THE 2015 LUSH PRIZE

SUPPORTING ANIMAL-FREE TESTING

Lush Prize for Training - 2015

Research Paper

1 Executive Summary

The Training Prize is one of six categories of award within the annual £250,000 Lush Prize which recognises outstanding achievements in education and training of available non-animal methods, as well as initiatives in raising awareness of the need for replacement of animals in toxicity testing. A £50,000 award fund is shared between all winners of the Training Prize each year.

Prize winning work may relate to training and outreach to researchers and industry, postgraduates or earlier-education audiences in schools, college or sixth form. Since its launch in 2012, the Lush Prize has awarded six organisations and individuals (two per year) from the UK, Italy, Bulgaria, Africa and the USA a total of £150,000 from the Training Prize fund.

This research paper includes the following:

- Facts and figures - how many animals are saved by training researchers in non-animal methods
- A review of the 2014 Training Prize winners
- A review of 2014-2015 activity of key organisations involved in training in non-animal methods
- Finally, a comprehensive reference section (updated for 2015) is included

This paper is intended as an update to the Lush Training Prize in 2015. It is also recommended that previous Lush Training Prize research papers (2012-2014) are reviewed for further useful information.

Finally, a number of organisations are identified as potential nominations for the 2015 Lush Training Prize:

1 The European Society for Toxicology In Vitro (ESTIV): Organises regular meetings and training workshops to disseminate information on research and education in *in vitro* toxicology across industry and academia as well as governments.

2 The Alternatives: Continue a campaign of education and training in alternative methods and replacing animals in research.

3 Proefdiervrij (The Dutch Society to Replace Animal Testing): Campaigns to bring an end to animal experiments in The Netherlands by providing regular lectures on non-animal methods to national universities.

4 The Mahatma Gandhi Doerenkamp Centre: For their educational workshops in promoting human 3D tissue models.

5 Jawaharlal Institute of Postgraduate Medical Education and Research: For successful replacement of animals with computer software models in pharmacology education.

2 Facts and figures- how many animals are saved by training researchers in non-animal methods?

In terms of training and education in non-animal methods, the number of animals potentially saved can be looked at in several ways:

- Literally, the number of animals officially used in 'training and education' – 179,981 are used for this purpose each year just in the EU, according to most recently published figures[1]. This could be training in either toxicity testing or more 'basic' research. The breakdown within this total is not easily estimated or clearly stated in official statistics; however, some limited though useful information is provided by some member states on the specific purpose of the training, for example surgical techniques for human or veterinary purposes. The Czech Republic also states that it provides training seminars and lectures to animal researchers and technicians, which include *'teaching of alternative methods to experiments on animals'.* Bulgaria reports its highest category of animal use as education and training

- The second number is much harder to quantify and relates to the number of animals potentially saved on an ongoing basis, as more researchers worldwide are made aware of non-animal methods, are trained in such methods and most importantly, use them as standard practice from then on

- Officially published figures state that over 1 million animals are used in toxicity tests each year in the EU alone[2]. However, an increasing number of animal tests continue to be carried out under the REACH legislation, which alone is estimated to have used more than 800,000 animals to date (many of whom were used despite the availability of non-animal tests[3]) and is predicted to total more than 13 million by the end of the programme, after its most intensive phase of animal testing (2014 onwards, with the final key submission deadline being 2018)[4]

1 Seventh Report from the Commission to the Council and the European Parliament on the Statistics on the number of animals used for experimental and other scientific purposes in the member states of the EU

2 Seventh Report from the Commission to the Council and the European Parliament on the Statistics on the number of animals used for experimental and other scientific purposes in the member states of the EU

3 Minimising Animal Testing for the Registration, Evaluation, and Authorisation of Chemical Substances (REACH) Regulation

4 REACH's death toll: 800,000 animals and counting! PETA International Science Consortium

Ongoing issues in the education and training of researchers in non-animal methods include:

- A lack of awareness that alternative, non-animal test methods not only exist but have been validated for use

- Availability of appropriate guidance for use of approved alternative methods, which should be provided by the relevant competent authorities. For example, the European Chemicals Agency (ECHA) responsible for REACH recently published much needed advice to accompany newly adopted skin-sensitisation test methods[5]

- A need for guidance on methods that have been approved for use, on the basis of inter-laboratory validation and approval. A recently published concept paper[6] by the European Medicines Agency (EMA) highlights how the uptake of alternative methods, although validated, approved and even included in Ph. Eur (European Pharmacopoeia) monographs[7], is being delayed as the method must first be demonstrated to function appropriately in each individual laboratory in which it will be used and for each specific medicinal product that it will be used to test (product specific validation) and that guidance on the requirements for this final stage of the validation process is currently lacking

3 2014 Lush Training Prize winners

Two winners of the Training Prize were each awarded £25,000 in 2014:

3.1 Prof. Ovanes Mekenyan, (Laboratory of Mathematical Chemistry[8], Bulgaria)

Professor Mekenyan won the prize, along with his team, for ongoing work on the QSAR (Quantitative Structure Activity Relationship) Toolbox, a pioneering software application that enables the implementation of various methods for categorising and assessing the toxicity of chemicals. The subsequent data gaps that arise can then be filled for the purpose of (eco) toxicity hazard assessments. The system provides the capabilities to reduce and eliminate animal testing, by maximising the advantage of already available experimental data to reliably estimate the hazard assessment of substances.

5 http://echa.europa.eu/documents/10162/21650280/oecd_test_guidelines_skin_sensitisation_en.pdf
6 EMA. Concept paper on transferring quality control methods validated in collaborative trials to a product/ laboratory specific context
7 https://www.edqm.eu/en/european-pharmacopoeia-background-50.html
8 www.oasis-lmc.org/

The LMC is a research team of 40 which was established over three decades ago and is based at the University of Bourgas. The LMC are experts in predicting toxicological and biological properties of chemical compounds, as well as development of unique mathematical methods for simulation of metabolism to predict skin sensitisation, mutagenicity and hormonal toxicity. To share this expertise, they provide training and consultation in many aspects of 'structure-activity' modelling, including IT-based evaluation of metabolic activity and reactions and building QSAR models. The LMC provides a free license for academic institutions, regulatory authorities and NGOs (available upon request) for evaluating *applicability domains* of QSAR models (i.e. if the toxicity test endpoint of the chemical can be reliably predicted with the method in question); selection of chemicals for strategic testing and finally the management of several databases on metabolites and transformations observed in different testing environments, as well as chemical databases including 2D/3D parameters, fate and (eco)toxicity data. The LMC also provides on-site training for researchers and industry representatives.

The LMC is well known in the computational chemistry and *in-silico* modelling field and also provides expertise via its collaboration on a number of EU projects with key players in the chemicals industry, including 3M, BASF, P&G, Dow Chemicals, L'Oréal, Givaudan, ExxonMobil, Unilever and DuPont as well as national regulatory authorities in Germany, France, Denmark, USA, Canada, Japan and Australia. The LMC continues its training activity since winning the Lush Prize and in April 2015, partnered with The International Council for Animal Protection in OECD Programmes (ICAPO) to offer QSAR Toolbox training courses to regulators at the US Environmental Protection Agency (EPA)[9].

3.2 The Africa Network for Animal Welfare[10] (ANAW)

ANAW was the second Training Prize winner in 2014, accepted by Dr Dennis Makau for their outstanding work in promoting alternatives to harmful use of animals in education across Africa.

Established in 2006, ANAW is based in Kenya but works as a Pan African non-governmental organisation campaigning across many areas. As well as being permanently ' on call' to help animals in distress across Kenya and surrounding regions, they work to influence policy and legislation, improving animal welfare and ending the use of animals in research. ANAW promotes a number of Alternatives to Harmful Use of Animals in Education and Training that can be used instead of live animals and actively advocate for the use of these alternatives with relevant institutions.

In September 2009, a workshop entitled 'The Africa Animal Welfare Workshop and a Seminar on Alternatives to Lab Animals in Education' was held in Nairobi, bringing

9 http://www.piscltd.org.uk/wp-content/uploads/2015/04/PR-QSAR-training.pdf
10 http://www.anaw.org/

together participants from 11 African countries, aimed at introducing and educating stakeholders on alternatives to animals testing. Participants represented various learning institutions, government agencies and professional associations.

Among the findings from the conference were that data on the number of animals used for testing was inadequate, due to lack of standard reporting procedures; local use of alternatives was limited due to lack of information and awareness; educators who play a pivotal role in the development of the school curriculum would benefit from further training on alternatives to lead to adoption in schools.

ANAW has since carried out several baseline studies to provide data which informs the campaign. Since 2010 to date, ANAW has been engaging students and members of staff in various institutions of higher learning, e.g. University of Nairobi, Baraton University and Kenyatta University. The approach has been mainly discussions, debates, workshops and seminar-like demonstrations on alternatives. The ultimate goal of this project is the replacement or the substitution of animals used in teaching/training with non-animal models.

In September 2013, ANAW organised the first International Pan African Animal Welfare Alliance (PAAWA) conference in Nairobi[11], sponsored by a number of key international animal rights and welfare organisations. The theme of the conference was 'Main-streaming animal welfare in Africa's development'. Among the alternatives showcased were models for use in education, to directly replace the use of animals in dissection.

4 Review of 2014-2015 activity of key organisations involved in training in non-animal methods

4.1 LARF (The Analysis and Research Laboratory of Pathophysiology)

LARF is based at the University of Genoa in Italy and headed by Dr Anna Maria Bassi. They offer a wide range of analytical services in *in-vitro* testing for the chemicals, drug and cosmetic industries[12].

The main activities of the LARF include setting up alternatives to animal testing models for the evaluation of the biological potential of chemicals, as well as standardisation and validation of *in-vitro* assays to be used for the toxicological evaluation of substances.

11 http://www.oie.int/doc/ged/D12970.PDF
12 http://www.larf.unige.it/

LARF was a winner of the Lush Training Prize in 2013 and continue their efforts in education and awareness of non-animal methods of toxicity testing, in particular training courses in animal-free cell culture research. For example, in December 2013, LARF ran its fifth theoretical and practical based course in 'Cell Culture: Alternative Methods'. The course provides key information on some alternative methods to animal testing, including human reconstituted tissue. Participants get the opportunity to learn and try out ready to use *in-vitro* models, all of which are entirely free of any animal derived materials. Reduced fees are offered to students to maximise attendance and raise awareness of this vitally important course.

Since winning the Lush Training Prize, LARF has seen an increase in interest in the courses it offers and more applications from international participants. LARF believes that continuing to raise awareness of the Lush Prize via effective promotion, event sponsorship, conferences and advertising will improve outreach, acceptance and discussion of replacing animals in toxicity testing.

4.2 XCellLR8

XCellR8 are a UK-based contract research organisation (CRO), fully committed to replacing animals in toxicity testing and with the aim of training others in doing so[13].

A previous Lush Prize winner, XCellR8 have, since 2008, trained over 300 researchers worldwide in using animal-free cell culture methods that are fully approved for regulatory use. Since winning the Lush Prize, XCellR8 are expanding their training programme, as well as continuing their work in offering animal-free testing methods, for example in skin sensitisation and genotoxicity testing.

XCellR8 are currently working on an exciting and innovative project towards replacement of the cruel and archaic LD_{50}[14], a lethal test which measures the toxicity of a substance when 50% of the animals (dosed with huge concentrations of the substance) have died. The LD_{50} has long been considered by industry to be not only outdated and unnecessary, but scientifically crude and unreliable in predicting human responses. Despite this widespread opinion, the most recently available statistics show that more than 340,000[1] animals suffer and die in LD_{50} and 'other lethal' toxicity tests each year in the EU alone, making the research and training initiatives of XCellR8 and other like-minded organisations more important than ever. With this in mind, in September 2014, XCellR8 initiated an eighteen month collaboration with FRAME (Fund for Replacement of Animals in Medical Experiments) and other partners to investigate viable replacement solutions for overcoming conflict between the EU Cosmetic Regulation (which bans the use of animal testing in cosmetics) and the chemicals testing regulation REACH (Registration, Evaluation, and Authorisation of Chemicals) which still requires animal testing and therefore impacts on chemicals to be used in cosmetic products.

13 http://www.x-cellr8.com/
14 http://www.x-cellr8.com/testing/in-development/

4.3 The Institute for In Vitro Sciences (IIVS)[15]

Based in Maryland, USA, IIVS was established in 1997 and is recognised as a world leading organisation in outreach and training in alternative methods to animal testing. IIVS have featured prominently in Lush Prize as a Training award winner in 2012.

Training workshops organised by the IIVS focus on discussion of the finer detail of *in-vitro* tests and the toxicological endpoints they meet. The workshops also involve participants who have extensive experience or specialised knowledge of the tests for intensive scientific review and debate, with the aim of clarifying and understanding the procedures required. Workshop reports are then widely distributed among the *in-vitro* testing community for feedback to develop and improve the assays.

A key, 'hands-on' training session offered by the IIVS each year is the ‘Practical Methods for In Vitro Toxicology Workshop. The objective of these workshops is to teach basic techniques of choosing *in-vitro* tests, appropriate laboratory procedures, data review and interpretation and how this is applied to the toxicological end points of the test(s). Comprehensive information, combined with hands on training and one-to-one interaction with expert supervisors enables attendees to use the assays with confidence, back in their own laboratories.

The IIVS also continues its invaluable toxicity training webinars, most recently in April 2015 on 'In Vitro 3T3 Phototoxicity Assay Practical Experiences: Assay Optimization and Challenges', provided free as part of the IIVS Education service, to allow new and existing users of the assay to learn, provide feedback and encourage discussion for best practice and improvement.

4.4 The Centre for Alternatives to Animal Testing (CAAT-Europe)

CAAT-Europe is based at the University of Konstanz . A winner of the 2014 Lobbying Prize, it was established in 2010 as the European branch of CAAT USA (located at the Johns Hopkins University in Baltimore). CAAT continues its ongoing mission to promote non-animal methods in research and education, by coordinating conference events and training workshops. Their forthcoming 'Joint Information Day on Biology Inspired Microsystems—Status and Future'[16] will focus on recent advances to enable the development of microfluidic ‘human-on-a-chip’ devices, to simulate organ function and interaction on a microphysiological scale, enabling a new level of physiologically relevant assays.

15 http://www.iivs.org/

[16] http://caat.jhsph.edu/programs/

4.5 Lush Prize conference activity 2014-2015

During the 2014-2015 Lush Training Prize cycle, the **9th World Congress** on Alternatives to Animal Use in the Life Sciences[17] was held. Several key sessions relevant to training and education included:

- 3Rs in academic education, training programs and anticipated needs
- Innovative training and teaching tools

These sessions each included several different presentations from international speakers. For example: assessment of training needs and knowledge gaps for scientists in available alternative methods in Korea, India and Brazil; a review of alternative tools and approaches to education and training; and successful educational initiatives to replacing animals by use of simulators in veterinary student training and computer software tools in pharmacology education[18].

Whilst many sessions at the World Congress remain broadly linked to the 3Rs (for example, some areas focus on the continued use of animals and sharing 'best practices' in education and training) sessions can be selected which relate only to the '1R' of r*eplacement.*

In September 2015, Lush Prize will also attend the **16th Congress hosted by the European Society for Alternatives to Animal Testing (EUSAAT) i**n Linz[19]. Of particular relevance to the Training Prize at EUSAAT 2015 is the 'Practical Training Course on Alternative Methods'[20], which will be focusing on established *in-vitro* and *ex-vivo* methods for assessing the eye irritation/corrosion hazard potential of chemicals and finished products. The two day intensive training course is free of charge and open to all participants of the congress but especially to those "interested in gaining knowledge and practical experience on advanced non-animal methods for toxicology testing".

5 Conclusion

The Training Prize continues to be an essential category of the Lush Prize, distinct from the equally important Lobbying and Public Awareness prizes. Not only does the Training Prize provide specific focus to the education and adoption of readily available, non-animal methods (from the simplest models to the more complex *in-vitro* assays), they also give critical insight into how this varies globally and the work that still needs to be done.

[17] http://www.wc9prague.org/scientific-program/program-overview/
[18] http://www.altex.ch/resources/153171_WC9_Theme_3.pdf
[19] http://www.eusaat.org/
[20] http://eusaat-congress.eu/index.php/congress/2015/2015-practical-training-course

6 Organisations active in training and providing educational materials

6.1 Africa Network for Animal Welfare (ANAW)

http://www.anaw.org/

Established in 2006 and based in Kenya, the ANAW has committed itself to spearheading a number of animal welfare of campaigns while building networks with governments, political leaders, media and other institutions to press for effective policy and legislation changes and for the protection and care for animals at national and community level. ANAW partners with international bodies and institutions of higher learning to promote use of alternatives to animals in labs. ANAW were awarded a Lush Training Prize in 2014.

6.2 The Alexandra Association, Monaco

http://www.alexandra-project.org

The Alexandra Association aims to develop and promote alternative methods to animal research for both scientific and ethical purposes in both toxicity testing and medical research. The founders of the association are experts in scientific research and technical innovation. The organisation is a previous Lush Prize nominee, recognised for ongoing efforts in education and training in alternative methods, including 'OpenSource' 3D Tissue Engineering in human tissue reconstruction and cell culture.

6.3 AltTox (Non-Animal Methods for Toxicity Testing)

http://www.alttox.org/

AltTox is a vital resource for anyone interested in animal-free science from a research or training perspective. Alttox provides various levels of useful information, from basic descriptions of toxicity tests, up-to-date information on alternatives and newsletters through to various tools and databases as well as information on forthcoming courses and events.

6.4 The Alternatives Research & Development Foundation (ARDF)

http://www.ardf-online.org/

Established in 1993, The ARDF, based in the USA, awards research funds that support the development, validation, and/or adoption of non-animal methods in biomedical research, product testing, and education. ARDF aims to bring ‘alternatives technology and compassion to modern laboratories and classrooms’.

6.5 'Alternatives Toxicity Services' (ATS)

http://www.alternativetoxservice.com/Homepage.aspx

ATS is a contract company based in both Genoa and London which offers companies high content screening services for evidence-based acute toxicity and neurotoxicity via a number of *in-vitro* tests, with the aim of promoting the principles of the 3Rs. While it must be noted that the services provided are not all animal-free (some use rat and mouse primary cells or cell lines) human cell based tests are also available. ATS also provides training services in cell culture methods.

6.6 Animal Aid

www.animalaid.org.uk

Animal Aid is one of the UK's most experienced and long-established animal rights organisations, campaigning for animals on a number of issues, including an end to animal testing. The education department at Animal Aid provides a school speaker training service whose speakers are available to present and train volunteers on animal testing. They can also provide educational materials for both teachers and pupils on request.

6.7 Animal Ethics Infolink

http://www.animalethics.org.au/education-and-training/alternatives-to-animal-use

Animal Ethics Infolink is an Australia-based online resource. While focus is broadly across the 3Rs, the site provides useful information on training and education materials in the replacement of animal testing

6.8 Animalearn

http://www.animalearn.org

Animalearn, based in the USA and a division of the American Anti-Vivisection Society (AAVS), continues to promote its highly useful 'Science Bank' for alternatives to animal use in education. The tool is an easy to use 'drop down' search facility on the Animalearn website, to find resources by education level (from early school stages through to medical training), type of animal or type of alternative (e.g. video, computer simulation, models and more). Animalearn also rewards students and schoolchildren for their achievements in educating others on the choice to object to dissection or question teaching curriculums that contain animal use.

6.9 CAAT- Centre for Alternatives to Animal Testing – John Hopkins University

The CAAT is based in Maryland, USA. As well as its US site it has European Headquarters at the University of Konstanz in Germany and operates Altweb, a website dedicated to the 3Rs and dissemination of information on humane science to researchers, students and educational staff. CAAT continues to provide workshops and educational materials in alternative methods. To date, CAAT has provided the following courses and events;

- In-Vitro Medical Device Testing
- Green Toxicology Information Day
- Functional Non-animal Biobarrier Models in Research and Risk Assessment
- DNT4 (Alternatives in Developmental Neurotoxicity Testing)
- Emergence of Systematic Review and Related Approaches in Toxicology - an EBTC Workshop

6.10 Cruelty Free International (formerly known as BUAV)

https://www.crueltyfreeinternational.org/

Cruelty Free International is one of the leading campaigning organisations against animal testing with successful undercover investigations exposing the hidden animal suffering in laboratories. The BUAV provides a 'Schools' guide also aimed at students, to raise awareness and provide a truthful insight into the realities of animal testing. They also produce a number of science reports providing further information.

6.11 DAAE (Doctors Against Animal Experiments)

http://www.aerzte-gegen-tierversuche.de

DAAE, based in Germany, is a charitable organisation of several hundred doctors and scientists who work in the medical field. DAAE supports the immediate abolition of all animal experiments on ethical and scientific grounds. In order to make the cruel and unscientific nature of animal experiments public, they provide scientifically-based information on animal experiments both for doctors and scientists, as well as for the general public. DAAE manage and update their own database to inform the public about the reality of animal experiments[21] as well as a database on *in-vitro* methods.

6.12 The Dr. Hadwen Trust (DHT)

http://www.drhadwentrust.org

The Dr Hadwen Trust (DHT) is the UK's leading non-animal medical research charity and a previous Lush Prize nominee, as well as funding a variety of research projects on an ongoing basis. DHT has awarded seven 'Summer Studentships' in 2014 to young researchers to enable them to continue their work in replacements to animal testing over the summer period. This year's projects support a variety of new methods into disease including Parkinson's disease, cancer and diabetes. The DHT launched the Summer Studentship scheme in 2012, to assist undergraduate students in gaining practical, laboratory-based experience in research methods to replace animals.

6.13 DsRAT - Dutch Society for the Replacement of Animal Testing

http://www.proefdiervrij.nl/

DsRAT supports scientists, entrepreneurs and the government in the development of these new techniques by providing educational materials, engaging in collaborations and initiating discussions about animal free solutions to ensure the future replacement of animal testing.

6.14 European Coalition to End Animal Experiments (ECEAE)

http://www.eceae.org

The European Coalition to End Animal Experiments (ECEAE) was formed in 1990 by organisations across Europe to successfully campaign to ban cosmetics testing on animals. Today, the ECEAE campaigns on all animal testing issues in Europe, bringing together extensive expertise, experience and knowledge from major European animal protection organisations, working with politicians and scientists to ensure that animals in laboratories are high on the European political agenda.

[21] http://www.datenbank-tierversuche.de/

6.15 European Partnership for Alternatives to Animals Approaches

http://www.epaa.org

The EPAA is a collaboration between the European Commission, European trade associations, and industry who are “are committed to pooling knowledge and resources to accelerate the development, validation and acceptance of alternative approaches to further the replacement, reduction and refinement (3Rs) of animal use in regulatory testing.” (It must be noted that the 3Rs remit of the EPAA is particularly broad in that, whilst 1R/replacements are highlighted, other initiatives include, for example, awards to laboratory animal staff).

6.16 ESTIV (European Society of Toxicology In -Vitro)

http://www.estiv.org

ESTIV promotes *in-vitro* methods both scientifically and educationally across Europe. ESTIV held its 2014 congress in The Netherlands with a theme of 'Making Sense of In-Vitro Methods'. Topics included long-term toxicity prediction using computer models and integrated, non-animal testing strategies in skin sensitisation. ESTIV also held a training course in January 2015 in Lisbon entitled 'Applied In-Vitro Toxicology Course'[22]. ESTIV is sponsored by a number of major chemical and pharmaceutical companies, most recently Roche.

6.17 EURL-ECVAM (The European Union Reference Laboratory for Alternatives to Animal Testing)

http://ihcp.jrc.ec.europa.eu/our_labs/eurl-ecvam

In June 2014, EURL-ECVAM released its 'Updated list of alternative test methods' submitted to the organisation for validation and acceptance as alternative methods to animal testing since 2008. EURL-ECVAM continues to organise a variety of workshops, courses and publish formal recommendations, as well as international outreach projects, most recently hosting a visit by the Korean Research and Testing Institute (KRT) to allow the KRT to gain insight into EURL ECVAM's approach towards the development, validation and international recognition of alternative methods to animal testing and to discuss best practices and main challenges with respect to their scientific evaluation. EURL-ECVAM also manages and updates two main databases, DB-ALM (Database for Alternative Methods) and TSAR (Tracking System on Alternative Methods), which are listed separately in this Appendix.

6.18 EUSAAT- the European Society for Alternatives to Animal Testing

http://www.eusaat.org

EUSAAT has been documented in previous Lush Prize research. The EUSAAT website was updated in 2014, to better serve all interested in alternatives to animal testing. One of EUSAAT's key aims is '*promotion of the use of non-animal tests in the area of education*'.

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22 http://www.estiv.org/docs/ESTIV_Training_InVitroTox.pdf?set=a.512417912102502.122630.422812001063094&type=1&l=27051111e7

6.19 The Human Toxicology Project Consortium (HTPC)

http://www.humantoxicologyproject.org

The HTPC is a major collaboration to advance a new paradigm in toxicity testing and pathway-based approaches to chemical safety assessment. The HTPC is active in co-sponsoring (with the IIVS and HSI) ground breaking training programmes for Chinese researchers in non-animal methods for cosmetics testing. HTPC also provide a number of useful information resources including videos on new technologies, such as high throughput drug screening and the 'Virtual Liver'. The consortium also communicates forthcoming events and training courses on it's website.

6.20 Humane Society International (HSI)

http://www.hsi.org

The HSI continues its highly successful 'Be Cruelty Free Campaign', engaging with stakeholders in Asia to progress towards phasing out mandatory animal testing for cosmetics. HSI, along with it's sister organisation the HSUS (Humane Society of the United States) and The Human Toxicology Project Consortium, recently awarded an $80,000 grant to the Institute for In Vitro Sciences (IIVS) to provide vitally needed, hands-on training in non-animal tests to China's government regulators and scientists.

6.21 The Institute for In Vitro Sciences (IIVS)

http://www.iivs.org

The IIVS, a former Lush Prize winner and nominee continues its outstanding efforts to disseminate free information via webinars and 'free to register' events and for its ongoing work with Chinese authorities in the education, training and adoption of non-animal methods to replace animal testing. The IIVS also continues to provide it's much needed 'Practical Methods in In Vitro Toxicology ' annual training courses.

6.22 INTERNICHE (International Network for Humane Education)

http:/www.interniche.org

A previous Lush Training Prize winner, Interniche produce a variety of educational materials relevant to study of human medicine, veterinary research and the life sciences and has led international efforts to implement the use of humane, alternative methods and teaching materials in education across a number of countries.

6.23 The Innovative Methods and Alternatives to Animal Research Unit, Australia

The Innovative Methods and Alternatives to Animal Research Unit based at the John Curtin Medical School at Australian National University[23] supports researchers in 'innovative methods to entirely replace the need for an animal model, or the replacement of an animal product in an assay or procedure (e.g. animal derived

23 http://jcsmr.anu.edu.au/research/research-facilities/innovative-methods-and-alternatives-animal-research-unit

antibodies for immunoassay)'. The Unit collaborates with a number of other academic centres in Australia, including the University of Sydney, specifically on a project involving animal-free cell culture methods for malaria and vascular pathology and Wollongong University's initiative to ' Replace Animals in Australian Testing'[24] which aims to 'create a network of researchers and other individuals or groups interested in advocating non-animal based research and in strengthening the Australian Government/NHMRC guidelines and their enforcement'

6.24 Joint Research Institute for Health and Consumer Protection (JRC)

https://ec.europa.eu/jrc/en/institutes/ihcp

The JRC 'Science Hub' collates a variety of information and forthcoming training courses and events. In June 2014, the JRC launched an online tool to identify chemicals useful for the development and validation of alternative methods to animal testing. CheLIST is the first worldwide attempt to compile a cross-referenceable 'list of substances lists'; its uniqueness consists of the combination of both regulatory and scientific areas, and its openness to integrate new lists to be considered in the database. For specific scientific, industrial or regulatory purposes chemicals are grouped and included in various lists. The fact that a given chemical is included in a specific list reveals many details about its properties. Easy access to such information, which is typically scattered across numerous databases, project websites and peer-reviewed literature, should facilitate the work of researchers looking for the right reference chemicals to develop, characterise or validate tests as alternatives to animal-based testing.

6.25 Laboratory of Mathematical Chemistry (LMC)

http://oasis-lmc.org/products/software/toolbox/training.aspx

Winners of the 2014 Training Prize and headed by Prof Ovanes Mekenyan, the LMC are the developers of the QSAR (Quantitative Structure Activity Relationship) toolbox. The LMC continues to offer on-site training (on request), as well as regular annual training courses, organised in co-operation with stakeholders such as ICAPO and REACH Monitor[25].

6.26 LARF (The Analysis and Research Laboratory of Pathophysiology)

http://www.larf.unige.it

LARF, headed by Dr Anna Maria Bassi was a winner of the 2013 Training Prize. LARF continues to devote its expertise to *in-vitro*, alternative methods of research including human cell cultures, 3D organ toxicity and investigation of mechanisms of cellular injury in disease e.g. cancer. LARF continues to organise training courses in

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24 http://lha.uow.edu.au/hsi/research/raat/index.html

25 http://www.reachmonitor.com/index.php?lang=2&aptd=4&id=38

alternative methods for young scientists as the organisation firmly believes in the dissemination of knowledge and data sharing.

6.27 Mahatma Gandhi-Doerenkamp Center (MGDC)

http://www.mgdcaua.org/
The MGDC has remained active in its aim of educating the Indian scientific community on the '3Rs' and alternative methods to animal testing.

6.28 National Anti Vivisection Society (NAVS) USA

http://www.navs.org
NAVS USA continues its campaign for compassionate science and education without animal use, providing educational materials and scientific information on alternative methods around the world.

6.29 National Anti Vivisection Society UK

http://www.navs.org.uk
NAVS UK continues to promote research projects via the Lord Dowding Fund. Projects have included alternatives to the use of animals in education and funding for teaching of humane alternatives to university students.

6.30 The NC3Rs

http://www.nc3rs.org.uk
The NC3Rs selects and awards research grant funding to projects considered under their '3Rs' (reduction, refinement, replacement) criteria.

6.31 NEAVS (New England Anti-Vivisection Society)

http://www.neavs.org
As part of it's 'Ethical Science Education Campaign', NEAVS continues to provide a number of educational outreach materials for schools and colleges, including posters and brochures on animal testing and alternative methods.

6.32 Netherlands Knowledge Centre on Alternatives to Animal Use (NKCA)

http://www.nkca.nl
The NKCA promotes the application of the 3Rs in the Netherlands. The Centre is a collaboration between the RIVM (National Institute for Public Health) and the University of Utrecht since 2010 and offers ‘animal testing alternatives’ modules as part of postgraduate training for professionals. NKCA also advises teachers on the animal-free testing models available for secondary schools, and recommends animal-testing alternatives as a potential subject for student projects.

6.33 PETA (People for the Ethical Treatment of Animals)

http://www.peta.org
PETA continues as one of the world's major animal rights organisations campaigning against animal testing, among many other issues. Most recently, and as highlighted in previous Lush Prize papers, PETA has directly funded Chinese scientists in

training in non-animal methods[26] as well as a hugely successful campaign by PETA India towards ending animal use in the national education curriculum. PETA's International Science Consortium (PISC)27 promotes and funds non-animal research methods and coordinates the scientific and regulatory expertise of its members.

6.34 SAFE (Save Animals from Exploitation)

http://www.safe.org.nz

SAFE are a New Zealand based organisation and 2013 'Public Awareness' Lush Prize winner, promoting a number of educational materials. They also offer school speaking services to educate and raise awareness on a variety of animal rights and welfare issues, including animal experiments. For example, SAFE recently presented at the 'Humane Education Symposium'.

6.35 SATIS- People for Animal Rights, Germany

http://www.satis-tierrechte.de/

SATIS continues to partner with Interniche to communicate a variety of educational materials on replacement methods to animal testing and continues to provide its information on national university rankings and Master's degree programmes. SATIS also communicates on innovative new technologies in medical research training, for example a training course in June 2014 on use of the 'RealSpine'[28], a highly realistic spine simulator for aspiring surgeons developed at the University of Leipzig. Junior doctors from different hospitals train using the tool under the guidance of experienced surgeons. While previously practiced on animals, simulation systems such as the 'RealSpine' are increasingly used. Training courses allow new surgeons to familiarise themselves with the complex structures of the spine and to identify risk structures in this area of the body, before any work on patients begins.

6.36 SEURAT-1 (Safety Evaluation Ultimately Replacing Animal Tests)

http://www.seurat-1.eu/

SEURAT-1 is an international scale collaborative project funded under the EU Seventh Framework Programme (FP-7). The SEURAT-1 Symposium on *future animal-free safety assessment* will take place on 4 December 2015 in Brussels[29].

6.37 The Alternatives

http://thealternativeseu.wordpress.com/2013/08/16/thealternatives-eu-is-born/

The Alternatives is an Italy-based non-profit organisation launched in August 2013 which actively promotes alternatives to animal experiments by providing a variety of information, scientific publications and its long term expertise in teaching human

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26 http://www.peta.org/blog/chinese-scientists-learn-non-animal-testing-thanks-peta/

27 http://www.piscltd.org.uk/

28 http://www.realspine.de/

29 http://www.seurat-1.eu/pages/library/events/seurat-1-symposium.php

based clinical research, as well as experience in engaging with educational authorities and regulators on replacements to animal testing.

7 2015 courses and workshops

Below are some examples of forthcoming events, courses and workshops in 2015. Other training courses and events are also listed within the updates for each organisation. This is not an exhaustive list and many other courses and events are available.

- 51st Congress of the European Societies of Toxicology (EUROTOX 2015) September 13–16, 2015; Porto, Portugal [http://www.eurotox2015.com/]

- European Congresses on Alternatives to Animal Testing (EUSAAT) September 20-23, 2015 Linz, Austria [http://www.eusaat-congress.eu/]
- Lush Prize 2015: Conference and Awards Ceremony; London; 20th Nov 2015 [www.lushprize.org]
- 3rd 'Animal Replacement Science 'Conference; (Date 12th November2015); UK;Dr Hadwen Trust [http://www.drhadwentrust.org/]
- The SEURAT-1 Symposium on *future animal-free safety assessment* will take place on 4 December 2015 in Brussels [http://www.seurat-1.eu/pages/library/events/seurat-1-symposium.php]

8 Web-based educational tools and research databases

The following is a suggested list of databases, knowledge bases or software, plus examples of educational tools in alternative methods, updated for 2015. (It is not an exhaustive list).

8.1 AnimAlt ZEBET – database for alternative methods to animal experiments

http://www.bfr.bund.de/en/animalt_zebet___database_for_alternative_methods_to_animal_experiments-62822.html
The German Federal Institute for Risk Assessment (BfR) incorporates ZEBET, which is the 'Centre for the Documentation and Evaluation of Alternatives to Animal Experiments'. It houses AnimAlt-ZEBET, a database aiming to provide scientists with information on alternative methods. It is accessible on the internet without licence fees in German and English and includes validated information on alternative methods. ZEBET also developed a continuing education course, 'Laboratory Animals, Animal Experiments and Alternative Methods', in 1992. Participation in the course is a "pre-requisite to the approval of an application for animal experiments". The course is offered as a "regular semester course at the Freie Universitaet Berlin"

and is also available on a “monthly basis as a commercial training programme” in both German and English.

8.2 The DataBase service on Alternative Methods, DB-ALM (EURL=ECVAM)

http://ecvam-dbalm.jrc.ec.europa.eu/

This database aims to “provide an overall picture on the state-of-the-art of alternative methods in use at all stages of development, validation or regulatory acceptance for a given topic area in the form of method summary descriptions and/or more detailed information to allow the transfer and use of a method by a laboratory”.

8.3 Data Infrastructure for Chemical Safety (DiXa)

http://www.dixa-fp7.eu/

The DiXa project states that “animal-based test models need to be replaced - preferably by robust, non-animal assays which better predict human toxicity , are less costly, and are socially more acceptable”.

The project has a number of collaborators including JRC European Commission, Maastricht University, Imperial College London and EMBL-EBI – a not-for-profit organisation that provides freely available bioinformatics tools and services to the public. DiXa has offered a considerable number of training courses (both on-site and online) and workshops focussing on next generation 'omics' technologies and data structures.

8.4 DEREK Nexus Toxicity Prediction Database

http://www.lhasalimited.org/products/derek-nexus.htm

DEREK is an expert toxicity prediction database pioneered by Lhasa Limited, a not-for-profit organisation and educational charity that facilitates collaborative data sharing projects in the pharmaceutical, cosmetics and chemistry-related industries.

8.5 Froguts

http://www.froguts.com/

An on-line virtual dissection which has been designed to give better understanding of frogs and other life forms by the use of instructional technology.

8.6 Go3R search engine

http://www.go3r.org/

This project, produced by Transinsight GmbH with ZEBET, aims to develop a “knowledge-based search engine for alternative methods to animal experiments”. It “provides an endpoint-centred semantic literature search for toxicological information (e.g. as required for REACH), highlights animal testing alternatives and organises 22 million abstracts listed in PubMed and TOXNET in an accurate table of contents, enabling fast bibliometric analysis and promising more exhaustive and selective recovery of relevant documents”.

8.7 Humane Society Veterinary Medical Association Alternatives in Education (HSVMA)

http://www.hsvma.org/resources#humane_alternatives

HSVMA offers a variety of educational and training materials including publications and databases offering information on alternatives to animal use. They include the Alternatives in Education database, Alternatives Database and Humane Teaching Methods resources, as well as others.

8.8 Sniffy the Virtual Rat

http://wadsworth.cengage.com/psychology_d/special_features/sniffy.html
An online 'virtual rat' simulation programme to aid student learning.

8.9 The Tracking System on Alternative Methods (TSAR - EURL-ECVAM)

http://tsar.jrc.ec.europa.eu/
This database is “a tool aimed at providing a transparent view on the status of alternative methods as they progress from purely scientific protocols submitted for pre-validation to being actively used in a regulatory context. This tracking system intends to cover all steps, from the initial submission for pre-validation until final adoption by inclusion in the EU legislation and/or related Guidance Documents, when appropriate. TSAR was updated in June 2014 following release of the EURL-ECVAM updated list of alternative methods.

8.10 QSAR Toolbox

http://www.qsartoolbox.org/
This technical database is for researchers, government bodies, chemical industry personnel and any interested stakeholders. The software works by grouping chemicals into categories in order to identify (and therefore fill) 'gaps' in ecotoxicity data which are needed for a complete risk assessment of a substance. The tool allows for entire categories of chemicals to be analysed, saving costs and animals from being used in unnecessary testing. In its 'Support' section, the toolbox also provides highly useful online training packages such as 'QSAR ToolBox Web Training' and step-by-step guides for prediction of specific endpoints, e.g. skin sensitisation.