Home Office

NON-TECHNICAL SUMMARY

Model development for oncology drug discovery.

Project duration

5 years 0 months

Project purpose

- (a) Basic research
- (b) Translational or applied research with one of the following aims:
  - (i) Avoidance, prevention, diagnosis or treatment of disease, ill-health or abnormality, or their effects, in man, animals or plants

Key words

tumour models, medicine discovery, cancer therapy, in vivo pharmacology, tumour microenvironment

Animal types	Life stages
Mice	Adult

Retrospective assessment

> The Secretary of State has determined that a retrospective assessment of this licence is not required.

Objectives and benefits

Description of the projects objectives, for example the scientific unknowns or clinical or scientific needs it's addressing.

What's the aim of this project?

The purpose of this Project Licence is to develop and establish new models to support the discovery and development of new medicines to treat cancer.

Potential benefits likely to derive from the project, for example how science might be advanced or how humans, animals or the environment might benefit - these could be short-term benefits within the duration of the project or long-term benefits that accrue after the project has finished.

Why is it important to undertake this work?

In 2022, as published by the World Health Organisation, there were an estimated 20 million new cancer cases and 9.7 million deaths. In UK alone according to Cancer Research UK data, over the last decade (between 2006-2008 and 2016-2018), the cancer incidence rates increased by 4% and they are projected to rise further by 2% in the UK in the next 10-15 years to come; meaning that many more cases of cancer will develop in patients which will not be merely due to age.

Despite the significant advancements in treatment of cancer over the last two decades, there are still many types for which tumour-targeted therapies are not available. In other cases, such therapies are available, but treatment is not effective for all patients and many patients who do respond to these therapies will eventually develop resistance and their tumour grows back. Of those patients diagnosed in the UK, only 50% will survive for 10 years or more following their diagnosis.

In this Project Licence we aim to develop and establish new complex in vivo models for cancer therapeutics that are expected to better mimic the target organ biology of the patient. These new models will complement the existing models already used to study the mechanisms involved in cancer development to enable the development of new medicines for cancer patients The intention of this PPL is to build models, such as colorectal orthotopic, but may in the future diverge from orthotopic tumour models to include models for colitis or infection protocols. Our intention is to design separate protocols of each new model that would go through internal approval process before being added to this project.

What outputs do you think you will see at the end of this project?

This work will help establish complex models, like orthotopic tumour models, colitis models or infection models to name a few, that will be used to advance our experimental cancer medicines through multiple phases of research and development by evaluating their activity in animal models of disease. These models will mimic patient biology more accurately and thus will help us to develop an insight into whether the new medicines work in more relevant clinical settings and possibly could also enable us to identify potential targets for new medicines and thereby expand treatment options for cancer patients.

Equally, use of complex models developed under this project work may also guide us to determine which of the experimental medicines should not be progressed further. In addition to the outputs

mentioned above, we expect to publish our results and to present our findings externally to scientific peers.

We expect that such more patient relevant models which reflect human disease more accurately may reduce the use of traditional, less reflective models, thus reducing the number of animals used for experimental work as they will be more accurate to predict the drug outcomes to enable decisions whether the new medicines can be progressed to the clinical trials in relevant disease indications.

Who or what will benefit from these outputs, and how?

This programme of work is expected to enable us to develop patient-relevant disease models. Models established using this licence will be used to test and progress new cancer medicines which, if successful, will have the potential to benefit millions of cancer patients across the globe in the longer term. However, as the discovery of the new medicine is a slow process, in the short term these models will help progress the right format of the ‘candidate medicines’ through the discovery pipeline. These candidate molecules, if approved for use in the clinics, will then be available to treat patients with cancer who otherwise are likely to die from their disease.

The development of new or improved cancer models will help us to target the right patient populations with our medicines which will increase the likelihood that those patients will benefit from the treatment.

The work carried out under this licence is also expected to contribute knowledge to the broader scientific community through the publication of our findings and presentations at internal and external scientific meetings on regular basis.

How will you look to maximise the outputs of this work?

Our team has an excellent track record of publishing the advances in discovery of new medicines as well as animal modelling. We aim to publish both successful and unsuccessful experimental results in relevant scientific journals, and to share our data and learnings with numerous collaborators to avoid duplication of research work and efforts. We present our research at national and international conferences for the benefit of the broader scientific community. This public dissemination of our results has the potential to lead to new collaboration and opportunities to develop new innovative experimental cancer models and medicines as well as to further characterise or find new associated indicators of disease (biomarkers).

Species and numbers of animals expected to be used

- Mice: 400

Predicted harms

Typical procedures done to animals, for example injections or surgical procedures, including duration of the experiment and number of procedures.

Explain why you are using these types of animals and your choice of life stages.

Mice are one of the most commonly used animals for biological research, especially cancer research. This is because many more tumour models are available for mice, and a wealth of published data exists to help guide the experimental plans and interpret results. This is also true for tumour immunology studies. The immune system of mice resembles that of humans in many respects which means that tumours can be grown in these animals to create patient-specific models to investigate new experimental cancer medicines along with their effect on the immune response to tumours.

This research project will use mice to support our efforts to discover and develop novel therapies for cancer to benefit these patients. Specifically, we will use mice to enable us to mimic the complex aspects of the disease as well as the properties of the medicines that are currently not possible in a laboratory setting or by using simplistic research models. It is important to undertake this program of work to support the development of new formats and technologies that are being developed for cancer therapy and test them in a complex live animal model that imitates the nature of the disease. This program of work will establish models which will be used by the team to progress new cancer medicines through the discovery and development pipeline.

We will also use immunocompromised mice; these are mice that have defect in their ability to produce an immune response which allows human samples to grow in them without rejection. We use models termed as 'humanised'; by injecting both human immune cells as well as human tumours to model specific aspects of the disease that we cannot do in 'mouse only' systems.

Typically, we plan to use adult mice (6-14 weeks old) at the start of our studies as the immune system is considered immature in younger mice and would not represent the biology of the cancer patients we aim to treat.

Typically, what will be done to an animal used in your project?

Animals are kept in high-quality facilities, free from pathogens (disease-causing organisms such as bacteria, viruses, and parasites) and with access to food, water, and environmental enrichment. In all the facilities used, the animal care staff are highly trained in rodent welfare and will ensure the animal suffering is minimised. Animals are housed in groups except in exceptional circumstances, for example when aggressive behaviour puts the welfare of the animal at risk or when cage-mates have been removed for experimental reasons.

Most of the animals will be used for studies to create tumour models that better recapitulate (mirror and predict) the clinical circumstances and/or patient disease patterns. The vast majority of tumours will result from either surgical implantation or specialised injection of tumour cells or tumour or self-organising 3D tissue cultures (so called organoid) fragments into a specific organ (e.g. cecum or colon).

In most studies, we will use advanced imaging techniques (such as bioluminescence imaging, ultrasound etc.) that will allow us to monitor the tumour growth. To undertake such imaging sessions animals will be anaesthetised so that consistent and reproducible measurements could be taken in a motionless, sleeping animal.

Blood samples may also be collected during some studies to measure levels of cytokines or medicine, or human immune cell components in humanised models. Small volume, max 10% of total blood volume in a living animal at any one given time-point or 15% of total blood volume in a 28 day period, blood samples are taken from a vein while the study is ongoing, whereas larger blood samples are taken at the end of study if a greater volume (usually total blood is collected) is needed. Such a procedure will always be carried out at the end of the study under a non-recovery anaesthesia.

To establish and characterise the new tumour models we may also inject medicines, such as those used as standard of care in patients like chemotherapy or our own experimental cancer medicine-candidates. Medicines are commonly injected into the peritoneal cavity (i.p.; into the abdomen), intravenously (i.v.; into the tail vein). Occasionally medicines may be administered orally (oral gavage; o.g. or p.o.) or under the skin (s.c.; subcutaneously).

At times medicines may only need to be administered once, but more often they may be administered according to a schedule that requires multiple administrations. The administration schedule is usually determined by the properties of the medicines like their effectiveness, stability inside the living body etc. For example, medicines injected into the peritoneal cavity are typically given two to three times per week, whereas those given orally would typically be administered once or twice a day, often for the duration of the study. In most cases our studies last approximately one to two months but on occasion when tumours grow slowly, they could last for 6 months.

Following is an example of typical steps in a study with an immunocompromised host animal to develop the orthotopic colorectal tumour model (Protocol 1):

1. implantation of a microchip under the skin (s.c.) for identification

2. injection of human immune cells into the tail vein (i.v.)

3. surgical implantation of tumour cells into a target organ (e.g. cecum or colon)

4. tumour measurement/ monitoring

5. administration of experimental or standard of care (SoC) medicine by one or more of the following routes: i.p. into the peritoneal cavity (typically this will be done twice a week for three weeks); intravenous i.v. into the tail vein (typically this will be done once or twice a week for 3-4 weeks); orally (by gavage; (typically this is done once or twice a day for the duration of the study)

6. collection of a blood sample(s)

At the end of procedures, all animals will be humanely killed. Tumour, blood and other organs may be collected for any analysis.

The steps in a typical study involving the non- immunocompromised host animal will be the same as above except for step 2 which will not be needed.

What are the expected impacts and/or adverse effects for the animals during your project?

In these studies, the likeliest sources of adverse effects are from surgical procedures, size and condition of the tumour, or in humanised models from graft versus host disease (GvHD). “Graft” here refers to transplanted human immune cells “host” refers to the animal.

Animals will undergo surgical procedures for tumour implants and are expected to experience pain due to the surgery and will be classified as moderate severity. Anaesthetic and pain relief (analgesia) will be provided when surgery is performed as per veterinary consultation.

GvHD is a systemic disorder that occurs when the graft's immune cells recognize the host as foreign and attack the recipient's body cells. Animals will be classified according to a scoring system that is in place and is based on the degree and duration of clinical observations such as body weight, activity level, posture, and body condition.

We will humanely kill any animals that have developed large tumours or have developed tumours that are impeding any movement or leading to significant abdominal swelling due to fluid accumulation to minimise unnecessary suffering.

At times, use of genetically modified mice is necessary for our work. Some of which will be immunocompromised mice, such mice may experience hock swelling. Mice will be assessed, using a score sheet, based on the size, capacity to grip, presence/absence of superficial lesion and gait. Affected mice may be given altered enrichment and/ or pain relief and/or anti-inflammatories in consultation with the veterinary advice. Mice that are unable to grip, reluctant to move or are affected bilaterally, with associated gait disturbance, will be humanely killed. Any treated mice that do not respond within 10 days of treatment onset will also be humanely killed.

Clinical signs will be seen in majority of the animals undergoing procedures in this Project License. Typically, clinical signs will be moderate in severity due to involvement of the surgical intervention. Animals are expected to recover well from surgery before they are enrolled for any drug treatment. From experience, clinical signs will include gradual weight loss of up to 20% from maximum weight, partial to marked piloerection, transient to intermittent hunching in the posture, subdued (toned down) but responsive behaviour, abnormal walking, short term ataxia (uncoordinated movements), intermittent diarrhoea. Some animals may also develop paleness in extremities.

Treatment of animals with cancer therapies may also lead to unwanted effects like those experienced by human patients. While humans may experience fatigue or fever soon after receiving the therapy, we observe similar responses in mice such as reduced mobility, hunched posture, and piloerection (bristling of fur). Most of these effects will be mild and of short duration; however, some animals may experience moderate effects like, gradual weight loss of up to 20% from maximum weight, partial to marked piloerection, transient to intermittent hunching in the posture.

For such animals we’ll have monitoring and control measures in place such as dosing animals early during working hours and observing animals for any adverse reactions and if animals are rapidly losing weight, then supportive measures such as wet mashed food or diet gels will typically be provided.

At the end of procedures, all animals will be humanely killed and humane endpoints will be applied under veterinary guidance as necessary.

Expected severity categories and the proportion of animals in each category, per species.

What are the expected severities and the proportion of animals in each category (per animal type)?

Moderate; 100%

What will happen to animals used in this project?

- Killed

Replacement

State what non-animal alternatives are available in this field, which alternatives you have considered and why they cannot be used for this purpose.

Why do you need to use animals to achieve the aim of your project?

This research project will use animals to support our efforts to discover and develop novel therapies for cancer to benefit these patients. Specifically, we will use animals to enable us to mimic the complex aspects of the disease as well as the drug properties that are currently not possible in a laboratory setting or by using simplistic research models. It is important to undertake this program of work to support the development of new drug formats and technologies for cancer therapy and test them in a complex live animal model that imitates the nature of the disease. This program of work will establish models which will be used by the team to progress new cancer medicines through the drug discovery and development pipeline.

We do conduct numerous in vitro experiments in the laboratory using cells, 3D tissue cultures (organoids mixed culture of cells of different origins and types; use molecular biology, and computer simulation modelling techniques to answer some of the questions, but it is still necessary to use some animals for research so that we can more accurately model the biology of the disease as well as the interactions of cancer cells with other cells and organs within a living body.

Isolated mixed culture of cells of different origin or 3D cell culture do not reproduce the complex nature of in vivo (in a live animal) biology. The use of animals will allow us to understand cancer in the organ of origin or as it spreads throughout the body. The most crucial aspect of our work is to understand the biology of the disease in an ‘as it is’ settings that resembles the patient situation more accurately, and then to extend this understanding in discovering the biology of different immune cells to harness them to attack tumours.

And it is not possible to fully recreate such complex system and interactions outside of a living animal. Thus it has to be a combination of in vitro and in vivo studies that provide the insight needed to understand cancer biology and develop new therapeutic approaches to treat it.

Which non-animal alternatives did you consider for use in this project?

Our department regularly uses computer modelling to fine tune the discovery of experimental medicines. A range of in vitro experiments are undertaken in laboratory dishes, containing single cell type or multiple cell types cultured together, which allows to study both direct interaction and indirect communication among different cell types. These are well-established 2-dimensional experiments that are useful to understand the specific ways that our experimental medicines affect tumour cell function.

We are now also regularly using more complex 3D experimental systems, such as patient-derived organoids and/or tumour slice culture system (TSC). In such system, the biological samples donated by patients are collected and processed (e.g. cut into thin slices in case of TSC) and then cultured in vitro. These methods preserve the spatial architecture and/ or the 3D structure of a patient tumour and are believed to be more representative of the biology of the whole tumour compared with the 2D experiments mentioned above.

Such experiments can only be undertaken for short durations of time due to practical considerations and/or viability of the patient material, however they are useful to find the lead experimental medicines that can be tested in animal models.

Why were they not suitable?

Cell-based methods are useful to gain an understanding of the way that experimental medicines impact the function of different cell types outside the body but cannot sufficiently demonstrate whether the cancer medicines remain stable after they enter the body, can reach the site of the tumour, or whether they are capable of inhibiting tumour growth in a live animal.

The 3D assay systems setup using the samples donated by patients (e.g. tumour slice or organoid cultures) are valuable additions to our experimental toolbox, however they have a short lifespan and can show modification of cellular functions but may not demonstrate that this effect can shrink a tumour.

None of the alternatives can demonstrate how the experimental therapies will behave in an organ specific pathological setting where biology could be very different due to numerous reasons like dysregulation (change in behaviour) of genes or due to impenetrable stroma (dense boundaries formed by some specific cell types and/or other components) in the tumour microenvironment, to name a few. The relatively simplistic in vitro experiments also cannot provide information like how the experimental medicines might be broken down by the body nor they can allow identification of specific signals produced in the body which can be linked to tumour growth inhibition or relapse.

Reduction

Explain how the numbers of animals for this project were determined. Describe steps that have been taken to reduce animal numbers, and principles used to design studies. Describe practices that are used throughout the project to minimise numbers consistent with scientific objectives, if any. These may include e.g. pilot studies, computer modelling, sharing of tissue and reuse.

How have you estimated the numbers of animals you will use?

This estimate is based on the way we anticipate running this model. Typically, few pilot studies will be run to establish surgical techniques and model conditions. Once these are established then validation studies will be run before the model can be run in the efficacy studies. The estimated number includes how many animals per study, how many studies of each type and some allowance for anticipated issues or changes in demand.

What steps did you take during the experimental design phase to reduce the number of animals being used in this project?

Our organization has a "Good Statistical Practice" program instituted by a team of Biostatisticians where animal experimental designs are formally reviewed before they start. This review is conducted by a researcher proposing the experiment and a supporting statistician team to ensure the goal, experimental design, and data analysis align. This process ensures the design is robust and that the data can be statistically reliably interpreted to answer the scientific question. In this process of design, it is ensured that elements of blinding and randomisation are also included, where possible. Animals are typically randomly assigned to the cages.

Blinding: All studies are blinded at the point of measurement. But because we work with experimental medicines that can have transient side effects, we need to be able to identify agents dosed and therefore the whole pipeline will not be blinded.

Randomisation: Randomisation is typically conducted based on body weight or tumour volume of the animals. A custom-built tool is generally be used to randomise animals to groups using minimisation (Altman and Bland 2005).

We also collaborate extensively within university and outside and use practical learnings from experience of such collaborators before and during setting up of the pilot experiment for new models.

Moreover, we also use the following guidelines and online tools while designing our animal studies:

- The NC3Rs Experimental Design Assistant, found at https://www.nc3rs.org.uk/experimentaldesign-assistant-eda

- The PREPARE Guidelines, found at https://norecopa.no/prepare

- UK Co-ordinating Committee on Cancer Research (UKCCCR’s) Guidelines for the welfare and use of animals in cancer research, updated in this paper: Workman et al. British Journal of Cancer; 2010: 102, 1555–1577.

- OBSERVE: guidelines for the refinement of rodent cancer models (De Vleeschauwer et. al., Nature Protocols; 2024: 19, 25712596).

What measures, apart from good experimental design, will you use to optimise the number of animals you plan to use in your project?

Small scale pilot studies will be carried out for each new tumour models establishment which then would be used to design next studies using the minimum number of animals needed to achieve the scientific objectives. We also implement innovative study designs to reduce animal numbers where

possible. We will analyse tissues from previous experiments and from collaborators whenever possible (e.g. to confirm the expression of target gene before selecting the appropriate tumour model for our experiments). We will avoid repeating experiments for additional data collection by collecting a wide range of tissues at the time of euthanasia. And we will aim to disseminate negative results from our studies i.e. cases where compounds or models were not effective, to inform the wider scientific community. This will reduce the need to repeat experiments in the future.

Refinement

Give examples of the specific measures (e.g., increased monitoring, post-operative care, pain management, training of animals) to be taken, in relation to the procedures, to minimise welfare costs (harms) to the animals. Describe the mechanisms in place to take up emerging refinement techniques during the lifetime of the project.

Which animal models and methods will you use during this project? Explain why these models and methods cause the least pain, suffering, distress, or lasting harm to the animals.

To mimic the organ specific features of a particular tumour type, we have to use complex experimental models where tumours may often develop inside the body of the animal. Such complex models may involve surgical methods to implant tumours, either in a cell suspension form via injection or that of tumour fragments.

Where possible, minimal invasive surgical methods will be used for implantation and imaging techniques to monitor tumour size. Such methods of tumour implantation are less painful for the animals and the distress caused is usually temporary that goes away in a couple of days. Methods will be chosen and put in place to allow the animals to be as mobile as possible, high standards of enrichments will be provided and the animals will be group housed wherever possible. Prior to start of any surgical procedure, we will agree with a Veterinary surgeon what pain relief medications or antibiotics are appropriate, both before and after the surgery. When recovering from surgery, we keep animals warm and monitor them closely until they display normal behaviours. They will be monitored closely on daily basis before they go on study. Where possible, appropriate imaging methods will be used to monitor tumour formation and progression.

We have also established methods like fine needle aspiration method which enables to sample tumours like similarly to biopsies taken from patients, and thereby reducing the need to run separate pharmacodynamic studies where possible.

Why can’t you use animals that are less sentient?

The mouse is the model organism that resembles humans most closely. The human and mouse genomes are almost of the similar size, and display an equivalent number of genes, which are functionally conserved. They are the least sentient species whose physiology is very similar to humans allowing us to adequately study the complex biology of human cancer and immune system and their interactions. Because many of our experimental therapies are designed to impact the immune system, it is essential that we use animal models that will be instrumental to generate data which can be

directly translated in meaningful design of clinical trials later. Currently less sentient model animals, like C. elegans, Drosophila or Zebrafish, are not suitable for research that involves interactions among different cell types (cancer cells, immune cells) of human original especially if we also want to model the organ specific biology of the disease for such interactions.

Our studies also monitor the growth of a tumour over a period of weeks to months therefore it is essential that the animals are conscious as the use of anaesthesia (an agent that induces a state of unconsciousness) would not be possible for such an extended period. In addition, the behaviour of conscious animals also often alerts us to adverse reactions to our therapies.

How will you refine the procedures you're using to minimise the welfare costs (harms) for the animals?

We are committed to refining our procedures to minimise harm to the animals and have a track record of doing so. We ensure small-scale pilot studies are carried out for establishing new tumour experimental methods, or therapy testing. We carefully monitor tumour burden including the use of whole-body imaging techniques when possible. We have implemented innovative study designs to reduce animal numbers and enhanced health checks to minimize suffering. General welfare of the animals is assessed by checking body weight and watching for the development of clinical signs such as activity levels, appearance of the coat, posture, and body condition.

We are constantly refining our surgical implantation techniques including that for patient-derived xenograft (PDX) tumour fragment passage. We are currently implementing the use of a trocar as a means of minimally invasive implant (a trocar is a veterinary device that can be used for implantation of small fragments of tissue subcutaneously without the need for wound closure. We are constantly refining the use of analgesia and anaesthetic regimens with constant inputs and discussion with Veterinary surgeon and animal welfare officers. We have developed a GVHD (graft versus host disease) scoring method that we are constantly refining to ensure welfare and scientific objectives are well balanced. We also intend to develop and continually refine separate scoring systems for each new complex model that we set up as such models may lead to new adverse effects that are outside the general clinical signs usually seen. Where possible we combine multiple experimental medicines that are to be injected via the same route at the same time, to minimize the number of injections administered to the animals. When unexpected events occur, these are thoroughly investigated to find out what happened so action can be taken to prevent a reoccurrence.

Animals may also be given extra bedding or enrichment to help support wellbeing and will be provided warmth during the surgical procedure and recovery phase thereafter. Animal losing weight approaching 8% of top recorded body weight will be provided food supplements like diet gels and/ or wet mashed food.

Hypodermic needles will always be discarded after a single injection so that blunted needles (which can cause unnecessary tissue injury and pain) are not used.

For tamoxifen usage, an internal guidance document developed by the Veterinary surgeons in the establishment will be followed.

Animals imported from outside the establishment will have a standard acclimatisation period as set by the establishment. The acclimatisation process is the period during which newly arrived research animals are allowed to fully recover from stress of transport to adjust to the new surroundings, feed, light/dark cycles, cage mates etc. Currently these are set at 7 days for national shipments or 14 days for international (overseas) shipments.

What published best practice guidance will you follow to ensure experiments are conducted in the most refined way?

Our practices follow the ARRIVE guidelines developed by NC3Rs for publication of our work in peer-reviewed journals (ARRIVE Guidelines version 2.0 released in July, 2020 can be found at https://arriveguidelines.org/).

Our practices incorporate many of the guiding principles of the PREPARE guidelines (Smith et al., PREPARE: guidelines for planning animal research and testing. 2017. Laboratory Animals). LASA (Laboratory Animal Science Association) also has a range of published guidance documents with principles that can be applied to our animal studies which are found at https://www.lasa.co.uk/current_publications/

Our team also closely follows the advances and best practices in 3Rs through the NC3Rs and establishment websites and via participation in conferences and events sponsored by organizations such as IAT (Institute of Animal Technology), LASA (Laboratory Animal Science Association, or NC3Rs about the best practices and refinements in the surgical as well as other procedures/ practices involving our in vivo work.

We also follow and incorporate well recognised and published guidelines to refine our workflows and best practices, like- UK Co-ordinating Committee on Cancer Research (UKCCCR's) Guidelines for the welfare and use of animals in cancer research, updated in this paper: Workman et al. British Journal of Cancer; 2010: 102, 1555–1577; as well as the latest published guidelines: OBSERVE: guidelines for the refinement of rodent cancer models (De Vleeschauwer et. al., Nature Protocols; 2024: 19, 2571–2596) for tumour burden monitoring, expected adverse events and for selecting the appropriate humane endpoints based on overall clinical signs including tumour burden.

How will you stay informed about advances in the 3Rs, and implement these advances effectively, during the project?

Our organisation is committed to the 3Rs and continues to follow advances in the community. We routinely hold Symposia and invite external speakers to talk on these topics and we have a dedicated 3Rs contact who regularly disseminates information related to 3Rs.

Our team is actively involved in promoting the 3Rs and participates in global 3Rs activities including an annual poster competition. This award was given to individuals working on the development of alternative models e.g. a team working on an ex vivo (taken directly from a living organism) tissue slice culture system in 2017.

Our team also is aware of advances in 3Rs through the NC3Rs and establishment websites and via participation in conferences and events sponsored by organizations such as LASA (Laboratory Animal

Science Association, IAT (Institute of Animal Technology) or NC3Rs.

We as organisation are also actively seeking to adopt and implement New-Approach Methodologies (NAMs) and Non-Animal Technologies (NATs) where such methodologies are available for the scientific purposes that align to our projects.