, be carried out in approved areas. At Imperial, the vast majority of work with animals takes place in speciaist facilities. However, there are some occasions where this is not feasible. For example, an academic may need to use a large piece of equipment, such as a magnetic resonance imaging scanner, which cannot be practically accommodated in our animal facilities. The room containing such equipment is assigned as a Designated Room and meets the standards of a specialist facility, as required by the Home Office.

As part of the governance changes, Imperial established a Designated Rooms Advisory Group with membership from all faculties to provide a clear and designated route for seeking advice or raising any issues around Designated Rooms. The Advisory Group is already having a positive impact. Having received an application for a Designated Room in an area that the members felt was not ideal, they were able, using their combined knowledge, to identify an existing area in a specialist facility at College that could serve instead. In this way, the Group is helping to provide solutions that meet the needs of researchers while also ensuring higher standards in animal welfare.

ANIMAL RESEARCH AT IMPERIAL: Governance structure



Investment in people

These changes to the governance model are significant. Imperial has also invested and created new, full-time, dedicated roles to ensure the successful implementation of the new structure and provide ongoing support.

These include:

- ***A Named Training and Competency Officer***, to ensure everyone working with animals is appropriately educated, trained and supervised
- ***A Project Manager*** to implement a new, online training record-keeping system (known as a-tune)
- ***A Quality Assurance and 3Rs Programme Manager***
- ***A Project Manager*** to support our ambition to gain international accreditation for our laboratory animal care
- ***An AWERB administrator***

Opposite: an animal technologist checks the temperature and humidity of the airflow supplying individually ventilated rat cages. Above: staff catch up in the corridor of one of Imperial's animal research facilities.

Take a look behind the scenes

1. Lighting
Ambient lighting is programmed to day and night, with dawn and dusk settings to reflect the natural environment. Some rooms also have red ambient lighting at night time, which rats and mice cannot see in, but humans can. Cages on the top row are shaded so they are exposed to the same amount of light as cages lower down.

2. Cage label
Each cage is labelled with the name of the lead researcher, project details, and the number of animals it contains. The label also has a unique barcode ID, so it can be stored and identified on a central computer system.

3. Ventilation
Filtered air is ducted into the individually ventilated cages, and is filtered once more as it is extracted, before being vented directly out of the building through the white ducts in the centre of the ceiling.

4. Two-level cage
This cage design provides more space for rats to exercise, and includes objects to make a more stimulating environment, such as nesting material and tunnels. Each cage is ergonomically designed so that one person can safely lift it.

5. Protective clothing
Everyone entering an animal room must put on a cap, lab coat, and disposable overshoes, gloves and face mask to protect both the animals and the handlers.

6. Change station
Stacks of cages are wheeled over to the change station where animals are transferred to the clean cages waiting on the left. The change station has its own ventilation unit. Yellow bump rails around the room protect the animals in their cages as they are moved around.

7. Floors, walls and ceilings
These are made from impermeable surfaces for regular washing and sanitising.

Professor Maggie Dallman, pictured in one of the College's zebrafish rooms, leads a research group working with a range of organisms from zebrafish to humans to study the basis for disease involving dysregulated immunity and inflammation and potential approaches to therapy. In addition to chairing AWERB, Maggie is also the College's Associate Provost (Academic Partnerships).

REFORMING WELFARE AND ETHICAL REVIEW

Professor Maggie Dallman, the new Chair of Imperial's Animal Welfare and Ethical Review Body (AWERB), talks about recent changes to how the College considers the welfare of animals in its care and the ethical considerations linked to this research.

Q. How does the College consider welfare and ethical issues associated with its animal research?

A. The College has statutory responsibilities under UK and EU law to review its animal research so that it is legally acceptable and conforms to best practice. It does this by having an AWERB, which reviews the welfare aspects and ethics of new project applications, disseminates good practice about the 3Rs, monitors animal welfare, and carries out mid- and end-term reviews for projects from a College perspective.

This review process considers whether a scientific proposal justifies the use of animals, as well as exploring practical issues on how the work will be carried out, including experimental design, how the animals will be looked after, what staff training might be required, and application of the 3Rs. These issues are important for both animal welfare and the quality of the science – treating our animals well produces better results.

We have a great responsibility to care for our animals in the same way that we care for our staff and students, and we show great respect to our animals when we have to work with them. The AWERB process is designed to make sure that when we do have to use animals, our work is carried out in the most efficient and effective way, to reduce the number of animals involved, refine the procedures that we use, and ensure that all our animal work is essential and cannot be carried out using alternatives.

Q. A year ago, Imperial committed to reform its AWERB. What are the main changes since then?

A. Over a relatively short time the College has made a lot of changes to the way that AWERB operates to help its work become more effective and progressive. These advances are designed to keep ethics and welfare at the heart of our research.

We began with a review of AWERB membership and the creation of a full-time administrator role. Our next major change was to put processes in place so that we could review all project applications in person, rather than assessing some of them by email, which had previously been the case. With approximately 170 project licence holders at Imperial, we have lots of applications, so we set up a structure that was better fit for purpose, with two new local AWERBs to review applications for mild or moderate scientific procedures and to refer on any proposals for severe ones to central AWERB.

Providing a review structure for our researchers, vets and Named Animal Care and Welfare Officers (NACWOs) to come together to consider all proposals face-to-face enormously strengthens the review process and enables us to share good practice effectively. Thanks to the local AWERBs, in just a few months we have been able to move from carrying out many of our reviews by email to reviewing all our applications in person. We've also become more nimble at responding to applications promptly, replying rapidly to any concerns raised, and translating lessons learnt into good practice to share with the community.

We have also made changes to how AWERB business is carried out. We provide more detailed information about the review process to project applicants in advance of meetings so they are aware of what they need to prepare, and have a better idea of what AWERB expects of them. We are in the process of developing an online application process to streamline and standardise the paperwork involved. And we have established a really inclusive environment at AWERB meetings to encourage open discussion and robust review of the research by all members.

Animal technologists at a change station in a mouse breeding room.

Q. What about the AWERB membership – who is involved in actually reviewing the research?
A. It's important that membership of our AWERBs represents a broad range of interests, expertise, seniority and roles, so we can consider our research from multiple perspectives. AWERB members include academics, a PhD student, a postdoctoral Junior Research Fellow, a statistician, vets, the NTCO, other technical staff representative of our animal research community, and lay members. The chairs of the local AWERBs and our 3Rs group sit on the central AWERB, to align the business of all three AWERBs and ensure tight communication on the development and application of the 3Rs. AWERB members also include our Establishment Licence Holder, and a research communicator to help us engage more effectively with people inside and outside the College about our work.

Central AWERB is now chaired by a senior academic at the College – currently myself – and supported by an experienced lay Vice-Chair. Inevitably, some members do have their own research programmes, myself included. If we ever need to take our own work to the AWERB then we ask colleagues to lead on the review so that it remains independent.

Q. How are the lay members selected and what is their role?
A. Involving lay people in the ethical review of our research increases the integrity of the review process. Their role is to bring independent perspectives to our discussions, and comment on whether they think the aims of the science really merit the use of animals, rather than commenting on the detail of the science.

Our lay members come from different backgrounds and have usually not been involved with animal research. They need to be sympathetic to the idea of working with animals in research, but they don't have to have done it themselves.

Q. Who else attends AWERB meetings?
A. The AWERB administrator supports AWERB business by providing essential resources for us to carry out our duties efficiently and in a timely fashion. The College's Home Office Inspector often attends our central AWERB meetings, which is helpful for us to double check the way we categorise our scientific procedures on the scale of mild-to-severe, as defined by the Home Office, and more generally to keep communications lines with the Home Office strong.

Q. How does welfare and ethical review fit into the College's overall framework of animal research?
A. AWERB is an interesting body as it sits outside the College's framework for managing animal research. This enables it to remain independent from the day-to-day operational requirements of running the facilities or managing large programmes of research.

As Chair of AWERB, I also sit on the College's Governance Board for Animal Research and the Management and Strategy Group for Animal Research, so that ethical and welfare issues are considered every time we discuss our work.

Q. Although the arrangements for ethical and welfare review are still quite new, can you give us an example of how they have changed processes?
A. One of our aims is to increase the sharing of good practice across our community. We recently had an application that included an excellent chart for assessing how animals were responding after surgery. It set out a very detailed protocol to look for clinical symptoms in the animal, which in this case happened to be a mouse. We felt that this was so valuable that we asked the project licence applicant if we could share that with our community, to encourage more people to use this comprehensive list of signs and symptoms to judge how well their animals are and to take appropriate action immediately if there is any sign of suffering beyond the terms of the licence.

Q. What's the ethical review process like from the point of view of a researcher?
A. Most research brought to AWERB will already have been peer reviewed by the scientific community, including consideration of the 3Rs. Coming to AWERB can therefore be a bit challenging for a researcher, as their work is being questioned again, but this time we are approaching things from a different perspective. The scientific validity of the work remains important, and indeed central to our understanding of the need for animal research, but at AWERB the focus is much more on the broader ethical, welfare and public considerations about the work.

You go to a committee meeting, stand up and present your work to the wide range of people represented on AWERB. You will also need to prepare yourself for questions, constructive challenges and scrutiny from all different directions.

We work really hard to ensure that it's not too combative, but we also want to make sure that our animal research is done in the best possible way from the perspective of welfare and ethics, as well as from the perspective of the science.

Researchers have told me that they go away from a review meeting feeling positive about the fact that they have had the undivided attention of so many experts who support their efforts to carry out cutting-edge science in a way that values and respects the animals used.

Q. What are your next priorities for welfare and ethical review at the College?
A. In 2014 we have taken some important steps to position welfare and ethical review at the heart of our research. For the future, I'm really keen to see this culture change continue, so that our whole animal research community understands and supports this essential part of our responsibilities as an organisation that carries out this work. There are a number of areas where I would like to see AWERB committing to new activities in the future.

Ethical considerations need to encompass the lifetime of a project, and AWERB will be expanding its involvement in reviewing projects at the mid-term to ensure that ethical and welfare aspects are considered alongside scientific issues throughout a project. Mid-term reviews are something that AWERB has only recently started to carry out; our recent reforms mean that the structure is now in place to discharge this responsibility more effectively.

Until now, the AWERB process has only considered animal research protected by UK and EU legislation and licensed through the College. In line with our aims to position ethical and welfare considerations at the heart of all our work, it is our ambition to apply similar considerations to collaborative research carried out by our staff at other organisations.

To fulfil our commitment to openness on animal research, I would also like AWERB to continue identifying and encouraging proactive communication and transparency about our animal research. You can read more about the significant steps we have taken in the past year to engage with people about our research on page 28, and I look forward to building on these in the year ahead.

I've had very positive conversations about these changes, which have got the College's scientific community engaged with the importance of this process in a way that didn't exist before. I am very grateful to our professional and lay Committee members and local AWERB chairs for their time and expertise, and look forward to progressing this important work in the year ahead.

"Researchers have told me that they go away from a review meeting feeling positive about the fact that they have had the undivided attention of so many experts who support their efforts to carry out cutting-edge science in a way that values and respects the animals used."

— *Professor Maggie Dallman*

Main AWERB reforms

- Chair, membership and terms of reference for central AWERB revised
- Pool of lay members established and new members appointed
- Application process streamlined and clarified
- Local AWERBs created to support interactions between researchers, CBS staff, NACWOs and vets
- All licence application reviews carried out face to face
- Full-time AWERB administrator post created and recruited

“We have a great responsibility to care for our animals in the same way that we care for our staff and students.”

– PROFESSOR MAGGIE DALLMAN, CHAIR, IMPERIAL’S ANIMAL WELFARE & ETHICAL REVIEW BODY

Left: Animal technologists discuss care regimes in the rabbit and guinea pig room.
Above: Rabbits are given hay, cardboard tubes and plastic balls to play with.
Below: The mouse house comes with an exercise wheel on its roof.

3Rs: REDUCTION, REPLACEMENT AND REFINEMENT

3Rs Group Chair Richard Reynolds (right) is Professor of Cellular Neurobiology. His research is leading to new ways of treating patients with progressive multiple sclerosis.

The 3Rs Group, set up by the College as part of the new governance model in May 2014, is designed to fulfil Imperial's aspirations to demonstrate good practice in implementing the 3Rs. It aims to do this by sharing the best approaches from across the College and from other organisations, and finding ways to support staff to adopt and implement improved practice to the fullest extent in all animal research work.

Professor Richard Reynolds, Deputy Head for Research in the Division of Brain Sciences, is chair of this new advisory group: "There are clear ethical reasons, in terms of animal welfare, why the 3Rs are so important. But increasing the focus on the 3Rs also makes sense from a research perspective. By creating a culture where we are constantly innovating to reduce, refine and replace animal research, we will also be enhancing the overall quality of the research we undertake."

"When you apply for an animal research licence, you have to state how you're replacing animal usage, reducing numbers and refining procedures, and we have always done this. What we want to do is make sure it's something we would naturally do in all our research for both ethical and scientific reasons. This may already be the case, but we want to instil it in the culture," he says. "We also want to remind our researchers to share the way they apply the 3Rs widely with other people working in similar areas through talks at conferences and in publications."

Professor Reynolds has assembled a committee of five academic staff of different seniority from across the College, together with animal technologists. The group meets every two months, and its first task is to gather knowledge about how the 3Rs are currently being applied across College.

"That's rarely been done before," he says. "There are approximately 170 project licence holders at Imperial, and until recently they have tended to work in isolation, so it's a major task."

The advisory group's work is at an early stage, but discussions with researchers have so far been very encouraging. "I didn't quite know what we were going to find when we started this. But everyone I've met so far has found it easy to tell me how they refine procedures and how they reduce the numbers of animals used. Everyone is paying attention to the 3Rs, which is good because it means Imperial is starting from a high baseline."

Professor Reynolds is eager to emphasise to researchers that applying the 3Rs is important not just from a legal and ethical perspective, but because it results in better science. "If your animals are under less stress because you refine the procedures you're using, the results are going to

be better, because you're focusing on the disease mechanism you're studying rather than other effects," he says. "You should be making sure you've got exactly the right number of animals for your experiment so you don't have to repeat the experiment."

Once the advisory group members have assembled a portfolio of 3Rs work from across the College, they will hold meetings to share good practice with other researchers. They have already launched awards for research staff and animal technologists, which include funding to present their work at conferences. Later they plan to hold workshops to generate new ideas. Professor Reynolds hopes to set up a College funding scheme for small research projects, to generate data for more substantive applications to external funders.

In his own research on multiple sclerosis (MS), Professor Reynolds uses post mortem human tissue to refine the questions that need to be investigated in an animal model. "You can do a lot of work with human tissue to work out disease mechanisms before you use animals," he says. His team developed a new model of MS in rats that better reflects what happens in patients. It provides more accurate and reproducible results, meaning that fewer animals have to be used overall.

Replacing animals completely in research on chronic diseases will be one of the biggest challenges, he says. "Currently it is not possible to replace animals everywhere. Conditions like Alzheimer's and rheumatoid arthritis occur over such a long time in a human, it's very difficult to model in a non-animal system. If a model doesn't reproduce that chronicity, it won't be a good way to test theories or drugs. Therefore, we need to address how to set up non-animal models of chronic disease. It's very difficult to do at the moment, but we can start by reducing numbers and refining experiments."

Reduction

Reducing the number of animals for testing new medicines

Dr Cesare Terracciano's work aims to reduce the need to use animals in research by improving methods for growing heart cells in the lab. Many new drugs fail to reach the market because of toxic effects on the heart. Research involving animals is currently integral to drug safety screening, but animal studies do not always reveal side effects that might occur in humans.

Dr Terracciano and his colleagues at the National Heart and Lung Institute are developing methods that would allow large amounts of human heart tissue to be grown in the lab and used for drug testing. Researchers can already grow small amounts of heart muscle from human cells but, in a petri dish, the cells do not develop all the features of heart cells in the body.

"These cells tend to be round and tend to be rather slow in their activity, simply because they're not challenged by their environment," says Dr Terracciano. "The heart is a very dynamic organ, which beats continuously and is subjected to very high pressures, and these are not present in culture."

In collaboration with the Institute of Biomedical Engineering at Imperial and the University of Southampton, Dr Terracciano's team has developed new surfaces that encourage cells to grow into regular lines as they do in the heart. Their studies so far have shown that cells grown using their methods behave more like cells in the heart.

Dr Terracciano was awarded a research contract in 2014 through the NC3Rs CRACK IT Challenges program that funds universities and small and medium enterprises to collaborate with industry to address scientific and technical challenges that will replace, reduce and refine the number of animals used in research.

"If we're successful in developing a platform that can be widely used for drug testing, we will be able to reduce dramatically the number of animals used for research and avoid harmful effects that new drugs might have on patients," says Dr Terracciano.

Dr Emerson is working with researchers at other institutions to help them adopt new techniques to significantly reduce the numbers of mice involved with assessing heart attack risk factors.

Refinement

Refining research into blood clotting

Dr Michael Emerson joined Imperial in 2005. He is Head of the Platelet Biology Group and his research focuses on the platelet blood cells responsible for triggering blood clots. He is looking at how risk factors such as pollutants can affect platelets in ways that increase the risk of a heart attack. Dr Emerson's group has recently been awarded its fourth award from the NC3Rs.

Dr Emerson says: "The nature of the research my group carries out – assessing platelet function in the context of other biological systems – requires an animal model. We inject the mice with a substance that activates platelets so that we can model conditions such as a heart attack.

Originally, the research was classed as a severe procedure by the Home Office, as it involved painful procedures and resulted in the death of the mice involved. Clearly there were major ethical opportunities to be gained from refining the way the research could be conducted.

My first NC3Rs grant was to refine the entire procedure so that it could be conducted under a general anaesthetic. This also allowed us to activate the platelets at a much lower level and measure the response using probes. These changes meant the mice involved in the research avoided the paralysis and suffering of the previous method, and also led to an 80–90% reduction in the overall numbers of mice used.

The second grant allowed us to infuse blood from humans, rather than other mice, into the recipient mouse. This reduced the number of mice required by a further 50%.

Our latest NC3Rs grant allows us to help increase uptake of this refined model among other institutes. This involves forming partnerships with research groups, identifying ways where they can reduce the number of mice involved in their research and providing training to help them reach this goal."

Replacement

New software for replacing animals

Dr Juliane Liepe joined Imperial in 2008. In 2013, she became one of a small number of researchers in the UK to be made an NC3Rs David Sainsbury Research Fellow. David Sainsbury Fellowships support exceptional, 3Rs-minded, early-career scientists.

Dr Liepe specialises in signalling processes during an immune response. She uses computational models to analyse imaging data from research involving animals. Her aim is to develop software to reduce or replace the animals required in future research.

The use of computational models has reduced the number of zebrafish needed for studying cell signalling processes.

> "The first time, we used 20 fish for the research and last time we used four. If you multiply that across similar research projects around the world, that's a big reduction in the number of animals."
>
> — *Dr Juliane Liepe*

Traditionally, mice were used to examine cell migration during this process. More recently, zebrafish have been used in this work, particularly for capturing images of the signalling processes. Dr Liepe says: "A lot of imaging data are collected but are usually used for presentation purposes rather than being analysed in detail. I felt there was a good opportunity to explore how computational models could use this data to reduce the number of animals required in future studies."

One year into the Fellowship, Dr Liepe and her collaborators are making significant progress on image processing, having moved from 2D to 3D data. The research has helped to develop computational models which are more efficient and reliable. Dr Liepe has spent a considerable amount of time developing software so that other researchers can use the same scripts to apply these methods to their own work. This will help further reduce the number of animals required in studies.

Another key part of Dr Liepe's work is developing statistics that allows cell migration behaviour to be quantified and used in a modelling system. Dr Liepe explains that this work is already leading to a reduction in the number of animals needed: "The first time, we used 20 fish for the research and this last time we used four. While that might not sound such a big number, if you multiply that across all similar research projects around the world, that's a big reduction in the number of animals being used. Biology is complex and so I don't think we will ever completely replace the need for some animal experiments because we will always need *in vivo* data. I do believe, though, that computational work will play a major role in reducing the numbers of animals required overall."

COMMUNICATING ABOUT ANIMAL RESEARCH

In January 2014, Imperial committed to more effective internal and external communication about animal research through its Action Plan.

A few months later, the College joined more than 70 UK organisations in signing the *Concordat on Openness on Animal Research,* which was developed in response to a 2012 opinion poll that showed the public wants to know more about what goes on in animal research. Here are some highlights of recent changes in the way that Imperial has become more open in how it communicates on this subject.

As an organisation that carries out animal research we have a responsibility to be transparent about what we do. We believe it's important to explain how and why we undertake research with animals, and to describe how it's regulated. If animal research has played a significant role in a scientific advancement, then we will say so — something that the College put into practice with its media releases over a decade ago.

The Action Plan and the Concordat have provided Imperial with further impetus to build on this foundation and communicate more widely about animal research, both within the College, and with external audiences.

Animal research newsletter for College researchers and animal technologists

In June 2014 the College launched the first issue of a monthly animal research newsletter for the community at Imperial. The original aim of the publication was to keep everyone working in animal research at the College informed about progress in implementing the College's Action Plan. But it soon grew into a popular publication with a broader remit to:

- Introduce staff recruited to the new roles set out in the Action Plan
- Celebrate and share good practice in the 3Rs, research and animal husbandry
- Improve mutual understanding of the respective roles of researcher and animal technologist
- Disseminate other internal and external news and broader animal research developments throughout the College's animal research community.

Making our staff and students aware of our work with animals

The College's *Annual Report and Accounts* for 2013–14 and its 2015–16 *Postgraduate Prospectus* feature prominent photographs and captions describing the College's work with animals, as part of our aims to make more people aware of our involvement with animals in research.

Building on this, the Provost's Board – responsible for delivering Imperial's core academic mission – agreed in December 2014 to let all new staff and prospective students know that Imperial carries out work with animals. It has agreed to include a formal statement to that effect in the further particulars used to recruit staff and in information for prospective students.

"My hope is that we can give our staff the confidence and support they need, so that talking about this important work becomes the norm rather than the exception."

— *Professor Maggie Dallman, Chair of AWERB*

Embedding a new approach to communications throughout the animal research governance model

The focus on communications in the Action Plan means that communications staff are represented on the Governance Board and the central AWERB. This enables us to enhance the way we communicate and engage with public audiences about our research with animals. Within the College community we can provide a more supportive culture for better communications, build stronger connections and share good practice.

Communicating about the process of animal research

In addition to communicating about the results of our research, we are also committed to raising awareness about the processes of how it is carried out and regulated.

In the past year we have published a series of online news stories on topics including progress with implementing the Action Plan, responses to external reviews into animal research at the College, and the College's commitment to the Concordat.

This information has been shared specifically with our collaborators and funders, many of whom are also Concordat signatories, as well as being made available to public audiences.

More opportunities for the public to find out about our animal research

In the past year, the College has committed to organising events in 2015 for stakeholders and public audiences about its work with animals, to support and further debate around the issues involved, and to build public awareness towards why this research is being done.

In March 2015, Imperial will be participating in the Open Lab Scheme run by Understanding Animal Research as part of British Science Week. This involves inviting schools to visit our animal research facilities and providing opportunities for students to meet scientists and explore why animals are used in research.

This approach is also feeding through into programming for large-scale College public events such as the Imperial Festival. It builds on work by our staff to share what they do with a variety of audiences. For example, one of our researchers is working on a science-art project (below).

In another example, animal technologist Amy Wathen won the prize for best first-time presenter at the 2014 Institute of Animal Technology congress for her talk about her work: "I got so much good feedback from other delegates. People said it made them feel more confident that there is real progression on openness. The more open senior academics are, the more technicians feel as though their work is receiving public support. To me, that's incredibly important."

During 2014 plans were firmed up to hold a public event to engage visitors with the role of animals in the College's biomedical research, and their contribution to improving animal and human health.

Enhanced communications about animal research

We have continued to develop the College's animal research web pages, originally launched in December 2013, so that they provide a good account of what we do and why and how we do it. The web pages include an expanding set of case studies of our work to promote better application of the 3Rs.

We also continue to highlight examples of where research involving animals has led to scientific advances. We do this through routes including:

- Committing to report annually on progress (through a report such as this one)
- Issuing media releases
- Publishing news stories on the College's online news service at **www.imperial.ac.uk/news**, where readers can leave comments and engage with the researchers about their work
- Giving public talks and supporting our staff to work with journalists to inform public debate.

In the summer of 2014, the College increased transparency by working closely with our animal technologists, researchers and a professional photographer to commission a series of photos to illustrate our animal facilities. The images depict some of the animals we work with, and provide an insight into how our staff care for them. They have been used in several of our publications, including this report.

Loop (work in progress) © Samantha Moore, an Animate Projects commission, supported by the Wellcome Trust

A watercolour sketch of zebrafish larvae as part of an animation project to foster partnerships between scientists and documentary makers. Dr Serge Mostowy is looking at how zebrafish respond to bacterial infections such as Shigella, *one of the main causes of dysentery. He is collaborating with animated documentary maker Samantha Moore on visualising the research.*

Committing to openness

The Concordat to Support the Career Development of Researchers

By signing the *Concordat on Openness on Animal Research* in May 2014, Imperial made the following commitments:

1. We will be clear about when, how and why we use animals in research
2. We will enhance our communications with the media and the public about our research using animals
3. We will be proactive in providing opportunities for the public to find out about research using animals
4. We will report on progress annually and share our experiences

FOR MORE INFORMATION

animal.research@imperial.ac.uk
www.imperial.ac.uk/animal-research/annual-report

Editor: Natasha Martineau
Contributors: Laura Gallagher, Kerry Noble, Sam Wong, Peter Zarko-Flynn
Production: Joanna McGarry

This publication is produced for Imperial's public audiences, and our funders, collaborators, staff, students and alumni. It is part of our commitment to report annually on progress with implementing our Action Plan for world class animal research, and forms part of our programme of activities to communicate more widely about our animal research.

This report is published by the Communications and Public Affairs Division. Additional multimedia content is available online.

www.imperial.ac.uk/animal-research