

Industry Report



UK animal experiment statistics indicate reluctance to embrace modern tools to advance British labs into the 21st century

Dr Lindsay Marshall

Recently published Home Office statistics [1], have revealed that a high number of dogs, mice, cats, rabbits and other animals – some 3.52 million - are still being used in British laboratories despite availability of high-tech and often more human-predictive non-animal approaches.

Humane Society International (HSI) Senior Scientist Dr Lindsay Marshall, who for 12 years managed a laboratory dedicated to animal-free research into respiratory diseases, offers views on some of the reasons that might be preventing a much higher uptake of non-animal techniques that could offer a viable alternative to the use of animal models in research and industry.

“As a scientist myself, I know all too well the drawbacks of relying on animals to study and treat human disease. The fact is that animal models fail far more often than they succeed, so it’s hugely frustrating and worrying to see the UK, year after year, failing to move away from outdated animal experiments. It’s high time UK research funding bodies stopped squandering British taxpayer money and charitable donations on dead-end research and made a serious investment in human organoids, organs-on-a-chip, computerised systems biology models and other advanced, non-animal technologies that are the true future of modern medical research.”

Dr Marshall pointed out that in 2010 the Government made a commitment to reduce animals used in scientific research; but almost 10 years after this declaration of intent [2], the UK remains one of the highest lab animal users in Europe. In those same years, non-animal technologies that can produce faster, cheaper and more human-relevant results, have advanced enormously:

- Computers are much better than animals at predicting possible toxic effects of chemicals and drugs [3]
- The discovery of induced pluripotent stem cells has helped to remove the ethical barriers to stem cell use [4]
- Scientists have created human-mimetic systems of almost every organ in the body. There is a human-on-a-chip for drug testing [5], a patient-on-a-chip is not far away [6] and chips have travelled to space to investigate the impact of ageing on the human body [7].

Dr Marshall is not alone in her opinion. A raft of academic reviews from expert scientists in a range of fields reach the same conclusion for conditions as diverse as autism, cardiovascular disease, liver disease, diabetes, and Alzheimer’s disease [8] and they call for more investment in human-relevant methods.

“I think that there are many reasons for a reluctance to move away from animals. There is a culture of inertia in research, where animal models have been developed in and are used by a lab, these will be ‘favoured’ by the researchers and they may see no reason to change or adapt to more relevant, human-focused approaches. Fear of the unknown. There’s an element of familiarity in how to use the animals and understanding the outputs from the animals, that enables persistence of animal models and does not take into account the huge species gap that exists between animals and humans that impacts translation efficiency. Anecdotally, we have heard of more junior researchers being taught and expected to use, the animal methods by their PI, despite a desire to use more human and humane approaches. There is also a requirement to consider the research question in applying non-animal approaches for the first time - there are no simple like-for-like replacements such that a single in vitro assay will stand in for an animal model. We (HSI) do not see this as a reason to continue using the animal models, or to spend scant research resources ‘tweaking’ existing animal models to create something

symptomatically similar to a human condition. Instead, we suggest that researchers look to articulate their research questions in a manner that reflects the novel methodologies emerging and that considers how these methods may be incorporated into a program of research in order to address a specific research question. We believe that framing the question to enable exploitation of the suite of continually developing non-animal methods that are rapidly advancing human relevant science, without compromising safety or discovery, is more likely to translate to much needed treatments and interventions, enables better understanding of human disease. Education and training are required (see below), but at all levels, not just newly qualified researchers.

Is the UK government investing enough in research structure support, funding, partnership incentives, graduate/technician education and training?

There are some initiatives already- eg the NC3Rs, the Medicines Discovery Catapult - but much of the funding for purely non-animal research is through charities and so is extremely limited and incredibly competitive. The NC3Rs funding for Replacement is combined with initiatives to refine and reduce animal use and it is apparent that this, estimated as around 3% of total research funding in the UK, is not sufficient to encourage the move away from animals. We feel that the Research Councils could use their strategic science roadmaps to help the transitioning of UK life science research to a human biology-based, non-animal paradigm (akin to the US National Academies vision of ‘Toxicity testing in the 21st century’ or Tox21), with augmented funding for cutting-edge human-relevant technologies and approaches such as human organoids, organs-on-a-chip and elucidation of pathways of human disease and disorders.

Education is an important point - there are recognised gaps in training not just for non-animal methods, but ethics and welfare, (see https://www.theguardian.com/higher-education-network/2016/dec/10/we-are-getting-animal-research-wrong-only-education-can-fix-it?CMP=share_btn_tw). Creating a UK workforce that understands the value and utility of non-animal approaches necessitates revising educational curricula to include modern, relevant, non-animal technologies (e.g. human pathways-based methods). Synchronising educational curricula with high level research objectives is needed to develop a strong, capable workforce—appropriately qualified researchers responsive to challenges facing UK science (and consistent with implementation of the Animal (Scientific Procedures) Act). The European Union has just announced their intention to develop online modules for training in non-animal approaches (<https://iivs.org/2019/07/16/iivs-partners-win-contract-from-ec-for-training-non-animal-testing-methods/>), but we obviously do not know of the UK’s ability to access this after October. Raising awareness is key, but has to go beyond educating budding scientists and tackle that inertia of the established researchers refusing to put down their mice!

What incentives do you feel could be more helpful to industry –for example, financial (eg through regulatory changes; tax breaks; employment assistance schemes) and through supported research partnership initiatives?

Actually, industry are leading the way- in the UK, the number of animals used for regulatory purposes is on the decrease, as the non-animal methods seem to be embraced by industry, perhaps due to the Tox21 initiative which was developed in the US and uses human cell-based assays to develop more efficient approaches in predicting how substances impact human health. Increases in data outputs and efficiency with

these approaches have vastly reduced the use of animals in toxicity testing such that 'only' 26% of procedures in the UK in 2018 were for regulatory purposes. One of the barriers to wider uptake of the non-animal approaches for regulatory purposes are the geographical differences in requirements and we at HSI have been calling for global harmonisation for regulatory requirement for some time, and through our work with intergovernmental bodies like the OECD, we are trying to accelerate global adoption of non-animal testing methods.

Recently, reviews of the need for animal research facilities in the UK have led to closure of the Wellcome Sanger Institute [9] illustrating the growing recognition within the scientific community that a paradigm shift away from animal use is essential for medical progress. Recognition that fewer animals are required due to a "rise in the use of alternative technologies" [10] is a step in the right direction, yet the Home Office animal use statistics indicate that there is much more work required to reduce the body count Dr Marshall added.

1. 2018 Home Office statistics: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/818158/annual-statistics-scientific-procedures-living-animals-2018.pdf
2. <https://publications.parliament.uk/pa/cm201011/cmhansrd/cm110718/wmstext/110718m0001.htm>
3. Passini, et al. 2017 Human In Silico Drug Trials Demonstrate Higher Accuracy than Animal Models in Predicting Clinical Pro-Arrhythmic Cardiotoxicity. *Front Physiol.*8:668. Luechtefeld et al. 2018 Machine learning of toxicological big data enables read-across structure activity relationships (RASAR) outperforming animal test reproducibility. *Toxicological Sciences.* 165 1, 1 September 2018: 198-212
4. <https://www.eurostemcell.org/lips-cells-and-reprogramming-turn-any-cell-body-stem-cell>
5. <https://hesperosinc.com>

6. Edington et al. (2018) Interconnected Microphysiological Systems for Quantitative Biology and Pharmacology Studies. *Sci Rep.* 2018 Mar 14;8(1):4530. doi: 10.1038/s41598-018-22749-0
7. <https://ncats.nih.gov/tissuechip/projects/space>
8. Savoji, et al. 2018 Cardiovascular Disease Models: A Game Changing Paradigm in Drug Discovery and Screening. *Biomaterials.* 10.1016/j.biomaterials.2018.09.036
- Boeckmans et al. 2018. Human-based systems: Mechanistic NASH modelling just around the corner? *Pharmacol Res.* 134:257-267. 10.1016/j.phrs.2018.06.029
- Muotri, A. R. 2016. The Human Model: Changing Focus on Autism Research. *Biol Psychiatry.* 79;8: 642-9.
- Bowman, et al. 2018. Future Roadmaps for Precision Medicine Applied to Diabetes: Rising to the Challenge of Heterogeneity. *Journal of Diabetes Research.* 10.1155/2018/3061620
- Clerc, et al. 2016. A look into the future of ALS research. *Drug Discov Today.* 21;6: 939-49
9. <https://www.sanger.ac.uk/news/view/sanger-institute-animal-research-facility-close><https://www.nature.com/articles/d41586-019-02002-y>
10. <https://chemicalwatch.com/77872/sanger-institute-announces-closure-of-animal-research-facility>
11. https://ntp.niehs.nih.gov/liccvam/meetings/liccvam-forum-2019/06-lee-ncats_508.pdf

Are you working with methods or ideas that could transform the need for animals in research? Are you a producer of technology that reduces the needs for such tests?

We would welcome your feedback on the above – please email heather@intlabmate.com



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