



Lush Prize 2016

Training Prize

Research Paper

Rebecca Ram, Scientific Consultant, Lush Prize

Executive Summary

The purpose of this research paper is to provide an overview of the **Training Prize**, one of the six categories of the £250,000 Lush Prize successfully awarded every year since 2012. The Lush Training Prize rewards individuals, teams or organisations involved in providing training and/or humane education on non-animal methods of safety (toxicity) testing. £50,000 is available in this category, for one overall winner or shared between two projects.

Over the last four years, the Training prize has awarded £200,000 to eight outstanding organisations across Europe, Africa and the USA for their work in educating researchers, students and regulators in both the acceptance and use of non-animal technologies.¹

This paper is intended as an update on the Lush Training Prize in 2016. It is also recommended that previous research papers (2012-2015) are reviewed for further useful information, including reviews and updates on prizewinning organisations, as well as background on training and education in non-animal technologies.

1 <http://www.lushprize.org/awards/training-prize/>

2016 update; ongoing challenges and successes in training, acceptance and enforcement of non-animal methods

Year on year, awareness of alternative methods increases worldwide, which is to be celebrated. Yet there remains the continuing challenge of not only ensuring resources are available for training and education but making sure that enforcement and monitoring of how (and if) methods are being implemented is carried out across industry and academia. Given both the scientific and ethical imperatives to replace animal tests, this responsibility should fall to national competent authorities and administrative agencies. Yet, several examples demonstrate how this is not the case, even when a test has been validated for use. This is in some cases due to intense effort devoted to the validation process, but perhaps a lack of appropriate follow up to see how tests are actually being used after they have been approved. One such example is the development of the human blood pyrogen test, by Hartung et al, with the potential to replace the same test in rabbits². First published in 1995, it was finally validated and accepted for use in 2009, yet instead of a decrease in rabbit use, annual numbers used for the test actually rose, meaning that *since the method was accepted at regulatory level, more than 800,000 rabbits have suffered and died needlessly, with 400,000 rabbits still used each year, worldwide.*

2 http://www.altex.ch/resources/altex_2015_2_079_100_FFTHartung.pdf

A similar concern is seen when reviewing the use of the well known LLNA (Local Lymph Node Assay (OECD 429³) for skin sensitisation. Although a reduction and refinement method as it still uses animals, its use should have been favoured over the more severe Guinea Pig Maximisation test (GPMT) since its regulatory approval in 2002. However, an analysis by Hartung et al. in 2007 showed that of 1450 skin sensitisation tests, only 50 were LLNA, with the remaining 1400 still using guinea pigs, demonstrating that enforcement, combined with removal of the unnecessary and outdated test method is the only way to save animals. Furthermore, the skin sensitisation Adverse Outcome Pathway (AOP) as highlighted in the 2015 Lush Black Box Prize⁴, now offers entirely human based test methods, which are already approved or (in the case of the human cell line activation (h-CLAT) test) undergoing approval and awaiting official publication at OECD level⁵⁶⁷.

The continued use of animals in toxicity tests, despite the availability of humane alternatives reinforces a vital need for the following:

- A sustained campaign in outreach, training, education and enforcement of non-animal methods.
- Equally important is the *active deletion of outmoded animal tests from regulatory guidelines*, to ensure uptake of alternatives and the prevention of animal suffering as soon as possible.

These represent the values and mission of the Lush Training Prize.

3 http://www.oecd-ilibrary.org/environment/test-no-429-skin-sensitisation_9789264071100-en

4 <http://www.lushprize.org/awards/black-box-prize/>

5 http://www.oecd-ilibrary.org/environment/test-no-442c-in-chemico-skin-sensitisation_9789264229709-en

6 http://www.oecd-ilibrary.org/environment/test-no-442d-in-vitro-skin-sensitisation_9789264229822-en

7 [https://www.oecd.org/env/ehs/testing/151216-Draft-h-CLAT-TG-After-Expert-Meeting-\(clean\)-Final.pdf](https://www.oecd.org/env/ehs/testing/151216-Draft-h-CLAT-TG-After-Expert-Meeting-(clean)-Final.pdf)

Lush Training Prize Winners - 2015

Two exceptional organisations were awarded Training Prizes in 2015, each receiving £25,000:

PETA International Science Consortium Ltd., (PISC) UK

PISC⁸ has undertaken a long term campaign to minimise animal testing under the large scale, EU chemicals testing regulation REACH (Registration Evaluation and Authorisation of Chemicals) which has resulted in an increase in toxicity tests on animals since it came into force in 2007. To do this, PISC's award winning work includes organisation of scientific webinars and face to face training sessions, to promote the use and acceptance of non-animal technologies and integrated testing strategies (ITS). By employing experts in relevant areas from EU agencies, industry and academia, the sessions (co-hosted by Chemical Watch) have an audience of thousands, including scientists, regulators and relevant industry stakeholders in need of education on the methods available.

Dimitry Leporsky⁹, Ukraine

Dimitry was awarded a 2015 Training Prize for his ongoing work over recent years (in collaboration with international organisation and former prizewinner InterNICHE), to ensure the use of animals is replaced with alternative methods in universities across the Ukraine, Belarus, Russia and Kyrgyzstan, by discussion and contract negotiation with teaching staff and department heads, to phase out and replace the use of animals by formal agreement. In the Ukraine alone, this has directly achieved an 85% success level in replacing both live animal use and dissections, saving more than 48,000 animals since 2008. Furthermore, since 2014, more than 18,000 animals have been replaced in other countries. To date, the cumulative total of animals no longer facing experiments or being killed is 684,047 for the Ukraine alone. Dimitry has also engaged in further educational initiatives with early career

8 www.piscld.org.uk

9 <http://www.gumannoe-obrazovanie.org/>

scientists to raise awareness of both the scientific and ethical arguments for using non-animal technologies in their research.

Organisations relevant to the Training Prize in 2016

With each new yearly prize cycle, as well as welcoming independent nominations, the Lush Prize also identifies relevant individuals or organisations who may be eligible for an award because of the work they have been doing, but may not otherwise nominate themselves. In these cases, the Lush Prize team reviews achievements and if considered appropriate, contacts such organisations to ask them if they would like to submit a nomination.

A 2016 update on organisations relevant to the Lush Training Prize is summarised below, some of which have either previously been awarded or shortlisted because of their ongoing work in education, training and dissemination of information related to non-animal methods. As always, some organisations relate to the 3Rs generally, rather than the specific 1R remit of the Prize; however, they are included to provide a more complete overview. This is not an exhaustive list and many other organisations who have previously been awarded, shortlisted or nominated can be reviewed in both previous background papers and on the Lush Prize website. The Training Prize continues to welcome nominations from other groups or individuals:

Instituto 1R de Promocao e Pesquisa Para Substituicao da Experimentacao Animal (1R Institute of Promotion and Research for the Replacement of Animal Experimentation) Brazil¹⁰

Established in 2015 from initiatives carried out over the last decade, the 1R Institute brings together expertise in toxicology, biochemistry, cell biology, biotechnology, physiology, public health, scientific education, law and rights and applied ethics.

10 <http://www.instituto1r.org/>

Three of the founding members of the institute include Lush Prize judge Professor Thalez Trés and two previous Young Researcher award winners, Dr Róber Bachinski (2014) and Dr Bianca Maragliani (2015).

The Institute describes its objectives as follows:

I – To promote ethics, peace, citizenship and human rights, by working in collaboration with professors, teachers and students to ensure students' rights to preserve their ethical principles concerning non-harmful animal use in classes.

II – To guide, through technical-scientific and/or juridical consulting and awareness campaigns, students, teachers, professors and society in general on humane methods of teaching/learning and research, especially for training and education. In this context, it aims to promote liberty and humane equality, following the Article 1 of the Universal Declaration of Human Rights. It also aims to promote freedom of expression and freedom of beliefs, assured by the Article 1 of the Brazilian Federal Constitution, and following the same constitution to promote and ensure the non-privation of rights for ideological convictions.

III – To promote and encourage the research and development of alternative methods, focusing on the final objective of replacing animal use in science and education.

In 2015 alone, the 1R Institute team have presented and participated in more than twenty national conferences and round table events, as well as providing numerous media interviews and released publications on the need for humane education in Brazil.¹¹ One of the institute's specific initiatives includes The Brazilian National Network for Humane Education (RedEH), an initiative to identify and gather professors and researchers involved in humane education and replacement of

11 Bachinski, R, Tréz, T, Alves, GG, *et al.* 2015. Humane Education in Brazil: Organisation, Challenges and Opportunities. *Alternatives to Laboratory Animals (ATLA)* 43, 337-344.

harmful animal use in teaching and training, now includes 25 professors, including representatives from Spain, Portugal and Colombia as international contacts ¹²

Róber Bachinski kindly provided the following update on the Institute's outreach and activities in 2015;

'Early in 2015, academic professors and researchers started in Brazil the 1R Institute of Promotion and Research for the Replacement of Animal Experimentation. The 1R Institute came from several projects already developed on Brazil, especially on Humane Education, expanding for R&I. Founder members come from different fields in the academia, including biochemistry and cell biology, microphysiology, in vitro and omics assays, immunology, humane education, law system, public policies and applied ethics. Through the Humane Education, the 1R Institute understands the academic support to 1R students, concerning to practical activities, scientific initiation opportunities, or even social-academic argumentation, as primordial for new scientific construct. These students will contribute to the change of scientific paradigm, nucleating academic movements and new research groups. Indeed many students against animal use for education are interested on scientific activities based on 1R science, for research and development and also for new humane education methods and approaches. The 1R Institute idealized the Brazilian National Network for Humane Education (RedEH) (Bachinski, Tréz, Alves, Garcia, & Simone, 2015), gathering Humane Education professors and researchers, supporting and spreading humane education methods. Currently, 28 professors from different Brazilian regions and Biological and Health science courses integrate the RedEH. The project is a horizontal self-managed team, where each one can propose projects or create specific programs. The 1R Institute was supported for RedEH members requesting a national recognition of Conscious Objection, addressed to the Brazilian National Council for the Control of Animal Experimentation (CONCEA), linked to The Ministry of Science, Technology and Innovation (MCTI). CONCEA published in February 3rd the "Brazilian Guideline for Animal Care and Use for Activities of Education and Research", delegating to institutes that uses animals the responsibility to offer alternative methods for Conscientious Objector students (5.1.1.O), and the development of an institutional ombudsman office*

12 <http://www.instituto1r.org/#!reddeh/cn8r>

for subjects related to animal use, including to support those students (5.1.1.J) (CONCEA & MCTI, 2016). Aiming the support for new scientific groups, the 1R Institute also created the 1R Researcher List, looking for Brazilian researchers supporting animal replacement, especially as potential new scientific groups or academic advisors for students and young researchers. Despite other scientific groups working on 3Rs, especially related to Governmental bodies, the 1R Institute did 24 conferences in Brazilian universities in Brazil and academic activities for students in Brazil. All conferences and interviews are moments for talk about new technologies and new approaches for a human-based and non-animal science.'

(* Note: CONCEA is the legal authority regulating animal use in Brazil)

Brazilian Network for Alternative Methods (RENAMA)

RENAMA was developed after a need was finally identified in 2008 for recognition of alternative methods in Brazil¹³.

Together with the Brazilian Centre for Validation of Alternative Methods (BraCVAM) RENAMA identifies and prioritises new test methods for validation and regulatory acceptance and encouraging recognition of non-animal technologies.

Key lab sites are involved in training and development in *in-vitro* strategies, for example acceptance and training in OECD-recognised test methods, as well as 'Organisation of Interlaboratory comparisons' to ensure consistency and harmonisation with test methods and Good Laboratory Practice (GLP). Increased recognition of OECD methods is required, yet to achieve this infrastructural setbacks must still be overcome.

It is also important to note that a key challenge in Brazil is that, even after validation and acceptance of alternative test methods, companies can take up to 5 years to

13 <http://www.atla.org.uk/brazilian-center-for-the-validation-of-alternative-methods-bracvam-and-the-process-of-validation-in-brazil/>

implement them - in the meantime further animals suffer unnecessarily. This is an issue that key national animal-protection groups are trying to address, as well as taking into account other practical and logistical factors such as resources, quality and availability of materials. For example, to overcome ongoing customs and import problems preventing the use of HRE (Human Reconstituted Epithelium or 'human skin in a test tube') donated and waste tissue from surgical procedures is used in some cases.

Romanian Centre for Alternative Test Methods (ROCAM)¹⁴

ROCAM was established in June 2015 and is hosted by the University of Agricultural Sciences and Veterinary Medicine (USAMV) in Cluj-Napoca at the Institute of Life Sciences. The centre describes its main goal as '*to promote excellence in the field of education, research and innovation*' and its efforts focus around three main working groups (WG) addressing Regulatory Affairs; Research and most relevant to the Training Prize - Education and Training. Very recently, the centre hosted a training event in 'In-silico modelling and tools under REACH'¹⁵

A Course in Alternatives¹⁶

The Alternatives is an organisation headed by Dr. Candida Nastrucci, who in collaboration with the Italian Regional Authority of Tuscany has implemented 'A Course on Alternatives' with a specific focus on replacement methods in research and education.

14 <http://rocam.usamvcluj.ro/>

15 <https://www.eventbrite.com/e/in-silico-modeling-and-tools-under-reach-tickets-22774010679?ref=ebtnebreg>

16 www.thealternatives.eu

Kirkstall Quasi-Vivo® Training Courses ¹⁷

Kirkstall is a UK based, cell culture technology company, formed in collaboration over the last decade through research from the University of Pisa. Kirkstall's headline product is Quasi-Vivo, a high throughput and high quality cell-culture system to mimic human metabolism which Kirkstall describes as:

17 <http://kirkstall.org/>

- *A route to replacement of animal testing with lower costs and the obvious ethical benefits*
- *More physiologically relevant models that can be a better prediction of what will happen in the clinical (in vivo) situation*
- *Opportunities for collaborative research at the forefront of advanced in vitro cell culture and disease modelling*

Kirkstall also provide 1 or 3 day training courses in Quasi-Vivo, to provide *in-vitro* researchers with an introduction to both theory and practice of advanced cell culture techniques through a combination of lectures, demonstrations and practical hands-on experience.

University of Milan, Master of Veterinary Biotechnology Sciences; 'Alternative Methods in Toxicology'¹⁸

In 2015, the University of Milan introduced a mandatory module to its veterinary masters course, described as including *in-vitro* replacement methods, in-silico demonstrations and integrated testing strategies. The course also includes theoretical study of alternatives in toxicological research and is currently expanding its practical content to include opportunities for further *in-vitro* laboratory experience.

ToxRead¹⁹ is a freely accessible software tool to assist chemical researchers in optimising their read across evaluations of similar groups of substances. The software, developed by Mario Negri Pharmacological Research in Milan, allows the user to provide the chemical of interest, the endpoint, and to choose a number of similar chemicals (up to six), to produce easy to read graphical results connecting the target chemical and the structural alerts with the most similar compounds.

18 Caloni, F. (2015) Teaching alternative methods in Toxicology in Veterinary Science. *ALTEX Proceedings EUSAAT 2015* Vol. 4 (2) [http://eusaat-congress.eu/images/2015/Abstractbook_EUSAAT_2015_Linz_2015_low_res.pdf]

19 <http://www.toxgate.eu/index.php>

The QSAR Databank (QsarDB)²⁰

QsarDB is described as a smart repository for (Q)SAR/QSPR models and datasets, readily accessible for discovery and exploration research. The databank currently contains over 360 predictive (Q)SAR models for physical-chemical properties, environmental toxicity, ecotoxicity, human health, toxicokinetic and other endpoints.

Qsar DB was developed by the Molecular Technology Group at the Institute of Chemistry in the University of Tartu, Estonia, who also provide training workshops on using the repository, for example at QSAR 2016²¹

²⁰ www.qsardb.org

²¹ <http://www.qsar2016.com/#!program/c15y>

Lush Training Prize outreach in 2015-2016

Lush Prize had a busy couple of weeks in September 2015, attending back to back toxicology conferences. At EUROTOX 2015, the 51st Congress of the European Societies of Toxicology (<http://www.eurotox2015.com/>) we engaged with researchers and toxicologists to inform and raise awareness on the Training Prize as well as the other five prize categories, all aimed at eliminating the use of animals in toxicity testing. Lush Prize also presented a poster entitled 'The Lush Prize – Rewarding innovative animal-free science around the world' (www.lushprize.org/poster).

Our abstract submission was also published in the official journal of EUROTOX 2015, Toxicology Letters (<http://www.journals.elsevier.com/toxicology-letters/>)

The theme of EUROTOX 2015 was 'Bridging Sciences for Safety'. While much of the conference and exhibition focussed on conventionally accepted methods of toxicity testing using animals, there were some key sessions on the 3R's, incorporating the specific aim of the Lush Prize - *replacement*. One particularly interesting session was a debate (between representatives from ECVAM and Procter & Gamble) on *in-vitro* methods that are available now and ready to be relied upon for human safety.

The second conference Lush Prize attended was the 19th European Congress on Alternatives to Animals hosted by EUSAAT (European Society for Alternatives to Animal Testing) and held each year at Johann Kepler University in Linz ²². The congress included a variety of relevant topics, including a "Practical Training Course on Alternative Methods"²³.

Lush Prize again presented its 2015 poster and networked with potential nominees, researchers and key figures in the field. Attendees were very interested to hear about the Prize and how they can nominate their own work, or that of others for an award in Training, Science, Lobbying, Public Awareness or as a Young Researcher. Training courses will once again be offered at EUSAAT 2016²⁴.

22 <http://www.eusaat.org/>

23 <http://eusaat-congress.eu/index.php/congress/2015/2015-practical-training-course>

24 <http://eusaat-congress.eu/index.php/congress/2016/2016-practical-training-course>

In April 2016, Lush Prize also attended the Pan American Conference on Alternative Methods 25 at Johns Hopkins University in Baltimore.

The conference was the first of its kind hosted by former Lush prizewinner CAAT (Centre for Alternatives to Animal Testing). The event addressed not only developments in the established 'reduction, refinement, replacement', but aimed to introduce a further '3Rs' in initiatives to replace animal testing, namely 'Roadmaps'; 'Relevance' and 'Read-Across'.

Conclusion

At the time of writing this paper, the Lush Prize continues to receive and review nominations for the 2016 Training Prize until the closing deadline of 24 July. Outreach for the Training Prize will continue into the 2016-2017 prize cycle.

References

Key organisations continue their work in training and education of non-animal methods, meaning that many references largely remain unchanged. Therefore, in addition to the organisations and individuals included above, it is highly recommended to review comprehensive reference and bibliography sections provided in previous Training Prize papers²⁶.

25 <http://caat.jhsph.edu/programs/workshops/PanAmerican/index.html>

26 <http://www.lushprize.org/awards/background-research-papers/>