ethical consumer | research and consultancy

Lush Prize - 2012 to 2022

What's been achieved on the road to ending animal testing in the last ten years?

A Research and Evaluation Paper

October 2022

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A. Executive summary

1. Introduction and Background

The first Lush Prize awards were held in London in November 2012. As it approaches its tenth anniversary, it makes sense to pause to evaluate the impact of the project and the changes that have been seen in that time. What's been achieved on the road to ending animal testing? And what can we say about the role the Prize has played?

This paper is broken down into three parts: direct impacts, bigger picture developments and conclusions.

2. Direct Impacts

Between 2012 to 2022 Lush Prize has awarded over 3 million EUR across 35 countries to 126 projects. For the vast majority of recipients, often leaders in their fields, the money would have been used to continue campaigning, lobbying, training or to fund innovative scientific research.

We then look at some endorsements and feedback from former winners on how the prize categories have evolved to meet the changing environment around them. This is followed by a timeline of key events over the ten year period.

We review how the prize continues to receive applications from high profile institutions in the field - including governments, universities and international collaborations. In addition, through increasingly successful spin-off annual conferences, the Prize is playing an important role in building a broad community of interest with the goal of ending animal use in toxicity testing.

We end this section by evaluating how the prize has performed against the project's original mission and goals - set in 2012. It is pretty clear that Lush Prize has achieved what it set out to do. It has also clearly created direct impact at the point where each of the prizes received an award, and which will continue to ripple out into the future. It has used the awards and conferences to raise awareness with some modest success by asking the right questions in a complicated space.

3. Bigger picture developments

Answering the question about the impact this has had on animal testing in the wider world is a more complicated one, and is what the next stages of this paper attempt to do.

We have identified the following 10 key developments, or changes, on the road to ending animal testing that have occurred in the period between 2012 and 2022, which are grouped into four themed areas: Science, Politics, Reasons not to celebrate too soon, and Reasons to be cheerful. They are:

Science (and Young Researchers and Training)
1 A rising awareness of the failure of the animal model
2 A rise of Organs on Chips and Computational Toxicology
3 AOPs (Adverse Outcome Pathways) are becoming embedded as a core knowledge framework

Politics (Lobbying and Public Awareness)
4 Bans on animal tested cosmetics have been rolling out globally
5 A rise of ambition for full replacement everywhere (roadmaps)
6 A rise of 3Rs centres and replacement ideas

Reasons not to celebrate too soon
7 Painfully slow decreases in animal use
8 Institutional inertia remains a real problem

Reasons to be cheerful
9 More discussion of human relevant science and less of 'alternatives'
10 Young scientists are increasingly being trained in and are enthusiastic about these ideas.

4. Conclusions

Lush Prize is just one player in an ecosystem of other institutions all pushing towards the same goal. It is clearly playing a role in contributing to the aggregate pressure for change.

The key difference of the Prize to the many other institutions discussed above is its focus on complete replacement (or simply 'animal-free') methods in the world of toxicity testing. Many other organisations work on this, but often as part of much bigger programmes, either addressing animal use more widely (campaigners), or concentrating mainly on new approach methods (NAMs) in drug discovery (scientists).

Lush Prize's background in animal ethics means that it has not compromised on the goal of complete replacement, nor on the use of animal ingredients. In a world where 3Rs and 'alternatives' have been, until recently, the mainstream approaches to addressing animal use in science, this remains another key difference for the project. Lush Prize has remained an unwavering voice for complete replacement.

10 years ago, when Lush Prize was being designed, we asked specialists how realistic it was to call for a world where all animal testing had stopped, and how long it might take to get there? Most said we needed to be in it for the long haul, and that it would take at least 20 years to achieve that goal. Exploring that question in more detail is the goal of this year's conference.

It would be wrong not to address the two counter-trends identified in the bigger picture developments section above. These were the slow decline in actual animal use and the related institutional inertia.

However, what Lush Prize (and others) are trying to do is very complicated. Making change happen in this context is not simple. Lush Prize was designed in 2012 - with its five awards - in full recognition that change in this area is complex and needs a multi-pronged approach. But, by and large, over the last 10 years the Prize has seen good positive trends, and experienced great feedback and encouraging growth.

Part B Direct Impacts

1. Distribution of prize money to winners

Between 2012 to 2022 Lush Prize has awarded over 3 million EUR across 35 countries to 126 projects.

Category	Science (£50,000)	Training (£50,000)	Lobbying (£50,000)	Public Awareness (£50,000)	Young Researcher (£10,000 x 5)
Total winners 2012 to 2022	12	15	16	15	68

In addition:

- In 2015, there was a Black Box prize where an additional £250,000 was awarded for *in vitro* replacement methods mapping to the Adverse Outcome Pathway (AOP) for skin sensitisation.
- There have been several winners of the Andrew Tyler[1] 'Lifetime achievement' and 'political achievement' awards

Year	2012	2013	2014	2015	2016	2017	2018	2020	2022
Total nomin-ations received	65	55	58	100	100	116	109	137	140

Total nominations received in 2022 was over double those received in 2012.
In 2018 the Lush Prize became biennial after Lush created another 'Spring Prize' for social and environmental regeneration.

[1]Andrew Tyler was a key Lush Prize judge from its inception in 2012 to his death in 2017.

Winners countries include:
Australia; Austria; Belgium; Brazil; Bulgaria; Canada; Chile; China; Denmark; France; Germany; India; Iran; Japan; Kenya; Luxembourg; Netherlands; New Zealand; Russia; Singapore; South Korea; Sweden; Switzerland; Taiwan; UK; Ukraine; USA.

2. Endorsements

Obviously each of the 126 projects would have been affected positively in some way. The 68 young researchers specifically receive funding for future projects. For the vast majority of other recipients, the money would have been used to continue campaigning, lobbying, training or to fund innovative scientific research.

The following are specific comments from winners:

"...very important in recognising our work and convincing others to replace animals"

"....visibility for research on alternative methods in Brazil. ...For the education field, it is very important, because more students know about researches on humane education and they come to ask for information....encouraging new techniques of education, focusing on toxicity testing in the 21st century"

"...not only funded my research but allowed me to engage in partnerships and keep on devoting my career to replacement methods..."

"...recognition for the work our group has done, it has assisted us to be a stronger force .... a huge boost for us financially, and has given us corporate support for an important ethical issue, despite the vested interests that we are faced with on a daily basis"

"..endorse our work with both political and scientific communities in India. Piece by piece,we are moving towards the removal of all animals from laboratories"

3. Continuing evolution

Each year the prize reviews the awards it gives and the type of work it looks to reward. The most recent significant review took place in 2019.

For the Science and Young Researcher awards Lush Prize decided to re-focus its criteria on projects most likely to lead to practical non-animal tests which could be accepted by regulators.
It listed the most promising approaches as including:

- Adverse Outcome Pathways (AOPs)
- Organs on a chip approaches, and
- Computational toxicology *(in silico* methods)

It also expressed particular interest in human relevant adverse outcome pathways for systemic toxicology or developmental toxicology.

4. Timeline

The timeline below shows key events in the ten years of Lush Prize. It is also being used in graphic form to communicate the Prize's history at its tenth year events.

Year	Lush Prize	Notable Winners	'Big picture'
2012	The Lush Prize is launched with 100 people in a paper tent in Shoreditch, London.	The Japan Anti-Vivisection Association wins a Public Awareness Prize.	The OECD approves a second alternative for eye irritation tests.
2013	The Prize makes its first ever science award to a 'computational toxicology' project.	The Swedish Fund for Research Without Animal Experiments wins a Lobbying Award.	The EU ban, prohibiting the sale of animal tested cosmetics, is fully implemented
2014	Lush Prize holds its first large conference on the theme 'Is 1R the new 3Rs?'	The Kenya-based Africa Network for Animal Welfare wins a Training prize.	India bans cosmetic animal testing and the import of animal-tested cosmetics.
2015	The first 'Black Box' prize is awarded by Brian May to five organisations for their work on new tests for skin sensitisation using Adverse Outcome Pathway research.	Bianca Marigliani from The Federal University of São Paulo, Brazil wins a Young Research Prize for her work on replacing fetal bovine serum (FBS) in animal tests.	New Zealand bans cosmetic animal testing for finished products and ingredients intended exclusively for use in cosmetics.
2016	Young Researcher Awards are extended to include 'Asia', 'Americas', and 'Rest of the World' and awards events held at multiple locations.	Vshine Animal Protection Association China receives a Public Awareness award for its Be Cruelty Free campaign.	The prize-winning skin sensitisation Adverse Outcome Pathway methods are approved by the OECD.
2017	Lush Prize launches a new 'Andrew Tyler' award for outstanding contributions towards ending animal testing.	Professor Jennifer Lewis's Bioprinting Team at Harvard University wins the Science Prize.	The Alliance for Human Relevant Science is Launched in the UK.
2018	The first Lush Prize awards are held in mainland Europe (Berlin, Germany) with a conference focussing on 'Organs on a Chip'	Thirteen scientists from countries including the USA, Brazil, Taiwan, Japan, China, Germany and Italy win Young Researcher awards.	The Netherlands Government launches it's 'Transitie Proefdiervrije Innovatie' initiative to become a world leader in 'animal free innovation'
2019-2020	Lush Prize goes fully virtual, hosting its first online conference and awards ceremony on the theme of 'Can big data replace animal testing?'	SOKO Tierschutz wins a Public Awareness prize for an undercover investigation of a Laboratory in Germany.	The seminal book, *Animal Experimentation*: *Working Towards a Paradigm Change,* is published with contributions from 51 authors including two from the Lush Prize team.
2021-2022	Lush Prize explores 'The role of public awareness in the replacement of animals in safety testing' and celebrates its 10th anniversary.	Our 2022 winners will be announced on November 18th.	The European Parliament votes (almost unanimously) for a European Union–wide plan for phasing out the use of animals in research and testing

5. The prize continues to receive applications from high profile institutions in the field

The following institutions have all been winners or connected to winning projects.

Government and international
European Commission Joint Research Centre
US Environmental Protection Agency, USA
OECD
Institute of Disease Control and Prevention, China

Universities
Liverpool John Moores University
Karolinska Institute
Institute of Food Safety, Wageningen University and Research Centre
University of Konstanz
Osaka City University Graduate School of Medicine
University of Konstanz
University Hospital Würzburg
University of Luxembourg
University of Leeds
Swansea University
Queensland University of Technology
Federal University of Goiás
Karlsruhe Institute of Technology
Ulm University
Takasaki University of Health and Welfare
University of Luxembourg
National University of Singapore
Harvard University
University of Pennsylvania
Wyss Institute-Harvard University
Institute of Biomedical Engineering, National Chiao Tung University Taiwan
Qinghai University
Charité-Universitätsmedizin
Cambridge University
Columbia University
Tsinghua University, China

Multinational corporations
BASF SE
Givaudan
Unilever
Proctor and Gamble

International Collaborations
Human Toxicology Project Consortium
Center for Alternatives to Animal Testing

The use of research papers within Lush Prize to identify and invite high performers to apply continues to play a key role in this. For example, scoping research is conducted during each nominations period, to identify science projects which score highly (according to pre-determined criteria) on their potential to develop NAMs and promote a shift away from animal tests.

Such projects (relevant to Science or Young Researcher categories) may often be within institutions where animal research is also carried out routinely. Lush Prize recognizes this and therefore ensures that prize funding is carefully ring fenced in such situations, to reward the best animal free safety science and continue to uphold its 'replacement' policy, also often providing a vital source of funding (particularly to Young Researchers) for animal-free methods which may otherwise be very difficult or refused.

Nevertheless it is still worth noting that the award still carries with it sufficient credibility (and cash) to attract people working on these issues at the highest level.

6. Building a community of interest though conferences and networking

(a) Our conferences

Following the success of increasingly formal conference discussions around the in person awards events in the early years, Lush Prize has gone on to host annual events looking to explore key issues with its winners and other experts. Recent online events have attracted more than 300 participants and high profile speakers.

2014 - Is 1R the new 3Rs?
2015 - Adverse Outcome Pathways – What, How and Where Next?
2016 - Regulating Chemical Safety – the future for animal use
2017 - Adverse Outcome Pathways (Seattle WC10)
2018 - Can Organ-on-a-Chip replace animal use in safety testing with advanced human focused approaches?'
2020 - Can Big Data Replace Animal Testing?
2021 - The role of public awareness in the replacement of animals in safety testing

(b) Our forum

In 2021, we set up the Lush Prize 1R Network - a forum and collaborative networking tool for Lush Prize winners and others to share expertise and actively participate in the paradigm shift towards human relevant science to replace animal use in research and safety testing. Although yet to achieve critical mass, it has proven some use in the evaluation of our work, and we are hopeful that it will become more active in the future.
Find out more at https://lushprize.org/background/lush-prize-1r-network

Lush Prize remains a unique voice in the field. It brings together campaigners and scientists in a way that was unusual 10 years ago. It also brings some glitz and chutzpah to an otherwise very technical area of science.

(c) Our sponsorship at other events and projects

As part of its goal of attracting high quality nominations for its awards, Lush Prize now makes small strategic sponsorships of 'replacement only' sessions at many major 3Rs conference annually. These include EUSAAT (European Society for Alternatives to Animal Testing) in Europe, ESTIV (European Socity of Toxicology In Vitro), the World Congresses, the Asian Congresses on Alternatives and most recently at the Microphysiological Systems (MPS) Summit (for organ on a chip approaches). Rebecca Ram, our Science Advisor, will often present at these events and many others too.

Lush Prize was also a sponsor in 2019 of the seminal 'replacement' publication, *Animal Experimentation*: *Working Towards a Paradigm Change.*and wrote two of the contributing chapters.

7. Evaluating Direct Impacts

The founding 'Aims and Objectives' of the Lush Prize in 2012 were longer than this short extract, but included the following:

Aims
- To expedite the replacement of animal tests in product safety testing by rewarding and funding strategic projects and interventions anywhere in the world.
- To raise public awareness of ongoing safety testing and the movement for change.
- To encourage the scientific, regulatory and campaigning communities to focus attention on animal-free toxicology testing.

Objectives
- The Lush Prize is an annual award of £250,000 designed to focus resources on bringing forward the day when all product safety testing takes place without the use of animals.
- The Lush Prize focuses on toxicity testing for consumer products in a way which complements the many projects already addressing the use of animals in medical testing.
- The Lush Prize is also choosing to focus attention on 21st Century Toxicology as a specific area of non-animal testing research which holds out the most hope for an animal-test free future.
- The Lush Prize also distinguishes itself by being a 1R rather than a 3Rs Prize.
- An annual awards ceremony and conference in November will: raise public awareness of ongoing safety testing and the global movement for change, focus attention on the individual winning projects and promote debate and collaboration around achieving this goal.

Evaluated against these eight points, it is clear that Lush Prize has achieved what it set out to do. It has clearly created direct impact at the point where each of the prizes received an award which will continue to ripple out into the future.
It has used the awards and conferences to raise awareness with some modest success by asking the right questions in a complicated space.

Answering the question about the impact this has had on animal testing in the wider world is a more complicated one, and is what the next stages of this paper attempt to do.

Part C Bigger picture developments

1 A rising awareness of the failure of the animal model

Lush Prize was set up to press particularly for an end to animal use in chemical safety testing. However, it is increasing awareness of the poor performance of animals in predicting human responses in drug development which has boosted the understanding of the need to replace animals in laboratories more widely.

The most commonly shared statistic is that 86-90% of drugs fail human trials either due to lack of effectiveness (efficacy) or safety concerns, despite having proved promising in earlier (preclinical) tests which are largely based on animal studies.[2]

This failure rate for drug development, despite attempts by some (including pro-animal research organisations) to describe it as a myth, is found again and again in study after study, and has become increasingly difficult to ignore as the decade has gone on.[3]

> *"The high clinical failure rate in drug development across all disease categories is based, at least in part, on the inability to adequately model human diseases in animals and the poor predictability of animal models. A notable systematic review, published in 2007, compared animal experimentation results with clinical trial findings across interventions aimed at the treatment of head injury, respiratory distress*
>
> *syndrome, osteoporosis, stroke, and hemorrhage. The study found that the human and animal results were in accordance only half of the time. In other words, the animal experiments were no more likely than a flip of the coin to predict whether those interventions would benefit humans.*
>
> *In 2004, the FDA estimated that 92 percent of drugs that pass preclinical tests, including "pivotal" animal tests, fail to proceed to the market. More recent analysis suggests that, despite efforts to improve the predictability of animal testing, the failure rate has actually increased and is now closer to 96 percent. The main causes of failure are lack of effectiveness and safety problems that were not predicted by animal tests."*
>
> Ayesha Akhtar[4]

This is not necessarily rising public awareness, but simply awareness from scientists trying to achieve particular goals. One result of this is that it has driven pharmaceutical companies

[2] Thomas DW, Burns J, Audette J, Carroll A, Dow-Hygelund C, Hay M. Clinical development success rates 2006–2015. 2016. Available at: https://www.bio.org/sites/default/files/Clinical%20Development%20Success%20Rates%202006-2015%20-%20BIO,%20Biomedtracker,%20Amplion%202016.pdf (Accessed 20/9/2019)

[3] Wong CH, Siah KW, Lo AW. Estimation of clinical trial success rates and related parameters. Biostatistics. 2019;20(2):273-86.,

[4] Akhtar A. The flaws and human harms of animal experimentation. Camb Q Healthc Ethics. 2015 Oct;24(4):407-19. doi: 10.1017/S0963180115000079. PMID: 26364776; PMCID: PMC4594046.

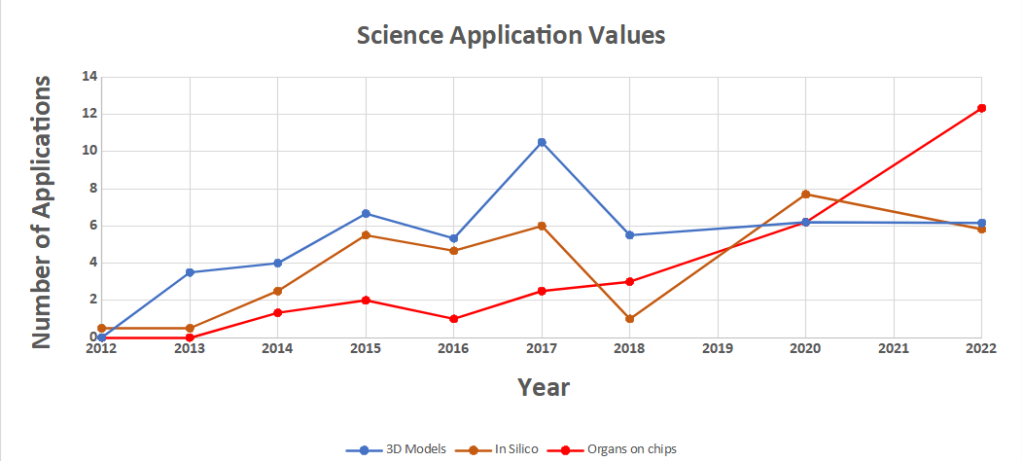
into diverting significant resources into developing more human-relevant methods such as organs on chips (see section 2 below).
It has also raised the question of whether the predictivity of chemical safety testing on animals is likely to be as poor as it is for drugs, especially given the global pace of safety testing required for new substances.

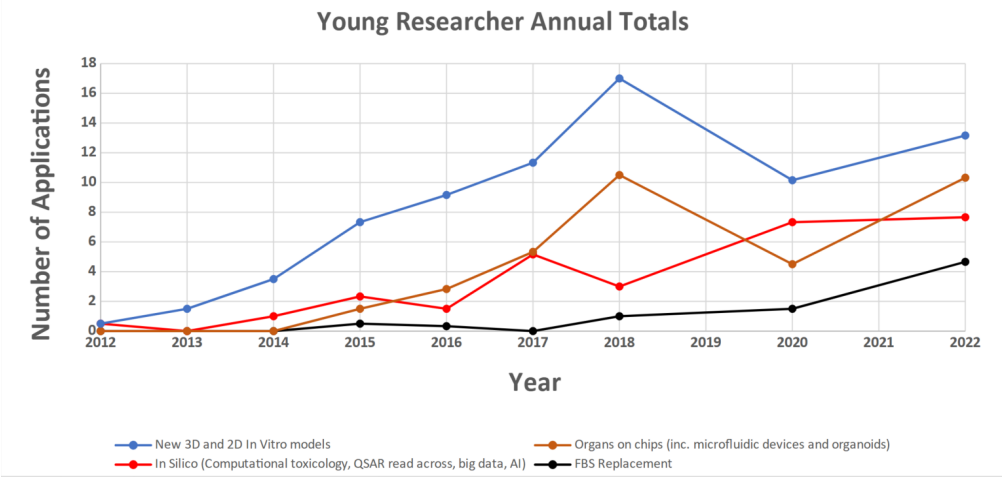
So although animal ethics provided the drive behind the establishment of Lush Prize in 2012, the equally valid argument that animal testing is simply poor science is driving a more widespread understanding of the need to bring an end to the 'old technology' of animal tests.

Despite this, as we see in section X below, animals are still routinely used in experimental disease research and in decades-old tests for drugs and other chemicals which are known to have major limitations and provide little or no human relevant information.[5]

2 A rise of Organs on Chips and Computational toxicology

In September this year we did a retrospective analysis of applications received for the Lush Prize awards each year. Although these are only a small sample within a much larger phenomenon, the graphs below show clear trends of increasing activity in these two areas.





[5] e.g. the archaic LD 50 or 'lethal dose test' which still used 11,758 animals in the UK during 2021 (mainly mice and some fish) and many thousands more across the EU.

In the wider world, the global organ-on-a-chip market, the vast majority of which use human cells, was valued at $103.44 million in 2020, and is projected to reach $1.6bn by 2030.[6] Its commercial impact is such that the first of an annual series of 'MPS World Summits' was held in the USA in June this year. (Organs on chips are know by a variety of other more technical names including Microphysiological Systems (MPS.)
The rising use of *'in silico'* or computational approaches to assessing toxicity has also been widely documented elsewhere.[7] Its increasing ability to predict adverse responses means that it is in greater use within the pharmaceutical industry and has become accepted by some regulators for some endpoints over the last few years, though still largely alongside data from animal tests .[8]

3 AOPs are becoming embedded as a core knowledge framework

The science-based Lush Prizes have always focused on human toxicity pathways in the context of 21st-century science, and in recent years the language has become dominated by the idea of human 'adverse outcome pathways' (AOPs).
An AOP is a toxicity pathway that links a Molecular Initiating Event to an Adverse Outcome (e.g. illness or death) via a defined series of biological steps.

Lush Prize judge, Dr Gill Langley wrote, for an internal research paper commissioned by Lush Prize in 2017, as follows:

> *"The AOP concept was only articulated in 2010 and as late as 2012 there were only 2-3 scientific papers per year that referred to it. But already the OECD has endorsed six AOPs, for different uses and five of them with relevance to human health. As at end-June 2017, 18 other AOPs are under review at the OECD, indicating a late stage in the endorsement process. These AOPs are for a range of toxic endpoints including embryo toxicity, epilepsy, learning and memory deficits, impaired fertility, liver tumours and others."*

In October 2022, the AOP Knowledge Base of the OECD listed 452 AOPs., many of which are based on human relevant adverse outcomes.[9]

Lush Prize also commissions an annual research paper on recently published Science research papers.

This June the author wrote: "From the PubMed search we identified a total of 2,254 articles published in the last two years and of potential interest to Lush. This represents a significant increase in publication rate compared with the 772 papers identified in the 18 months (May 2018 – Nov 2019) preceding the previous, 2020, Lush report. Of these 2,254 articles, 932

[6]https://www.alliedmarketresearch.com/organ-on-chip-market March 2022

[7]The role of 'big data' and '*in silico'* New Approach Methodologies (NAMs) in ending animal use – A commentary on progress. Rebecca N.Ram' DomenicoGadaleta, Timothy E.H.Allen. Computational Toxicology Volume 23, August 2022, 100232

[8] Ibid at p5

[9] https://aopkb.oecd.org/#aops

(41%) relevant titles were from the “Adverse Outcome Pathways” and “AOP” searches; a further 309 (14%) relevant projects from the “Organ on a chip” search, 93 (4%) from the “Microphysiological system(s)” search; and finally, an additional 920 titles (41%) from the “Computational toxicity” and “*in silico* toxicology” searches."

These 932 papers compare with the 2 to 3 annually identified in 2012.

Although complicated for non-scientists to understand, what AOPs can do is "Organize information about biological interactions and toxicity mechanisms into models that describe how exposure to a substance might cause illness or injury."[10] Having done that they can then "Suggest cell- or biochemical-based tests for pathway elements that could be used to develop testing strategies for targeted toxicity."[11]

In this way, AOPs can provide a conceptual basis for non-animal testing strategies which can in theory replace all animal use. And because they can demonstrate a detailed understanding of how a chemical causes injury, they show up animal models as a less sophisticated technology.

It is for this reason that Lush Prize named its 'special award' the Black box prize - to draw attention to that fact that AOPs can provide a view inside the 'black box' of an outdated animal test model.

4 Cosmetics testing bans have been rolling out globally

2013 - the year after Lush Prize was launched - marked the final implementation of the Cosmetics Directive in Europe. This legislation prohibited the sale of and testing on animals of cosmetics and their ingredients across the European Union. Leading up to this period this issue had been a key focus for European activists.

The EU bans, accompanied by sustained campaigns from animal protection and humane research groups led to similar animal tested cosmetics bans being adopted around the world. The significance of the EU market, and the desire of other countries not to have conflicting regulations which may hamper their businesses, has also had a critical role to play.
The Humane Society International, a key campaigner in this area has a timeline of the bans listed on its website - an edited version of which follows here.[12]

2013
March: Norway bans cosmetic animal testing and the sale of animal-tested cosmetics.
March: The full European Union ban on the sale of animal-tested cosmetics takes effect.
January: Israel implements a prohibition on the sale of all cosmetics that have been tested on animals.

2014
November: India bans the import of animal-tested cosmetics.

[10] https://ntp.niehs.nih.gov/whatwestudy/niceatm/comptox/ct-aop/aop.html
[11] Ibid
[12] https://www.humanesociety.org/resources/timeline-cosmetics-testing-animals

June: China implements a rule to remove mandatory animal testing for so-called ”ordinary” cosmetics, such as shampoo or mascara, manufactured in China.
May: India bans cosmetic animal testing.
January: São Paulo, Brazil, bans cosmetic animal testing.

2015
December: South Korea passes a law to partially ban the manufacture and sale of animal-tested cosmetic products and ingredients if government-recognised, non-animal alternatives exist.
July: Turkey bans cosmetic animal testing and the sale of animal-tested cosmetic products and ingredients where a validated alternative exists, effective January 2016.
June: Canada introduces the Cruelty-Free Cosmetics Act, legislation to ban cosmetic animal testing and the sale of animal tested ingredients.
April: Taiwan introduces legislation to ban cosmetic animal testing and the sale of animal tested ingredients.
March: New Zealand bans cosmetic animal testing for finished products and ingredients intended exclusively for use in cosmetics.

2016
December: Switzerland passes an ordinance to ban the sale of animal-tested cosmetics, effective May 2017.
October: Taiwan bans cosmetic animal testing for finished products and ingredients, effective 2019.
November: India bans the import of animal-tested cosmetics.

2017
December: Rio de Janeiro, Brazil bans cosmetics animal testing and the sale of animal-tested cosmetics.
December: South Africa introduces legislation to ban cosmetics animal testing and the sale of animal-tested cosmetics.
February: Guatemala becomes the first country in the Americas to ban cosmetics animal testing.

2018
June: Canada Cruelty-free Cosmetics Act, legislation to ban cosmetics animal testing and the sale of animal tested ingredients, passes the Senate.

2019
March: Australian government passes a ban on the use of new animal data for cosmetics safety.

2021
September: Mexico passes a law to ban cosmetics animal testing and the sale of animal-tested cosmetics.
May: New cosmetics regulations go into effect in China, opening a potential pathway for import of so-called “ordinary” cosmetics, such as shampoo and mascara, without the need for new animal testing.

For non-European campaigners, cosmetics testing on animals is still a key campaign. ONG Te Protejo a previous Lush Prize winner, has an ongoing campaign in Chile for example.[13]

5 A rise of ambition for full replacement everywhere (roadmaps)

It appears that campaigners and politicians have been emboldened by the rapid pace of development of human biology based testing, and are beginning to publish 'roadmaps for transitioning away from animal research'.

5.1 The Netherlands

The first of these appeared in the Netherlands in December 2016 and was called the "Transition Programme for Innovation without the use of animals (TPI)".[14] The National Committee for the protection of animals used for scientific purposes (NCad) published an opinion that some use of animals that is currently required by law for safety testing of chemicals, food additives, pesticides, and (veterinary) medicines as well as the commercial launch of biological products (e.g., vaccines) could be phased out, with some tests stopped as soon as 2025. For other research areas ten-year plans would be implemented for reducing the numbers of animals used.

Although the eye-catching 2025 phase out date originally speculated does not feature specifically in the program, the ambition has not gone away. Minister Schouten explained in a letter in December 2018 how the Netherlands was still "a forerunner in the international transition with animal-free innovation', and the target date was less strictly defined, because, 'By letting go of the year, and with it resistance, progress can be made. But this does not mean that the ambition for animal-free innovation has been abandoned or lessened'."

5.2 The USA

In 2019, the US Environmental Protection Agency (EPA) came up with something similar. The Frank R. Lautenberg Chemical Safety for the 21st Century Act[15] contained the first ever national United States requirement for the EPA and chemical companies to consider and use alternatives to animals in chemical testing. The EPA was also required to create a strategic plan to replace and reduce animal tests, provide incentives to use non-animal alternatives, and report regularly to Congress on its progress.[16]
So in September 2019, the EPA announced its intention “to aggressively reduce animal testing”: “EPA will reduce its requests for, and funding of, mammal studies by 30% by 2025 and eliminate all mammal study requests and funding by 2035.”[17]

[13]https://ongteprotejo.org/incidencia/
[14] Transition Programme for Innovation without the use of animals (TPI). https://www.transitieproefdiervrijeinnovatie.nl/english)
[15] passed into law in 2016.
[16]Physicans Committee for Responsible Medicine. Lush Prize Recognizes Physicians Committee Lobbying to Replace Animals in Testing. https://www.pcrm.org/news/good-science-digest/lush-prize-recognizes-physicians-committee-lobbying-replace-animals 11.11.17.
[17] Environmental Protection Agency. Administrator Wheeler Signs Memo to Reduce Animal Testing, Awards $4.25 Million to Advance Research on Alternative Methods to Animal Testing. News Release,

It further noted that “any mammal studies requested or funded by EPA after 2035 will require administrator approval on a case-by-case basis.[18] The EPA also will come as close as possible to excluding from its approval processes any reliance on mammal studies conducted after January 1, 2035, including those performed by third parties, subject to applicable legal requirements, including the Administrative Procedure Act.”

However, by 2021the EPA New Approach Methods (NAMs) work plan made no commitment to the 2035 deadline. Instead, it aimed “to ensure its regulatory framework is robust and flexible enough to accommodate the development and the use of NAMs; establish baselines, measurements and reporting mechanisms to track progress in meeting its goals; establish scientific confidence in NAMs and demonstrate application to regulatory decisions; develop NAMs that fill critical information needs; and continue to engage and communicate with stakeholders to incorporate their knowledge and address concerns as EPA moves away from vertebrate animal testing.”[19]

5.3 The European Union

In September 2021, the European Parliament voted overwhelmingly in favour of a Resolution calling on the European Commission to establish an EU-wide Action Plan for the active phase-out of the use of animals in experiments. The plan "shall include milestones and targets to incentivise progress towards the replacement of the use of animals with non-animal and human-based methods".[20] One of the core ideas of the resolution was also to promote new, more human-relevant, technologies such as organ-on-chip.

In March 2022, politicians and NGOs criticised the European Commission for providing, “in a weak response, only a list of fragmented initiatives that could eventually lead to some reduction in the use of animals and it is not taking steps to implement the requested action plan to phase out animal experiments. This leaves the EC with a status quo approach, leading to little impact and no sustainable reduction of the use of animals in areas where so much more can be achieved.”[21]. Concerns are heightened by forthcoming revisions to major EU chemicals legislation under the European Green Deal such as some around REACH (Registration Evaluation and Authorisation of Chemicals) which are likely to *increase* animal tests.

As well as government institutions and politicians, campaigners everywhere are beginning to publish their own road maps.

10.09.19. https://www.epa.gov/newsreleases/administrator-wheeler-signs-memo-reduce-animal-testing-awards-425-million-advance.

[18]Environmental Protection Agency. Administrator Memo Prioritizing Efforts to Reduce Animal Testing, September 10, 2019. https://www.epa.gov/research/administrator-memo-prioritizing-efforts-reduce-animal-testing-september-10-2019

[19]EPA drops target date to end mammalian toxicity testing by 2035 | ALTEX - Alternatives to animal experimentation ; New Approach Methods Work Plan (epa.gov))

[20] Eurogroup for Animals. A win for Parliament. 16.09.21. https://www.eurogroupforanimals.org/news/win-animals-european-parliament-votes-favour-comprehensive-plan-phase-out-experiments-animals.

[21] (Eurogroup for Animals. European Commission disregards wishes of the European Parliament by failing to take concrete steps to phase out animal experiments. 2.3.22. https://www.eurogroupforanimals.org/news/european-commission-disregards-wishes-european-parliament-failing-take-concrete-steps-phase)

5.4 Campaigners Road Maps

Animal Free Research UK published its report Modernise Medical Research in 2021.[22]
It encourages the government to “create a new department or ministerial position tasked exclusively with accelerating the replacement of animals. This role would undertake activities such as producing detailed plans, facilitating collaboration and leading the reform of international guidelines on the testing of medicines.”
AFRUK’s report explores moves in various countries to transition towards human-centred research with takeaways on how the UK government can learn from each example, along with a series of practical policy recommendations.

Also in 2021, PETA proposed a 'Research Modernization Deal' for a strategy for replacing the use of animals in experiments with human-relevant methods.[23]

Menschen für Tierrechte - Bundesverband der Tierversuchsgegner e.V. (People for Animal Rights Germany - Federal Association against Vivisection) have set out how they believe the complete replacement of animal procedures can be achieved in a "Master plan for an end to animal experiments".[24]

And in the UK, it was the pharmaceutical industry (and the Medicines Discovery Catapult a project funded by Innovate UK, an agency of the UK government) that has published suggestions "to develop technologies to humanise drug discovery in order to improve research productivity for industry."[25]

5.5 Opinion polls

A survey in September 2021 for Cruelty Free International found general support for the idea of a phase out date with:

- 65% of Great Britain wants to see a binding plan in place to phase out animal testing.
- 66% also agree that a target date should be set for the end of all animal experiments.[26]

Another survey in 2020 by Savanta ComRes for Cruelty Free International found:

- 72% of EU citizens think Europe should set targets and deadlines to phase out animal testing.[27]

6 A rise in 3Rs centres and replacement ideas

[22] Animal Free Research UK. How Can the UK Lead the World in Science and Animal Welfare. https://www.animalfreeresearchuk.org/how-can-uk-the-lead-the-world-in-science-and-animal-welfare/.
[23] People for the Ethical Treatment of Animals. PETA Outlines a New Deal to Revamp Laboratory Research. https://headlines.peta.org/research-modernization-new-deal/
[24] Baumgartl-Simons, C. and Hohensee, C. How Can the Final Goal of Completely Replacing Animal Procedures Successfully Be Achieved? In: Animal Experimentation: Working Towards a Paradigm Change. pp88-123. Eds Herrmann, K. and Jayne, K. Brill, 2019.
[25] State of the Discovery Nation 2018 and State of the Discovery Nation 2019 Medicines BioIndustry Discovery Catapult and BioIndustry Association
[26] https://crueltyfreeinternational.org/latest-news-and-updates/poll-two-thirds-brits-want-see-animal-tests-phased-out-and-deadline-set
[27] https://crueltyfreeeurope.org/what-we-do/latest-news-and-updates/poll-72-eu-citizens-want-phase-out-plan-animal-tests

Sixty years ago Russell and Burch's '*Principles of Humane Experimental Technique'* proposed the 3Rs (refinement, reduction and replacement) as an overarching idea or framework to embed ideas of animal welfare into scientific research which used animals.

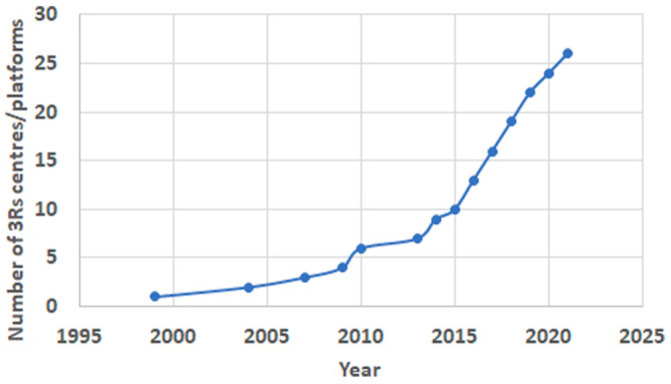
In most modern societies this 3Rs approach has become a popular 'compromise' position between animal advocates and scientific research bodies, and it is now formally embedded in legislation around the world as well as into the management plans of universities, institutes and commercial testing organisations everywhere.

6.1 3Rs Centres

EU Directive 2010/63 on the protection of animals used for scientific purposes became formally applied across the EU in January 2013. It was the first time that the 3Rs were specifically mentioned in EU legislation and resulted in many European countries implementing the 3Rs in their national legislation. In many cases this led to the formation of 3Rs centres and platforms.

These centres promote the 3Rs across the scientific community and provide training, as well as embedding the 3Rs in policy, practice and regulations.[28] EURL ECVAM organised events in 2015 and 2016 to network the Three Rs centres and platforms at the European level. [29]

Norway's 3R centre Norecopa lists 50 global 3R centres or platforms on its website although not all use the phrase '3R' in their title.[30] All of these are in Europe except eight. The others include India, New Zealand, Japan, Canada, Brazil, 'developing countries, particularly in Africa' and two in the USA.



The cumulative increase in the number of Three Rs centres and platforms in Europe over recent years.

[28] https://www.nc3rs.org.uk/who-we-are/our-mission
[29] Neuhaus, et al. 2022. The Rise of Three Rs Centres and Platforms in Europe. Alternatives to Laboratory Animals. Volume 50, Issue 2, March 2022, Pages 90-120.
[30] https://norecopa.no/search?q=*&sf=all&fq=cat%3A3R+Center&fq=db%3A3r&sort=name+asc&p=1&t=strict

Despite the advancement of replacement ideas, there still seems to be an eagerness to establish centres with a broad 3R rather than 1R focus in countries that don't yet have them. Recently created 3Rs centres and platforms include:

- 3Rs Centre Czech Republic - created in 2019
- Ukrainian 3Rs Center - created in 2020
- i3S - the Portuguese Three Rs centre - instigated in 2021
- France Center 3R (FC3R) - inaugurated in 2021
- Luxembourg 3Rs Platform - Preparatory meetings began in 2021 and the platform is currently in the development and mapping phase.[31]

And a counter trend of a rise in replacement ideas

However, as we have discussed above, growing evidence of the poor reproducibility of animal research[32], and its very high failure rate in drug discovery, is creating a crisis of confidence on the ability of animal tests to accurately predict human responses generally.

Because of this, two obvious questions arise:
(a) what is the point of reducing animal numbers in a test if we're not sure that the outcome is useful to predict a human response?
(b) what is the point of refining the way that a test is conducted if we're not sure that the outcome is useful to predict a human response?

It is also instructive to note that the rise of 'roadmaps', described in section 5.4 above, are all looking for a vision of complete replacement at some future time. Therefore it is looking like the 3Rs itself is becoming a redundant paradigm,

As concluded in 2019 in a co-authored paper by former Lush Prize winners the Centre for Alternatives to Animal Testing (CAAT) and the Joint Research Centre (JRC) : *"Our strategy may not promise an imminent end to the use of animals in science, but it will bring us closer to an era in which the 3Rs are increasingly perceived as a solution to a receding problem. Russell and Burch themselves surely would have welcomed these positive changes".*[33]

6.2 1Rs Networks

Because of this, there are the first signs of an emergence of alternative 1R networks with an explicitly different agenda.

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[31] Neuhaus, et al. 2022. The Rise of Three Rs Centres and Platforms in Europe. Alternatives to Laboratory Animals. Volume 50, Issue 2, March 2022, Pages 90-120

[32]https://www.researchgate.net/publication/325973998_Getting_personal_with_the_reproducibility_crisis_interviews_in_the_animal_research_community

[33] Herrmann, K., Pistollato, F. and Stephens, M. (2019) "Beyond the 3Rs: Expanding the use of humanrelevant replacement methods in biomedical research", ALTEX - Alternatives to animal experimentation, 36(3), pp. 343-352. doi: 10.14573/altex.1907031.

In 2022, the Alliance for Human Relevant Science and Animal Free Research UK launched a 'Community of Practice' which may help initiate a scientific shift of behaviour towards Replacement rather than 3Rs. It describes this project as:
“A one-of-its-kind online community aimed at improving communication among biomedical scientists […] The Animal Free Research Community of Practice is an interactive network for members to share their work, ideas, challenges and passion among like minded peers.”[34]

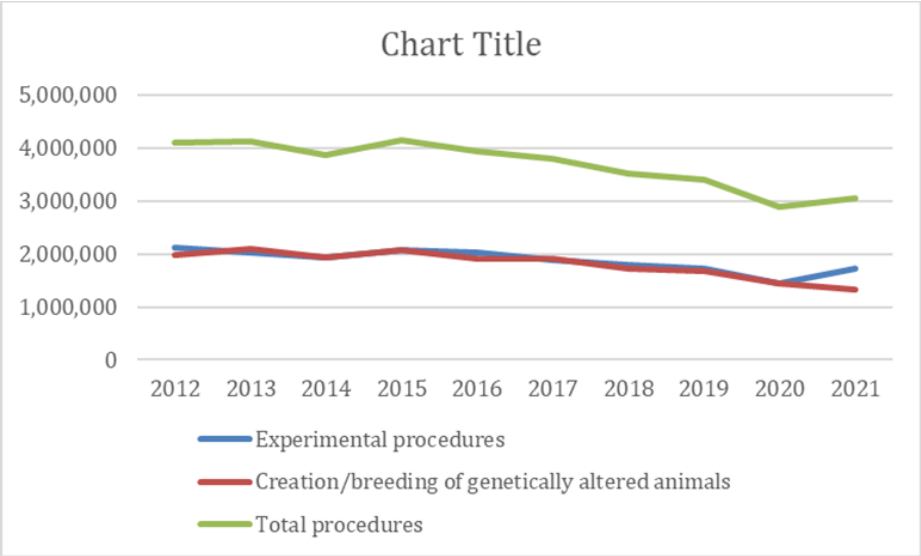
A similar network was established by Lush Prize in November 2021. The Lush Prize 1R Network aims “to create a collaborative network to share expertise and assist members, and others, in working towards the complete replacement of animal use in research and testing, with a particular focus on replacing animals in chemical safety assessment.” The LP1RN includes campaigners as well as scientists.[35]

7 Painfully slow decreases in animal use

7.1 The UK

In the UK, where data collection is of comparatively better quality compared to other countries, the figures include:

- ‘animal tests’ (for chemical safety e.g. cosmetics, food, drugs, industrial chemicals) as well as
- ‘animal experiments’ (experimental or ‘basic’ and ‘applied’ disease research which precede the later phases of drug development and testing (clinical trials)).



[34] https://www.animalfreeresearchuk.org/community-of-practice/
[35] https://lushprize.org/background/lush-prize-1r-network/

Year	Experimental procedures	Creation/breeding of genetically altered animals	Total procedures
2012	2,129,067	1,980,961	4,110,028
2013	2,017,468	2,104,114	4,121,582
2014	1,925,583	1,941,856	3,867,439
2015	2,079,550	2,062,630	4,142,180
2016	2,022,675	1,913,839	3,936,514
2017	1,885,933	1,903,440	3,789,373
2018	1,801,948	1,718,256	3,520,204
2019	1,729,914	1,673,568	3,403,482
2020	1,443,317	1,439,993	2,883,310
2021	1,726,980	1,329,263	3,056,243

Total procedure numbers appear to show a slow downward trend, declining by at 25% from 4 million in 2012 to 3 million in 2021. These numbers relate to live animal use only and do not include the countless more which are killed and used for their tissues in *'in vitro'* research.

2021 figures show some encouraging signs including a 24% decrease in regulatory tests (including a 21% decrease in skin sensitisation tests) and no eye irritation tests for the first time ever. However, there are still animals used for tests which have alternatives and which should therefore be 'zero', e.g. 357 mice still used in skin sensitisation tests. Also sadly some increases in certain species, e.g. a 17% rise in the use of monkeys in 2021

Of over 3 million animal procedures in 2021, 1.7 million were experimental procedures and the remaining 1.3 million were to create/breed genetically modified (GM) animals 'not used in procedures'. These include thousands of animals deliberately bred to suffer harmful and painful mutations such as cancer, heart disease or birth defects.

Furthermore (and contrary to public perception), less than 12% of all procedures carried out are 'required by law' ('regulatory purposes') and even then there is scope for better use of NAMs instead of animals. The vast majority are for experimental research, mostly in academia (universities and medical research institutes), and though these animal procedures require permission via personal and establishment Home Office licences, they are not legally required

7.2 In Europe

In Europe (The EU-28 + Norway), the most recent numbers available for animal use are from 2019 (published July 2022). These show 10.4 million animal procedures which was a 1.5% decrease on 2018. It's important to note that the EU figures only include counts of live animal use and exclude (rather critically) other categories such as 'animals killed solely for organs and tissues' and 'animals bred and killed without being used'. Adding these numbers takes the yearly total to estimates of between 18-23 million.[36]

[36] https://www.altex.org/index.php/altex/article/view/1755/1722

A recent report by Cruelty Free Europe concludes - based on current animal test numbers - that " Assuming animal tests continue to follow a linear decrease at around 1% per year, it will be another 100 or more years (around 2126) before there are no more animal experiments in the EU.[37]"

All EU animal experiment statistics published to date are publicly available for anyone to read at the European Commission website [38]

7.3 Understanding the figures

There are two main reasons why observing a slow decline may actually represent more of a victory for campaigners than it might first seem.

The first is due to the presence of REACH in the equation. REACH is one of the most ambitious attempts to systematically test a large body of chemicals that the world has ever seen. ECHA received 33,363 registration dossiers for 11,114 substances manufactured or imported in quantities of between 1 to 100 tonnes/year. These were the final figures achieved by the third and final REACH deadline in 2018. For all three registration deadlines of 2010, 2013 and 2018 combined, the agency has received 88,319 dossiers for 21,551 chemicals.[39]
According to the HSE, "For a single, high-tonnage substance, with no pre-existing data, and no attempt to minimise animal testing, registration and subsequent fulfilment of the information gaps could require over 5,000 animals (assuming little or no avian testing)."[40]
With a programme of this size going on in the background, you might have expected animal testing to rise - at least during the registration period.

In addition, between 2012 and 2022 the EU economy grew at a rate of about 1.6% per year.[41] This would mean that the whole European economy grew by about 17% over the same period. This is another reason why you might expect actual animal test numbers to increase. The arrival of new substances in a growing economy, such as CBD, and the need to test new approaches to compostable packaging, are just two such examples.

An actual decline, even though slow, against this backdrop is another reason to suspect that something structural may be going on too. However, to paint a full picture, it's noted that REACH (and some of its 'sister' chemical regulations) are due to be revised soon under the European Green Deal and Chemical Strategy for Sustainability, with additional classes of chemicals to be included and great concern over large scale increases in animal tests.[42]

However, an important additional reason why true animal testing numbers for REACH are not reflected in the EU statistics is because the majority of REACH testing is done outside the EU.[43] This may mean observing a decline here may be more apparent than real.

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[37] Cruelty Free Europe Reducing and replacing animal experiments Europe needs an action plan (1).pdf;
[38] Animals used for scientific purposes - Environment - European Commission (europa.eu)
[39] https://chemicalwatch.com/67362/more-than-21000-substances-registered-under-reach
[40] https://www.hseni.gov.uk/reach-minimisation-animal-testing
[41] https://tradingeconomics.com/european-union/gdp-annual-growth-rate
[42] Can Europe replace animal testing of chemicals? (acs.org)

7.4 Opinion surveys in the UK also show painfully slow decreases in public support for animal use

The percentage of people supporting a ban on the use of animals for any form of research in the UK has seen a small increase over the survey period from 21% in 2012 to 27% in 2018.[44]

The surveys reveal that the public have limited knowledge of the issue but are interested in finding out more. However, there is a caveat when it comes to what the public thinks it knows about animal research. In its 2018 report Ipsos makes the following comments:

> *"Misperceptions about animals and testing of cosmetics persist – and have grown. Testing cosmetics and ingredients for cosmetics on animals has been banned since 2009 across the European Union (and the sale of cosmetics that have been tested on animals elsewhere in the world has been banned since 2013). Even so, this year 38 per cent of the public believe testing cosmetics on animals is allowed in the UK. This is a significant increase from 2014, when 31 per cent believed this to be the case."*
> *"It is important to acknowledge this gap between public perceptions and reality, as it suggests that those members of the public who say they feel informed about the use of animals in research do not necessarily hold accurate views on the topic."*[45]

This does not appear to have changed since 2018 either. A YouGov survey in 2021 found that "only 34% correctly said that testing of cosmetic ingredients is illegal in the UK, while 37% didn't know and 29% incorrectly said it was legal."[46]

8 Institutional inertia remains a real problem

8.1 A threat to the animal testing ban from REACH

It has long been a bone of contention for campaigners that the EU's cosmetics testing ban and its REACH chemical safety regulations issue conflicting instructions in some cases, such as where a cosmetics ingredient could be used in other products.

Newspapers have therefore reported that "hundreds of cosmetic products sold in the UK and Europe contain ingredients that have been tested on animals".[47]

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[43] Upholding the EU's Commitment to 'Animal Testing as a Last Resort' Under REACH Requires a Paradigm Shift in How We Assess Chemical Safety to Close the Gap Between Regulatory Testing and Modern Safety Science - PubMed (nih.gov) and Number of animals used in EU chemical tests doubles | Cruelty Free Europe

[44] Public attitudes to animal researchttps://yougov.co.uk/topics/health/articles-reports/2021/11/17/where-do-britons-stand-animal-testingh in 2018. Ipsos MORI on behalf of the Office for Life Sciences

[45] www.ipsos.com/sites/default/files/ct/news/documents/2019-05/18-040753-01_ols_public_attitudes_to_animal_research_report_v3_191118_public.pdf

[46]

However since 2020, new areas of concern opened up when REACH regulators began to insist on 'safety' tests for purely cosmetic ingredients for reasons of 'workers protection'.[48] This has led to a high profile pushback from industry and the general public.

In November 2020, major brands under the HSI Animal-Free Safety Assessment Collaboration, including Avon, P&G and L'Oreal, signed an open statement claiming that ECHA and its Board of Appeal were undermining the EU animal testing ban on cosmetics.

This was followed by a formal petition (European Citizens Initiative) called 'Save cruelty free cosmetics' which was supported by all the major animal campaign groups as well as major cosmetics brands. It was signed by more than 1.4m citizens by its deadline in August this year and is now awaiting a formal response from the European Commission.

8.2 A wider problem

In a sense this issue is indicative of a wider problem of institutional inertia. As Pandora Pound and Rebecca Ram note in a BMJ open science paper[49]:

> *Researchers may also be reluctant to relinquish animal models due to 'psychological lock-in', the phenomenon of beliefs persevering in the face of contradictory evidence. As Frank suggests, for researchers using animal models, belief in the value of their work may have hardened as a result of being questioned about it on ethical grounds. In addition, because of the closed nature of animal research, scientists using animal models may not have been exposed to the usual diversity of academic opinion and debate, leading to beliefs and practices becoming entrenched. Furthermore, they may not perceive it to be in their interests to change; referring to 'institutional lock-in', Frank notes that a huge infrastructure perpetuates animal research within universities, whereby academic departments benefit from funding, professional associations, conferences and academic programmes devoted to animal research, all of which make it harder to embrace new approaches.*[50]

[47] https://www.theguardian.com/environment/2021/aug/19/hundreds-of-uk-and-eu-cosmetics-products-contain-ingredients-tested-on-animals;
https://www.altex.org/index.php/altex/article/view/2291

[48] https://www.cosmeticsdesign-europe.com/Article/2022/08/26/Animal-testing-ban-cosmetics-EU-needs-protection-via-European-Citizens-Initiative-says-Dove

[49] Pound P, Ram R Are researchers moving away from animal models as a result of poor clinical translation in the field of stroke? An analysis of opinion papers
BMJ Open Science 2020;4:e100041. doi: 10.1136/bmjos-2019-100041

[50] Frank J, *Technological lock-in, positive institutional feedback, and research on laboratory animals. Structural Change and Economic Dynamics2005;16:557–75.*doi:10.1016/j.strueco.2004.11.001

9 Rise of the language of human relevant science

The focus of the game changing 2007 report Toxicity Testing in the 21st Century was all about a transition to superior predictive technologies based on human biology.[51] Since then, and given the rise of awareness of the failure of the animal model identified in point 1 above, there is now more discussion of how the language of human relevance might be core to removing animals from laboratories.

Lush Prize held its (now) annual conference in 2021 on the theme of the role of public awareness in the replacement of animals in safety testing.

The third panel session asked "What Role Can the Public Understanding of Science Play in Ending Animal Testing?"

During this panel, Dr Aysha Akhtar from the Center for Contemporary Sciences, an organisation promoting non-animal research methods in the USA, raised some important points about the language used by organisations in this field. Her comments include the following:[52]

> *"We need to change the narrative. As a community we have done a poor job of informing the public. We get too complex when we talk about animal testing and the replacement of animal testing."*
> *Stop using the word 'NAMs'. New Approach Methodologies - the public will have no idea what that means. […] Stop using the word alternatives - we are well beyond the idea of human-relevant testing methods being alternatives. They can actually be better."*
> *I started using the term human-biology-based testing methods to emphasise that these testing methods are based on human biology. When you talk about that, people get it."*
> *I would argue that we always need to use the word 'human biology' or 'human-specific' or 'human-relevant'."*
> *The thing the animal testing industry fear the most is an educated public. The public are ready for a change in the narrative about animal testing."*
> *Use simple words: "'We can revolutionise medical research to make it much more relevant to human biology. It will save not only animals but save humans'. Keep it simple. That is the type of language that the animal experimentation industry uses. We need to do the same thing."*
> *At CCS we have adopted the word 'artificial animal models', because they are artificial. They are artificially-created diseases in animals. The more you start using language like this the more it seeps into the public's mind. Language is so key to this."*

[51] Melvin E. Andersen, Daniel Krewski, Toxicity Testing in the 21st Century: Bringing the Vision to Life, *Toxicological Sciences*, Volume 107, Issue 2, February 2009, Pages 324–330, https://doi.org/10.1093/toxsci/kfn255

[52] Dr Aysha Akhtar, Center for Contemporary Sciences. Lush Prize Conference 2021 - Panel 3. https://vimeo.com/showcase/9070582/video/651485177

In another example of the shift-towards a language of human relevance, Safer Medicines Trust, Dr Hadwen Trust (now Animal Free Research UK), Kirkstall (a Lush Prize winner), Cyprotex and CN Bio Innovations launched the Alliance for Human Relevant Science in the House of Commons on 8th February 2017. The late Sir David Amess MP, a dedicated parliamentary advocate for non-animal methods, hosted the event, which was full to capacity with senior scientists and MPs whose enthusiasm and support were palpable. The Alliance spoke about how it aimed to help to speed the transition away from animal testing, towards more efficient and predictive models based on human biology. Sir David said: "Britain is a world leader in life science research. But we had better look to our laurels if we do not want to be left behind, while others take the lead in embracing more predictive tools based on human biology. I wish the new Alliance every success with this hugely important initiative."[53]

9.1 Alternatives to animal testing

Within this context, the notion of describing non-animal tests as 'alternatives' is also seen as problematic. An 'alternative' suggests a direct replacement with the aim of producing a similar outcome. Yet animal research is so poor at predicting and reproducing outcomes in humans, that we are not looking for an 'alternative' but for a better way to solve a problem or 'solution'. In fact, next generation risk assessment (NGRA) methods do not replace animal tests, instead they supersede them by providing better data.

'Alternatives' is a term that's been used for a long time and so its familiarity is still widespread, with the two main scientific journals in the field of non-animal research both using it;
ALTEX – Alternatives to Animal Experimentation
ATLA - Alternatives to Laboratory Animals
ALTEX is the journal of the Center for Alternatives to Animal Testing. Other organisations in this field include EUSAAT - the European Society for Alternatives to Animal Testing.
The terms 'alternative' and 'replacement' can both have different meanings to different people. They do not necessarily refer to the complete replacement of animals and are at times used to refer to one animal that is used in place of another. For example, mice have been referred to as a replacement to non-human primates;[54] minipigs as an alternative approach to using dogs and non-human primates;[55] and zebrafish larvae "as a new alternative model […] replacing and reducing […] mammals."[56]

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[53] https://www.humanrelevantscience.org/launch-event/

[54] Home Office. 2014. Working to Reduce the Use of Animals in Scientific Research. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/277942/bis-14-589-working-to-reduce-the-use-of_animals-in-research.pdf;

[55] (Forster et al. 2010. The RETHINK Project on Minipigs in the Toxicity Testing of New Medicines and Chemicals: Conclusions and Recommendations. Journal of Pharmacological and Toxicological Methods, 62(3), pp. 236–242)

[56] (Academy of Medical Sciences. Animals in research. https://acmedsci.ac.uk/file-download/65265472)

For a fuller explanation of why ‘alternatives’ are not always what they seem, see When Is an Alternative Not an Alternative? Supporting Progress for Absolute Replacement of Animals in Science. [57]

10 Young scientists are increasingly being trained in and are enthusiastic about these ideas.

10.1 Number of Young Researcher nominations received

The Young Researcher award category reflects the ongoing interest and enthusiasm of the Lush Prize to invest in early career scientists wishing to start (or continue) a career in cutting edge science without animals. We continue to receive high quality research proposals, including advanced *in vitro* methods (e.g. Multi organ chip, 3D spheroid and IPSC methods) *in silico* (e.g. chemical screening via machine learning and artificial intelligence (AI) models) and NAMs strategies which incorporate many of these different method types.

The growing interest in non-animal research is reflected in the number of Young Researcher nominations received, which has generally increased year on year, the exception being 2020, when the COVID-19 pandemic was a likely factor. 2022 saw a return to pre-pandemic levels of nominations, as shown in the table below.

Year	2015	2016	2017	2018	2020*	2022
Total YR nominations received	26	27	38	55	47	54

*Slight decrease in 2020 likely due to COVID-19 pandemic

In 2016, 2017 and 2018 the Lush Prize was pleased to award a 'bonus' number of YR bursaries, (a total of fifteen each year instead of the usual five) allocated across three geographical regions- 'Young Researcher Asia', 'Young Researcher Americas' and 'Young Research Rest of the World' to address the need to provide funding to young scientists who are often ‘lone voices’ in pursuing animal free research interests.

Successful winners explained how - aside from gaining urgently needed funding for their research materials and equipment- the recognition of winning the award itself raises awareness in their establishments and shines a spotlight on the issue of how unreliable animal use is and why it must end. While their success is not always received positively, many brave young scientists have been driven to continue their award-winning research in the face of criticism over not pursuing animal studies.

Our 2016 YR Asia winner from Japan explained

[57] Redmond, C. 2019. When Is an Alternative Not an Alternative? Supporting Progress for Absolute Replacement of Animals in Science. In: Animal Experimentation: Working Towards a Paradigm Change. https://brill.com/view/book/edcoll/9789004391192/BP000034.xml

'My main reasons to work in this field are ethics and the simple fact that animals are not good a model for humans. It is flawed to consume an animal's life without considering the differences between animals and humans in accordance with safety test guidelines ....I come up against barriers in trying to avoid the use of animals in my work.. One is it's difficult to obtain human tissue for study without data on animal testing…using animals is required in Japan…. To break the barrier, I and many scientists have risen up and launched the community from this year. The other is it's difficult to get research funding for non-animal research ..where the majority of researchers believe that animal testing is scientifically the most relevant to assess safety. I need the support of the community to achieve an animal testing free future"

10.2 It's just better science

Over the Lush Prize's first decade, the young researcher nominations have evolved to embrace the latest advances in human relevant, animal-free technologies but, for many early career scientists, it is simply the 'better science' they are used to.

Encouragingly, increased interest in non-animal methods (from early to senior career research level) has been apparent in recent years. The drive for change towards New Approach Methods/Non-Animal Methods (NAMs) is due in no small part to younger generation scientists, who have graduated alongside the emergence of modern technologies in toxicology and biomedical research. As a result, they do not necessarily hold the belief that animal-based methods are the so called 'gold standard'.

One of the key positive findings from interviews with previous Young Researcher prize winners is that "Young scientists don't always have the prejudices about animal testing being the 'best' way of doing things", which evidence suggests is a more typical 'collective belief' of senior researchers in industry and academia, who have grown accustomed to using animals – often via repeat research grants or salaries to do so - over long careers.[58]

Funding for animal research is still the mainstream route and far easier to obtain, as laboratory institute and funding infrastructure are built on decades of the same types of animal procedures being carried out again and again. This is termed 'well established' models, which in turn result in cycles of repeat funding. This is particularly true in academic research, where animal use 'lock in' is prevalent, reflected in the testimonies received in many nominations, for example where researchers are committed to continuing their NAMs research,"despite the vested interests that we are faced with on a daily basis".

Encouragingly, evidence suggests that while the number of animals used in labs is declining only slowly, the number of researchers is increasing, reflecting a shift to some extent towards NAMs and related technologies. For example, the number of EU based researchers in R& D increased by nearly 30% between 2010-2020.[59], [60]

[58] https://pubmed.ncbi.nlm.nih.gov/26753946/
[59] https://ec.europa.eu/eurostat/statistics-explained/index.php?title=R%26D_personnel#R.26D_personnel
[60] https://www.altex.org/index.php/altex/article/view/1134/1131

To be clear, gaining funding for young scientists remains challenging, but is moving (very slowly) in the right direction, as recognition for NAMs improves. Young Researcher funding channels offered by the Lush Prize and other stakeholder organisations, such as those enrolling for summer schools , travel bursaries or other studentships- continue to fulfil a vital role.

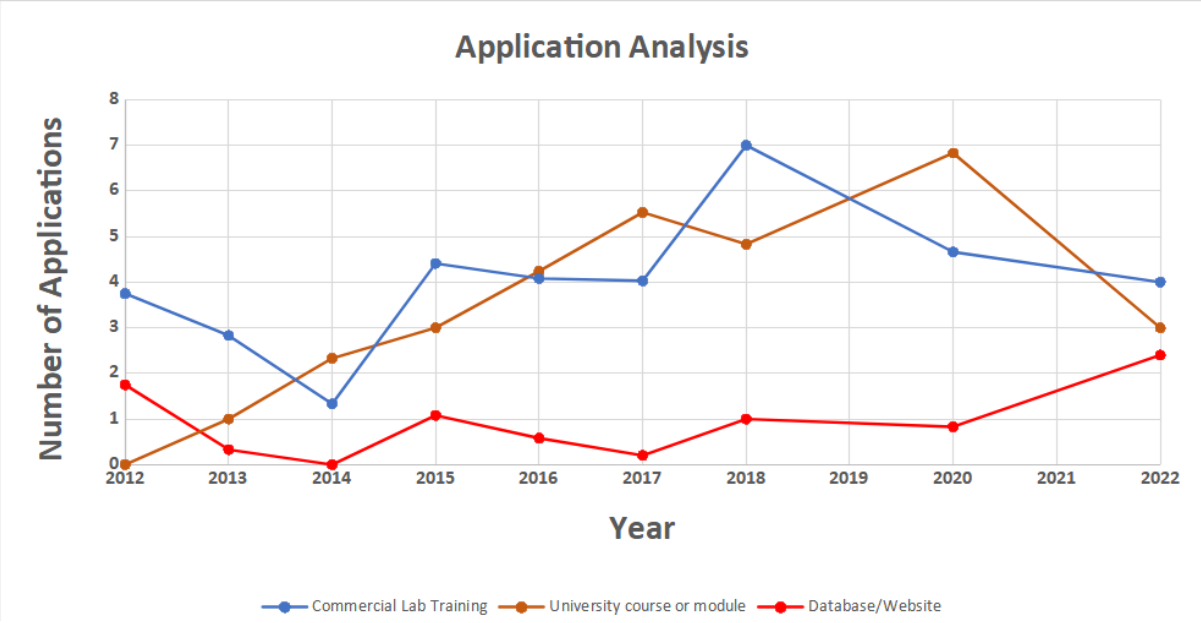
10.3 And a rise in training projects

There is sometimes a disconnection between the rapid advancement of technologies that avoid using animals and the education of scientists in these fields. Eurogroup for Animals noted that " There is little point in having the most advanced technologies in the world if very few people know how to use them".[61]

Over the ten years of Lush Prize there has been a greater use of the internet to support online training. The outbreak of the Covid-19 pandemic in 2020 hastened the take up of online approaches due to the lockdowns around the world resulting in the cancellation of in-person workshops and training.

Some training courses usually held in-person were able to move online during the pandemic, including the Physicians Committee for Responsible Medicine's Summer School on Innovative Approaches in Science, JRC Summer School on Non-animal Approaches in Science and the European Society of Toxicology In Vitro's Applied Training Course.

An additional benefit of online training, such as webinars and online conferences, is that people can attend from a greater number of countries who may be restricted by financial costs or other factors in attending in-person. Recordings of these sessions can be more conveniently viewed later by people in other time zones.



[61] https://www.eurogroupforanimals.org/news/action-plan-transition-animal-free-innovation-concrete-way-forward

The Table above shows the types of projects applying for Training Category awards over the Prize's ten year period.

Below are some of the main training courses (excluding those offered by universities to their students) that focus on the replacement of animal use. All of these courses / platforms were launched since Lush Prize began in 2012.

AFRUK Summer Student Programme
Website: https://www.animalfreeresearchuk.org/summerstudent/programme/

Summer School on Innovative Approaches in Science - Physicians Committee for Responsible Medicine
Website: https://www.pcrm.org/ethical-science/ethical-education-and-training/ERA21

JRC Summer School on Non-animal Approaches in Science (European Commission's Joint Research Centre)

The European Society of Toxicology In Vitro (ESTIV) Applied Training Course
Website: https://www.estiv.org/projects-activities/training-course/about-the-course/

Center for Alternatives to Animal Testing (CAAT)
Course 1: Animals in Research: Law, Policy, and Humane Sciences (online course)
Website: https://www.jhsph.edu/courses/course/36166/2022/187.625.81/animals-in-
Course 2: Toxicology 21: Scientific Applications / Evidence Based Toxicology
Website: https://www.coursera.org/lecture/toxicology-21/center-for-alternatives-to-animal-testing-6BjRq and https://www.coursera.org/learn/evidence-based-toxicology

PETA Science Consortium International webinars
Website: https://www.thepsci.eu/training-videos-webinars/

CPHMS - The Centre for Predictive Human Model Systems (India)
Website: https://aic.ccmb.res.in/student-innovators-program/

Altertox Academy
Website: https://academy.altertox.be/trainings/

Berliner Landestierschutzbeauftragte - Animal Welfare Commissioner of Berlin
Website: https://www.youtube.com/channel/UC7WgnOtO4Ez6HiDRITLEWZg/featured

Part D: Conclusions and evaluation

1 Contributing to the aggregate pressure for change

Trying to assess the indirect impacts of the activities of a single civil society group in complex global social change projects is fraught with difficulty. Lush Prize is just one player in an ecosystem of other institutions all pushing towards the same goal. These include big global campaign groups like HSI and international academic projects like the Centre for Alternatives to Animal Testing (CAAT), as well as hundreds of other national projects and individuals.

All of the bigger picture developments which we have identified in the previous section would certainly have happened in some way without the presence of the Prize. And the first four particularly were already on long trends before the Prize came along.
1 A rising awareness of the failure of the animal model
2 A rise of Organs on Chips and Computational toxicology
3 AOPs are becoming embedded as a core knowledge framework
4 Cosmetics testing bans have been rolling out globally

When assessing the impact of other campaigns, at Ethical Consumer we use the expression 'contributing to the aggregate pressure for change'. The strategic rewarding and financing of the 126 key projects that the prize has done (that we covered in Part B) will all have helped move each of these developments on a little bit.

2 A unique project in the centre of toxicology conversations

The key difference of the Prize to the many other institutions discussed above is its laser-like focus on complete replacement in the world of toxicity testing. Many other organisations work on this, but often as part of much bigger programmes, either addressing animal use more widely (campaigners), or concentrating mainly on drug discovery (scientists).

Others do exist in this space, such as the excellent Animal Free Safety Assessment Collaboration (of which Lush is a member).[62] However Lush Prize, which has five awards which include campaigners, lobbyists and young researchers, has created a very broad tent. There are no other communities of interest quite like it. At Lush Prize events, undercover lab investigators can come into the same room as scientists and campaigners for cruelty free shopping and be treated as equals. More importantly they can see how they are part of a wider movement for change.

And because Lush Prize sits in the middle of all this and learns about all the projects going on around the world it is uniquely placed to bring them together. One of the most important impacts the prize has had over the years is when winners meet up with others to form 'horizontal future collaborations' independently of the Prize. The two classic examples we

[62] www.afsacollaboration.org/

use are Lush's own relationship with XCellR8 and the talent pool for recruitment into HSI (Humane Society International) that the awards have become! But there are others too.

3 An unwavering voice for complete replacement

Lush Prize's background in animal ethics means that it has not compromised on the goal of complete replacement, nor on the use of animal ingredients. In a world where 3Rs and 'alternatives' have been, until recently, the mainstream approaches to addressing animal use in science, this remains another key difference for the project.

Although many will know this already, some winners and applicants will learn that this is (both scientifically and ethically) a tenable or viable position to hold. And, as we mentioned above, Lush Prize's sponsorship of 'replacement only' session at 3Rs conference reinforces this idea with more mainstream players too.

Because of this, the impact of the Prize on the four other positive developments we identified, which are about more subtle changes to language and ideas, could have been more significant. These are:
5 A rise of ambition for full replacement (roadmaps)
6 A rise of replacement ideas and 3Rs centres
9 More discussion of human relevant science and less of alternatives
10 Young scientists are increasingly being trained in and are enthusiastic about these ideas

Of course, Lush Prize will have just been contributing to these too as part of 'aggregate pressure for change. However, they are arguable newer phenomena too, becoming more visible in the years since the Prize began. Perhaps the Prize's confidence has given confidence to others that holding this position will not be seen as weird or hopelessly idealistic.

4. How long before the goal of complete replacement is met?

10 years ago, when Lush Prize was being designed, we asked specialists how realistic it was to call for a world where all animal testing had stopped, and how long it might take to get there? When we got an answer, most said we needed to be in it for the long haul, and that it would take at least 20 years to achieve that goal.

So, ten years in, does it feel like we are halfway through? Does progress feel quick enough? Or does the light at the end of the tunnel still feel 20 years away?

It is interesting to note, in this context, the dates that appeared (and then disappeared) in the institutional roadmaps discussed in C5 above. They included 2025 (for some), 2032 and 2035 which are in roughly the same ballpark as 'another 10 years' from 2022.

It is also interesting to note that, even the most aggressive promoters of animal use in toxicology testing, are suggesting that 20 to 40 years might be doable. ECHA's former executive director, Bjorn Hansen, said on chemical testing without using animals in 2021 "we're currently 40 years away from being able to effectively predict toxicity of chemicals, but with focused investment and regulatory needs driving the work, this could be reduced to 20 years."[63]

Responding to Dr Hansen, Professor Thomas Hartung, described the limitation of predictive toxicology as the "overestimation of the quality of the animal testing predicting human health effects". "As long as we set the wrong goal – reproducing the animal findings – we effectively block change. From my point of view, it takes rather limited time and investment".

Asking this question is on the agenda for Lush Prize's 2022 conference in November. Perhaps we can update this paper after that?

5. Unsticking the institutional inertia?

It would be wrong not to address the two counter-trends identified in the bigger picture developments section above. These were the slow decline in actual animal use and the related institutional inertia.

The first point to note is an obvious one. What Lush Prize (and others) are trying to do is very complicated. Toxicity testing on animals has become embedded in institutions around the world over many decades. Different countries have different regulatory regimes and different cultures and different political systems. Even regulations within advanced, world leading institutes (e.g. the EU), greatly lack harmonization and coherency. Making change happen in this context is not simple.

Obviously it would be great if comprehensive international government action could divert funding towards non animal methods and prevent regulations from encouraging greater animal use. And it is important to push for it. However, global change rarely happens in such a logical and sensible way. The current frustrations in trying to address climate change and tax avoidance in a coherent way are just two cases in point.

On the related question of how long it will take for organs on chips to be accepted as replacements to animal models, Professor Don Ingber, founder of the Wyss Institute at Harvard, expects a much more piecemeal approach to reform.

> *"This process will probably occur gradually and involve replacement of one particular animal model at a time....this will probably be decided on the commercial battlefield, which is now possible given that there are many companies manufacturing organ chips as well as automated control systems to run them.*[64]

[63] https://chemicalwatch.com/275371/echa-head-we-are-40-years-away-from-effective-predictive-toxicology - admittedly this was a slightly different question - but is closely related.
[64] Ingber, D.E. Human organs-on-chips for disease modelling, drug development and personalized medicine. *Nat Rev Genet* **23**, 467–491 (2022). https://doi.org/10.1038/s41576-022-00466-9

However this is not to say that there can be no tipping points or breakthroughs along the way.

Lush Prize was designed in 2012 - with its five awards - in full recognition that change in this area is complex and needs a multi-pronged approach. As we mentioned above, innovating and evolving these awards in an ongoing way is baked into the way the project is run. It is likely to change again (even before the 2024 awards cycle) following some useful contributions from our community.[65] But, by and large, over the last 10 years the Prize has seen good positive trends, and experienced great feedback and encouraging growth.

[65] Such as the suggestion of a prize for innovation at health charities and environmental groups