

# Lush Young Researcher Prize 2014

**Background Paper** 



# **1 Executive Summary**

The Lush Prize, now in its third year, awards and encourages individuals or organisations who have contributed to its global initiative to end animal testing in the fields of science, public awareness, lobbying, training and finally young researchers who wish to develop a career in animal-free toxicology. The total yearly prize fund is £250,000. The 2014 'Young Researcher' category of the Lush Prize, as in previous years welcomes nominations from early career scientists who are keen to progress in research without animal testing and this year, the award offers four £12,500 bursaries, to reward research and development specifically in methods of *entire replacement* of animals in toxicity testing. To date, Lush Prize is pleased to have awarded eight winners from six countries a total of £100,000 from the Young Researcher fund. As in previous years, the research behind the Lush Prize is also important in recognising individuals, campaigning organisations or research institutes who might not otherwise be nominated for their achievements.



# 2 Methodology

This research paper is based on the following:

- A brief review of last years' findings
- Where are we now? The current situation, developments and key issues regarding toxicity testing in animals
- The key players in the field the ethical early career scientists
- A review of organisations, research institutes, public bodies and societies who provide a network of educational and career opportunities for young researchers
- The way forward for the Young Researcher Prize and it's links to the Training Prize category

A note on terminology; Lush Prize refers to testing without animals as 'non-animal' methods. They are validated, scientifically robust methods of safety testing in their own right. The use of terms such as 'alternatives' or 'replacement' methods (while useful for clarity sometimes) may suggest that animal testing is the 'gold standard' of safety testing, when much of the scientific industry along with a wealth of research evidence confirms that, aside from the suffering involved, animal tests do not reliably predict human responses. In addition, the term 'alternatives' is also used to describe the 3Rs methods, previously summarised as follows:

- Refinement: minimise suffering and distress to animals
- Reduction: minimise the number of animals used
- Replacement: avoid the use of living animals

As in previous years, the Lush Prize uses a 'replacement filter'. Whilst reduction or refinement methods are positive steps, they are not achievements. Therefore, Lush Prize considers only the final 'R' (replacement) to be a genuine alternative as the other 2Rs still involve animals. This also aligns with the Lush Prize eligibility criteria which outline the '1R of replacement' rather than refinement or reduction.



# 3 A brief review of last year's findings

To discuss the relevance of the Young Researcher prize, a number of key animal protection organisations have been contacted and interviewed during previous research for the Lush Prize. Some of these contacts are quoted and provide useful updates throughout this paper.

As highlighted in previous Lush Prize research, the key messages remain the same; although the acceptance and recognition of new technologies is growing at an encouraging rate, animal-free toxicology is still the 'less travelled' path and any early career researcher trying to progress in this area is likely to meet at least some resistance or challenges along the way. That said, the environment for discussion of alternatives to animal use is expanding, therefore it is vital to be persistent and remain true to one's values in pursuing career and networking opportunities. A very proactive attitude is needed- ethical scientists must seek out their chances, but the rewards can be hugely successful.

It is also clear from previous Lush Prize papers that continuing to promote the antianimal testing message to all relevant individuals in the young/early career researcher field, as well as communicating at an earlier stage of education is vital. 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'.*<sup>1</sup> An unbiased view and fresh perspective on cutting edge science is essential, combined with raising awareness earlier in the educational system. There is also a strong link between the Young Researcher and Training prizes, as the awards are relevant to those involved in the education of a number of audiences, from children in early stage schooling through GCSE/A level to undergraduate and through postgraduate level and beyond. These issues are discussed later in this paper and it is recommended that the Young Researcher and Training Prize papers are both reviewed, given their considerable connection.

Lush Prize research in 2013 also involved extensive interviews and feedback from previous prize winners which provided valuable information regarding ongoing attitudes to non-animal research and its acceptance in the scientific community, as well as how meaningful the individual bursaries offered by the Young Researcher Prize have been to date.

<sup>&</sup>lt;sup>1</sup> Lush Young Researchers Prize 2012- Research Paper

# 4 Where are we now? The current situation, developments and key issues regarding toxicity testing in animals

# 4.1 The EU cosmetics marketing ban

As reviewed previously by Lush Prize, a major development in the campaign to end animal testing came last year on 11<sup>th</sup> March 2013, when the final ban on the import and sale of animal tested cosmetics came into force across the EU. This completed a series of deadlines, starting with a ban on animal testing of finished cosmetic products (back in Sep 2004) followed by a similar ban on testing for cosmetic ingredients(11 March 2009). The extended marketing deadline until 2013 acknowledged that non-animal methods for certain areas of toxicity testing where not yet available and to allow extra time for their research and development. These broad areas of toxicity testing are as follows;

- Repeated dose toxicity
- Reproductive toxicity
- Toxicokinetics
- Skin sensitisation
- Carcinogenicity

It's important to note that each of these areas include many individual tests and can use varying numbers of animals. For example, a reproductive toxicity test may use a minimum of almost 1000 animals.<sup>2</sup>

Although the good news is that in theory, all animal testing is now banned under the EU Cosmetics Regulation (and this specifically means that if a company wants to test any ingredient *solely for cosmetic purposes*, it can no longer test it on animals in the EU <u>or</u> sell it in the EU if it has been tested on animals anywhere else in the world) there are loopholes to be aware of. Substances can still be tested on animals under other types of legislation (for example REACH, the EU law concerning the *R*egistration, *E*valuation and Authorisation of *Ch*emicals) which are still ultimately used in cosmetics. Such ingredients may be of 'multipurpose' use and the cosmetics sector itself has stated that it obtains 90 % of its ingredients from other industries such as food or industrial chemicals. <sup>3</sup>

Furthermore, animal testing for cosmetics still continues outside the EU. Similarly, there are no such prohibitions on animal use in any other areas of chemicals testing such as biocides, food, pharmaceuticals or industrial chemical safety and while general reference is made to animal welfare and the 3Rs in these areas, animal testing is still heavily replied upon. It is important to note claims that animal use is avoided 'whenever possible' or that animals are only used 'when there is no legally available alternative'. These statements sound ethically reassuring, but mask the fact that many areas of the animal research industry have at best a reactive, rather than

<sup>&</sup>lt;sup>2</sup> BUAV: EU adoption of alternative method is too slow: <u>http://www.buav.org/article/1495/eu-adoption-of-alternative-method-is-too-slow</u>

<sup>&</sup>lt;sup>3</sup> Commission staff working document on the animal testing and marketing ban and on the state of play in relation to alternative methods in the field of cosmetics :<u>http://ec.europa.eu/consumers/sectors/cosmetics/ files/pdf/animal\_testing/ia\_at\_2013\_en.pdf</u>



proactive attitude to moving away from animal research and will only use alternatives if they happen to come along.

But there is some good news. The EU cosmetic ban has had a positive influence outside its borders, as both India and Israel have recently announced bans on animal tested cosmetics (and household products). <sup>4 5</sup> On a further positive note, there has been some progress in moving away from animal testing in 'non-cosmetic' areas. For example, the recently published (June 2014)second report <sup>6</sup> by the European Chemicals Agency (ECHA) on REACH indicates that companies are making some use of alternative testing strategies, specifically that

"Building categories and predicting substance properties by read-across is the most widely used method. This means filling a data gap for a substance by using information from similar substances. Combining information together from different sources (weight of evidence) is the second most common method, followed by computer modelling (qualitative/quantitative structural-activity relationship, (Q)SAR)."

However, it is important to be realistic and view this information in context. While it is clearly a welcome move for companies to reduce animal use and maximise use of existing alternatives, these efforts are no substitute for what is still vitally neededgenuine, mainstream investment by all relevant stakeholders (academia, industry, government agencies and public bodies) to develop (or complete validation of) nonanimal methods that are still considered 'lacking' and which until available, will result in animals still being used. Despite the REACH legislation mandating the avoidance of animals wherever possible, the aforementioned latest ECHA report also indicates that at least 4.887 new animal tests have been conducted for REACH since its launch in 2007, with the number of tests more than doubling since 2009, from 1,849 to 4,887 and a three-fold increase in the number of reproductive toxicity tests carried out (which as stated earlier can use almost 1000 animals per test). As REACH continues until its final deadline in 2018, further animal tests will significantly increase this figure, unless radical changes are made. Equally important to note is that these animal tests are conducted for all manner of purposes, for chemicals which may be used in everything from laundry detergent to drain cleaner to slimming foods, simply so that companies can market new or 'innovative' products.

All of this means that there is considerable scope for early career researchers working in a broad range of scientific or technical fields to get involved in non-animal methods. This is coupled with the fact that the *in-vitro* toxicity testing market is projected to be worth \$17,227 million by 2018. <sup>7</sup> Again, the EU cosmetic testing bans have played a key part in driving this growth.

<sup>&</sup>lt;sup>4</sup> Ban sale of animal tested products: PETA to Government: <u>http://articles.economictimes.indiatimes.com/</u> 2014-04-20/news/49266222\_1\_household-products-cosmetics-animal-tests

<sup>&</sup>lt;sup>5</sup> Import Ban on Animal tested products goes into effect in Israel :<u>http://altweb.jhsph.edu/news/2012/</u> Israel\_bans\_testing.html

<sup>&</sup>lt;sup>6</sup> European Chemicals Agency (ECHA): The Use of Alternatives to Testing on Animals for the REACH Regulation. Second report under Article 117(3) of the REACH Regulation

<sup>&</sup>lt;sup>7</sup> In-Vitro Toxicology Testing Market worth \$17,227 Million by 2018: <u>http://www.prnewswire.co.uk/news-releases/in-vitro-toxicology-testing-market-worth-17227-million-by-2018-253586361.html</u>



## 4.2 <u>Mainstream funding and development of 3Rs including non- animal methods</u>

The importance of funding offered by the Lush Prize continues to grow. This is especially relevant to the Young Researcher Prize, as the bursaries won will be directly funding methods to replace the use of animals in 'frontline' research. As highlighted in 2012 research conducted for the Lush Prize, a major setback with the availability of non-animal methods is a lack of finance. The fact that ongoing reliance on animal research means it continues to receive the vast majority of funding. Furthermore, those interested in non-animal research not only have to maintain momentum on their specific ideas and methods, but also face a need to continually look for funding or sponsorship, which ultimately impacts on the amount of time they directly spend on their research, as acknowledged by PETA in an interview with Lush Prize in 2012;

<sup>•</sup>.people may have good ideas about non-animal methods but they're continually going to be seeking support...and funding for those'<sup>8</sup>

To provide some up to date figures to illustrate, in 2012-2013 in the UK, over £300 million of public funding was spent on projects which '*include an element of animal use*' .In contrast, just under £9 million was awarded to 3R's projects broadly termed as 'alternatives' ,with the NC3Rs awarding £7 million of this total.<sup>9</sup> The NC3Rs state that of the funding they provide, '*around 55 per cent of research awards are directed primarily at replacement, 25 per cent for reduction and 20 per cent for refinement*'. <sup>10</sup> Therefore within the £9 million, a much lower total was awarded to genuine non-animal (replacement) methods as a significant amount of 'alternatives' funding is donated to the '2Rs' which still involve animals. For example, previous NC3Rs funding includes projects which develop scales for recognising facial expressions of pain in monkeys <sup>11</sup> or facial grimace scales in rabbits.<sup>12</sup> To add further perspective, since it was established in 2004, the NC3Rs has awarded just over £37 million in project funding. Based on the above figures, this equates to 12% of *just one year's* government funding of projects which include animal research.

Research carried out by the BUAV in 2013 revealed the stark lack of funding devoted to alternatives to animal testing across the EU member states. Just €18.7 million was devoted to methods relating to the 3Rs in 2013 by only seven countries, with most member states failing to assign any funding at all and half not responding. Given that the most recently available figures (for 2011) show the total combined annual science R&D (research and development) budget for the EU to be almost **€257** 

<sup>&</sup>lt;sup>8</sup> Interview with PETA, 20 August 2012

<sup>&</sup>lt;sup>9</sup> Hansard Written Answers :Animal Experiments 11 March 2014:<u>http://www.theyworkforyou.com/wrans/?</u> id=2014-03-11a.188641.h

<sup>&</sup>lt;sup>10</sup> NC3Rs Funding Schemes: <u>http://www.nc3rs.org.uk/landing.asp?id=27</u>

<sup>&</sup>lt;sup>11</sup> Quantifying the behavioural and facial correlates of pain in laboratory macaques: <u>http://www.nc3rs.org.uk/</u> researchportfolio/showcatportfolio.asp?id=324

<sup>&</sup>lt;sup>12</sup> The Rabbit Grimace Scale- a new method for pain assessment in rabbits: <u>http://www.nc3rs.org.uk/news.asp?</u> id=1833



**billion**, the amount spent on alternatives is wholly inadequate, equating to just 0.007% of expenditure. <sup>13</sup>

These figures demonstrate the importance of independent funding for non-animal research that the Lush Prize offers. At its launch in 2012, the £50,000 total prize money for the Young Researcher Prize was allocated to five potential winners. This has now changed slightly to four prizes of £12,500 to increase funding awarded to individuals, whilst still recognising the work of several researchers .Feedback from previous prize-winners has indicated that the bursaries provide a meaningful amount, therefore the slight increase in funding across four awards will be of even more benefit to go towards both research expenses and the cost of consumables.

# 4.3 Validation and acceptance of non-animal methods

A further rate limiting factor in non-animal methods is their validation and acceptance, as highlighted previously by Lush Prize research. Some of the methods now available have taken decades to attain even partial approval for use. Added to this is the confusion caused by different rates of validation according to various guidelines, for example European Test Methods Regulation vs the OECD guidelines <sup>14</sup>. However, on the positive side, the rigorous validation and testing process only adds to the weight of evidence that non-animal methods provide highly accurate and human-relevant technologies, where animal testing continues to fail. Furthermore, no animal test has ever been validated and scrutinised to the same scientific degree as non-animal methods. Rather, animal based methods defined as 'well characterised' or 'well defined' simply means that they have been carried out in duplicative tests over and over again, with little or no translation into a clinical setting. A very recently published article by the Editor of the British Medical Journal highlights this, by asking 'How productive and predictive is animal research?' and concluded that 'Funds might be better directed towards clinical rather than basic research, where there is a clearer return on investment in terms of effects on patient care.' <sup>15</sup>

There is also a well-established 'Catch 22' situation with acceptance of non-animal methods, whereby regulatory agencies feel unwilling or unable to accept such data, largely due to the fact that they are not used to seeing it as much and so continue to rely on animal based data. This in turn means that the industry is unwilling to invest time and money in non-animal methods as there is a risk that they will not be approved. This was highlighted by Prof. Coenraad Hendriksen, the Chair of 'Alternatives to Animal Use' of the University of Utrecht to the European Parliament recently;

<sup>&</sup>lt;sup>13</sup> Taylor, K. (2013) BUAV : EU member state government contribution to alternative methods. *ALTEX*:<u>http://www.altex.ch/resources/epub\_Taylor\_140124.pdf</u>

<sup>&</sup>lt;sup>14</sup> Wagner, K. et al. (2012) Inconsistencies in Data Requirements of EU Legislation Involving Tests on Animals ALTEX:<u>http://www.altex.ch/resources/altex\_2012\_3\_302\_332\_Wagner11.pdf</u>

<sup>&</sup>lt;sup>15</sup> How predictive and productive is animal research? BMJ: 5<sup>th</sup> June 2014:<u>http://www.bmj.com/content/bmj/348/</u> bmj.g3719.full.pdf

"...manufacturers are reluctant to invest in alternative tests without having assurance of regulatory acceptance. At the same time and the other way around - the regulators are reluctant to assure acceptance in the absence of data.' <sup>16</sup>

This again emphasises a clear contrast in attitudes and bias when compared to the animal testing community, for example in the UK where basic or 'fundamental' research (also termed 'blue sky' research, as highlighted in the Lush Prize 2012 paper) which, far from being met with apprehension, reluctance or claims of 'high risk', is actively encouraged and accounts for 30% of all animals used annually, continually receiving large-scale investment and public funding. There is no legal requirement to perform basic or 'fundamental' research on animals, yet a highly-demand led system is in place.

# 4.4 "Banning animal testing will stifle innovation"

This was a claim that was regularly made by industry as the 2013 EU cosmetics ban came into effect (*"the ban acts as a brake on innovation"*.<sup>17</sup>) Far from impeding research, the bans (both 2009 and 2013) had the opposite effect and were the direct drivers for the launch of new research into non-animal methods through large scale, multinational projects, (for example ReProTect <sup>18</sup>) as these critical deadlines approached. Research and development of new methods is innovation in itself and provides the perfect opportunity for those who genuinely want to be involved in cutting edge, next generation science, without causing animal suffering. The EU has led the way in progress to alternative methods of testing to animals and is considered 'a leader in innovation', something which should be reflected in the opportunities it offers young researchers and emerging graduate scientists.

# 4.5 <u>Toxicity testing is toxicity testing, regardless of purpose</u>

The validated and accepted non-animal (replacement) toxicity testing methods that are now available have been developed largely due to EU bans on both the testing (March 2009) and the marketing (March 2013) of cosmetic ingredients on animals. As a result, discussion of replacing animals in toxicity testing is far more common and perhaps considered more acceptable in the cosmetics field. However, young researchers working or studying in other areas of toxicity may feel less able to speak out about their research interests, especially in replacement /non-animal methods as these are seen as more controversial than '2Rs' (reduction or refinement) approaches. It is therefore important to recognise that these methods are now of essential use in other chemicals testing sectors, such as the food or pharmaceutical industries. This demonstrates that when a non-animal method is developed and accepted, it can potentially be applied to the testing of any

<sup>&</sup>lt;sup>16</sup> Animal Testing- Science or Tradition? Summary of Proceedings- Expert Seminar European Parliament 19<sup>th</sup> Feb 2014: <u>http://www.sidonia.pl/files/12iii14.pdf</u>

<sup>&</sup>lt;sup>17</sup> Europe Bans Marketing of Cosmetics Tested on Animals: <u>http://ens-newswire.com/2013/03/11/europe-bans-marketing-of-cosmetics-tested-on-animals/</u>

<sup>&</sup>lt;sup>18</sup> ReProTect <u>http://www.opentox.org/meet/opentox2011/talks/OpenTox2011\_Talk-Schwarz.pdf</u>



substance, for any purpose. This may encourage young researchers to voice their interests in non-animal methods.

This is especially relevant as, despite alternatives being developed in areas such as cosmetics, toxicity testing in animals continues in many other industries. For example, in the UK in 2013, over 375,000 toxicity tests (from a total 4.12 million experiments) were performed on animals (mice, rats, rabbits, guinea pigs, dogs, cats, monkeys, birds and fish).<sup>19</sup> Another important point with regard to the Young Researcher Prize is that almost half of all animal experiments in the UK are carried out at universities. One of the most concerning findings is that an increase in GM (genetically modified)animal use (mainly mice) and an increasing use of zebrafish is in some aspects being considered an 'alternative', as highlighted by FRAME (Fund for Replacement of Animals in Medical Experiments).<sup>20</sup>

Latest figures <sup>21</sup> also show that over 1 million animals (1,004873 from a total of just under 11.5 million animals) are used in toxicity testing across the EU each year. Of these, 111,166 animals are used in tests that aren't even required by law (categorised as 'no regulatory requirements') The archaic and much criticised LD <sub>50</sub> / LC <sub>50</sub> (lethal dose or lethal concentration test which tests the amount of substance required to kill 50% of the animals) accounts for the majority of the animals used each year, along with other lethal tests (34%) with the other main use simply being categorised as 'other' toxicology tests. (22%) followed by chronic/sub chronic toxicity and reproductive toxicity. There is no official figure for the number of toxicity tests still conducted on animals worldwide (from the estimated yearly total of 115 million animals <sup>22</sup> used in all experiments) as many countries omit this information or do not even count numbers of animals used, however a revised estimate by Lush Prize puts the number of toxicity tests carried out on animals worldwide as almost 9.5 million (from a total 118 million animal experiments)<sup>23</sup>.

Despite ongoing development and validation of alternatives in some of these areas however, thousands of animals continue to be used in all types of toxicity tests, as summarised below:

<sup>&</sup>lt;sup>19</sup> Statistics of Scientific Procedures on Living Animals (2013) -UK Home Office:<u>https://www.gov.uk/government/uploads/attachment\_data/file/327854/spanimals13.pdf</u>

<sup>&</sup>lt;sup>20</sup> Home Office statistics on lab animal use released -FRAME:<u>http://www.frame.org.uk/home-office-statistics-on-lab-animal-use-released/</u>

<sup>&</sup>lt;sup>21</sup> Seventh Report on the number of animals used in scientific procedures (2011): <u>http://eur-lex.europa.eu/</u> resource.html?uri=cellar:d2e73ac5-60d0-11e3-ab0f-01aa75ed71a1.0001.01/DOC\_1&format=PDF

<sup>&</sup>lt;sup>22</sup> Taylor, K. et al. (2008) Estimates of Worldwide Laboratory Animal Use in 2005: BUAV <u>http://www.buav.org/</u> \_lib/userfiles/files/Science\_Reports/Estimates\_For\_Worldwide\_Laboratory.pdf

<sup>&</sup>lt;sup>23</sup> Lush Prize 'A Global View of Animal Experiments 2014' - <u>http://www.lushprize.org/wp-content/uploads/</u> <u>Global\_View\_of-Animal\_Experiments\_2014.pdf</u>



Test	Description
Acute and sub-acute toxicity testing Methods (including lethal dose tests such as LD <sub>50</sub> )	Tests of one-off or short term duration, usually via oral, dermal or inhalation dosing (usually mice or rats)
Skin Irritation	Test to check for (reversible) damage to the skin by topical application of a substance to the animals' shaved bare skin (usually rabbits)
Skin Sensitisation	Test to check for (irreversible) damage to the skin by topical application of a substance to the animals' shaved bare skin (usually rabbits)
Eye Irritation/Corrosion	The Draize rabbit test –substance is instilled into the eyes of albino rabbits to check for irritation/corrosion (reversible/irreversible injury) to the cornea, iris and conjunctiva for up to 21 days
Sub chronic and chronic toxicity	Longer term (weeks/months/years) repeated dose toxicity tests (oral/skin/inhalation) usually for 28 or 90 days ( longer studies of 1-2 years are also conducted) rodents and non-rodent species (dogs or non-human primates)
Carcinogenicity	Oral/dermal/inhalation of substances to check for development of cancerous lesions, typically rats for 2 years duration.
Developmental Toxicity	To check for effects during pregnancy of animals and foetuses(female rats and rabbits)
Mutagenicity & Genotoxicity	Test to check effects of DNA damage which may or may not be passed onto offspring or lead to cancer - several types of test including lethal testing in rodents
Reproductive Toxicity	To check for effects on the reproductive function of male and female animals and development of offspring. Long term dosing of parent animals before mating, during mating, pregnancy and birth of offspring for entire generations of animals. Large numbers of animals used per test. e.g. Extended One Generation Reproductive Toxicity Study for one chemical uses 960 animals
Toxicity to aquatic vertebrates	Fish are used to test for both acute and chronic toxic effects; tests include the 96-hour $LC_{50}$ test, (lethal concentration to 50% of the fish). Chronic fish tests may start with eggs, embryos, or juveniles, and last from 7 to more than 200 days

'Other Toxicology' tests * *T	The latest EU statistics state that these 'other' tests
ind	include 'neurotoxicity, toxicokinetics, testing of
bid	iological evaluation of medical devices:
int	itracutaneous testing of reactivity in rabbits, studies
int	ito the penetration of nanoparticles through tissue
ar	and their biocompatibility, studies into the evaluation
of	of sensitization potential of dyestuffs used in the
te.	extile industry and pharmacological studies
ind	included in safety tests) and target animal studies
ca	arried out on companion animals to different
re	egulatory standards ( e.g. US EPA, FDA) tests to
de	etermine the residues of veterinary medicaments in
ca	alves and in broilers, test to determine the non-
to.	poxicity and irreversibility of toxins and efficacy of
va	accines (blue tongue, clostridium)

In its 2013 progress report <sup>24</sup> on the development, validation and regulatory acceptance of alternative methods, EURL-ECVAM (EU Reference Laboratory for alternatives to animal testing) summarised that

"Overall, good progress has been made in the validation and regulatory acceptance in areas such as local toxicity where the underpinning science is more advanced and mature alternative methods are available. For very complex endpoints on the other hand, such as chronic systemic toxicity, carcinogenicity or reproductive toxicity, efforts are predominantly focused on research and development where the emphasis is on the integration of a variety of methods based on mechanistic understanding. The future is bright however, since considerable advances in new in vitro technologies, systems biology, bioinformatics and computational modelling are driving a paradigm shift in toxicological testing and assessment where non-animal methods will ultimately become the tools of choice.'

# 4.6 A year on from the 2013 marketing ban- work still to be done

Despite the EU animal-tested cosmetic bans being the major driver of non-animal toxicity testing methods in recent years, there is still much more to be done. This is illustrated very clearly given that 'Over 80% of the world allows animals to be used in cruel and unnecessary cosmetics tests and these animal tested cosmetics can be purchased in every country across the globe."<sup>25</sup>

Although the 2013 EU marketing ban on animal tested cosmetics did finally go ahead, the European Commission had previously considered the possibility of delaying the deadline on the basis of recommendations that the alternative methods

<sup>&</sup>lt;sup>24</sup> EURL ECVAM progress report on the development, validation and regulatory acceptance of alternative methods (2010-2013):<u>http://ihcp.jrc.ec.europa.eu/our\_labs/eurl-ecvam/eurl-ecvam-releases-2013-progressreport-development-validation-regulatory-acceptance-alternative-methods</u>

<sup>&</sup>lt;sup>25</sup> Cruelty Free International: Animal tested cosmetics are for sale in every country in the world:<u>http://www.crueltyfreeinternational.org/en/the-issue</u>



still 'missing' would take much longer to be developed. For example, estimates of another 5-9 years were proposed for skin sensitisation and toxicokinetic methods to be developed and possibly even longer for full replacement in these areas. No estimates were provided at all for when repeat dose toxicity, reproductive toxicity or carcinogenicity tests on animals might be developed. These timelines were estimated in a report published by the Commission in 2011.<sup>26</sup> In the three years since then, aside from the introduction of the 2013 ban itself (which went ahead regardless of the alternatives available, which was great news) further work has been ongoing in the areas of toxicity testing which still need development. For example, in 2013 the Joint Research Centre (JRC) published its EURL-ECVAM Strategy to Avoid and Reduce Animal Use in Genotoxicity Testing'. <sup>27</sup>Similarly, the five-year long NOTOX project <sup>28</sup> launched in 2011 and involving a network of scientific expertise from several countries works 'towards the replacement of current repeated dose systemic toxicity testing in human safety assessment'. NOTOX is part of a wider project funded under the EU Seventh Framework Programme (FP-7) known as SEURAT (Safety Evaluation Ultimately Replacing Animal Testing) which combines the research efforts of over 70 European universities, public research institutes and companies and regularly posts open vacancies and research opportunities. <sup>29</sup> Of particular relevance is that SEURAT recently hosted a 'Young Scientists Summer School' to discuss replacement of repeat dose toxicity testing in animals. 30

<sup>&</sup>lt;sup>26</sup> Alternative (non-animal) methods for cosmetics testing: current status and future prospects—2010: <u>http://ihcp.jrc.ec.europa.eu/our\_activities/alt-animal-testing-safety-assessment-chemicals/report\_2010/fulltext.pdf</u>

<sup>&</sup>lt;sup>27</sup> EURL ECVAM Strategy to Avoid and Reduce Animal Use in Genotoxicity Testing:<u>http://publications.jrc.ec.europa.eu/repository/bitstream/111111111/30088/1/jrc\_report\_en\_34844\_online.pdf</u>

<sup>&</sup>lt;sup>28</sup> NOTOX: Predicting long term toxic effects using computer models based on systems characterization of organotypic cultures: <u>http://www.notox-sb.eu/</u>

<sup>&</sup>lt;sup>29</sup> SEURAT (Safety Evaluation Ultimately Replacing Animal Testing): <u>http://www.seurat-1.eu/</u>

<sup>&</sup>lt;sup>30</sup> Young scientists from JRC's EURL ECVAM at the second SEURAT-1 Summer School: <u>https://</u> www.eurtd.com/seurat-1/2014/summer-school/

# 5 The key players in the field – the ethical early career scientists

As previously highlighted, there remain ongoing prejudices towards switching from animal to non -animal research. Resistance to change, combined with 'comfort' in repeating accepted, conventional methods allows the animal research industry to maintain the 'status quo', despite ever increasing recognition that animal testing is a flawed, overrated and outdated system. It must also be noted that the industry has for decades consisted of a network of not only researchers, but breeders, suppliers and transporters of animals across the world who rely on animal testing to continue. There are other factors to consider, for example some scientists(especially senior level researchers) have based their entire careers on using animals and are unable or unwilling to consider anything else or they may view switching to non-animal research as the unattractive option of 'starting again'. This may also apply to earlier career individuals who have followed the mainstream route into animal based toxicology to progress their careers to date, for example since leaving university. This is echoed by several previous prizewinners who felt that the undergraduate level of their education was the most challenging in trying to avoid using animals. Nevertheless, one of the 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'.<sup>31</sup>

Research for Lush Prize conducted during its launch in 2012 provided a useful summary of various awards and funding programmes available to early career scientists. An updated summary of these is shown below, with some new additions in bold. It should be noted that these prizes cover any or all of the 3Rs, rather than just replacement and the list is not exhaustive.

Name of award, prize or bursary	Organisation behind award
3Rs Science Award	The European Partnership for Alternative Approaches to Animal Testing (EPAA)
Russell & Burch Award	Humane Society of the United States
Charles River Laboratories' Excellence in Refinement Award	Charles River Laboratories/ CAAT, (Johns Hopkins Center for Alternatives to Animal Testing)
David Sainsbury Fellowships	National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs).
NC3Rs Studentships * (a more detailed summary of these is provided below)	National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs).

<sup>&</sup>lt;sup>31</sup> Lush Young Researchers Prize 2012- Research Paper

LRI Innovative Science Award	The European Chemical Industry Council (CEFIC), in conjunction with the Society of Environmental Toxicology and Chemistry (SETAC), the Association of European Toxicologists and European Societies of Toxicology (EUROTOX), the International Society of Exposure Sciences (ISES) and Chemical Week
Macquarie University Eureka Prize for Outstanding Young Researcher	Australian Museum/Macquarie University
Society for In Vitro Biology Young Scientist Award	Society for In Vitro Biology
Colgate-Palmolive Postdoctoral Fellowship Award in In Vitro Toxicology	Society of Toxicology, sponsored by Colgate Palmolive
Scholarships alternatives to animal testing	Juliana von Wendt Fund, Finland
EPAA 3R Laboratory technician Prize (awarded for the first time in 2013)	The European Partnership for Alternative Approaches to Animal Testing (EPAA)
Colgate Palmolive Grants for Alternatives Research	Society of Toxicology, sponsored by Colgate Palmolive
Colgate Palmolive Awards for Student Training in Alternative Methods	Society of Toxicology, sponsored by Colgate Palmolive
Bjorn Ekwall Memorial Award	Bjorn Ekwall Memorial Foundation
CAAT Recognition Award	CAAT, (Johns Hopkins Center for Alternatives to Animal Testing)
Doerenkamp-Zbinden Award	Doerenkamp-Zbinden Foundation
ECETOC Science Awards	ECETOC(European Centre for Ecotoxicology and Toxicology of Chemicals)
Japanese Society for Alternatives to Animal Experiments (JSAAE) Society Award	Japanese Society for Alternatives to Animal Experiments (JSAAE)
Three R's Award	New Zealand National Animal Ethics Advisory Committee

Nordic Prize for Alternatives to Animal Experiments	The Swedish Fund for Research Without Animal Experiments, the Danish Alternative Fund and the Finnish Juliana von Wendt Fund
2015 Felix Wankel Animal Welfare Research Award	Faculty of Veterinary Medicine of the Ludwig-Maximilians-University Munich
for a variety of animal welfare issues, including awarding outstanding experimental and innovative scientific papers aiming at or resulting in the replacement or reduction of animal testing.	The award (up to €30,000) may be divided among several prize winners.

\*To provide further information on the types of scholarships available to young researchers, below is a summary of the 15 PhD studentships currently funded by the UK NC3R's. The full list is shown to illustrate the types of research on offer, however it must also be noted that the studentships below cover the broader '3Rs', rather than the 'replacement only' criteria that the Young Researcher Prize requires.

Location	Description
University of Aberdeen with Marine Science Scotland	Development of a method for non-lethal sampling from individual fish to investigate host responses to ectoparasites.
University of Birmingham with University of Oxford	Creating an <i>in vitro</i> model of pathogenic ossification to explore methods for dispersion.
University of Edinburgh	Motor neuron regeneration in larval zebrafish.
The Babraham Institute, University of Cambridge	Towards engineering a multi-cell lineage multi-organism intestine.
University of East Anglia with University of Liverpool	Development of a non-mammalian, pre- clinical screening tool (FETOX) for predictive analysis of drug safety.
University of Glasgow with University of Edinburgh	An <i>in vitro</i> model to investigate the role of oestrogen and oestrogen metabolism in pulmonary vascular disease.



University of Hertfordshire with GlaxoSmithKline.	DM-MAP: Drug and Metabolite Microsampling Analytical Platform for preclinical medicines development
University of Leeds	Development of an <i>in vitro</i> system to determine the causes of aberrant, leukaemogenic V(D)J recombinant reactions.
University of Liverpool	Developing molecular therapies for glaucoma using an <i>ex vivo</i> human organ culture system.
University of Oxford	Development of a patient-derived cellular model of circadian disruption in bipolar disorder
Royal Holloway, University of London with University College London.	Find the target of valproic acid; pioneering the use of a non-animal model for basic biomedical (epilepsy) research
Royal Veterinary College	Replacing rodent models for investigating the influence of the microbiome upon innate immune responses and resistance to pathogens.
University of Southampton	Exploitation of an <i>ex vivo</i> disease model to characterise early events in retinal degeneration.
University of Strathclyde	Developing microfluidic systems for high- throughput studies of functional neuronal networks.
University of Sussex	Development of a refined model of neuropathic pain: a model without frank nerve injury.

As highlighted by EURL-ECVAM <sup>32</sup>, a key factor in the development of non-animal methods is the integration of a number of test methods (or 'battery') which successfully address endpoints, especially those which are considered more complex or in-depth. (For example, several alternatives available in skin testing examine how a substance may react in various stages of topical application, absorption, irritation or corrosion which provide very targetted and quantitative results, especially when compared to a crude skin test in rabbits or guinea pigs).

<sup>&</sup>lt;sup>32</sup> EURL ECVAM progress report on the development, validation and regulatory acceptance of alternative methods (2010-2013):<u>http://ihcp.jrc.ec.europa.eu/our\_labs/eurl-ecvam/eurl-ecvam-releases-2013-progressreport-development-validation-regulatory-acceptance-alternative-methods</u>



Therefore,non-animal methods which are still in testing or validation, or 'gaps' in the development of methods where the biggest use of animals still lies, such as reproductive or chronic toxicity, could allow the Lush Prize to potentially channel ideas or research themes for specific replacement projects. This may also help young researchers to specialise in key areas. For example promotion of helpful materials could aid those who wish to get involved in animal free toxicology and need an area to focus on to progress further.

Never before has there been a better opportunity for young researchers to focus on this specialist area, not only to save animals from unnecessary pain and suffering, but to pave the way for a career in cutting edge innovation. As highlighted by the New England Anti-Vivisection Society (NEAVS) in a previous interview with Lush Prize, linking an early career scientist's research to increased income and sponsorship is key;

"I think the solution for graduate students who want to do more progressive in vitro research is to find the granting agencies that will help bring money in [to an institution].... The key to changing institutions is bringing in grant dollars. When someone who wants to develop in vitro alternatives can show that they can bring in million dollar grants, then institutions are going to have to accept it. They're not going to turn money away even if they want to try to suppress a certain ideology"<sup>33</sup>

Therefore, if a researcher has ideas but can also say ' if you fund me, I propose to cut your costs, save you time, increase income and improve your business ', whilst this might be a challenge, their proposals are much more likely to be considered.

<sup>&</sup>lt;sup>33</sup> Interview with NEAVS, 20 August 2012



# 6 A review of organisations, research institutes, public bodies and societies which provide a network of educational and career opportunities for young researchers

Earlier education is key; raising awareness as soon as possible

There is significant connection between the Young Researcher and Training Prizes with regard to educational issues in animal testing and alternatives. For the 2013 prize cycle, Lush Prize conducted extensive reviews of school curriculums, educational materials and university level information on both dissection and animal testing and interviews with key campaigning organisations and research institutes. As an update to this research, the next section reviews some of these organisations which currently operate highly successful educational and training packages for schools, colleges and universities, as well as more specific research initiatives, funding opportunities and events specifically aimed at early career scientists who wish to find out more. Further details on *all* organisations referenced in this paper can be found in Appendix 1.

**Alttox** is an essential tool for graduates and young scientists interested in pursuing a career in toxicity testing without animals. It is an online forum for exchange of information and news on non-animal toxicity tests methods, with a toxicity testing resource centre, useful links to other organisations and forthcoming events and training courses. It also invites commentaries in a section entitled 'The Way Forward' <sup>34</sup>

Established in 1993, **The Alternatives Research & Development Foundation (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'. <sup>35</sup>

**Animal Aid**'s education department operates a school speaker training service whose speakers are available to present and train volunteers on a number of animal rights issues, including animal testing. They can also provide educational materials for both teachers and pupils on request. <sup>36</sup>

**BUAV** (British Union for the Abolition of Vivisection) provides a 'Schools' guide <sup>37</sup> 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 <sup>38</sup>

<sup>&</sup>lt;sup>34</sup> AltTox- Non-animal methods for Toxicity Testing: <u>http://www.alttox.org/</u>

<sup>&</sup>lt;sup>35</sup> Alternatives Research and Develpment Foundation :<u>http://www.ardf-online.org/</u>

<sup>&</sup>lt;sup>36</sup> Animal Aid: Education Department :http://www.animalaid.org.uk/h/n/EDUCATION/

<sup>&</sup>lt;sup>37</sup> What's wrong with animal experiments? A guide for students: BUAV:<u>http://www.buav.org/\_lib/userfiles/files/ Guides/BUAV\_SchoolsGuide.pdf</u>

<sup>&</sup>lt;sup>38</sup> BUAV Science Reports: <u>http://www.buav.org/humane-science/science-reports/</u>



**The Center for Alternatives to Animal Testing (CAAT)** <sup>39</sup>based at John Hopkins University in Maryland, USA has had key involvement in the Lush Prize to date. As well as it's 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 as well as others. CAAT and ALtweb are vital sources of information (such as events or latest updates on studentships or sponsorships available to apply for) to those wishing to pursue or maintain a career in non-animal methods.

**DAAE-** (Doctors Against Animal Experiments) based in Germany run projects for young people and have offered research fund prizes <sup>40</sup>

The **Dr Hadwen Trust** (DHT), the UK's leading non-animal medical research charity, as well as funding a variety of research projects on an ongoing basis, has awarded seven 'Summer Studentships' in 2014 <sup>41</sup> 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. Funding is offered for a period of up to eight weeks and includes a budget for research consumables. Additionally, in 2014 the DHT is looking for a student (aged 18+) to take up a free bursary place to attend and represent the DHT at the British Science Festival from 6-11 September in Birmingham<sup>42</sup>.

# 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 covered this year included long term toxicity prediction using computer models and integrated, non-animal testing strategies in skin sensitisation. ESTIV is also offering a training course in January 2015 in Lisbon entitled 'Applied In-Vitro Toxicology Course' and welcomes young scientists. ESTIV is sponsored by a number of major chemical and pharmaceutical companies, most recently Roche.

For early career scientists who are interested in specific opportunities to gain experience in the *validation* of alternative methods, **EURL-ECVAM** (**The European Union Reference Laboratory for Alternatives to Animal Testing**) represents a focal point of EU activity on alternative test methods and in response to the

<sup>&</sup>lt;sup>39</sup> John Hopkins University Centre for Alternatives to Animal Testing : <u>http://caat.jhsph.edu/</u>

<sup>&</sup>lt;sup>40</sup> Doctors Against Animal Experiments (Germany):<u>http://www.aerzte-gegen-tierversuche.de/en/projects/school-project</u>

<sup>&</sup>lt;sup>41</sup> Dr. Hadwen Trust Summer Studentships Projects 2014: <u>http://www.drhadwentrust.org/research-and-funding/</u> <u>summer-studentships-current-portfolio</u>

<sup>&</sup>lt;sup>42</sup> Would you like to be the DHT's Geek4aWeek? <u>http://www.drhadwentrust.org/latest-news/news-and-views/</u> post/254-would-you-like-to-be-the-dhtas-geek4aweek



requirement by the recently amended EU directive on animal research (2010/63/EU) set up EU-NETVAL (the European Union Network of Laboratories for the Validation of Alternative Methods). EU-NETVAL currently consists of 26 'member' laboratories <sup>43</sup> which may be of interest to young scientists to monitor regularly for up and coming career opportunities or internships. Opportunities may be on offer either at these sites directly, or other sites associated with them. It is important to note that many of these labs are not exclusively dedicated to alternatives to animal use and may also conduct animal research. For example the UK member is HLS (Huntingdon Life Sciences) a global scale animal testing laboratory. Some of the EU-NETVAL labs are also listed separately below where they offer specific other educational or career opportunities in non-animal methods.

**FICAM**, the Finnish Centre for Alternative Methods\_<sup>44</sup> is the centre of expertise for alternative methods to animals and the EU-NETVAL member laboratory for Finland. FICAM focuses on the development and validation of human cell and tissue culture 2D- and 3D-models. FICAM has a strong core of scientific education and training in non-animal methods and states that '*students can perform research both for MSc and doctoral (Ph.D. and MD) degrees. The students for MSc degree come from other study programs, and they will only perform the practical research in FICAM. The students for doctoral degree usually belong to graduate schools'. Since 2007, FICAM has also provided special courses in cell and tissue culture for toxicology schools which would be directly relevant to young scientists, as well as being linked to the Finnish Consensus Platform for Alternatives (<u>FINCOPA</u>) and organisation of yearly networking events and seminars.* 

Fund for the Replacement of Animals in Medical Experiments (**FRAME**)<sup>45</sup> have provided key information in previous Lush Prize research. FRAME is based in Nottingham, UK and operates the FRAME Alternatives Laboratory (FAL) as well as providing training schools in experimental design and statistics in association with universities throughout the UK, Europe and Scandinavia. FRAME's mission is to promote the replacement of animals in medical experiments, and the use of nonanimal methods for predicting human adverse reactions, as well as to promote the development and evaluation of *in vitro* and other non-animal alternatives in peer reviewed scientific journals and relevant scientific research. FRAME also publishes ATLA, the Alternatives to Laboratory Animals Journal.

The Humane Research Trust (UK) is a registered charity dedicated to medical research without animals. The HRT encourages scientists to develop innovative alternatives and focuses on 'educating the next generation of researchers'. Their statement of policy is 'No animals or animal tissue to be used. Applications need to show some advance in technique, or use existing techniques in areas where it is the

<sup>&</sup>lt;sup>43</sup> EU-Netval -European Union Network of Laboratories for the Validation of Alternative Methods: <u>http://</u> <u>ihcp.jrc.ec.europa.eu/our\_labs/eurl-ecvam/eu-netval/EU-NETVAL-list-labs-updated-13-01-2014.pdf</u>

<sup>&</sup>lt;sup>44</sup> FICAM- The Finnish Centre for Alternative Methods: http://www.ficam.fi/

<sup>&</sup>lt;sup>45</sup> FRAME Training Schools in Experimental Design - <u>http://www.frame.org.uk/training-schools/</u>



norm to use animals, which will lead to a reduction in animal usage and a benefit to human health."<sup>46</sup>

**The International Foundation for Ethical Research (IFER)** based in Chicago, USA awards cutting edge new technologies that replace animals in research, testing and education. IFER offers graduate student fellowships which provide \$12,500 plus \$2,500 for supply costs. They operate a number of eligibility criteria for interested applicants.<sup>47</sup>

**INTERNICHE (International Network for Humane Education) produce** a variety of educational materials relevant to study of human medicine, veterinary research and the life sciences.

The **Lord Dowding Fund for Humane Research (LDF)** funds medical research projects which replace the use of animals. Detailed information on the LDF, the types of projects it funds and how to apply can be found on their website. Although the LDF currently states that funding availability is limited, one-off funding may be considered for research consumables. The LDF also states that 'Although we are always keen to promote studies into alternatives to animal experimentation, we unfortunately don't provide funding purely for individuals at the PhD or post-graduate level'.<sup>48</sup>

The Australian based **Medical Advances Without Animals Trust (MAWA)** is a registered charity which aims to advance medical science to improve human health and therapeutic outcomes without using animals or animal products. The Trust provides "research and equipment grants, fellowships, scholarships, bursaries and sponsorships to scientists and scholars throughout Australia in a competitive award process, and funds a range of other initiatives to further MAWA's goals".<sup>49</sup>

The **Netherlands Knowledge Centre on Alternatives to Animal Use (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.

The **Physicians Committee for Responsible Medicine** (PCRM) in the USA promotes alternatives to animal research and campaigns for the use of non-animal methods in medical education. They provide a wealth of scientific educational materials, information on courses and career opportunities and internships. The

<sup>&</sup>lt;sup>46</sup> Humane Research Trust – Applying for Funding <u>http://www.humaneresearch.org.uk/application-for-funding/</u>

<sup>&</sup>lt;sup>47</sup> IFER Graduate Fellowships for Alternatives to the Use of Animals - <u>http://www.ifer.org/fellowships.php</u>

<sup>&</sup>lt;sup>48</sup> Lord Dowding Fund- Applying for Funding:<u>http://www.ldf.org.uk/research/49/52/298/</u>

<sup>&</sup>lt;sup>49</sup> MAWA Funding Initiatives :<u>http://mawa-trust.org.au/pdf/MAWA%20Funding%20Initiatives.pdf</u>



PCRM also campaigns on a broader scope for higher standards of ethical research and the benefits of preventative medicine. <sup>50</sup>

**SAFE** (Save Animals from Exploitation) are a New Zealand based organisation and previous 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'. <sup>51</sup>

**Scientists for Global Responsibility (SGR)** are based in the UK and promote ethical awareness in science and technology. They provide an 'ethical careers' section on their website which includes resources to help scientists and engineers gain a deeper understanding of ethical issues in science, design and technology and help them choose an ethical path in this area. Materials include briefings, presentations, articles and other resources, as well as an 'ethical employers' contact list.<sup>52</sup>

**SET** based in Germany is the Foundation for the Promotion of Alternate and Complementary Methods to Reduce Animal Testing. SET offers the opportunity to gain funding for projects which focus broadly across the 3Rs. SET also have an interest in funding training and education initiatives. <sup>53</sup>

As referenced earlier in this paper, the EU research project known as **SEURAT (Safety Evaluation Ultimately Replacing Animal Tests)** recently hosted it's second 'Young Scientists Summer School' in collaboration with ESTIV (European Society of Toxicology In Vitro to discuss replacement of repeat dose toxicity testing in animals.

The Swedish Fund for Research Without Animal Experiments supports alternatives in basic and applied research in various areas, including the development of computer simulation systems, toxicology, and training of laboratory personnel and courses in alternatives. The fund has awarded over 30 million SEK since 1971 and currently awards projects totalling € 80 000-160 000 each year. <sup>55</sup>

The <u>**3R Research Foundation (Switzerland)</u>**: awards annual prizes for research directly impacting on the 3Rs. They have key areas of interest that they emphasise</u>

<sup>&</sup>lt;sup>50</sup> PCRM:Education and Training - <u>http://www.pcrm.org/research/edtraining/</u>

<sup>&</sup>lt;sup>51</sup> SAFE Education :<u>http://www.safe.org.nz/Education/</u>

<sup>&</sup>lt;sup>52</sup> SGR Ethical Careers: <u>http://www.sgr.org.uk/projects/ethical-careers</u>

<sup>&</sup>lt;sup>53</sup> SET Funding and Proposals: Guidelines and Criteria <u>http://www.stiftung-set.de/research\_funding/</u> <u>guidelines\_and\_criteria.html?L=1</u>

<sup>&</sup>lt;sup>54</sup> SEURAT-1 Young Scientists Summer School <u>https://www.eurtd.com/seurat-1/2014/summer-school/</u>

<sup>&</sup>lt;sup>55</sup> Projects Funded by the Swedish Fund <u>http://www.forskautandjurforsok.se/in-english/Grants/</u>



to grant applicants, one of which is alternative methods to acute and chronic toxicity testing. <sup>56</sup>

**HemiBio** is one of six projects funded under the SEURAT programme. The aim of HeMiBio is to generate a liver-simulating device (Hepatic Microfluidic Bioreactor) mimicking the structure and function of the human liver. Hemibio states that there is a great need for suitable human cells to be used in toxicity testing, due to the often poor concordance between animal models and toxic effects in humans. The project was set up in 2011 as part of the drive to find suitable non-animal methods to meet the requirements of the (then) forthcoming marketing ban on animal tested cosmetics. HemiBio also plans a series of education and training opportunities for young scientists. Workshops and courses cover topics such as cell biology, genetic engineering of stem cells and 2D or 3D-culture devices. HemiBio also promotes job and study opportunities as well as events including Summer and Winter Schools for young scientists.<sup>57</sup>

<sup>&</sup>lt;sup>56</sup> 3Rs Research Foundation - Principal areas for financial support of research projects :<u>http://www.forschung3r.ch/en/guidelines/focus.html</u>

<sup>&</sup>lt;sup>57</sup> Third HeniBio Winter School for Young Scientists: <u>http://www.hemibio.eu/training-a-education</u>



# 7 Resources & selected bibliography

# Appendix 1: List of websites of organisations and documents used to help inform this report

## **Alternatives Research and Development**

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

The mission of the Alternatives Research and Development Foundation is to fund and promote the development, validation and adoption of non-animal methods in biomedical research, product testing and education

### Altox

### http://www.alttox.org/

AltTox.org is a website dedicated to advancing non-animal methods of toxicity testing through online discussion and information exchange.

### **Animal Aid**

#### http://www.animalaid.org.uk

Animal Aid is the UK's largest animal rights group and one of the longest established in the world, campaigning peacefully against all forms of animal abuse and promoting a cruelty-free lifestyle. Animal Aid investigates and exposes animal cruelty, and the evidence found is often used by the media, bringing these issues to public attention.

#### **Björn Ekwall Memorial Foundation**

#### http://www.bemf.eu/

The Scandinavian Society for Cell Toxicology (SSCT) established the Björn Ekwall Memorial Foundation in 2001. The main goal of the BEMF is to honour the memory of Dr. Björn Ekwall by giving a reward to the scientists who have substantially contributed to the field of cell toxicology, e.g. by developing new in vitro tests, or via mechanistic or validation studies.

#### **British Toxicology Society**

#### http://www.thebts.org/

The BTS is a learned society for toxicologists in the UK and represents the interests of approximately 1,000 members.

# The Campaign to End All Animal Experiments (BUAV)

#### http://www.buav.org/

Leading UK antivivisection campaigning organisation with a vision to "create a world where nobody wants or believes we need to experiment on animals". Also acts as secretariat to the ECEAE (European Coalition to End Animal Experiments)

#### **Cruelty Free international**

#### http://www.crueltyfreeinternational.org/

Cruelty Free International is the global campaign to end animal testing for cosmetics, calling on governments and regulators around the world to introduce a ban on the testing of animals for cosmetic products and ingredients.



# 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.

### **Dr Hadwen Trust for Humane Research**

### http://www.drhadwentrust.org

The Dr Hadwen Trust for Humane Research (DHT) is the UK's leading medical research charity that funds and promotes the development of techniques and procedures to replace the use of animals in biomedical research and testing.

# **European Consensus Platform for Alternatives (ECOPA)**

#### http://www.ecopa.eu

ECOPA is a consensus between animal welfare, industry, academia and governmental institutions in various countries as an efficient way to stimulate research into alternatives to animal experiments and enforce the acceptance of alternatives in experimental practice.

### European Centre for Ecotoxicology and Toxicology of Chemicals

#### http://www.ecetoc.org/

ECETOC is Europe's leading industry association for developing and promoting top quality science in human and environmental risk assessment of chemicals.

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

http://ihcp.jrc.ec.europa.eu/our\_labs/eurl-ecvam

EURL-ECVAM was established in 2011, due to the increasing need for new methods to be developed and proposed for validation in the European Union.

# EUROECOTOX

#### http://www.euroecotox.eu/

Europeon Network established to promote the integration of European activities on the replacement and reduction of animal experiments in ecotoxicology.

# The European Partnership for Alternative Approaches to Animal Testing (EPAA)

http://ec.europa.eu/enterprise/epaa/index\_en.htm

A voluntary collaboration between the European Commission, European trade associations, and companies from seven industry sectors. The partners 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.



# FICAM (The Finnish Centre for Alternative Methods)

## http://www.ficam.fi

FICAM is the centre of expertise for alternative methods to animal experimentation in Finland. FICAM develops and validates human-cell-based tissue/organ models, shares information on alternative methods, educates experts, and acts as the Finnish reference laboratory for EURL-ECVAM (European Union Reference Laboratory for Alternatives to Animal Testing).

# Fund for the Replacement of Animals in Medical Experiments (FRAME) <u>www.frame.org.uk</u>

The ultimate aim of FRAME is the elimination of the need to use laboratory animals in any kind of medical or scientific procedures. FRAME is dedicated to the development of new and valid methods that will replace the need for laboratory animals in medical and scientific research, education, and testing.

### HemiBio

#### http://www.hemibio.eu/

HemiBio is one of six projects funded under the SEURAT programme. The aim of HeMiBio is to generate a liver-simulating device (Hepatic Microfluidic Bioreactor) mimicking the structure and function of the human liver. Hemibio states that there is a great need for suitable human cells to be used in toxicity testing, due to the often poor concordance between animal models and toxic effects in humans. The project was set up in 2011 as part of the drive to find suitable non-animal methods to meet the requirements of the (then) forthcoming marketing ban on animal tested cosmetics. HemiBio also plans a series of education and training opportunities for young scientists. Workshops and courses cover topics such as cell biology, genetic engineering of stem cells and 2D or 3D-culture devices. HemiBio also promotes job and study opportunities as well as events including Summer and Winter Schools for young scientists

# The Humane Research Trust (UK)

#### www.humaneresearch.org.uk

The Humane Research Trust is a registered charity dedicated to medical research without animals. The Trust raises the necessary finance to fund and promote pioneering medical research into human disease without the use of animals or animal tissue. Their aim is to eliminate the need for animals in human medical research. The Humane Research Trust works with scientists, funding a wide range of research at a number of UK hospitals and universities. The Trust also funds lectureships and studentships, which help to spread the message that humane research is the cost effective way to promote human health, quickly and with a clear conscience.

# **Humane Society International (HSI)**

### http://www.hsi.org/

**HSI** is one of the only international animal protection organizations in the world working to protect all animals—including animals in laboratories, farm animals, companion animals, and wildlife. HSI has recently seen huge success in Asia with its



Be Cruelty Free campaign and engagement with stakeholders in China and Korea to bring an end to animal testing and promote use of non-animal methods.

# The International Foundation for Ethical Research (IFER)

## http://www.ifer.org

IFER supports the development, validation and implementation of innovative scientific methodologies that advance science and replace the use of animals in research, testing and education.

## **INTERNICHE (International Network for Humane Education)**

#### http://www.interniche.org

The aim of INTERNICHE is to achieve high quality, fully humane education and training in medicine, veterinary medicine and biological science. They support progressive science teaching and the replacement of animal experiments by working with teachers to introduce alternatives and with students to support freedom of conscience.

### Institute for In Vitro Sciences

#### http://www.iivs.org/

The Institute for In Vitro Sciences, Inc. is a non-profit research and testing laboratory dedicated to the advancement of in vitro (non-animal) methods worldwide.

#### In Vitro Jobs

#### http://www.invitrojobs.com/

Many researchers have a strong interest in animal-free research, but find information on institutions and research groups who use animal-free methods hard to come by. InVitro Jobs was set up by People for Animal Rights (Menschen für Tierrechte -Bundesverband der Tierversuchsgegner) in Germany. The aim is to enable researchers to access animal-free research easily. The site includes an upto-date list of research groups active in the development of animal-free techniques and, job vacancies. The site also aims to provide students with the opportunities to contact research groups to obtain information for their studies and to promote cooperation, networking and the exchange of ideas between researchers.

# John Hopkins University Centre for Alternatives to Animal Testing (CAAT) <a href="http://caat.jhsph.edu/">http://caat.jhsph.edu/</a>

CAAT believes the best science is humane science. Their programs seek to provide a better, safer, more humane future for people and animals.

# Lord Dowding Fund for Humane Research (LDF)

#### http://www.ldf.org.uk

The objectives of the LDF are to support, sponsor, and fund better methods of scientific and medical research for testing products and curing disease, which replace the use of animals and fund areas of non-animal fundamental research which lead to the adoption of non-animal research methodology.

# Medical Advances Without Animals Trust (MAWA)

http://mawa-trust.org.au/



**MAWA** is a registered charity which aims to advance medical science to improve human health and therapeutic outcomes without using animals or animal products. The Trust provides "research and equipment grants, fellowships, scholarships, bursaries and sponsorships to scientists and scholars throughout Australia in a competitive award process, and funds a range of other initiatives to further MAWA's goals

# The Marchig Animal Welfare Trust

#### http://www.marchigtrust.org

Based in Scotland, the Marchig Animal Welfare Trust is a charity which focuses on all areas of animal protection from cruelty and abuse. Established in 1989 by Madame Jeanne Marchig of Geneva, because of her deep concern for nature and animals, the trust awards grants to a wide variety of projects including "promoting alternative methods to animal experimentation and their practical implementation".

# National Anti-Vivisection Society (NAVS)

#### http://www.navs.org.uk

The NAVS group is comprised of four NGOs working to end the suffering of animals: the National Anti-Vivisection Society; Animal Defenders International; the Lord Dowding Fund for Humane Research; and the Animal+World Show.

# The National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs)

#### http://www.nc3rs.org.uk/

The National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs) is an independent scientific organisation, tasked by the Government with supporting the UK science base through the application of the 3Rs. The NC3Rs is the UK"s largest funder of 3Rs research. NC3Rs is also behind <u>www.crackit.org.uk</u> a programme designed to replace, reduce and refine (the 3Rs) the use of animals in research. It includes a funding competition for research and development to solve 3Rs challenges identified with sponsors from the industrial and academic sectors, and a technology partnering hub to accelerate the sharing, validation and uptake of potential 3Rs methods.

# The Netherlands Knowledge Centre on Alternatives to Animal Use (NKCA)

#### http://www.nkca.nl/

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

# The New England Anti-Vivisection Society (NEAVS)

#### http://www.neavs.org/

US-based animal advocacy organization, whose mission is to end the use of animals in research, testing and science education and replace it with scientifically



superior and humane non-animal alternatives. NEAVS advocates for all animals in laboratories and classrooms through education, public outreach, legislation, policy change, and legal action. The organisation is closely affiliated with the American Fund for Alternatives to Animal Research (AFAAR).

# PETA (People for the Ethical Treatment of Animals)

#### http://www.peta.org

PETA continues its campaigns as one of the world's leading animal rights organisations. A previous Lush prizewinner and nominee, PETA's most recent victories include engagement with government officials in both China and India to end animal testing and promote the use of alternatives, as well as direct funding of researchers in China to provide training in non-animal methods.

### Physicians Committee for Responsible Medicine (PCRM)

http://www.pcrm.org/

The PCRM promotes alternatives to animal research and campaigns for the use of non-animal methods in medical education. They provide a wealth of scientific educational materials, information on courses and career opportunities and internships. The PCRM also campaigns on a broader scope for higher standards of ethical research and the benefits of preventative medicine

# Platforms and Funds for Alternatives to Animal Experimentation, Live Kleveland

http://oslovet.norecopa.no/platform/report/ecopaplatforms.pdf

A report from The Norwegian Reference Centre for Laboratory Animal Science & Alternatives, Norwegian School of Veterinary Science, Oslo, Norway 2005

# Juliana von Went Fund for Research Without Animal Experiments

#### http://www.jvws.org/

The Juliana von Wendt Fund, founded in 1971, is a Finnish charity, which supports humane methods of scientific and medical research. The Fund awards yearly grants to Finnish researchers developing and applying non-animal methodology in a wide range of fields including toxicity testing, cancer research, surgery, antibody production, computer assisted drug modelling, tissue culture techniques, higher education etc. Methods replacing exceptionally harmful use of animals are prioritised, as well as projects which are most relevant for human or animal welfare. From 1996 onwards the Fund has awarded The Scandinavian Research Prize for Alternatives to Animal Experiments together with the funds of Sweden and Denmark.

# **SAFE** (Save Animals from Exploitation)

# www.safe.org.nz

SAFE are a New Zealand based organisation and previous 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.

# SET (Foundation for the Promotion of Alternate and Complementary Methods to Reduce Animal Testing) Germany



### http://www.stiftung-set.de/index.php

**SET** based in Germany, offers the opportunity to gain funding for projects which focus broadly across the 3Rs. SET also have an interest in funding training and education initiatives.

# 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). SEURAT recently hosted its second 'Young Scientists Summer School' in collaboration with ESTIV (European Society of Toxicology In Vitro) to discuss replacement of repeat dose toxicity testing in animals.

# Scientists for Global Responsibility (SGR)

http://www.sgr.org.uk

**SGR** are based in the UK and promote ethical awareness in science and technology. They provide an 'ethical careers' section on their website which includes resources to help scientists and engineers gain a deeper understanding of ethical issues in science, design and technology and help them choose an ethical path in this area. Materials include briefings, presentations, articles and other resources, as well as an 'ethical employers' contact list

# The Swedish Fund for Research Without Animal Experiments

http://www.forskautandjurforsok.se/index.php

The Swedish Fund supports alternatives in basic and applied research in various areas, including the development of computer simulation systems, toxicology, and training of laboratory personnel and courses in alternatives. The fund has awarded over 30 million SEK since 1971 and currently awards projects totalling  $\in$  80 000-160 000 each year

# The 3R Research Foundation (Switzerland)

# http://www.forschung3r.ch/en/information

The 3Rs foundation awards annual prizes for research directly impacting on the 3Rs. They have key areas of interest that they emphasise to grant applicants, one of which is alternative methods to acute and chronic toxicity testing

# Appendix 2: Example companies which use only non-animal, alternative or human based technologies

# Asterand (UK and USA)

#### http://www.asterand.com

Asterand is the leading global provider of high quality, well characterized human tissue and human tissue-based research solutions to drug discovery scientists. Their mission is to provide human-based solutions to accelerate the identification and validation of drug targets and enhance the selection of drug candidates with an increased likelihood of clinical success.



# **Biopta (UK)**

#### http://www.biopta.com

Biopta is the leading company focussed on the use of fresh functional human tissues in drug development. Based in Glasgow, UK, and Maryland, USA, the Biopta Group has been providing contract research services to the pharmaceutical industry since 2002 and has established itself as the world leader in the use of fresh functional human tissues to better predict drug activity prior to clinical trials.

## Simugen

#### http://simugen-global.com/

SimuGen is an international computational biology company focused on predicting human toxicity early on in drug discovery. The company combines traditional, genomic, high content (HCS) in vitro screening and traditional cell endpoints, to produce high throughput screens for use alongside other early ADME (Absorption Distribution Metabolism Excretion) testing. SimuGen offers comprehensive toxicology screening services (HT-X<sup>™</sup>) and high-throughput decision analytics software (HT-Stream<sup>™</sup>) for customers' drug programmes. SimuGen's goal is to meet a major market gap that is not adequately addressed by current toxicogenomics - to accurately predict toxicity in the early stages of drug discovery.