People for the Ethical Treatment of Animals Foundation (PeTA) – Written evidence (LSI0043)

Summary

1. The UK has provided valuable leadership concerning the replacement of animals used in research, and in ensuring the promotion of new technologies.[1] However, there are many opportunities that the UK has yet to exploit. In this submission, we wish to draw the Committee's attention to areas where we should build on relevant national and international initiatives, and to comment on ways in which existing requirements regarding the use of animals in experiments may be affected by the UK's decision to leave the European Union.

2. We recommend that the House of Lords Science and Technology Select Committee (the Committee) explicitly identify scientific advances that provide opportunities to fully replace animal use in areas of biomedical research and regulatory testing, many of which we discuss in further detail in the appendix[2], and reiterate the requirement, as set out in the Animals (Scientific Procedures) Act 1986, to promote the replacement, reduction and refinement of animal use (the 3Rs).

3. Furthermore, there is a considerable societal demand for the ethical concerns surrounding experiments on animals to be fully addressed, and we recommend that this be reflected in any new industrial strategy. In addition, there is growing evidence that replacing failing animal studies currently used in preclinical pharmacology and toxicity testing is necessary to address late-stage failures in the drug-development process.

4. Our key recommendations can be summarised as follows:

    - **Science and Innovation:** Increase innovation by funding more non-animal research that focuses on human biology-based interventions.
    - **Industrial Strategy:** Increase investment in reliable, innovative animal-free methods and bold policy initiatives that work towards ending the use of animals in life sciences research.
    - **NHS procurement and collaboration:** Support NHS-researcher collaboration initiatives, such as biobanking, to integrate the NHS directly into the development of new human-relevant technologies.
    - **Responsibility and accountability:** Make the Life Sciences Industrial Strategy accountable to citizens through Parliament. The Government's role should be to formulate the strategy and seek the endorsement of

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1 CRACK IT. Replacement. n.d. Retrieved from https://crackit.org.uk/primary-rs/replacement. Accessed September 2017.

2 Appendix can be found at https://www.peta.org/wp-content/uploads/2017/04/Trump_Team_Packet_r5_72.pdf 'Advancing Biomedical Research and Regulatory Policies for Human and Animal Health', January 2017.

Parliament, allowing full parliamentary scrutiny of relevant proposals and budgets.

- **Brexit**: Increase transparency in relation to animals used in scientific procedures and establish a clear policy within a legislative framework which sees a commitment to the development, validation and implementation of non-animal methods.

Science and Innovation

1. How can investors be encouraged to invest in turning basic life science research into new innovations in treatment? Why has investment been lacking in this sector? Does the research base have the necessary infrastructure to be world-leading?

5. A likely reason for the poor investment in life science research is the high attrition rates seen in the development of new therapies, which is caused by the use of experiments on animals that are poorly predictive of toxicity and efficacy in humans.[3] The appendix[4] includes further information on specific areas of research that should be ended immediately due to the failure of experiments on animals to lead to human therapies. Attrition represents a significant financial burden for industry – the cost of developing a drug is estimated at $1778 million, however without attrition this reduces to $394 million.[1] As animals are not sufficiently predictive of human responses, their continued use will not address this issue.[5] Investment in non-animal technologies, on the other hand, could increase returns and encourage new investors.

6. While we recognise the UK has initiated activity likely to further non-animal technologies, for example through the Innovate UK's "A non-animal technologies roadmap for the UK"[6] it appears that the proportion of the UK's science budget currently allocated to non-animal research remains relatively small and that this continues to be a major obstacle to the advancement of this innovative field.[7] Most of the Government's work towards the promotion and funding of innovative non-animal research methods is performed by the National Centre for the Replacement, Refinement and Reduction of Animals in

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3 Non-Animal Technologies Special Interest Group. Potential applications of non-animal technologies. n.d. Retrieved from https://connect.innovateuk.org/web/non-animal-technologies/applications-and-opportunities. Accessed August 2017.

4 Appendix can be found at https://www.peta.org/wp-content/uploads/2017/04/Trump_Team_Packet_r5__72.pdf 'Advancing Biomedical Research and Regulatory Policies for Human and Animal Health', January 2017.

5 Hartung T. Food for Thought Look Back in Anger – What Clinical Studies Tell Us About Preclinical Work. *ALTEX.* 2013;30(3):275-291.

6 Innovate UK. A non-animal technologies roadmap for the UK Advancing predictive biology. 2015. Retrieved from https://www.gov.uk/government/publications/non-animal-technologies-in-the-uk-a-roadmap-strategy-and-vision. Accessed September 2017.

7 Ram R. Young researchers – the ethical challenge. *Alternatives to laboratory animals: ATLA.* 2015;43(6), 72-7.

Research (NC3Rs). However, the core funders of the NC3Rs - the Medical Research Council (MRC) and the Biotechnology and Biological Sciences Research Council (BBSRC) – dedicate only a small fraction of this funding towards non-animal technologies. For instance, only £1.2 million of the BBSRC's £332 million research budget in the 2015–16 period was dedicated to the 3Rs.[8] In total, the NC3Rs have an annual budget of only £10 million.[9]

Recommendation

7. The new Life Sciences and Industrial strategy must outline how the UK will increase investment in non-animal methods, and communicate the economic benefits that such investment will inevitably bring.

2. Why has the UK underperformed in turning basic research in the life sciences into intellectual property? What needs to be done to address this historic weakness in the UK and grow new companies to commercialise new research and related technologies in the life sciences?

8. Companies and researchers with the potential to develop new therapeutic products would benefit from regulatory changes to allow greater use and acceptance of non-animal preclinical pharmacology and toxicology testing.

9. Currently, researchers developing therapies that show promise in non-animal models of disease, for instance by producing changes in human-relevant models at the cellular or molecular level, may be presented with a restrictive choice between demonstrating the effect in an animal model (that may poorly predict effects in humans, see appendix[10]) or not taking their project forward.

10. Many scientists have come to realise that most of the published findings from experiments on animals over the past 20 years are either inaccurate or false. A 2015 analysis concluded that between 50 and 89 percent of all preclinical research could not be reproduced, which, at the most conservative U.S. estimate, results in an approximate annual spend of $28 billion on misleading experimentation.[11]

11. Likewise, several standard "animal models of disease" have been called into question by researchers themselves and their inherent failings are likely to hinder rather than advance promising new therapies.[12]

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8 Biotechnology and Biological Sciences Research Council. Research Spend by Research Topic and Investment Mechanism. n.d. Retrieved from http://www.bbsrc.ac.uk/about/spending/research-spend-topic-investment-mechanism. Accessed July 2017.

9 National Centre for the Replacement Refinement & Reduction of Animals in Research. Our Funding. n.d. Retrieved from https://www.nc3rs.org.uk/about-us/funders. Accessed September 2017.

10 Appendix can be found at https://www.peta.org/wp-content/uploads/2017/04/Trump_Team_Packet_r5_72.pdf 'Advancing Biomedical Research and Regulatory Policies for Human and Animal Health', January 2017.

11 Freedman LP, et al. The economics of reproducibility in preclinical research. *PLOS Biol.* 2015:13.6:e1002165.

12 Langley, et al., (2015). *Lessons from Toxicology: Developing a 21st-Century Paradigm for Medical*

12. While there are many factors at play in the failure of experiments on animals to predict human outcomes reliably—including reporting and publication bias, poor study design, and inadequate sample size—intrinsic biological and genetic differences between species contribute significantly to problems in extrapolating results from nonhuman animals to humans. According to a 2014 review paper in the BMJ:

> *"Several studies have shown that even the most promising findings from animal research often fail in human trials and are rarely adopted into clinical practice. For example, one study found that fewer than 10% of highly promising basic science discoveries enter routine clinical use within 20 years… [I]f research conducted on animals continues to be unable to reasonably predict what can be expected in humans, the public's continuing endorsement and funding of preclinical animal research seems misplaced".*[13]

13. New ways of integrating research findings and evidence into health policy and practice are needed to ensure uptake and implementation of evidence-based interventions, with a focus on exclusively human biology-based technologies.

Recommendation

14. The UK must move away from animal-based research and encourage and support the progression of scientists who focus on innovative mechanistic methods including *in silico*, *in vitro*, and *in chemico* models. This approach would increase our fundamental understanding of disease and also mitigate the risk from unreliable experiments on animals, which can lead to promising cures being discarded and to the progression of dangerous drugs, due to differences between human and animal biology and physiology.

    Furthermore, we recommend that a systematic review of all areas of research using animals be conducted, as this would be an effective catalyst for a shift in research priorities towards human-relevant innovations. Our appendix may serve as a starting point for such a review.[14]

3. What can be done to ensure the UK has the necessary skills and manpower to build a world class life sciences sector, both within the research base and the NHS?

15. Universities must be required to offer modules on animal free approaches, including in toxicology courses. A lack of specific courses and guidance for young scientists and a perceived lack of choice regarding careers in science

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Research. Environmental Health Perspectives, 123(11), pp. A268-A272.

13 Pound P and Bracken MB. Is animal research sufficiently evidence based to be a cornerstone of biomedical research? *BMJ*. 2014:348:g3387

14 Appendix can be found at https://www.peta.org/wp-content/uploads/2017/04/Trump_Team_Packet_r5_72.pdf 'Advancing Biomedical Research and Regulatory Policies for Human and Animal Health', January 2017.

means that the UK is currently at risk of lacking the required skill-set to be a world leader in innovative and cutting-edge scientific methodology.

16. Furthermore, scientists using animal-free methods are often pushed to test on animals by funding bodies, journal reviewers, and the regulatory authorities. For example, the Coalition Government's Delivery Plan "Working to Reduce the Use of Animals in Research" noted that conservatism among scientific journal editors and peer reviewers is a barrier to the uptake of non-animal methods, as publications tend to downplay the significance of non-animal research.[15]

Recommendation

17. In order to promote the skills required to build a world class life sciences sector in the UK, researchers, in particular those in their early careers, should be given greater incentives to develop animal-free methods. Incentives might include allocating more funding to PhD research based on *in vitro*, *in silico*, and *in chemico* methods; government awards for promising non-animal technologies being developed by early career researchers (the Lush prize may provide a potential framework),[16] and reduced taxation for laboratory equipment bought to implement non-animal research, similar to the VAT exemption for medical research.[17]

4. How does the UK compare to other countries in this sector, for example Germany and the United States?

18. The UK's reliance on animal-based research is a significant obstacle to our becoming world leaders in the life sciences sector. Many of the world's leading scientists are now focusing on non-animal human-relevant research, due to the overwhelming evidence that tests using animals do not provide results that are applicable to humans.

19. The Netherlands National Committee for the protection of animals used for scientific purposes (NCad)[18] has set bold objectives regarding replacement of animal use, having called upon the relevant Minister to focus "*heavily on innovations without laboratory animals", noting that by doing so "the*

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15 Department for Business, Innovation & Skills, Department of Health, and Home Office. Working to reduce the use of animals in research: delivery plan. 2014. Retrieved from https://www.gov.uk/government/publications/working-to-reduce-the-use-of-animals-in-research-delivery-plan. Accessed September 2017.

16 LUSH. Why We Need a Prize. n.d. Retrieved from http://lushprize.org/background/need-prize/. Accessed September 2017.

17 HM Revenue & Customs. VAT Notice 701/6: charity funded equipment for medical, veterinary etc uses. Retrieved from https://www.gov.uk/government/publications/vat-notice-7016-charity-funded-equipment-for-medical-veterinary-etc-uses/vat-notice-7016-charity-funded-equipment-for-medical-veterinary-etc-uses. Accessed September 2017.

18 Netherlands National Committee for the protection of animals used for scientific purposes (NCad). NCad opinion Transition to non-animal research. 2016. Retrieved from https://www.ncadierproevenbeleid.nl/documenten/rapport/2016/12/15/ncad-opinion-transition-to-non-animal-research. Accessed August 2018.

Netherlands will be able to achieve its objective of becoming an international leader in innovation without laboratory animals in the fields of applied and translational research by 2025." In plans accepted by the Dutch government, the NCad has envisaged phasing out tests on animals for the toxicity assessment of chemicals, food ingredients, pesticides, veterinary medicines, and vaccines by 2025. Were the UK to follow suit, we would inevitably see a surge in scientific innovation leading to better protection of human health and the environment. For example, when the European ban on using animals to test cosmetics came into effect, there was a thriving expansion in revolutionary, humane approaches that had numerous applications; and scientists can now perform high-tech, sensitive tests using 3-dimensional tissue models produced from human cells to evaluate whether chemicals irritate the skin and eyes.

20. In addition to the scientific case for replacing the use of animals in research and testing, NCad's public consultation also highlighted moral and ethical issues.[19] These issues must also be considered in the UK, particularly as the 2016 Ipsos Mori survey[20], commissioned by UK's Department of Business, Energy and Industrial Strategy, noted that 74% of respondents agree with the statement: "*there needs to be more work done into alternatives to using animals in scientific research*" and that 26% of respondents would like to see a ban on any use of animals in research. The 2016 survey also found 59% of people disagreed with the statement "*it does not bother me if animals are used in scientific research*".

21. The uptake of new non-animal techniques provides an opportunity for the proposed UK Life Sciences Strategy to meet both scientific and ethical objectives by further promoting new human biology based technologies.

Recommendations

22. The UK must create an innovative and forward-thinking life sciences sector by promoting the development of non-animal research techniques and the replacement of animal use. It is necessary to recognise and act upon the shortcomings associated with animal use in biomedical research, and to foster more human-relevant technologies. Strategic priorities on the replacement of animals in research are presented in the appendix[21].

23. The existing 2014 UK Delivery Plan[22] and subsequent 2015 publication[23],

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19 Opinion of the Netherlands National Committee for the protection of animals used for scientific purposes (NCad). Transition to non-animal research. 2016. Retrieved from https://www.ncadierproevenbeleid.nl/ documenten/rapport/2016/12/15/ncad-opinion-transition-to-non-animal-research. Accessed September 2017.

20 Clemence, M. and Leaman, J. Public attitudes to animal research in 2016. *A report by Ipsos MORI for the Department for Business, Energy & Industrial Strategy*. 2016. Retrieved from https://www.ipsos.com/sites/default/files/publication/1970-01/sri-public-attitudes-to-animal-research-2016.pdf

21 Appendix can be found at https://www.peta.org/wp-content/uploads/2017/04/Trump_Team_Packet_r5_72.pdf 'Advancing Biomedical Research and Regulatory Policies for Human and Animal Health', January 2017.

"Working to Reduce the use of Animals in Scientific Research" should be updated, and more ambitious goals set.

The recommendations from Innovate UK's 2015 Non-Animal Technologies Roadmap for the UK[24] should be implemented, and the recognition that the "*market potential for non-animal technologies is huge [. . .] one of a series of emerging technologies that could drive future UK economic growth*" should be acknowledged and incorporated into all life sciences strategies.

Industrial Strategy

5. What can be learnt from the impact of the 2011 UK Life Sciences Strategy? What evidence is there that a strategy will work for the life sciences sector? How can its success be measured against its stated objectives?

24. The 2011 UK Life Science Strategy discusses ways to strengthen the UK's life sciences industries and how to better incorporate exciting investment environments into regulatory processes. A significant area worthy of investment is the advancement of alternative methods for hazard assessment. In particular, the novel systems and approaches under development which are driving our mechanistic understanding of physiological processes and human disease, for example organs-on-chips, computer models, adverse outcome pathways (AOPs) and integrated approaches to testing and assessment (IATAs).

25. Innovate UK's roadmap for non-animal research states that the global market for cell-based assays in drug discovery, safety, and toxicology will reach $21.6 billion by 2018 and that the 3-dimensional cell-culture market is expected to grow to approximately $2.2 billion in 2019.[25] However, the 2011 UK Life Science Strategy did not discuss this investment opportunity and had only one reference to the use of animals in experiments, *i.e. "We are aiming to reduce the use of animals in scientific research, and are supportive of all work directed at developing alternatives and improving standards."*

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22 Understanding Animal Research. Government announces Delivery Plan for reduction of animals in research. 2014. Retrieved from http://www.understandinganimalresearch.org.uk/news/communications-media/government-announces-delivery-plan-for-reduction-of-animals-in-research/. Accessed August 2017.

23 Department for Business, Innovation & Skills, Department of Health, and Home Office. Working to reduce the use of animals in research: delivery report. 2015. Retrieved from www.gov.uk/government/uploads/system/uploads/attachment_data/file/417441/Delivery_Report_2015.pdf. Accessed August 2017.

24 Innovate UK. Non-animal technologies in the UK: a roadmap, strategy and vision. 2015. Retrieved from https://www.gov.uk/government/publications/non-animal-technologies-in-the-uk-a-roadmap-strategy-and-vision. Accessed August 2015.

25 Innovate UK. A Non-Animal Technologies Roadmap for the UK: Advancing Predictive Biology. 2015. Retrieved from https://www.nc3rs.org.uk/sites/default/files/documents/NonAnimalTechCO082_RYE_4_nrfinal2.pdf. Accessed July 2017.

26. By mandating a move away from animal experimentation and towards more advanced human relevant scientific methods, the UK has the opportunity to expedite the development of new technologies that will streamline drug development, making the process safer, cheaper, and more effective. Developing these technologies also allows for the creation of interdisciplinary research teams that will be fundamental in creating the "human disease models of tomorrow".[26]

27. Aside from the economic benefits of non-animal technologies, the 2011 strategy also failed to address the growing concern about the lack of applicability of results from experiments on animals to humans, a concern which is supported by mounting evidence. As discussed earlier, systematic reviews demonstrate that animal studies are misleading and actually hinder medical progress by diverting economic and intellectual resources from methodologies better suited to curing human disease.[27]

28. This was also addressed by Sir Alexander Fleming, who's discovery of penicillin is mentioned in the Ministerial Foreword of the 2011 UK Life Science Strategy report as a notable UK-based life sciences achievement. Sir Alexander Fleming once stated "*How fortunate we didn't have these animal tests in the 1940s, for penicillin would probably have never been granted a license, and probably the whole field of antibiotics might never have been realized*."[28]

29. The absence of a discussion of these issues, which are central to the sustainable development of a truly innovative life sciences sector, means that **the 2011 UK Life Science Strategy report failed to meet its stated objectives**.

Recommendation

30. The UK government must stop funding experiments on animals, which have failed to provide effective treatments and cures for human diseases, and instead increase investment in reliable, innovative non-animal methods and bold policy initiatives that work towards ending the use of animals in life sciences research. This will result in the development of more effective and reliable methods for toxicity assessment and alleviate the suffering of millions of animals.

6. (If published) Does the strategy contain the right recommendations? What should it contain/what is missing? How will the life sciences strategy interact with the wider industrial strategy, including regional

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26 hDMT Institute. White Paper: Towards Precision Medicine in Future Healthcare: Organ-on-Chip Technology and hDMT. 2016.

27 Ioannidis JP. Extrapolating from animals to humans. *Sci Transl Med*. 2012; 4(151):151ps15.

28 People for the Ethical Treatment of Animals. *Animal Testing Is Bad Science: Point/Counterpoint*. n.d. Retrieved from https://www.peta.org/issues/animals-used-for-experimentation/animal-testing-bad-science. Accessed August 2017.

and devolved administration strategies? How will the strategies be coordinated so that they don't operate in 'silos'?

31. The report makes some interesting and valuable recommendations, however it does not address the use of animals in experiments nor the development of non-animal technologies, and therefore disregards important opportunities.

Recommendations

32. The report makes the recommendation that the *"UK should attract 2000 new discovery scientists from around the globe."* In order to do this, it is important to invest in new and exciting science. Complex (cell-based) and virtual (computer-based) models of human tissues and organs, such as novel dynamic systems created from engineered human tissues, are acknowledged as one of the most exciting research areas in 21st century toxicology.[29]

33. The report makes the recommendation to *"support a 50% increase in the number of clinical trials over the next 5 years and a growing proportion of change of practice and trials with novel methodology over the next 5 years."* We recommend the use of human-relevant models in pre-clinical studies to maximise the success of clinical trials. More than 90% of treatments entering clinical trials fail to gain approval, mostly due to insufficient efficacy and/or unacceptable toxicity, because of the limited predictive value of preclinical studies.[30] In fact, the inherent limitations of existing methods for evaluating chemical safety has led the National Institutes of Health, the US Environmental Protection Agency, the US Department of Defense (Defense Advanced Research Projects Agency), the European Commission and European industry to invest hundreds of millions of dollars in the development of more relevant, efficient methods, which are based on understanding mechanistic human biological pathways.[31] If the UK were to also increase investment in these methods, it would lead to a reduction in the time it takes to bring new and novel treatments to market. As an example, the organs-on-chips models being developed at Harvard University's Wyss Institute are predicted to play a pivotal role in streamlining clinical trial processes.[32]

34. The report recommends *"[i]n the next five years, the NHS should engage in fifty collaborative programmes in late-stage clinical trials, real world data collection, or in the evaluation of diagnostics or devices. The UK should be in the top quartile of comparator countries, both for the speed of adoption and*

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29 Knudsen TB, Keller DA, Sander M, et al. FutureTox II: In vitro Data and In Silico Models for Predictive Toxicology. Toxicol Sci. 2015;143(2):256-267.

30 Plenge RM, Edward M Scolnick, D Altshuler. Validating therapeutic targets through human genetics. *Nat Rev Drug Discov.* 2013;12(8):581.

31 NTP Interagency Center for the Evaluation of Alternative Toxicological Methods and the Human Toxicology Project Consortium. BioMed21 - A Human Pathway-based Approach to Disease and Medicine White Paper. 2017. Retrieved from https://ntp.niehs.nih.gov/iccvam/meetings/biomed21-2017/whitepaper-final-22june.pdf. Accessed September 2017.

32 Esch EW, Bahinski A, Huh D. Organs-on-chips at the frontiers of drug discovery. *Nat Rev Drug Discov*. 2015;14(4):248-260.

the overall uptake of innovative, cost effective products, to the benefit of all UK patients by the end of 2023." We recommend encouraging collaboration between researchers and the NHS in human-relevant innovations to expedite the development of new and effective healthcare products, and this can be achieved through increased funding. We further discuss the implementation of NHS biobanking collaborations for the improvement of patient outcomes without the need for increased resources in question 12.

35. The report also discusses strengthening STEM education. For the long term improvement of the UK's life science sector, it is important to implement a well-rounded and exciting curriculum within the life sciences. This must include the latest *in vitro, in silico* and *in chemico* innovations, as well as information on the limitations of experimenting on animals.

9. How do the devolved administrations and city regions fit into the strategy? Scotland has its own life sciences strategy, how will the two interact?

36. With regard to animal experimentation, the Scottish Parliament and Welsh and Northern Irish assemblies have no legislative competence. The Home Office is the sole regulator in England, Scotland and Wales and the Department of Health, Social Security and Public Safety is the regulator in Northern Ireland. Therefore, to achieve harmonisation of regulatory testing requirements and application of testing and assessment strategies within the life sciences sector, it is essential that a UK life sciences strategy applies to the whole of the UK and is adopted as such across all regions.

Recommendation

37. We recommend that the UK government works closely with each of the devolved administrations to seek harmonisation to the greatest possible extent.

NHS procurement and collaboration

12. How can collaboration between researchers and the NHS be improved, particularly in light of increased fiscal pressures in the NHS? Will the NHS England research plan help in this regard? How can the ability of the NHS to contribute to the development of and adopting new technology be improved?

38. Increasing financial pressure within the NHS is limiting the resources and structures that are available to facilitate high-quality research. However, research cannot deliver improved patient outcomes without the input of patients and clinicians,[33] and as stated in the recent Life Science Industrial Strategy, "*[a]ny credible life sciences strategy in the UK must have the NHS as*

[33] Wyld L, Smith S, Hawkins NJ, Long J, Ward RL. Introducing Research Initiatives into Healthcare: What Do Doctors Think? *Biopreserv Biobank*. 2014;12(2):91-98.

an active participant".[34] Fortunately, there are areas where increased collaboration between researchers and the NHS can expedite the development of new technologies, without requiring increased resources. For example, the successful partnering between Medtronic Health Solutions and the NHS Hospital Trusts,[35] or even widespread implementation of collaborative biobanking strategies.

39. Institutional biobanking, *i.e.* the organised collection of biological materials during routine healthcare procedures for the purposes of research, is an essential resource in improving our mechanistic understanding of disease. Qualitative research has shown that successful integration of research initiatives such as biobanking into hospitals can be achieved through early collaboration between the implementing team and healthcare professionals.[36] It also found that financial incentives were not necessary, and that doctors were encouraged to take operational responsibility for these initiatives as long as their contributions were properly acknowledged.

40. By supporting biobanking initiatives and encouraging innovative work with these materials, the NHS can directly contribute to the development of new and exciting technologies, whilst shifting the testing paradigm away from experiments on animals and towards mechanistic human-relevant studies.

Recommendation

41. We recommend that the strategy includes the implementation of several pilot biobanking initiatives, with an aim to make such initiatives compulsory. The experience from these initial studies should be used to develop other promising NHS-researcher collaborations.

Responsibility and accountability?

13. Who should take responsibility for the implementation of the Life Sciences Industrial Strategy and to whom should they be accountable? What should the UK Government's role be? What should the role of the academic, charitable and business sectors be?

42. The academic, charitable and business sectors should always be subject to appropriate levels of scrutiny and transparency when in receipt of public funds. We welcome the Research Councils UK support for making the outputs from

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[34] Life Sciences Industrial Stratey Board led by Professor Bell. Life Sciences Industrial Strategy – A report to the Government from the life science sector. 2017. Retrieved from https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/640696/life-sciences-industrial-strategy.pdf. Accessed September 2017.

[35] Life Sciences Industrial Stratey Board led by Professor Bell. Life Sciences Industrial Strategy – A report to the Government from the life science sector. 2017. Retrieved from https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/640696/life-sciences-industrial-strategy.pdf. Accessed September 2017.

[36] Wyld L, Smith S, Hawkins NJ, Long J, Ward RL. Introducing Research Initiatives into Healthcare: What Do Doctors Think? *Biopreserv Biobank*. 2014;12(2):91-98.

such research publicly available[37] and fully endorse the European Commission's decision to ensure that all projects receiving Horizon 2020 funding are required to ensure journal articles are openly accessible, free of charge. In particular, we believe raw data should be made publicly available as described in the European Commission's 2013 fact sheet on open access in Horizon 2020[38].

Recommendation

43. The Life Sciences Industrial Strategy should be accountable to citizens through Parliament. The Government's role should be to formulate the strategy and seek the endorsement of Parliament, allowing full parliamentary scrutiny of relevant proposals and budgets.

15. Does the Government have the right structures in place to support the life science sector? Is the Office of Life Sciences effective? Should the Government appoint a dedicated Life Sciences Minister? If so, should that Minister have UK-wide or England-only responsibilities?

44. We believe that appointment of a Life Sciences Minister will help ensure public accountability.

Brexit

17. How should the regulatory framework be changed or improved after Brexit to support the sector?

45. In the wake of Brexit, the Government must commit to maintaining, at a minimum, a ban on animal experiments deemed illegal in the EU. However, this is an ample opportunity to become a global leader in the life sciences by phasing out tests on animals and investing in cutting-edge non-animal research methodologies.

Recommendations

46. The following key issues should be considered in developing a national legislative framework for the safety assessment of pharmaceuticals, industrial chemicals, pesticides, biocides and consumer products. These recommendations aim to ensure an efficient testing process now and lay the foundation for a more protective and humane testing paradigm in the future.

    The UK government must work with other world leaders to harmonize and promote international acceptance of non-animal testing methods.

47. Prioritising the use of alternatives is consistent with existing national and international legislation. For example, Directive 2010/63/EU contains clear

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[37] Research Councils UK. Open Access. n.d. Retrieved from http://www.rcuk.ac.uk/research/openaccess/ Accessed September 2017.

[38] European Commission. Fact sheet: Open Access in Horizon 2020. 2013. Retrieved from https://ec.europa.eu/programmes/horizon2020/sites/horizon2020/files/FactSheet_Open_Access.pdf. Accessed September 2017.

requirements that animal tests should only be performed when approaches which do not use animals cannot be undertaken. Article 4.1 states: "Member States shall ensure that, wherever possible, a scientifically satisfactory method or testing strategy, not entailing the use of live animals, shall be used instead of a procedure." Furthermore the Animals (Scientific Procedures) Act 1986 (ASPA) states: "Project licence holders are required to ensure that their programme of work does not involve any regulated procedures for which there is a scientifically satisfactory alternative method or testing strategy that does not entail the use of a protected animal."[39]

48. This philosophy is preserved across other legislation that involve the use of animals in toxicity tests. For example, promoting non-animal methods is an objective of REACH, with the regulation containing a number of specific measures intended to minimise animal use *as well as* more general provisions to establish and enforce the requirement that testing on animals should only be performed as a last resort. In the US, the amended TSCA[40] now requires the US Environmental Protection Agency to justify any information requests that require testing on vertebrate animals and encourage the development and use of alternatives that provide equivalent or better scientific results. In accordance with the UK's Animals (Scientific Procedures) Act of 1986 (ASPA), UK chemicals legislation must require new and existing non-animal methods to be used in place of tests on animals.

Integrated approaches to testing and assessment (IATAs) that draw on *in silico*, *in chemico* and *in vitro* methods should be advocated.

49. IATAs are pragmatic, science-based approaches for chemical hazard assessment based on the integrated analyses of existing information complemented by new information generated by testing.[41] IATAs combine information from various sources, for example (quantitative) structure activity relationships ([Q]SAR), read-across, *in chemico, in vitro, ex vivo, in vivo* and omic technologies. The integration of information from key events within specific toxicity pathways results in assessments that are significantly more predictive of human health effects than those based on testing in animals. The information used to create an IATA can include:

    - Adverse outcome pathways (AOPs) are analytical constructs that describe a sequential chain of causally linked events at different levels of biological organisation leading to adverse health effects. AOPs are

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39 Animals in Science Committee and The Rt Hon Norman Baker. Consolidated version of ASPA 1986. 2014. Retrieved from https://www.gov.uk/government/publications/consolidated-version-of-aspa-1986. Accessed September 2017.

40 US Environmental Protection Agency. The Frank R. Lautenberg Chemical Safety for the 21st Century Act. 2016. Retrieved from https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/frank-r-lautenberg-chemical-safety-21st-century-act. Accessed August 2017.

41 Organisation for Economic Cooperation and Development. Integrated Approaches to Testing and Assessment (IATA). 2017. http://www.oecd.org/chemicalsafety/risk-assessment/iata-integrated-approaches-to-testing-and-assessment.htm. Accessed August 2017

pivotal to the mechanistic understanding of the effects of new treatments and their side effects. For example, AOPs can be used in the study of drug-induced liver injury, which is a prominent reason for premarketing and postmarketing drug withdrawal.[42]

- Grouping and read-across strategies allow prediction of health effects for a particular substance based on data from other substances deemed as similar due to, for example, their structure, physicochemical properties, or toxicokinetics. These approaches represent the state of the art in toxicity prediction and are used in product design and regulatory decisions as part of pharmaceutical design and development.[43]

- *In silico* approaches such as [Q]SARs and physiologically based pharmacokinetic (PBPK) models can be combined with existing data and information generated by *in vitro* methods in integrated testing strategies to assess the hazard potential of new treatments. A major proportion of *in silico* approaches were developed by the pharmaceutical industry for use in drug discovery.[44]

- *In vitro* methods based on cultured human cells and tissues provide human-relevant information. Despite a continuing increase in the use of *in vitro* (and *in silico*) tests by the pharmaceutical industry and a growth in this area of £1 billion since 2002, the Home Office figures for animal use in the UK by commercial organisations have stayed largely unchanged.[45] Investment in this area must increase.

There should be greater transparency in relation to the use of animals in scientific procedures.

50. High quality regulation depends on the capacity of the public and concerned stakeholders to evaluate the work of the regulator and hold them to account. The government should therefore improve the regulatory framework following Brexit to promote openness and transparency by implementing the following legislative changes:

Repeal Section 24 of the amended Animals (Scientific Procedures) Act 1986 (ASPA)

Section 24 prevents any effective, comprehensive evaluation of the regulation of experiments on animals and should be entirely repealed. No controls on the release and dissemination of information regarding experiments on animals should be required other than those already

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42 Vinken M. Adverse outcome pathways and drug-induced liver injury testing. *Chem Res Toxicol*. 2015;28(7):1391-1397.

43 Chackalamannil S, ed. Rotella D, ed. Ward S, ed. *Comprehensive Medicinal Chemistry III.* Elsevier; 2017.

44 Raunio H. In Silico Toxicology – Non-Testing Methods. *Front Pharmacol*. 2011;2:33.

45 Goh JY, Weaver RJ, Dixon L, Platt NJ, Roberts RA. Development and use of in vitro alternatives to animal testing by the pharmaceutical industry 1980–2013. *Toxicol Res-UK*. 2015;4(5):1297-307.

established in other existing legislation, including the Freedom of Information Act (2000).

Revise ASPA to allow for a public commenting period on all project licence applications before ministerial approval

Currently, the processes of evaluation and authorisation of new life sciences research which uses animals is conducted without public oversight. The removal of barriers to information held by public bodies would save resources, reduce late-stage failures in the drug-development process and ensure uptake of innovative new treatments. Project licence applications and retrospective reviews should be made publicly available (which can be done without identifying the establishments or the individual researchers, and also without revealing information that is genuinely commercially confidential). A similar system has been implemented through REACH, where stakeholders are able to submit data to fill information gaps in order to prevent duplicate animal testing.

51. Improving transparency by repealing Section 24 and allowing a public commenting period on all project licence applications will allow greater scientific and ethical scrutiny, improve the application of the 3Rs and increase collaboration and innovation, resulting in a more progressive life sciences sector.

The UK must establish a clear policy within a legislative framework which codifies a commitment to the development, validation and implementation of non-animal methods.

52. EU Directive 2010/63/EU[46] requires member states and the European Commission to contribute to the development and validation of alternative approaches, and encourage research in this field. In the absence of further UK involvement in this effort at EU level effort, it will become even more important to ensure that a coherent 'Replacement strategy' is developed.

53. Similarly, Regulation (EU) No 1291/2013 establishing Horizon 2020[47] identifies as a priority the need for research aimed at "understanding the molecular basis of disease," specifically through making use of systems biology and related tools, within the Societal Challenge of "improving the lifelong health and wellbeing of all." These EU policy objectives should be firmly embedded within UK national policy.

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46 Directive 2010/63/EU of the European Parliament and of the Council, of 22 September 2010 on the protection of animals used for scientific purposes. Retrieved from http://eurlex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2010:276:0033:0079:en:PDF. Accessed August 2017.

47 Regulation (EU) No 1291/2013 of the European Parliament and the Council of 11 December 2013 establishing Horizon 2020 - the Framework Programme for Research and Innovation (2014-2020) and repealing Decision No 982/2006/EC. Retrieved from http://ec.europa.eu/research/participants/data/ref/h2020/legal_basis/fp/h2020-eu-establact_en.pdf. Accessed August 2017.

The UK must remove the 'gold-plating' constraints currently imposed by Directive2010/63/EU on the protection of animals used for scientific purposes.

54. For those animals currently being used in scientific procedures, Brexit provides ample opportunity to implement higher housing and care standards as the UK will no longer be constrained by Article 2 of Directive 2010/63/EU, which requires observing "*the general rules laid down in the TFEU*".

55. Raising standards, such as cage sizes, beyond the minimum requirements laid out in the EU Directive must be allowed following Brexit and not interpreted as 'gold-plating'. As advances are made in animal welfare science it is essential that the UK allows for flexibility in its national legislation that seeks to improve animal welfare, implement measures pertaining to the 3Rs and takes into account the significant public concern caused by animal experimentation.

56. However, as our prior responses and recommendations demonstrate, the most effective and efficient way to make the UK world leaders in the life sciences is to end the use of all animals in experiments. We can provide additional information on housing and care standards upon request.

18. To what extent should the UK remain involved with and contribute to agencies such as the EMA post Brexit?

57. Harmonisation is an important tool in reducing the number of animals used in experiments, for example by preventing duplicate testing, therefore working with European agencies is vital. However, the UK should only align itself with ventures that facilitate its goal to have one of the world's most advanced life science sectors based on the use of human-relevant animal-free approaches.

Recommendations

European Medicines Agency (EMA)

58. In 2015, the EMA released a strategy of its work to 2020 which, despite the extensive use of animals in the authorisation of new human and veterinary medicines, did not address the subject of experiments on animals. Therefore, the Medicines and Healthcare products Regulator Agency (MHRA)'s future work with the EMA should focus on demonstrating the superior abilities of non-animal tests to predict the effectiveness of new medicines. Innovative UK regulations could lead to the formation of new and improved European regulations.[48]

European Chemicals Agency (ECHA)

59. Although the REACH regulation aims to improve the protection of human health and the environment from the risks that can be posed by *chemicals*, it includes a number of commendable provisions to reduce the use of animals that can be

[48] Galsworthy M, McKee M. A plan for UK science after the European Union referendum. *Science*. 2017;355(6320): 31-32.

incorporated into the whole life sciences sector, in particular in Articles 13 and 25.

60. Article 13(1) states: "*Information on intrinsic properties of substances may be generated by means other than tests, provided that the conditions set out in Annex XI are met. In particular for human toxicity, information shall be generated whenever possible by means other than vertebrate animal tests, through the use of alternative methods, for example, in vitro methods or qualitative or quantitative structure-activity relationship models or from information from structurally related substances (grouping or read-across).*".

61. Article 25 of the REACH regulation requires that "*[i]n order to avoid animal testing, testing on vertebrate animals for the purposes of this Regulation shall be undertaken only as a last resort.*"

62. Similar provisions must be incorporated into the new UK strategy.

The European Union Reference Laboratory for alternatives to animal testing (EURL-ECVAM)

63. EURL ECVAM was established to validate methods which reduce, refine or replace the use of animals for the safety and efficacy testing of chemicals, biologicals, and vaccines.[49] They also promote the development and dissemination of alternative approaches, the application of these approaches within industry and their regulatory acceptance. The UK should now increase its work on the validation of new methods and continue working with EURL-ECVAM post Brexit, either through the NC3Rs or a new body created to focus primarily on replacement and validation efforts.

The European Food Safety Authority (EFSA)

64. EFSA has previously underlined the importance of implementing risk assessment approaches that lead towards the replacement of tests on animals for assessing food and feed toxicity.[50] More recently, it launched the OpenFoodTox database of chemical hazard in food and feed, a tool to help risk assessors prioritise toxicological testing strategies and carry out risk assessments without the use of animals. The UK should now focus on producing similar initiatives.

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[49] The European Union Reference Laboratory for alternatives to animal testing. n.d. Retrieved from https://eurl-ecvam.jrc.ec.europa.eu/. Accessed September 2017.

[50] Barlow S, Chesson A, Collins JD, et al. Existing approaches incorporating replacement, reduction and refinement of animal testing: applicability in food and feed risk assessment. *The EFSA Journal*. 2009;1052:1-77