Lush Training Prize 2012

Research Paper

Executive Summary

The Lush Training Prize aims to reward individuals and organisations involved in training researchers in non-animal methods. The training prize recognises that many involved in testing of chemicals are not aware of the range of non-animal methods available or trained in using them. Establishing training programmes around the world makes a huge difference to the field. The prize wishes therefore to reward individuals, teams or organisations who have excelled in this field.

Difficulties in defining 'training'

In conducting research for this report it became quickly apparent that training, in the context of non-animal alternatives, could be interpreted as including many things, from training in new techniques to publishing databases and educating school children. It also became clear that this area is much neglected in comparison with research, with very few organisations working specifically on alternatives training. For the 2012 Lush Prize the criteria for this category have been left fairly loose, so as to more usefully inform the research process, rather than focussing in on any one narrow area at this stage.

Areas included in the research

Much of the training uncovered appears to be quite ad hoc, such as one-off training days, or booklets on alternatives. A summary of a few such smaller initiatives is included. The research looks at organisations/initiatives in the following categories: training organisations and programmes, databases, toolboxes, search guides and other web based resources, short training courses, alternatives teaching centres, industry collaborations, commercial organisations providing training in *in vitro* methods, societies, and funders of animal alternatives. In conducting this research it became apparent that hands-on training overlaps to an extent with web-based information sharing.

Outstanding projects

This paper has applied a 'replacement only' filter to the projects looked at, in line with the replacement focus of the Lush Prize. This means that the alternatives centres, some of which are doing great work on replacement, were not included, as they also promote reduction and refinement. The following three organisations stood out in the loose definition of training we have chosen to use. The rationale for selecting them varies – from the extent of their work in training to their relevance to the specific area of chemical testing – key to all however is their global reach:

- Institute of In Vitro Sciences
- InterNICHE
- The International QSAR Foundation

Conclusion

The research indicates that training in non-animal methods is a much neglected area in

general. Despite this a small number of organisations doing outstanding work in this area were identified.

The issue of animal experiments and testing is often painted as a moral one, with perceived human need pitched against animal welfare/rights. The fact that animals appear to be used in experiments out of a combination of habit, laziness, poor communication, lack of co-ordination, bureaucracy and an unwillingness to change is not something that often features in public debates about animal testing and experimentation; these issues are perhaps not considered as interesting as the deeper philosophical discussions over animal use. Yet it is arguably in this area where more of an immediate difference can come in pushing for change as these are changes that can be implemented today without the need for either ethical arguments being won, laws being changed or scientific breakthroughs being achieved. A much more comprehensive, systematic approach to encouraging the use of existing non-animal methods is required both in toxicology and beyond – from classrooms through universities to the commercial testing laboratories themselves. It would seem that in this area, with quite simply better communication, many animals' lives could be saved.

1. Methodology

In the period under review (2011-12), two major international conferences on alternatives to animal testing have taken place: the 8th World Congress on Alternatives and Animal Use in the Life Sciences (WC8 at Montreal); and the European Society for Alternatives to Animal Testing (EUSAAT 14 at Linz). Abstracts of these conferences were reviewed to find mention of any relevant organisations, projects or programmes. A number of relevant journals were also reviewed for the period, including ATLA[1] and ALTEX[2], as well as a number of relevant websites including AltTox.org[3], and Altweb[4]- described as global clearing houses for information on alternatives to animal testing.

Much of the work in this area takes a "three Rs" (3Rs) approach, first described by Russell and Burch in 1959 in their book 'The principles of humane experimental technique', which are guiding principles for the use of animals in research in many countries:

- **Replacement** refers to the preferred use of non-animal methods over animal methods whenever it is possible to achieve the same scientific aim.
- **Reduction** refers to methods that enable researchers to obtain comparable levels of information from fewer animals, or to obtain more information from the same number of animals.
- **Refinement** refers to methods that alleviate or minimize potential pain, suffering or distress, and enhance animal welfare for the animals still used.

The Lush Prize seeks to reward achievements in **replacement** only, i.e. projects which focus on replacing the use of animals entirely.

Reviewing the literature above yielded a lot of useful information on training, with a loose definition applied, and how it relates to other areas. However very few projects or organisations focusing on hands-on training, specifically in replacement, were found.

It became apparent that hands-on training overlaps to an extent with information sharing, certainly in terms of the aim/importance of training in the context of the Lush Prize – i.e. to share information about existing non-animal methods. So some databases, search guides and other such projects are looked at.

Opinion was canvassed, within the 'alternatives community' on what the training element of the Lush Prize could or should include. This was done by looking at relevant literature, and via telephone and email conversations with a small number of individuals.

1 The official journal of FRAME (Fund for the Replacement of Animals in Medical Research) in the UK.

2 The official journal official journal of CAAT, the Center for Alternatives to Animal Testing at the Johns Hopkins University Baltimore, USA, EUSAAT, the European Society for Alternatives to Animal Testing, t4, the transatlantic think tank of toxicology (Baltimore, Utrecht, Konstanz) and the Doerenkamp chairs in Germany, India, The Netherlands, Switzerland and USA.

3 www.alltox.org

4 http://altweb.jhsph.edu

2. Consultation

The following is a summary of the information gathered through seeking expert advice and reviewing the literature. Although by no means comprehensive, a variety of useful information was yielded.

Thomas Hartung, Bas Blaauboer and Marcel Leist, all of whom are 'Doerenkamp-Zbinden-Chairs' (see page 24) at different 'Centres for Alternatives' discuss the matter in some depth in the article 'Food for Thought … on Education in Alternative Methods in Toxicology.' This focuses mainly within academia, although it does touch on reaching out beyond academic circles. They raise the following questions to begin with:

- Do we need education on alternatives or on a new toxicology?
- Do we need to create new courses and curricula or modify the current ones?
- Whom do we need to target, the next generation (students), current practitioners (post-graduate level), senior management (decision makers), or all of them?
- Which areas of study and work environments should be targeted: biology, chemistry, medicine, veterinary medicine, other life sciences, risk assessors, lawyers, policy makers, regulators, etc.?
- How can we achieve coverage of large numbers of target audiences? How to network and synergise in a situation of diaspora, i.e. where the different offers and competence centres are widely dispersed?
- Is “alternative methods” the right catch phrase or should we label it “new toxicology?”
- Are we teaching alternatives or are we teaching with alternatives?
- Which modern communication tools accelerate and optimise education?[5]

They argue, within academia, the importance of teaching an alternative approach, rather than alternative methods, and that knowledge of specific alternative approaches is probably not that important. Instead, learning how to find alternative methods by queries to pertinent databases is required, so that every researcher considering animal use or its alternatives should know about how to find relevant alternatives. They argue that this, however, is only one step: the researcher must be willing to seriously consider alternatives in the first place. They raise therefore the importance of teaching the limitations of an animal approach and highlight the paucity of publications critiquing animal methods from a scientific perspective. Teaching a method-critical view of alternatives is probably even

5 Food for Thought … on Education in Alternative Methods in Toxicology, Thomas Hartung[1] , Bas Blaauboer[2] and Marcel Leist[3], Doerenkamp-Zbinden-Chairs for [1]evidence-based toxicology, Johns Hopkins University, Baltimore, USA; [2]Alternatives to Animal testing in toxicological Risk Assessment, Utrecht University, the Netherlands; [3]In Vitro toxicology and Biomedicine, University of Konstanz, Germany

more important for the future toxicologist than teaching specific methods themselves. New methods come and go, they say, but the principal limitations of modelling and testing remain. The pace of new technologies coming to the laboratory makes it almost useless to teach any approach, except as an example, whereas the principles of statistically valid experimental design, of documentation, of data analysis and visualisation, are much longer-lived. Training in statistics and experimental design of course can bring about reduction and refinement, but not the replacement which the Lush Prize aims to reward. The content of teaching alternative approaches they say should be three-fold – alternative methods, alternative thinking about quality assurance and the limitations of current approaches. The latter they say will perhaps have the most important impact on animal use, especially in the fields of basic research and agent discovery (which together make up two thirds of all animal use), where classical alternative methods are rare and the central implementation mechanism of validation is often not feasible. Frequently it is overestimation of the quality and predictive value of the animal model that leads to its use. Teaching of an alternative approach is necessary at many diverse places in many different curricula – thus pointing out the need for new forms of teaching. Very few individuals are actively teaching alternative approaches, they say. Many of the players in the field are anchored in industry, research institutes, the regulatory arena, or NGOs, thus they contribute to academic education only via adjunct appointments, if at all.[6]

Nick Jukes, Co-ordinator of InterNICHE, the International Network for Humane Education, agrees that there is insufficient focus on education and training. Research and testing dominate the discussions, he says, and the role of effective education and training is often neglected, despite being crucial to both. He argues that what is really needed is comprehensive training which provides not only practical skills in an alternative science, but also a realistic and unbiased overview of the current situation, including the obstacles and opportunities for realising the vision of full replacement in toxicology. Strategic guidance on how to go forward together is lacking. “The field is very compartmentalised, and there are many vested interests that contribute to an inertia. These include not only practical and economic vested interests, but also the emotional, such as attachment to animal experimentation and limited commitment to the process of replacement. What's needed is real visionary leadership and co-ordination.” Echoing Hartung *et al,* he says that more studies concerning alternatives, including systematic reviews, are needed, in order to lift the scientific and ethical level of the debate. Related to this, more focus and publicity is needed concerning the consumer safety advantages of alternatives in general and in vitro toxicology in particular.[7]

Nick goes on to say that the use of alternatives to harmful animal use at school and university level (animal experiments and dissection of purpose-killed animals) has positive impacts in the fields of education and training, and in those of research and testing. The auditing of courses to better identify teaching objectives and best practice methods of meeting them should also be encouraged, he says. The implementation of suitable

6 Food for Thought … on Education in Alternative Methods in Toxicology, Thomas Hartung, Bas Blaauboer[2] and Marcel Leist[3], Doerenkamp-Zbinden-Chairs for [1]evidence-based toxicology, Johns Hopkins University, Baltimore, USA; [2]Alternatives to Animal testing in toxicological Risk Assessment, Utrecht University, the Netherlands; [3]In Vitro toxicology and Biomedicine, University of Konstanz, Germany

7 Communication with Nick Jukes, InterNICHE via email

humane tools and approaches will then bring the pedagogical and other advantages of alternatives, as evidenced in published studies, to the education and training process. Similarly, he says that acknowledgement of the existence of the 'hidden curriculum' and the implicit messages and lessons that it puts across is important. These can include teaching the 'acceptability' of harmful animal use and giving the impression there are no alternatives; discouraging critical thinking and teaching conformity; and supporting the process of desensitisation. The use of alternatives can obviate this negative hidden curriculum. Nick concludes that there is a need for support and training courses in curricular transformation and in curricular design, as well as in specific alternative methods, for teachers; and a need for support for students who conscientiously object to harmful animal use and who motivate for alternatives. The higher levels of knowledge and skills acquisition, the positive attitudes developed, and a familiarity with alternatives developed at a younger age, are all very important issues for the uptake of alternatives in toxicity testing and for consolidating the route from an alternative education to a humane science. Educating the trainers at professional level is equally important – 3Rs courses and those for future researchers and technicians either still use animals or do not focus enough on replacement. Nick refers to misunderstandings and avoidance by various bodies on the true nature of the 3Rs in research and testing – that non-animal replacement is the ideal.[8] This is something that has become apparent in conducting this research.

Hartung *et al* highlight three areas where education is needed. One is conceptualisation. This relates specifically to the required paradigm shift in thinking for the move into '21st Century Toxicology'. It is frequently forgotten that most research in the field addresses technical problems within already established concepts; therefore, a step back is required to look at the bigger picture. Another is knowledge transfer, which concerns the integration of alternatives fields within academia.[9]

Most directly relevant to the focus of this research, Hartung *et al* also highlight the importance of breaking down barriers, which refers to the considerable barriers which exist at the market end of the pipe-line of method development for alternative safety evaluation, despite the documented success of 3Rs methods and problems posed by animal experiments. Technical/scientific barriers are linked to the validation problem, legal and regulatory issues exist, in addition to conceptual and psychological barriers with the latter closely linked to the reputation of the scientific area of new toxicology (3Rs methods) outside academia. In particular, end-users and regulators need confidence in the validity of the methods. The transition to new methods is often additionally hampered by inertia and a preference to use old, well-acquainted technology. A lack of trust is also part of the problem, due to a lack of information or erroneous information about newer methods. Here, academic institutions and teaching can play an important, two-fold role. Contributing to the dissemination of knowledge outside academia through centres, using their independence from lobby groups, and with good scientific reputations, such groups provide credibility to the validity of alternative approaches, and, by doing so, break down

8Communication with Nick Jukes, InterNICHE via email

9Food for Thought … on Education in Alternative Methods in Toxicology, Thomas Hartung[1] , Bas Blaauboer[2] and Marcel Leist[3], Doerenkamp-Zbinden-Chairs for [1]evidence-based toxicology, Johns Hopkins University, Baltimore, USA; [2]Alternatives to Animal testing in toxicological Risk Assessment, Utrecht University, the Netherlands; [3]In Vitro toxicology and Biomedicine, University of Konstanz, Germany

many conceptual barriers.[10]

Michael Balls, Chairman of the trustees of FRAME (Fund for the Replacement of Animals in Medical Experiments), raised the issue of problems early on, related to the validation stage: that in a validation study, it is the test procedure which has to be put to the test, not the competence of those who perform it. He feels there should therefore be a training stage before the actual validation study testing begins. Later on, when the developers of a validated test made it available for use, its reputation would be damaged, if those who tried to use it lacked the necessary competence and concluded that it didn't work, he says, and therefore he sees this as an area where training should be targeted.[11]

Troy Seidle, Director of Research & Toxicology for the animal welfare NGO Humane Society International (HSI) agrees that training could potentially cover a lot of ground, but for the purposes of the Lush Prize he felt it would be best interpreted as referring to activities aimed at the dissemination of knowledge, information and skills to promote and support the increased use of available and accepted non-animal test methods and testing strategies by end-users in industry, regulators, and academics/students. In his opinion, focusing on 'accepted' approaches distinguishes training from lobbying, and focusing on test methods keeps it specific to toxicology rather than the wider world of animals in research or education. He sees training as less a post-validation activity as a post-regulatory acceptance activity (i.e., the step after validation) – bridging the knowledge and experience gap once the legal hurdles have been surmounted. He feels this should be kept separate from topics such as data sharing or open access/non-proprietary techniques, which he sees as a business/economic issue rather than one that can be solved through an educative approach.[12]

The Institute for *In Vitro* Sciences (IIVS) is a contract laboratory for *in vitro* toxicology, assay optimisation and validation, workshops and training, working very much at the market end of the alternatives development pipeline. In an abstract they presented at WC8, IIVS argued that with the recent advancements in the adoption of a considerable number of alternative methods to animal testing by the OECD, and the global harmonisation of world commerce, the importance of providing education on the adopted alternative methods throughout the world is becoming increasingly necessary. This training should include: the specifics of the *in vitro* test method protocols; the importance of ensuring good laboratory practices; proficiency, reliability and relevance of the method for regulatory purposes; calls for an education preferably based on practical demonstrations and/or hands-on-training. Such training is essential for scientists performing *in vitro* tests, and is also key for regulators to gain the necessary understanding and make critical assessments of the in vitro data. Furthermore, such training could favour standardisation of regulatory assessment and decisions on hazard properties of chemicals across the

10 Food for Thought … on Education in Alternative Methods in Toxicology, Thomas Hartung[1] , Bas Blaauboer[2] and Marcel Leist[3], Doerenkamp-Zbinden-Chairs for [1]evidence-based toxicology, Johns Hopkins University, Baltimore, USA; [2]Alternatives to Animal testing in toxicological Risk Assessment, Utrecht University, the Netherlands; [3]In Vitro toxicology and Biomedicine, University of Konstanz, Germany

11 Communication with Michael Balls, FRAME, via email

12 Communication with Troy Seidle, HSI via email

world.[13]

Nick Jukes raises the importance of keeping scientists and others updated in developments in knowledge and techniques, in the changes and implementation of laws such as REACH, and in information retrieval. Training in search techniques for alternatives, he says, is needed. In applications (protocols) for research and testing on animals, researchers should be required to demonstrate to animal use / ethics committees which websites and databases – and of those, which *specific pages* – they have visited, as part of the proof that they have searched effectively. This is not yet the norm. This supports the view of Hartung *et al*, that conducting the search is one thing, but the researcher must be willing to seriously consider alternatives in the first place, to avoid it merely being considered a box-ticking exercise. Hartung *et al* see animal use committees as a promising target group for training along with institutional ethical review boards, as these are made up of individuals with a key role in influencing the actual use of animals and animal alternatives.[14]

One of the abstracts from WC8 stresses the importance of open-access journals in sharing information on alternatives. The abstract cites PubMed Central, a free digital archive of biomedical and life sciences journal literature directly related to the US National Institutes of Health (NIH) Public Access Policy, and BioMed Central and PLoS (Public Library of Science), both publishers of peer-reviewed scientific and medical research literature freely available as public resources, as good examples.[15] Another abstract stresses the importance of involving human information providers i.e. those trained in information access, in accessing comprehensive information on alternative techniques.[16]

Christiane Hohensee, project leader at In Vitro Jobs – an organisation which aims to make finding research and job opportunities in this area easier – agrees that training and education could include many things. Her observations were that courses could be offered in these fields of education and training: cell culture handling, conservation, quality management etc; e-learning platforms; skills labs with dummies/mannequins, and information about their producers; body donation programs; multimedia computer simulation programmes; workshops; information days; web platforms and open access / data sharing possibilities.[17]

Nick Jukes argues that the existence of new human tissue banks is promising, but availability of this biological material needs to be much more widespread to support effectively *in vitro* labs. Similarly, more animal body donation programs, with associated

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13 International practical training on in vitro methods E. Hill 1 and C. Eskes 2 1Institute for In vitro Sciences, Inc., Gaithersburg, USA; 2Services & Consultation on Alternative Methods, Agno, Switzerland ehill@iivs.org

14 Food for Thought … on Education in Alternative Methods in Toxicology, Thomas Hartung[1] , Bas Blaauboer[2] and Marcel Leist[3], Doerenkamp-Zbinden-Chairs for [1]evidence-based toxicology, Johns Hopkins University, Baltimore, USA; [2]Alternatives to Animal testing in toxicological Risk Assessment, Utrecht University, the Netherlands; [3]In Vitro toxicology and Biomedicine, University of Konstanz, Germany

15 Open-access journals and the increased availability of animal alternatives information M. W. Wood 1, C. Howard 2 and L. A. Hart 1 1University of California, Davis, USA; 2Johns Hopkins Center for Alternatives to Animal Testing, Baltimore, MD, USA mwwood@ucdavis.edu

16 People making information matter D. Jensen U.S. Department of Agriculture, Beltsville, USA danna.jensen@ars.usda.gov

17 Communication with Christiane Hohensee of In Vitro Jobs via email

animal cadaver, organ and tissue banks, are needed, both for use in education and training and for the development and testing of veterinary medicines.[18] He also says that humane students need to see that there is a realistic future for them, citing 'invitrojobs' as a useful example in terms of encouragement and information about job opportunities in the field.[19] Thinking bigger, setting up an in vitro lab may sometimes be a considerable investment and a major change in practice; is there enough support and training in managing the transition to in vitro toxicology, he asks.[20] Theodora Capaldo, President and Executive Director of the *New England Anti-Vivisection Society* says many small laboratories developing non-animal techniques have given up because they can't be guaranteed a market – something that would change if it were made mandatory to use available non-animal methods once they have become validated. This is not the case where she is based, in the US but is increasingly becoming more the case here in Europe (see Lobbying paper).[21] However training in what may appear to be the entirely separate area of business management/strategy and marketing could perhaps also help here.

Hartung *et al* conclude 'We are far from having a consistent concept for education of alternative approaches. The suggested means to create this include: intense learning experiences and exchangeable teaching materials such as lecture materials, text books, and e-learning resources; a textbook that addresses elements of the alternative approach rather than a list of alternative methods; sharing of such teaching materials in a depository; establishing a network of academic teachers; a project to develop curricula and channel them to the respective institutions in the various disciplines; providing support to school teachers. With the increasing popularity of e-learning, i.e. internet and computer-based teaching, they argue this could be a useful approach. Education they say, represents a key opportunity to advance the field of alternatives which has been largely underexploited so far.'[22]

Both within and beyond academia and industry, says Nick Jukes, awareness about replacement and specific alternative methods from the public, from animal welfare / animal rights / anti-vivisection groups, from students and scientists, and from politicians and law-makers, is lacking. Educating *all* parties is crucial he says. So education *about alternatives,* as well as training *in them,* is needed. As an illustration, he points out that if environmentalists had argued clearly for non-animal techniques for testing chemicals when REACH was being discussed, then more progress could have been made. They too need education and training, he says.[23] Hartung *et al* echo this, saying that it is quite remarkable that there is currently – despite considerable similarity in anti-establishment approach – a substantial divide between environmental and animal welfare activists, with many environmental groups in favour of animal testing to generate data on hazards and risks of environmental chemicals. More recent discussions of current approaches, with a focus on

18 Communication with Nick Jukes, InterNICHE via email

19 Communication with Nick Jukes, InterNICHE via email

20 Communication with Nick Jukes, InterNICHE via email

21 Communication with Theodora Capaldo, NEAVS

22 Food for Thought … on Education in Alternative Methods in Toxicology, Thomas Hartung[1] , Bas Blaauboer[2] and Marcel Leist[3], Doerenkamp-Zbinden-Chairs for [1]evidence-based toxicology, Johns Hopkins University, Baltimore, USA; [2]Alternatives to Animal testing in toxicological Risk Assessment, Utrecht University, the Netherlands; [3]In Vitro toxicology and Biomedicine, University of Konstanz, Germany

23 Communication with Nick Jukes, InterNICHE via email

quality of data and throughput capabilities are however, they say, bringing on board more stakeholders with a longer perspective.[24]

24 Communication with Nick Jukes, InterNICHE via email

3. Conclusions and recommendations

The research, both from consultation with experts and trawling through the wealth of information that exists on alternatives (see data section below), indicates that training in non-animal methods is a much neglected area in general. Despite this, a small number of organisations doing outstanding work in this area were identified.

Outstanding projects
This paper has applied a 'replacement only' filter to the projects looked at, in line with the replacement focus of the Lush Prize. This means that the alternatives centres, some of which are doing great work on replacement, were not included, as they also promote reduction and refinement. The following three organisations stood out in the loose definition of training we have chosen to use. The rationale for selecting them varies – from the extent of their work in training to their relevance to the specific area of chemical testing – key to all, however, is their global reach:

- Institute of In Vitro Sciences
- InterNICHE
- The International QSAR Foundation

Conclusion
Even within the relatively small world of alternatives there appears to be a lack of joined up thinking and communication, certainly in practical terms, with seemingly endless duplication of on-line resources as just one very concrete example. The actual work of conducting practical hands-on training to implement non-animal methods appears to be left at present down to the hard work of motivated non-profit organisations. All three of the projects considered outstanding in this report are non-governmental, non-profit organisations.

The issue of animal experiments and testing is often painted as a moral one, with perceived human need pitched against animal welfare/rights. The fact that animals appear to be used in experiments out of a combination of habit, laziness, poor communication, lack of co-ordination, bureaucracy and an unwillingness to change is not something that often features in public debates about animal testing and experimentation; these issues are perhaps not considered as interesting as the deeper philosophical discussions over animal use. Yet it is arguably in this area where more of an immediate difference can come in pushing for change as these are changes that can be implemented today without the need for either ethical arguments being won, laws being changed or scientific breakthroughs being achieved. A much more comprehensive, systematic approach to encouraging the use of existing non-animal methods is required both in toxicology and beyond – from classrooms, through universities to the commercial testing laboratories themselves. It would seem that in this area, with quite simply better communication, many animals' lives could be saved.

Data section – organisations and initiatives identified in this area

4. Organisations involved with small-scale or one-off initiatives

In order to give an accurate picture of training in non-animal techniques and related activities a summary is given of just some of the smaller initiatives going on in this area, and some which have happened in the past. Many are exciting and innovative, or simply good work, but aren't big enough, or recent enough to be considered for the Lush Prize. This gives a broader indication of what work is going on in this area – this summary is by no means comprehensive:

- The UK's Royal Society for the Prevention of Cruelty to Animals (RSPCA) has produced a seemingly useful document – The 'R' of Replacement: The potential for implementing alternatives to the use of animals in research and testing.[25]

- The UK's National Centre for the 3Rs (NC3Rs) has produced a leaflet 'Acute toxicity testing of chemicals: opportunities to avoid redundant testing and use alternative approaches'.[26]

- The UK Health and Safety Executive (HSE) and UK REACH Competent Authority have produced a short guide 'REACH – Minimisation of Animal Testing (2010)' a leaflet which provides a brief summary of the opportunities available to REACH registrants to minimise animal testing.[27]

- Earlier this year People for the Ethical Treatment of Animals (PETA) Foundation produced “QSARs and REACH: A Guide to Sources of Information and Advice” a free resource for potential REACH registrants, identifying sources of information and expertise on the use of Quantitative Structure Activity Relationships (QSARs).[28]

- Last year the first textbook on alternatives in Chinese was published, albeit with a 3Rs rather than solely replacement focus.[29]

- The British Union for the Abolition of Vivisection (BUAV) has been involved in advising Government and researchers on alternatives to animal experiments in India.[30]

- From 2004 – 2007 the European Commission sponsored a project 'In Vitro Train'[31] which organised courses on the theoretical background and practical training of in

25 http://www.google.co.uk/url?sa=t&rct=j&q=rspca%20the%20r%20of%20replacement&source=web&cd=1&ved=0CCMQFjAA&url=http%3A%2F%2Fwww.rspca.org.uk%2FImageLocator%2FLocateAsset%3Fasset%3Ddocument%26assetId%3D1232728172320%26mode%3Dprd&ei=VRtRULOsHcao0QXavoGgCQ&usg=AFQjCNFANydL-vK-chOXoYKnJKSI8Ph9vg&cad=rja

26 www.nc3rs.org.uk/trackdoc.asp?id=1155&pid=53

27 http://www.hse.gov.uk/reach/resources/18animaltesting.pdf

28 http://www.altex.ch/en/index.html?id=17&ncat=1&nid=227

29 http://www.altex.ch/en/index.html?id=17&ncat=1&nid=158

30 http://www.buav.org/international-work

31 http://userpage.fu-berlin.de/~invitrot/

vitro methods for toxicity testing, providing attendees with sufficient experience to go on and apply the techniques to their own needs, disseminating the use of in vitro alternative methods and developing and/or validating new in vitro alternatives in the field of skin and eye toxicity. However the initiative does not seem to have been repeated.

- A DVD on cell culture methodologies for middle schools, high schools, and universities prepared by the Italian Platform for Alternatives, though back in 2006.[32]

- Many organisations publish guides on how to search for information, e.g. FRAME in the UK[33]

32 Food for Thought … on Education in Alternative Methods in Toxicology, Thomas Hartung[1] , Bas Blaauboer[2] and Marcel Leist[3], Doerenkamp-Zbinden-Chairs for [1]evidence-based toxicology, Johns Hopkins University, Baltimore, USA; [2]Alternatives to Animal testing in toxicological Risk Assessment, Utrecht University, the Netherlands; [3]In Vitro toxicology and Biomedicine, University of Konstanz, Germany

33 www.frame.org.uk/page.php?pg_id=139

5. Training organisations

5.1 The Institute for In Vitro Sciences

The Institute for In Vitro Sciences (IIVS) stands out as the main organisation involved in training of *in vitro* methods to those in industry. Founded in 1997, IIVS describes itself as a leading provider of *in vitro* testing in support of toxicological safety evaluations. Scientific programs coupled with educational and outreach initiatives have established IIVS as a global leader in the advancement of alternatives to animal testing. IIVS is a non-profit organisation operating as a centre of excellence for *in vitro* (non-animal) methods used for product safety testing purposes. IIVS's knowledge of the science and application of alternatives to animal experiments is recognised by regulatory agencies worldwide, it says. It provides education and training for chemical and personal care product companies internationally, enabling them to successfully apply non-animal methods within their product testing programs. IIVS also performs testing services in its own quality controlled laboratories providing access to its expert scientific team on a contract basis. The institute has ongoing programmes in the emerging markets of Brazil, China and Russia.[34]

IIVS also conducts training with and on behalf of NGOs such as People for the Ethical Treatment of Animals (PETA) and Humane Society International (HSI). In China last year the organisation worked with PETA in parallel with the organisation's lobbying activities in the country (see lobbying paper for further details). In Brazil in 2011 together with HSI and SeCAM (Services & Consultation on Alternative Methods), IIVS ran a training course "to better familiarise government authorities and industry scientists with internationally recognised non-animal tests. The event was very successful as it gathered broad participation of Brazilian regulators, industry and university scientists. The cosmetics sector was particularly well-represented, and expressed its willingness to further explore regulatory aspects of cosmetics testing in Brazil."[35]

Information on another planned initiative, again in Brazil, was highlighted in the abstracts of the World Congress: A practical workshop is currently being organised in Brazil by IIVS, SeCAM, University of Goiás and a local organising committee comprised of representatives from government, regulatory agencies, academia, industry and scientific associations. Such an inclusive composition allows for transparent and open discussions on the aims and goals of the workshop. The practical training will be provided by IIVS on assays that are currently accepted at the OECD level, and will focus on the technical steps of the adopted in vitro protocols, good laboratory practices, and finally the interpretation of results for regulatory purposes.[36]

IIVS is clearly pro-active at an international level in promoting the adoption of non-animal *in vitro* methods, and providing the practical hands-on training required to realise this.

5.2 InterNICHE

34 www.iivs.org

35 www.hsi.org/news/news/2011/12/brazil_cosmetics_121511.html

36 International practical training on in vitro methods E. Hill 1 and C. Eskes 2 1Institute for In vitro Sciences, Inc., Gaithersburg, USA; 2Services & Consultation on Alternative Methods, Agno, Switzerland ehill@iivs.org

InterNICHE is the International Network for Humane Education. According to its website InterNICHE aims for high quality, fully humane education and training in medicine, veterinary medicine and biological science. It supports progressive science teaching and the replacement of animal experiments by working with teachers to introduce alternatives and with students to support freedom of conscience.

InterNICHE is an open network comprising students, teachers and animal campaigners based on free association. The organisation works in partnership with any individual, group or department that shares the common goals of replacement of harmful animal use and investment in high quality ethical science. InterNICHE is a non-profit organisation which relies on donations and grants for its activity.

InterNICHE produced the video *Alternatives in Education* (1999), where teachers from a variety of disciplines demonstrate the alternatives that they use in their courses and which is available in nearly 20 languages. It has also published two editions of '*from Guinea Pig to Computer Mouse*' (1997, 2003), a book which fully describes over 500 products designed for progressive life science education and addresses teaching objectives in detail and assesses different pedagogical approaches. The organisation has also written many academic papers on the subject.

InterNICHE also offers a number of Alternatives Loan Systems across the world – libraries of products available for free loan, as well as literature, support and advice for teachers and students. The network also organises regular conferences, seminars and training with international speakers and trials of alternative methods and networking opportunities, and provides small grant funding for the development and purchase of alternatives.[37]

The new InterNICHE website, with an Alternatives Database and Studies Database, launched earlier this year, can in itself can be seen as a valuable training tool – a collaborative, content-rich, multi-language resource, developed to meet the needs of teachers and trainers, students, ethics committees, alternatives producers, and campaigners internationally. The site comprises news, information, database access, and downloads provided by InterNICHE. Functionality has been introduced that enables user-friendly upload of multi-language content from all parties, and which facilitates the process of translation.[38]

The Studies Database provides references, abstracts and other details for over 750 published studies and books on humane education, alternatives and related themes. It is searchable by discipline, author and keyword. Each study has been researched and included for its relevance to the pedagogical, ethical and economic issues presented by the use of animals, alternatives and technology in education and training. The Studies Database has been published to facilitate free access to information that can support curricular transformation and replacement of animal experiments. A comments facility has been established to encourage critique and debate. The database can help identify specific alternative tools and approaches to enhance practical classes, and in parallel with the InterNICHE Alternatives Database can be linked into alternative search strategies for universities and training centres. Links from individual studies to the PubMed database allow users to identify related citations. Studies about cutting edge technology and

37 www.interniche.org

38 www.interniche.org

techniques in medical training, often developed to ensure effective training and to help guarantee patient safety, are included for impact of the latter in replacing animal experiments and consolidating the implementation of non-animal training techniques.[39] [40]

In the period 2011-2012 InterNICHE has been involved in humane education and training outreach across the globe including in South Africa, Mexico, Iran, Portugal, Russia and China.

Clearly InterNICHE is working very much at the educational end of training in alternative methods, rather than with those in industry. Given the cultural shift that would seem to be required across the life sciences to facilitate a move away from animal models and testing, and the extent and international reach of the organisation's work, InterNICHE is considered to make an important contribution in this area.

6. Databases/Toolboxes/Search Guides/Other Web Based Resources

6.1 The International QSAR Foundation

The International QSAR Foundation (IQF) *says its vision* is to significantly reduce the use of animal tests without loss of public safety. Its mission it says is to develop computerised tools as alternatives to animal testing in order to decrease our reliance on animal tests in regulation, research and education. To achieve this the charitable organisation serves as a focal point for non-testing alternative methods to:

- build a scientific consensus on the best approaches in predicting the outcomes of animal tests
- make quality data from past animal tests more accessible to scientists around the world
- create new methods of predicting chemical hazards that currently cannot be adequately predicted and demonstrate the reliability of QSAR-based methods in hazard identification (QSAR = Quantitative structure–activity relationship).

The IQF has an online training program in QSAR methods and the QSAR Application Toolbox which is being developed by OECD member countries. The training program is designed for scientists charged with developing safety assessments for chemical manufacturers and distributors as well as for those charged with evaluating submitted assessments for new chemicals or those already used in commerce.

OECD QSAR Toolbox

The IQF website states that the QSAR Toolbox was developed under the aegis of OECD to facilitate the use of the 'category approach' and QSAR methods to fill data gaps in classification and labelling. Use of the Toolbox saves resources, reduces the need for animal testing, and greatly accelerates the hazard assessment process. The Toolbox provides the ability to:

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39 www.altex.ch/en/index.html?id=17&ncat=1&nid=212

40 www.interniche.org/studies

- make estimates of the relevant endpoints for single chemicals, linked to the chemical structure or 'CAS number' (unique numerical identifiers assigned by the Chemical Abstracts Service to every chemical described in the open scientific literature);
- obtain summary information on the validation processes and results of the model so that the user can decide for which regulatory purpose the estimate can be used;
- obtain a list of analogues for a chemical, together with their experimental, or estimated environmental, toxic or health effects;
- obtain estimates for metabolite activation/detoxification information for the chemical and interface with IUCLID 5 (International Uniform Chemical Information Database, the categorisation schema used during substance registration under the REACH regulation) with an ability for automated submission of estimated values for registration purposes.

The organisation appears to hold approximately annual QSAR Toolbox Training Workshops for OECD Stakeholders with two held in 2011-2012.[41]

More detailed information was found in an abstract from WC8 which says the OECD QSAR Toolbox it is a software application intended to be used by governments, industry and other stakeholders to fill gaps in (eco)toxicity data needed for assessing the hazards of chemicals. The two main pillars of the system are (i) the knowledge-base for grouping chemicals into toxicologically meaningful categories and (ii) databases with measured PhysChem, fate, and toxicity data. The grouping engines allow selection of analogues accounting for underlying interaction mechanisms and metabolism. Read-across and trend analysis are used to predict the endpoint values for a target chemical. The data gap filling methods also include a library of QSAR models to estimate missing experimental values. Each estimated value can be individually justified based on category hypothesis, quality of measured data and computation method used for categorisation and data prediction. As the rationales for analogues selection are often based on common mechanisms of action, good regulatory acceptance is expected for predictions provided by the Toolbox. Since October 2010 the OECD QSAR Toolbox version 2.0 is available for free and can be downloaded from the OECD website. Version 2 is available both as a distributed version and as a stand-alone version.[42]

Effectopedia

The International QSAR Foundation's website also contained an undated announcement from it and The Institute of Biophysics and Biomedical Engineering at the Bulgarian Academy of Sciences of the launch of the alpha version of Effectopedia, an online encyclopaedia and graphical editor for adverse outcome pathways (AOPs). This open source and free software is designed to fill the last remaining gap in the use of QSAR to estimate adverse effects of chemicals without additional animal testing.[43]

41 www.qsari.org

42 The OECD QSAR toolbox, O. Mekenyan 1, S. Dimitrov 1, T. Pavlov 1, T. Schultz 2, R. Diderich 2, D. Hirmann 3 and T. Netzeva 3 1Laboratory of Mathematical Chemistry, Bourgas, Bulgaria; 2Organization for Economic Co-Operations and Development, Paris, France; 3European Chemical Agency, Helsinki, Finland, omekenya@btu.bg

43 The OECD QSAR toolbox, O. Mekenyan 1, S. Dimitrov 1, T. Pavlov 1, T. Schultz 2, R. Diderich 2, D. Hirmann 3 and T. Netzeva 3

These freely available web-based systems, which can by nature be accessed from anywhere in the world are obviously much welcomed initiatives.

6.2 ECVAM/Joint Resource Centre

ECVAM, the European Centre for Alternative Methods is housed in The European Commission's Joint Research Centre (JRC) a department of the European Commission providing independent scientific and technological support for EU policy-making. ECVAM was established in 1991 pursuant to a requirement in Directive 86/609/EEC that the EC and its member states actively support the development, validation, and acceptance of methods to replace, reduce, or refine the use of animals in laboratories. The specific duties of ECVAM are "to: Coordinate the validation of alternative test methods at the EU level; act as a focal point for the exchange of information on the development of alternative test methods; set up, maintain and manage a database on alternative procedures; promote dialogue between legislators, industries, biomedical scientists, consumer organisations, and animal welfare groups, with a view to the development, validation, and international recognition of alternative test methods." To this end, ECVAM has organized more than 60 scientific workshops and task forces.[44]

The ECVAM Search Guide

The “ECVAM Search Guide”, produced by The European Centre for the Validation of Alternative Methods (ECVAM) is aimed at untrained database users and will be most relevant where comprehensive searches are required as part of authorisation processes for animal experiments and where regulatory requirements mandate the application of the 3Rs. A major challenge to locate relevant high quality information about a proposed field of scientific investigation is the exponential increase of scientific publications in the recent past. Over the last years the electronic resources, originally developed to offer a potential solution to this problem, have shown a similar proliferation. The question arises: how best to search for information specifically on the 3Rs in the World Wide Web that is heterogenic, constantly changing and growing? The ECVAM Search Guide provides a systematic step-by-step search procedure and user guidance to facilitate the location of the desired information on 3Rs alternatives in addition to an inventory of relevant resources providing an answer to the question: What can I find where? The project has been initiated and sponsored by ECVAM and represents the outcome of a close collaboration with the National German Centre for Documentation and Evaluation of Alternatives to Animal Experiments (ZEBET – see below) and an international project advisory team composed of scientists and representatives of ethical and regulatory authorities in support.[45] The ECVAM Search Guide “Good search practice on animal alternatives” by Annett J. Roi and Barbara Grune is available as a free pdf in the online EU

1Laboratory of Mathematical Chemistry, Bourgas, Bulgaria; 2Organization for Economic Co-Operations and Development, Paris, France; 3European Chemical Agency, Helsinki, Finland, omekenya@btu.bg

44www.alttox.org

45The ECVAM search guide – Good search practice on animal alternatives A. J. Roi 1, B. Grune 2, D. Butzke 2, A. Luch 2, G. Pellegrini 1 and J. Kreysa 11European Commission, Joint Research Centre, Ispra, Italy; 2ZEBET – Federal Institute for Risk Assessment, Berlin, German annett.roi@jrc.ec.europa.eu

Book Shop[46]

It seems unfortunate that the key benefit cited is help with authorisation of animal experiments – rather than a desire to help users find genuine replacement/non-animal alternatives!

ECVAM's DataBase service on Alternative Methods

The DB-ALM, ECVAM's DataBase service for ALternative Methods, (http://ecvam-dbalm.jrc.ec.europa.eu) has been publicly available since 2006, providing ready-to-use information as peer-reviewed data sheets. The database includes alternative methods at all stages of development and validation. For the time being its focus is on, but not restricted to, toxicity assessment methods, and can be widened to mode of action and other experimental approaches. As of 2011 152 method-summary descriptions and 130 INVITTOX (IN VItro Techniques in TOXicology) protocols were included providing all the information needed to use the tests. The aim of INVITTOX or DB-ALM Protocols is to enhance the acceptance and adoption of alternative techniques to animal experimentation by disseminating adequately documented methodological information at all the stages of development, validation and regulatory acceptance. The information provided should be detailed enough to allow the method to be transferred to another laboratory without the need of additional support. In addition DB-ALM provides 82 evaluations and details on formal validation studies, 9,163 test results, 5,321 bibliographic references and contacts on over 200 persons/institutions active in the field of alternatives. As of 2011 the service had over 2,200 registered users from 75 countries coming from academia, industry and regulatory authorities. Making information on alternatives easily accessible is key during authorisation processes for animal experiments. For this reason ECVAM has committed to continuing to enhance its DB-ALM, both with regard to content and user interface. In addition, ECVAM's Search Guide project will provide search procedures and user guidance to facilitate the location of information on any 3Rs alternative together with an inventory of relevant resources.[47]

A good potential replacement initiative, although with no particular 2011-2012 focus.

6.3 NORINA (A Norwegian Inventory of Alternatives)

NORINA is an English-language database containing information on over 3,900 audiovisual aids that may be used as alternatives or supplements to the use of animals in teaching and training, including dissection alternatives, at all levels from Junior School to University. The information in the database has been collected from 1991 onwards.

NORINA was created and developed by Senior Consultant Karina Smith at the Laboratory

46 http://www.altex.ch/en/index.html?id=17&ncat=1&nid=232, http://bookshop.europa.eu/en/the-ecvam-search-guide-pbLBNA24391/?CatalogCategoryID=Gj0KABst5F4AAAEjsZAY4e5L

47 Promoting the use and development of alternative methods for regulatory purposes and in research – ECVAM's DataBase service on ALternative Methods (DB-ALM) A. J. Roi, L. Farina, D. Kopustinskiene, M. Koszturova, G. Pellegrini and J. Kreysa European Commission, Joint Research Centre (JRC), Institute for Health and Consumer Protection (IHCP), European Centre for the Validation of Alternative Methods (ECVAM), Ispra, Italy Annett.J.Roi@jrc.ec.europa.eu

Animal Unit at the Norwegian School of Veterinary Science. NORINA was taken over by Norecopa in 2011. The project is now financed by Nordisk Samfunn mot Smertevoldende Dyreforsøk.[48]

6.4 AltTox.org

AltTox.org is an interactive, online resource for professionals interested in advancing toxicology to better protecting human health or to reduce reliance on animal use. AltTox is intended to supplement more conventional means of sharing information, such as books, journals, and static websites. Its scope goes beyond that of websites that cover the activities of individual institutions or organisations. At the same time, it maintains a sharp focus on *in vitro* and *in silico* methods and relevant integrated testing strategies, and does not dilute its coverage by addressing other toxicological methods, fields of bio-medical science, or areas of alternative methods. AltTox users include scientists, regulators, advocates, politicians, and others in industry, government, academia, and non-governmental organisations worldwide. The site provides relevant, concise, and up-to-date content, written in accessible language, as well as an interactive community platform (AltTox Forum), an extensive set of essays on “The Way Forward,” a calendar of upcoming meetings, and listings of a variety of helpful resources. As of August 2011, the website averaged over 8,000 visitors per month in the preceding year (an increase of 25% from the previous year) and nearly 17,000 page views per month. The website has a global reach, with 40% of visits from North America, 32% from Europe, and 22% from Asia. AltTox, as of August 2011, had approximately 60 “Way Forward” essays, over 1,200 subscribers to its monthly newsletter (AltTox Digest), and over 300 registered members of the AltTox Forum. Interested parties are encouraged to visit and contribute to AltTox regularly.[49]

6.5 AnimAlt ZEBET – database for alternative methods to animal experiments

The German Federal Institute for Risk Assessment (BfR) was set up in November 2002 to strengthen consumer health protection. It is the scientific agency of the Federal Republic of Germany which is responsible for preparing expert reports and opinions on the safety of substances and products. In this context, the Institute plays an important role in improving consumer protection and food safety. "Identify risks – Protect health" is the guiding principle for the work of the institute. BfR reports to the Federal Ministry of Food, Agriculture and Consumer Protection (BMELV). It enjoys independence in respect of its scientific assessments and research.

The BfR incorporates ZEBET the “Centre for the Documentation and Evaluation of Alternatives to Animal Experiments”. One of the tasks of ZEBET is to provide scientists from industry, universities and public authorities with information on alternative methods in a database developed for that specific purpose. Since February 2000 the ZEBET database on alternative methods to animal experiments has been accessible without license fees on

48 http://oslovet.norecopa.no/fag.aspx?fag=57&mnu=databases_1

49 AltTox.org: Communication platform for 21st Century ToxicologyM. Stephens 1, H. Kojima 2, G. Patlewicz-Tier 3, H. Spielmann 4 and L. Talley 1 1The Humane Society of the United States, Washington, USA; 2Japanese Center for the Validation of Alternative Methods, Tokyo, Japan; 3DuPont Haskell Global Centers for Health and Environmental Sciences, Newark, USA; 4Free University Berlin, Berlin, Germany mstephens@humanesociety.org

the Internet in German and English through the German Institute for Medical Documentation and Information (DIMDI). The ZEBET database offers validated information on alternative methods. Methods must fulfil at least one of the 3Rs.

The state of development and the scientific or official acceptance of alternative methods is also assessed and documented, with methods ascribed their stage in progress towards regulatory acceptance - "development", "validation", "scientific acceptance" and "regulatory acceptance". The documents in the ZEBET database are classified in data fields, e.g. designation of the method, keywords, evaluation, summary and references.[50]

6.6 Go3R search engine

Go3R is a semantic search engine, developed by the Technical University Dresden and ZEBET that 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. Go3R makes use of expert knowledge on Three Rs methods and regulatory toxicology, laid down in a network of concepts, terms and synonyms, to ‘recognise’ the contents of documents. The web-based search engine Go3R was created over the last three years to allow finding relevant hazard information and data as well as currently updating information on available test methods that meet the requirement to replace, reduce and refine animal testing. Go3R provides an endpoint-centred literature search to all scientists and regulatory authorities seeking toxicological information. Search results are presented automatically linked to an "intelligent table of contents" which enables the user to sort the literature listed in PubMed or the Toxicology Data Network (TOXNET) in a fast and comprehensive manner. Retrieved documents are automatically organised in categories relating to the IUCLID5 chapters. To enable Go3R to sort documents by the toxicological endpoint being investigated, complex endpoint-specific search queries have been compiled and integrated into the search engine. Dependent upon the endpoint, up to 100% of relevant documents containing either in vitro or in vivo hazard information were correctly sorted into the respective IUCLID5 category. Since Go3R can be customised to search in different databases, the IUCLID5 categorisation is also applicable to the screening and sorting of unpublished in-house data, and it can also be used to group substances. The ‘3Rs specific searches’ section of the table of contents recognises 3Rs-relevant documents and sorts these by 3Rs-specific information. Since important information on 3Rs alternatives is published not only in scientific journals, but also on dedicated internet sites, Go3R further allows searching the entire world-wide-web employing a Google-based search tool with prior ranking of information from 3Rs relevant websites. This option supports the retrieval of information on the status of validation and regulatory acceptance of specific test methods or their Standard Operating Procedure.[51]

50 http://www.bfr.bund.de/en

51 Using the Go3R Search Engine to Collect Toxicological Data and Three Rs-relevant Information for REACH Registration Dossiers U.G. Sauer,1 T. Wächter,2 M.R. Alvers,3 B. Grune,4 L. Hareng,5 B. Huhse,4 R. Landsiedel,5 A. Langsch,5 B. Wareing5 and M. Schroeder6 1Scientific Consultancy — Animal Welfare, Neubiberg, Germany; 2TU Dresden & Transinsight GmbH, Dresden, Germany; 3Transinsight GmbH, Dresden, Germany; 4Federal Institute for Risk Assessment, Berlin, Germany; 5BASF SE, Ludwigshafen, Germany; 6TU Dresden, Dresden, Germany

6.7 Toxicology and Environmental Health Information

The Toxicology and Environmental Health Information Program (TEHIP) maintains a comprehensive web site with access to resources produced by TEHIP and other government agencies and organisations. Its flagship resource is TOXNET, an integrated database system of hazardous chemicals, toxic releases and environmental health. TOXNET's use is supported by the TOXNET and Beyond Training Class Schedule and Workbook. The workbook corresponds to the one-day class *TOXNET and Beyond: Using the National Library of Medicine's Environmental Health and Toxicology Portal* offered by the National Library of Medicine Training Center (NTC).[52]

6.8 UC Davis Center for Animal Alternatives Information

The UC Davis Center for Animal Alternatives Information gathers and disseminates information concerning animal alternatives. The Centre places special emphasis on disseminating information concerning models, computer programs, and other animal alternatives in education through every level of public and private education. It also seeks to provide investigators who use animals with information on the most current methods for improving all aspects of animal care during their work. The centre acts as coordinating office for the UCD campus on improved and alternative methods for the use of animals. It is currently developing resources to:

- enable access to the literature of alternatives to animals
- present at conferences and workshops on topics relevant to the centre and to alternatives
- disseminate information to UC campus and California academic libraries and offices for news, science, administration, and animal care
- provides guidance in efficient use of existing information resources, in both print and electronic formats.

Clearly this institution has a very strong 3Rs focus.[53]

6.9 Altweb Guide to Searching for Alternatives

Altweb, published by CAAT/The Johns Hopkins School of Public Health (see below) is described as the global clearing house for information on alternatives to animal testing. It publishes its own search guide on its website, which it describes as a step-by-step approach to an alternatives search including databases, policies and regulations and sample searches.[54]

52 www.nlm.nih.gov/pubs/factsheets/tehipfs.html, http://toxnet.nlm.nih.gov/

53 http://lib.ucdavis.edu/dept/animalalternatives

54 http://altweb.jhsph.edu/resources/searchalt/index.html

6.10 The Humane Society Veterinary Medical Association Alternatives in Education Database

The HSVMA's Alternatives in Education Database contains thousands of entries of alternatives to the harming or killing of animals for many levels of education. To locate a particular alternative, the user simply needs to type in a key word or phrase and hit "search." The advanced search option allows the user to search for an alternative by species, medium, discipline, educational level or any combination of these categories. Once an alternative is accessed the user will find a description of it, as well as a source for the product (i.e. manufacturer, supplier, distributor.) To purchase or obtain a particular alternative, the user simply has to click on the source of the product, and is taken directly to the link, if available, for the source.[55]

6.11 European Resource Centre for Alternatives

The European Resource Centre for Alternatives (euRCA) was unfortunately closed due to lack of funding.[56]

7. Short Training Courses

7.1 The Hamner Institutes for Health Sciences

The Hamner Institutes for Health Sciences (The Hamner), www.thehamner.org, is an independent, non-profit organisation that offers an open, collaborative and cross-disciplinary approach to translational biomedical research. Based in North Carolina, The Hamner strives to act as a catalyst with global academic institutions, industries, and government to support innovative research and rapid technology development. Over the past 36 years, Hamner scientists have been recognised world-wide for their research contributions and training programs in environmental health sciences and chemical risk assessment. The Hamner has since broadened its mission to include translational research in bio-pharmaceutical safety, oncology, and nano-safety.

Advances from Hamner research have contributed significantly to our understanding of human health concerns that include exposure to environmental chemicals, adverse events from prescription drugs, cancer prevention, and lung disease. Building upon this international reputation for excellence, The Hamner is poised for continued growth and exploration of new opportunities to protect public health and prevent human disease.

The institute appears to have some involvement with animal testing, however it does offer education and training in replacement techniques. This year's courses include the five-day course 'Physiologically Based Pharmacokinetic (PBPK) Modelling and its Applications – Learn to apply an effective computational tool to support in vitro to in vivo extrapolation, human health risk/safety assessment, and drug development', in the USA[57] and two three-four day Computational Systems Biology and Dose Response Modelling Workshops in Italy and India.[58]

55 http://alted.hsvma.org/

56 www.eurca.org

57 http://www.thehamner.org/about-the-hamner/education-training/pbpk-modeling/

58 http://www.thehamner.org/about-the-hamner/education-training/dose-response-modeling/

7.2 Alternative Methods for Animal Use in Toxicology course at Milan veterinary faculty

The veterinary faculty of Milan established a mandatory course entitled Alternative Methods for Animal Use in Toxicology as part of the curriculum of the two-year Masters Program in Veterinary Biotechnology Sciences, starting in the 2010-2011 academic year, it is a 6-credit course totalling 48 hours – 24 theoretical and 24 practical.

7.3 In Vitro Models (Skin) Sensitisation

Summer course July 3rd to 6th 2012, the University of Applied Sciences Utrecht.

7.4 Practical Training Course on Integrated Fluidic Models for In Vitro Testing

17-18 September 2012, organised by Istituto Superiore Di Sanita, Environmental and Primary Prevention Department and the Interdepartmental Research Centre "E. Piaggio" University of Pisa.

7.5 International Society for Stem Cell Research (ISSCR) Stem Cell training courses

Nine more of these short courses were scheduled to take place in various cities in Europe, the US and Puerto Rico at the time of writing this report (mid-September 2012). The Society also runs various regularly occurring courses and seminar/meeting series

8. Funders of alternatives

8.1 Doctor Hadwen Trust

The Dr Hadwen Trust for Humane Research (DHT) is one of the UK's leading medical research charities that funds and promotes the development of techniques and procedures to replace the use of animals in biomedical research and testing. In the main it awards grants to scientists for their projects in a variety of research settings, however this year the Trust launched a new Summer Studentship Scheme to help UK undergraduates gain practical lab experience while investigating alternatives to animal-based research. The DHT says the scheme enables students to extend their studies over the summer period by working in a real research environment. Each award is worth £180 per week, up to a maximum of 8 weeks, with a separate budget of up to £500 available for consumables. The research undertaken must be directed towards replacing the use of living animals in current procedures within the applicant's laboratory or in the wider field. The Trust will not support (in this scheme or any other) research that requires or involves the use of living animals in any way, even if the ultimate aim may be to replace their use. The scheme does focus specifically on medical research or testing.[59]

8.2 Doerenkamp-Zbinden Foundation

Founded in 1982 on the initiative of its namesakes, Hildegard Doerenkamp and the late Prof. Gerhard Zbinden, the Doerenkamp-Zbinden Foundation was created to promote and reward "exceptional achievements in animal protection in biomedical research." From its

59 www.drhadwentrust.org

inception through the mid-1990s, the foundation focused primarily on reducing the suffering of animals used in experiments, awarding roughly a dozen refinement-oriented grants of up to $50,000 per year for up to two years. The foundation has financed a number of endowed professorships at various universities.

More recently, the foundation has been reorganised to focus exclusively on replacement and reduction initiatives and has renamed itself the Doerenkamp-Zbinden Foundation for Animal-Free Research. Under this new mandate, a Foundation Professorship for In Vitro Methods for the Replacement of Animal Experiments has been established at the University of Konstanz in Germany, complementing the Doerenkamp-Zbinden Endowed Chair for Evidence-based Toxicology at John Hopkins University. The foundation also awards an annual prize for outstanding achievement, above and beyond its ongoing grants program.[60]

8.3 Swedish Fund for Research Without Animal Experiments

The Swedish Fund for Research Without Animal Experiments is a private organization financed by public donations that "promotes the development and validation of replacement alternatives to animal experiments by awarding grants to research projects." The fund, active since 1964, is one of the first organisations in the world to award grants specifically for the replacement and reduction of animal experimentation. The fund regularly sponsors the annual workshops of the Scandinavian Society of Cell Toxicology, and routinely awards grants for university courses on alternatives as well as for laboratory personnel training.[61]

8.4 FRAME

Fund for the Replacement of Animals in Research UK based organisation, the main aim of which it says is to find scientific methods that remove the need for laboratory animals in laboratories including alternative research and testing methods such as cells in culture, computer-based approaches, the use of donated human cells and tissues, or studies on volunteers. FRAME advocates a 3Rs approach. Some of its studies are office-based but FRAME supports laboratory research at the University of Nottingham, and grants have also been awarded to other scientists working on the development of non-animal methods. The organisation also campaigns in a number of areas and lobby for changes in legislation, where appropriate.[62]

9. Alternatives Teaching Centres

9.1 In vitro toxicology training programs at Mahatma Gandhi-Doerenkamp Center (MGDC).

The Mahatma Gandhi-Doerenkamp Center (MGDC) has been established in India by the Doerenkamp-Zbinden Foundation (DZF), Switzerland (see above) to motivate the teachers

60 www.alttox.org
61 www.alttox.org
62 www.frame.org.uk

and students to take to “alternatives” in place of animals in life science education along the lines of the 3Rs principle. Additionally, it is also a mandate of the centre to inculcate non-animal methods in toxicity testing and research. The latter is aimed to be achieved by providing intensive training to the stakeholders in *in vitro* toxicology, this has been achieved through a series of workshops. An article published in Altex reported on the tenth such *in vitro* toxicology workshop, held in June 2012, organised in conjunction with the Gandhi-Gruber-Doerenkamp Chair for Alternatives in Education and *in vitro* Toxicology, Bharathidasan University, Tiruchirappalli, India. Through their programs for faculties, scientists, and students, the two organisations, according to the article, are constantly engaged in bringing about progressive changes in animal use in education, research, and risk assessment by sensitising and motivating the stakeholders towards implementation of the 3Rs concept. Campaigning by MGDC, in collaboration with NGO organizations working in India, such as People for Animals (PfA), I-CARE, PeTA and InterNICHE, and with the support of a few enlightened teachers, has resulted in the University Grants Commission designing specific guidelines for phasing out dissections from the life science curriculum in universities and colleges in India. Subsequently, the Ministry of Environment and Forests, Government of India, has also directed medical, veterinary, and pharmacy faculties to redesign their curriculum in such a way as to avoid unnecessary killing of animals. Sensitisation by MGDC is done along two different streams, one for the faculties and students towards familiarisation and implementation of the 3Rs concept in education by the adoption of digital tools and other humane approaches, and the other for those engaged in research and testing with an appeal to avoid unnecessary killing of animals and instead adopt *in vitro* and *in silico* tools. MGDC's *in vitro* toxicology workshops are aimed the latter mission, The 10th workshop, entitled “Techniques in Animal Cell Culture and In Vitro Toxicology”, conducted on June 1-10, 2012, at MGDC involved participants including faculty, students, and scientists from across the country. A number of experts illustrated the history and successes of *in vitro* methods on global, national, and personal levels. The workshop was a blend of technical lectures, demonstrations and hands-on training on each of the exercises, starting with an introduction on basics of animal cell culture, through primary culture, to adoption of molecular techniques. The response from the participants was said to be highly positive and endorsed the goals of the MGDC.[63, 64]

This is clearly very much in line with the Training element of the Lush Prize, i.e. training of non-animal methods in toxicity testing and research. However it is, unfortunately, framed within a wider 3Rs context, whereas the Lush Prize wishes to focus on and prioritise organisations with a strong 1R/replacement commitment.

9.2 CAAT and CAAT-Europe

The 30 year old Johns Hopkins Center for Alternatives to Animal Testing (CAAT) is a small, non-profit centre, part of the Johns Hopkins University Bloomberg School of Public Health based in Baltimore. CAAT says it is dedicated to improving health for both people and animals. CAAT promotes humane science by supporting the creation, development,

63 http://www.altex.ch/en/index.html?id=17&ncat=1&nid=236

64 In vitro toxicology training programs at Mahatma Gandhi-Doerenkamp Center (MGDC), India: a status report and a review M. D. Zeeshan, A. Riyasdeen, A. Radha, F. Kunnathodi and M. A. Akbarsha Bharathidasan University, Tiruchirappalli, India mdzeesh@gmail.com

validation, and use of alternatives to animals in research, product safety testing, and education. CAAT seeks to effect change by working with scientists in industry, government, and academia to find new ways to replace animals with non-animal methods, reduce the numbers of animals necessary, or refine methods to make them less painful or stressful to the animals involved.[65]

CAAT-Europe is a more recently established corresponding European Center for Alternatives to Animal Testing, housed at the University of Konstanz which seeks to co-ordinate transatlantic activities to promote education in humane science and participates in and coordinates publicly and privately funded European projects. The University of Konstanz has twenty years of prior experience in alternatives to animal experiments. CAAT-Europe plans to develop a joint education programme between the Johns Hopkins School of Public Health and the University of Konstanz. The programme will include e-courses, CAAT's existing certificate program on humane science (see below), a student exchange, and collaboration in the International Graduate School.[66] [67]

Both Centre's are endowed with Doerenkamp-Zbinden Chairs, professorships founded by the Doerenkamp-Zbinden foundation (see above) in order to promote research and teaching in the 3Rs and in the field of new toxicological approaches as formulated by the National Research Council of the USA in 2007 in its vision and roadmap document "Toxicology for the 21st century".

CAAT's academic programmes educate students and professionals in the research field about alternatives and humane science, helping them gain a better understanding of the 3Rs and their role in improving the quality of science. The Humane Science and Toxicology Certificate Program is central to CAAT's academic program, with a curriculum consisting of six courses, offered both in the classroom and online, through the Johns Hopkins Bloomberg School of Public Health. The certificate programme[68] is open to anyone with an undergraduate or graduate degree in public health or the biomedical sciences, as well as to students in any degree-granting program at the Johns Hopkins University. In an important step designed to make the Certificate Program easily accessible to a wide audience in business, legal, and regulatory communities, CAAT has worked to make the Humane Science and Toxicology Certificate Program available entirely online. CAAT also offers a free online course: Enhancing Humane Science/Improving Animal Research. This course provides a broad overview of diverse topics in humane science, including experimental design, humane endpoints, environmental enrichment, post-surgical care, pain management, and the impact of stress on the quality of data. The self-paced course consists of 12 audio lectures with accompanying slides, resource lists, and study questions, and is available on the CAAT website.[69]

65 http://caat.jhsph.edu/

66 http://cms.uni-konstanz.de/leist/caat-europe/

67 Center for Alternatives to Animal Testing – Europe (CAAT-Europe) M. Daneshian 1, T. Hartung 1,2 and M. Leist 1,3 1CAAT-Europe, University of Konstanz, Germany, 2CAAT, Johns Hopkins University, USA, 3Chair for in-vitro toxicology and biomedicine, University of Konstanz, Germany mardas.daneshian@uni-konstanz.de

68 http://commprojects.jhsph.edu/academics/prop.cfm?id=32

Clearly these courses include a strong if not exclusive refinement element.

CAAT and CAAT-Europe are key collaborators in the Transatlantic Think Tank of Toxicology T[4] which has organised workshops to develop a framework programme for the teaching of alternative methods, with what appears to be a stronger emphasis on replacement and a particular focus on 21st Century Toxicology.[70]

Relevant to the specific focus of this research, CAAT has organised a forthcoming Joint Information Day on Organotypic 3D-Cell Culture Models and Engineered Tissues, in October.

10. Other alternatives centres

Little training on replacement was found at any of these institutions.

10.1 Netherlands Center for Alternatives to animal use (NCA)

NCA is an academic institute within the Utrecht University Faculty of Veterinary Medicine created to act as a focal point for coordinating research and disseminating information on alternatives to animal experiments. To this end, the centre works in close collaboration with the Netherlands Organization for Health Research and Development, whose Program Committee on Alternatives to Animal Experimentation determines funding priorities for 3Rs research in Holland, as well as with the Dutch division of ECOPA (see below). NCA also performs extensive educational outreach, including: publication of the NCA Newsletter; maintenance of a Dutch database on alternatives; organisation of scientific workshops and symposia; participation in national and international networks of experts and instruction in the subject of alternatives to animal use during laboratory animal science classes.[71]

10.2 Nordic Information Centre for Alternative Methods (NICA)

Founded in 1998 by the Scandinavian Society for Cell Toxicology and financed largely through grants from Swedish animal welfare and 3Rs organizations, NICA aims to provide information about alternatives to animal experiments. NICA's core activities include providing online access to the Multicenter Evaluation of *In Vitro* Cytotoxicity (MEIC) and MEIC monographs on time-related human lethal blood concentrations (MEMO) databases, establishing and maintaining a database of alternative projects in the Nordic countr**ies and providing advice to members of ethical and animal care committees.**

10.3 The 3R Foundation

The 3R Foundation, based in Switzerland is a cooperative institution set up in 1987 by the Parliamentary Group for Animal Experimentation Questions, a number of chemical/pharmaceutical companies and the Foundation for Animalfree Research. The organisation is supervised by the Federal Department of Home Affairs. The aim of the 3R Foundation is to promote alternative research methods to animal experimentation through grants for research projects as well as to implement and promote the 3R principles. The

69 http://caat.jhsph.edu/

70 http://altweb.jhsph.edu/about_us/t4.html

71 www.alttox.org

organisation supports first and foremost projects aimed at developing new methods or refining accepted methods (validation) which offer improvements vis-à-vis standard animal experimentation.

The 3R Foundation provided a learning programme in German and English for individual, professional further training from 2005 on its website.[72] The programme offered the opportunity to test knowledge of various topics via the internet. However for technical and financial reasons the Foundation no longer offers its learning programme via the internet, a situation which is currently under review.

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

The NC3Rs was established in 2004 as an offshoot of the UK Medical Research Council (MRC) Centre for Best Practice for Animals in Research, with a mandate to serve as a focal point for 3Rs and animal welfare research and related initiatives in the UK. An independent organisation, financed by and accountable to a range of government, industry, and other stakeholders, the NC3Rs is principally active in the areas of research funding, publications and information dissemination and forum for stakeholder interaction

10.5 AltLab

The new alternative lab (AltLab) was opened in the summer of 2009 thanks to donations from the Norwegian Animal Protection Alliance and the University of Bergen to teach and train students, researchers and animal technicians. The AltLab contain several animal models, multimedia programs and surgical items. In the AltLab, users can learn intubation, blood sampling and different surgery techniques like transplantation of veins and organs, and injections. The AltLab also contains a library for selected books, DVDs and multimedia programs. The AltLab appears to be very much focussed on training towards the future use of animals, avoiding the use of animals at the training stage.[73] [74]

11. Industry Collaborations

11.1 The In Vitro Testing Industrial Platform (IVTIP)

IVTIP is an association of 45 companies with an active interest in (i) supporting and applying the principles of the 3Rs, and (ii) promoting the adoption of the fourth R (societal Responsibility). Member companies are represented globally from the following sectors: consumer products, pharmaceuticals, chemicals, cosmetics, and independent contract research organisations. IVTIP has established close contact with the European Commission in relevant Framework Programmes, ECVAM and EPAA (see above and below). Recently, it has initiated a close collaboration with ESTIV (European Society for In

72 http://3R-training.tierversuch.ch

73 The new alternative laboratory for training and teaching J. G. Stormark University of Bergen, Bergen, Norway joanna.stormark@biomed.uib.no

74 www.uib.no/dyreavdelingen/en/resources/alternatives-lab-at-the-bbb-unit

Vitro Toxicology) and CAAT-Europe in order to improve the flow of relevant knowledge between academia, industry and regulatory authorities, to stimulate the application of in vitro tests by industry and to facilitate their acceptance by regulatory authorities. IVTIP endorses the US NRC's "Toxicity Testing in the 21st Century" strategy as the ultimate replacement of animal experimentation for regulatory/safety testing and focuses on the implementation of innovative strategies. IVTIP provides inter-national discussion forums to address selected topics (e.g., "Toxicity Testing in the 21st Century" (Antwerp, Belgium, 2009), "Integrated Testing Strategies" (Geneva, Switzerland, 2010), and "Limitations of 3D Tissue Models" (Monaco, 2011)), and to identify and discuss novel tools, approaches and technologies in terms of relevance and applicability. The outcome of these discussion forums are published as peer reviewed papers in relevant journals. IVTIP has become an important stakeholder in the ongoing discussions on new regulations involving in vitro testing, thereby ensuring effective dissemination through transfer of both technology and knowledge.[75]

11.2 European Consensus Platform for Alternatives (ECOPA)

ECOPA is an EU-wide umbrella group for national "consensus platforms" comprising academic, government, industry and animal welfare stakeholders working cooperatively to advance the 3Rs in member states. The stated mission of ECOPA is "to facilitate the exchange of scientific information, expertise and experience between national consensus platforms, industry, science, animal welfare and EU and government institutions to enhance the further development and implementation of the 3Rs in animal experimentation in Europe and worldwide." To this end, ECOPA organises conferences and seminars, maintains an online repository of 3Rs databases and animal welfare legislation, and supports scientific and educational initiatives that are consistent with its mission.

11.3 European Partnership for Alternative Approaches to Animal Testing (EPAA)

The EPAA was established in 2005, as a joint initiative of the European Commission (EC) and a number of companies and trade associations for the purpose of pooling knowledge and resources to accelerate the development and acceptance of 3Rs methods in regulatory toxicology. Governed by a Steering Committee comprising both EC and corporate representatives, the EPAA originally carried out its principal work through five working groups with the following mandates:

- Mapping of past and current 3Rs activities to share successful approaches and better inform the planning and prioritisation of subsequent actions
- Prioritisation, promotion, and implementation of future research based on the application of the 3Rs
- Identification, dissemination, and implementation of best practice in the 3Rs, implementation of the 3Rs in regulation and decision-making, v*alidation and acceptance.*

75 The industrial applicability of in vitro methods: the role of the In Vitro Testing Industrial Platform (IVTIP) B. De Wever 1, E. Roggen 2, C. Krul 3, A. Poth 4 and S. Mikulowski 5 1ALTEXA Development, Monaco; 2Novozymes, Denmark; 3TNO, The Netherlands; 4Harlan Cytotest Cell Research, Germany; 5Biovator, Sweden marianna_gaca@bat.com

Projects of the EPAA are currently organised into three platforms:

The Science Platform involves the prioritization, promotion, and implementation of future research based on the application of the 3Rs with activities including workshops and reports on recent advances in computational and systems biology; chronic repeat dose systemic toxicity; *in vitro* metabolism; and *in vitro* ADME (absorption, distribution, metabolism, and excretion).

The 3Rs in Regulation Platform involves promoting implementation of 3Rs in EU regulatory testing with activities including a review of acute systemic toxicity and alternative approaches; a feasibility study for replacing the two-generation study reproductive toxicity study with a one-generation study; identification of priority areas for implementing 3Rs in regulatory testing; promoting closer collaboration of ECVAM (see above) and industry to support test method validation; and identifying and proposing strategies for overcoming barriers to validation and regulatory acceptance.

The Communication & Dissemination Platform promotes the identification, dissemination, and implementation of best practice in the 3Rs, including two limited-access databases developed by the EPAA:

- In-house Review Database – an inventory of alternative methods used by companies in product safety evaluations
- Research Review Database – a compilation of ongoing 3Rs research projects in the EU, intended to facilitate identification of gaps in research and inform direction of future research.[76]

12. Commercial organisations providing training in *in vitro* methods

12.1 XCellR8

XCellR8, www.x-cellr8.com says its goal is to maximise the productivity of cell culture-based research, by providing easy access to specialist technical support, training courses, and in vitro contract testing and says it is fully committed to the development of in vitro alternative methods.

XCellR8 offers training courses in diverse aspects of cell culture, from introductory cell culture techniques to complex primary model systems. All of its courses are run by scientists with direct experience in the relevant subject and in delivering technical training.

The company provides training on a one-to-one basis or to entire project teams and organises an annual "Cell Culture Techniques Fast Train" event which it says allows delegates to fast-track their knowledge in a new subject or to stay up to date with the latest developments.

The organisation is based in the UK but is now planning training events in the USA.

There are many other commercial organisations offering contract in vitro services which may well offer some forms of training but no other organisations came up, in this respect, in the process of this research.

76www.alttox.org

13.1 Societies

There are a number of *In Vitro* societies such as the European Society Of Toxicology In Vitro and American Society for Cellular and Computational Toxicology and The Dutch-Belgian Society for In Vitro Methods (INVITROM). These all have some relevance to this area. INVITROM, for example, is a joint initiative among academic centres in Belgium and the Netherlands whose mission is the "promotion of the development, the application and the acceptance of *in vitro* models in the biomedical research." Information exchange, including the organisation of an annual symposium, is a key function of INVITROM. So too is fostering collaboration between research institutes, industry, and regulators in support of more rapid development and acceptance of *in vitro* models, paradigms, and strategies.[77]

77 www.alttox.org