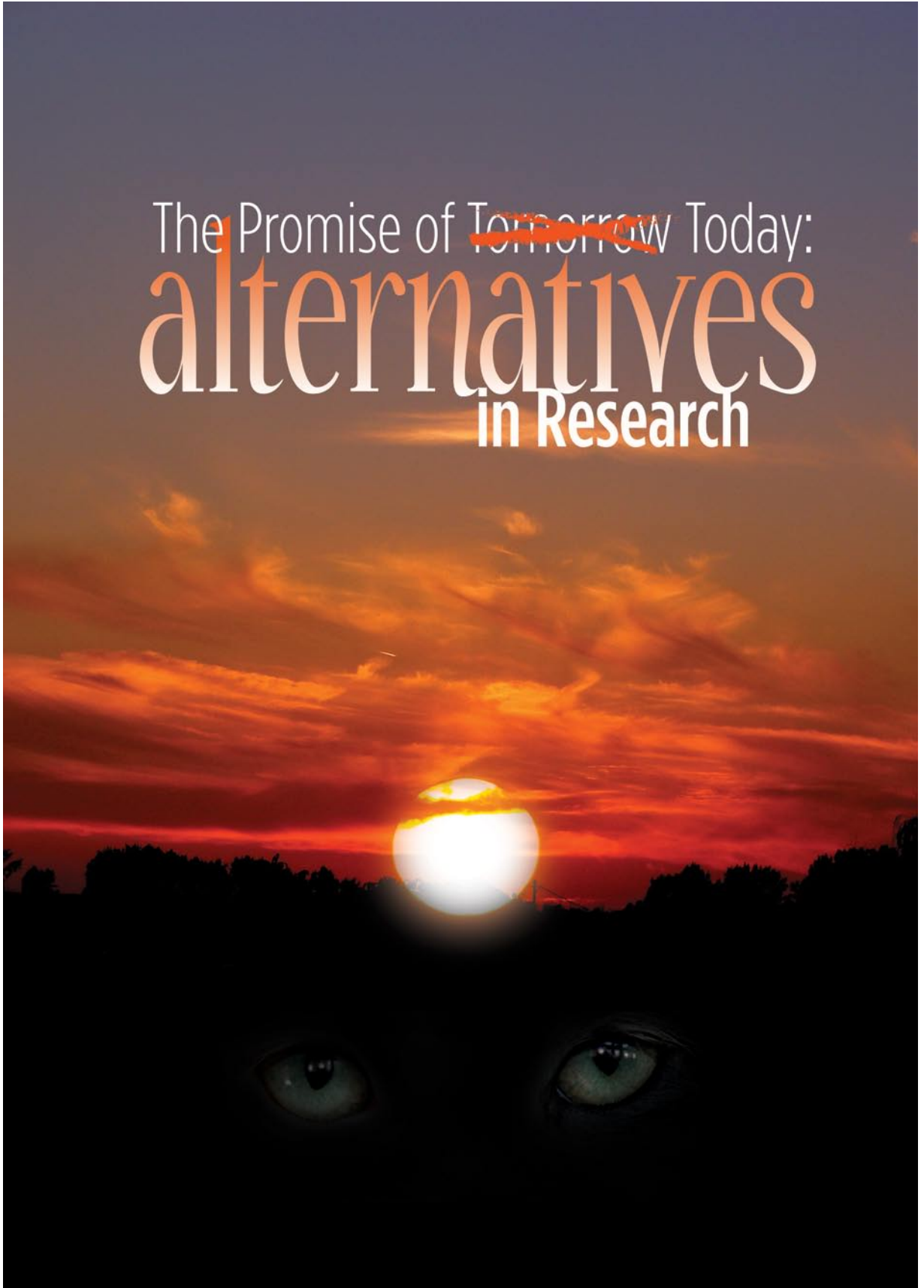




A PUBLICATION OF
THE AMERICAN
ANTI-VIVISECTION
SOCIETY

The Promise of ~~Tomorrow~~ Today: alternatives in Research



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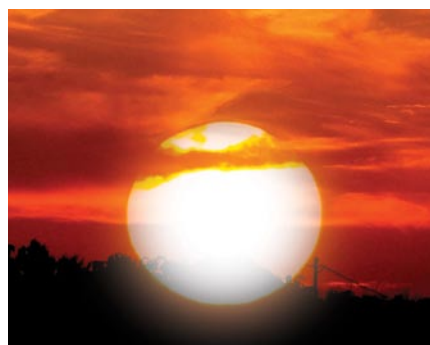
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Who Are We?



Founded in 1883, the American Anti-Vivisection Society (AAVS) is the oldest non-profit animal

advocacy and educational organization in the United States dedicated to ending experimentation on animals in research, testing, and education. AAVS also opposes and works to end other forms of cruelty to animals. We work with students, grassroots groups, individuals, teachers, the media, other national organizations, government officials, members of the scientific community, and advocates in other countries to legally and effectively end the use of animals in science through education, advocacy, and the development of alternative methods to animal use.

AAVS has two main divisions, each involved in specific activities. Animalearn is the education program of AAVS, which focuses on ending vivisection and dissection in the classroom. From elementary through college levels, Animalearn helps countless individuals make their classrooms more humane. Animalearn operates the most aggressive dissection alternatives lending library in the country, The Science Bank; it provides alternatives to using animals, from basic dissection, through psychology experiments. Animalearn also participates in national teacher conferences and hosts workshops to help teachers learn ways of educating without harming other living creatures. Animalearn's National Humane Educators Network links interested parties with speakers across the country, bringing the message of humane education to thousands.

The Outreach division of AAVS educates the general public about animal issues through one of the top-rated literature collections in the animal advocacy movement and the informative AAVS website. Our quarterly publication, *AV Magazine*, and bi-monthly newsletter, *Activate For Animals*, provide comprehensive up-to-date information on the scientific and ethical dimensions of animal experiments and alternatives. Both publications encourage AAVS members and supporters to become actively involved in our campaigns. Outreach staff also travel to speaking engagements and conferences and place advertisements in national publications to spread the AAVS message across the country.

The Alternatives Research & Development Foundation (ARDF), an affiliate of AAVS, awards grants to scientists and educators working to develop non-animal methods of investigation. ARDF's unique program provides the necessary resources for the development of alternatives to the use of animals, and it advocates the use of alternatives through the internet and by participating in conferences and seminars. Through these endeavors, ARDF works to promote scientific solutions for today with humane visions for the future.

We ask you to become a member of AAVS and help us to end the use of animals in science through education, advocacy, and the development of alternative methods. It is only through the support of members and other individuals that we are able to continue our vital and successful programs.

FIRST WORD



It's an honor for me to introduce this issue of the *AV Magazine* on alternatives. As you may know, I serve as President of both AAVS and our affiliate, the Alternatives Research & Development Foundation (ARDF). The foundation was established in 1993 to create an independent entity to further develop AAVS's support of alternatives. Our research grants for alternatives now total approximately \$1.5 million. You can read about some that were recently awarded in the ARDF Update, and I imagine you will be impressed with the innovative nature of these studies.

The potential for animal replacement is tremendous when an alternative method is successful. One project funded by ARDF resulted in an efficient, inexpensive replacement for growing small to medium quantities of monoclonal antibodies (MAbs). MAb production had traditionally been done in animals' abdomens, with considerable suffering involved. The new *in vitro* method was not only a scientific innovation; it provided a winning argument when AAVS and ARDF petitioned the National Institutes of Health (NIH) in the late 1990s. The resolution of the petition was that NIH required its grantees to produce MAbs using an *in vitro* method, unless there was scientific justification otherwise. We estimated that this policy shift had the potential of replacing one million animals a year.

But that points to a key factor in the success of alternatives: using them! Change requires motivation and there would be no alternatives science success without animal advocates like AAVS members pushing companies and governments to move away from using animals. Alternatives policy is the focus of more than one article in this issue of *AV Magazine*, and we are delighted and grateful to Thomas Hartung for writing an article comparing the European and American systems for advancing alternatives through validation. To many people, Dr. Hartung is probably the single most influential person in the world today on alternatives, having the position of head of the European Centre for the Validation of Alternative Methods (ECVAM).

Dr. Hartung gave a provocative closing speech at the recent 6th World Congress on Alternatives & Animal Use in the Life Sciences, of which ARDF was a major sponsor. The Congress was held in August 2007 in Tokyo—the first time in East Asia, where scientific research is booming. The challenge was to give a boost to alternative methods, and impress upon officials there that animal-based research is not the gold standard but only one method of investigation, and a flawed method at that. Over 950 people attended from dozens of countries, including China, Korea, and Thailand.

Thanks in part to your support of ARDF, we played a significant part in bringing together scientists with animal advocates and government officials to align all the players on a path for the future of non-animal research. There is good reason for hope. I keep in mind the classic quote by Sir Peter Medawar, Nobel-prize winner: "The use of experimental animals on the present scale is a temporary episode in biological and medical history."

Change is in the air. Read on, and stay tuned to developments by staying involved with AAVS and ARDF.

An Introduction to Alternatives

**By Sue Leary,
AAVS & ARDF President**

On June 12, 2007, a news release was sent out by the National Academy of Sciences, entitled "Report Calls for New Directions, Innovative Approaches in Testing Chemicals for Toxicity to Humans." It described how a committee of scientific experts, appointed by the National Research Council, had conducted an in-depth examination of how best to devise regulatory testing systems that would protect public health. Recognizing the disadvantages of old, crude test protocols that merely force animals into contact with chemicals and observe the effects that may or may not correlate with a human response, the committee pointed to a new way.

The release highlighted their recommendations, saying, "The report outlines a new approach that would rely less heavily on animal studies and instead focus on *in vitro* methods that evaluate chemicals' effects on biological processes using cells, cell lines, or cellular components, preferably of human origin. The new approach would generate more-relevant data to evaluate risks people face, expand the number of chemicals that could be scrutinized, and reduce the time, money, and animals involved in testing."

If any single thing could be a sign that alternatives have achieved acceptance by the mainstream science community, an endorsement by the National Academy of Sciences might be it. *Chemical*

& Engineering News and *Chemistry World* magazine both reported extensively on the new report, and animal advocates could not be faulted for celebrating.

But, of course, the idea of alternatives to animal research has been around for a while. How did it develop, what is different today, and what is needed to move this vision forward?

What is an alternative?

By definition, an alternative refers to a choice, typically, between two or more options that are equivalent in some way, such as "I don't really want to see that movie; what's the alternative?" A second definition of alternative suggests a deliberately different way of looking at something, a kind of subtle challenge of the status quo, such as 'alternative medicine,' 'alternative lifestyle,' or 'alternative schools.'

Interestingly, 'alternative' as used in reference to animal

research, can mean both. It can refer simply to a particular alternative method, such as a cell culture or a computer model that substitutes for an animal test. It can also refer to 'alternatives research,' an interdisciplinary field of science that by design is not using animals in a traditional way.

Anti-vivisection advocates in the early years may not have used the word 'alternatives,' but they certainly urged scientists to find another way of doing their work that did not use animals. It was not until 1959, though, that British researchers William Russell and Rex Burch proposed an alternatives research approach in a book, *The Principles of Humane Experimental Technique*. In it, they articulated the "3Rs" of replacement, reduction, and refinement.

A relatively straightforward concept, the 3Rs suggest that we Replace animals where possible, Reduce the numbers

of animals used, and Refine the procedures to ensure minimum invasiveness. The fascinating full text of the Russell and Burch book, including such chapters as "The Concept of Inhumanity," is available on the web at http://altweb.jhsph.edu/publications/humane_exp/het-toc.htm.

Their work was developed further, applying the principles to real research problems, by an organization in England, the Fund for the Replacement of Animals in Medical Experiments (FRAME), funded by animal advocates. As early as the 1970s, countries in Europe, such as The Netherlands, started to put comprehensive policies in place to at least recognize and consider animal suffering in cost/benefit analyses of the value of research projects.

But largely, the work of Russell and Burch was ahead of its time and not very well known until the 1980s when



animal advocates and industry adversaries needed to move beyond the impasse of identifying the problem of animal suffering in testing and toward a solution.

Advocates push for alternatives

Although there were many factors involved, if one person were to be identified with persuading big consumer product companies in the U.S. to turn from animal testing to alternatives, it would have to be New Yorker Henry Spira. Starting with the campaign to stop the Draize rabbit eye irritancy tests, launched in the late 1970s, Spira brought together organizations throughout the growing animal protection movement to demand that consumer product companies stop business as usual and seriously commit to alternatives. In doing so, new common ground was finally identified between advocates who objected to animal tests and scientists who were obligated by law to conduct some kind of test to demonstrate the safety or efficacy of a given product or drug.

Animal advocacy organizations were also willing to divert significant resources to funding alternatives research. AAVS did so enthusiastically and went even further to establish the Alternatives Research & Development Foundation (ARDF) to focus on that work exclusively.

Alternatives started to be specifically mentioned in laws. The Animal Welfare Act includes a requirement "...that the principal investigator considers alternatives..." The Congressional reauthorization of the National Institutes of Health included directing the enormous research agency to encourage alternatives. In the newly functioning European Union, a 1986 directive stated that an alternative must be used "when reasonably and practicably available."

As laboratories started to deliver alternative methods for consideration, it was decided that some official agency needed to 'validate' them, or a poorly performing alternative method could sour the science community and the public on alternatives. Elsewhere in this magazine, articles examine the European and U.S. validation entities; and as you will see, there have been some obstacles to rapid progress in the U.S., in part due to institutional expectations and structural issues. In contrast, Europe's validation body is well-funded and highly productive, and contributes a great deal to regulatory acceptance of alternatives.

International conferences to bring scientists from various disciplines—mainly toxicology—have been organized. The 1st World Congress on Alternatives &

Animal Use in the Life Sciences took place in 1993 in Baltimore, Maryland. Animal protection organizations participated and helped fund the meeting. The same applied to the 6th World Congress, in Tokyo in August 2007, which was co-sponsored by ARDF with the intent of bringing knowledge of alternative methods to Asia, where an increasing amount of animal research is being conducted.

Technology and political will

The 3Rs are now widely accepted in science, but what is new is the technology that permits more replacement methods than ever before. Cell cultures have progressed beyond a single fragile layer in a petri dish. Now, all varieties of cells, corresponding to the organs of interest in a study, such as the eye or skin or lungs, grow in multi-layer systems, and simulate human responses in new ways.

From micro-arrays to gene chips to use of specialized cell lines, the push is on to find high-performing *in vitro* methods to look at the effects of substances on human bodies and systems by looking at what happens to genes, proteins, and basic cell functions.

Europe's commitment to non-animal testing of cosmetics, and the scientific leadership there, have provided an enormous boost to the field. The willingness of governments and industry to work together culminated in the formation of the European Partnership for Alternative Approaches to Animal Testing, launched in November 2005. This group provides leadership and coordination, and conveys an understanding of accountability to the public values that demand that animal tests be avoided.

Moving forward

What would help alternatives development move more quickly in the U.S.? Here are a few ideas that AAVS and ARDF have been promoting:

Funding

The most important trigger of change is widespread and significant financial support. Private and public funds must be increased to develop, validate, and implement alternative methods, not only for purposes of testing but for basic research. There is evidence in the number of applications received by ARDF's annual grant program of substantial intellectual interest in conducting such work by well-qualified scientists. In response, ARDF has tripled its grant budget in the last five years. (see ARDF Update, p. 26)

Policy

Having alternatives principles integrated at all levels into policies that govern research would strongly deliver a consistent message. The mandatory European directive mentioned above, stating that alternatives must be used if reasonably and practicably available, has evidently been a major force for change in forming a variety of decisions. In contrast, voluntary cooperation is, by definition, unenforceable.

Improved training of young scientists

In The Netherlands, graduate students are required to take a comprehensive course on ethics and alternatives before they are permitted to perform experiments on animals. They now have a community of scientists who understand the principles and techniques of humane science and reinforce the standards. Other countries, including the U.S., should implement such a program.

Incorporating alternatives experts in the composition of the Institutional Animal Care and Use Committees (IACUCs)

In the U.S., the system of oversight relies on IACUC approval of animal experimentation. At this level, informed alternatives searches and incorporation of alternatives principles would go far to prevent animal use in at least some basic research.

Among the recommendations of a recent National Research Council's report, "Toxicity Testing in the Twenty-First Century: A Vision and A Strategy," are coordination of efforts and scaling up resources committed to alternatives development. In unusually strong language, the report says that a critical factor for success is the creation of an institution that fosters multidisciplinary research. The report warns that if the research is dispersed among different locations and organizations without a core organizing institute to enable communication and problem-solving across disciplines, there will be less chance of success within a reasonable time frame.

Conclusion

Animal advocates are sometimes inaccurately portrayed as anti-science or against human health. This could not be further from the truth. Although the development of alternatives is not a simple process, this technology is aimed at leading to greater scientific advances and protection of human health. The good news is that alternatives are where excellence in science blends perfectly with the highest ethical stand towards animals. **AV**

Interagency Coordinating Committee on the Validation of Alternative Methods:

A Missed Opportunity or Potential For Progress?

By **Nina Mak, AAVS Research Analyst**

& **Nicole Perry, AAVS Outreach Coordinator**



In 1993, Congress recognized the growing need for scientifically sound alternatives to animal testing when it drafted the Revitalization Act of the National Institutes of Health (NIH). NIH, the primary federal agency directing medical research in the U.S., acts under the auspices of 27 Institutes and Centers, the majority of which utilize animals in their research. However, under the NIH Revitalization Act of 1993, one such institute was charged with creating a plan for certifying alternative toxicological testing methods and promoting acceptance of these methods within the scientific community.¹

The Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) was born in September of 1994 as an ad hoc committee of the National Institute of Environmental Health Sciences (NIEHS).² Composed of representatives from 15 federal agencies, the committee worked for nearly two years publishing a report to fulfill its mandate. “Public concern about animal use,” they wrote, “...has resulted in recent legislation requiring scientists to consider, prior to using animals, alternatives that do not use animals, that reduce the number used, or that minimize their pain and distress.”³ Upon completion, this report outlined a process for validating alternative methods in a

way that was designed to be useful to the scientific community at large.

With the release of its final report, titled “Validation and Regulatory Acceptance of Toxicological Test Methods,” ICCVAM was established as a standing committee in 1997.⁴ Using its report as an outline, ICCVAM was responsible for implementing its proposed plan.

Finally, with the enactment of the ICCVAM Authorization Act of 2000, the standing committee graduated to permanence under the National Toxicology Program’s Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM).⁵ The law was enacted “[t]o establish, wherever

feasible, guidelines, recommendations, and regulations that promote the regulatory acceptance of new or revised scientifically valid toxicological tests that protect human and animal health and the environment while reducing, refining, or replacing animal tests and ensuring human safety and product effectiveness.”⁶

The law named 15 agencies as members of the Committee, all of which are still involved, and designated a sixteenth category for “any other agency that develops, or employs tests or test data using animals, or regulates on the basis of the use of animals in toxicity testing.”⁷ Members of ICCVAM include representatives from the Agency for Toxic Substances and Disease Registry, Consumer Product Safety Commission, Department of Agriculture, Department of Defense, Department of Energy, Department of the Interior, Department of Transportation, Environmental Protection Agency, Food and Drug Administration, National Institute for Occupational Safety and Health, National Institutes of Health, National Cancer Institute, National Institute of Environmental Health Sciences, National Library of Medicine, and the Occupational Safety and Health Administration.⁸

In addition, the law created a Scientific Advisory Committee on Alternative Toxicological Methods (SACATM) to advise ICCVAM and NICEATM on priorities related to developing, validating, and implementing alternatives. The law authorized a number of voting SACATM members, including at least one representative from a national animal protection organization.⁹

Evaluation Process

ICCVAM was created with the purpose of reducing, refining, and replacing the use of animals in toxicological testing. One way that it attempts to do this is by sharing information among agencies to eliminate duplicate tests and harmonize testing practices. Another way is by evaluating proposed methods and communicating its findings to the public with press releases.

When a new method is proposed, peer review panels are convened, which must assess the usefulness and risk of the proposed method, eventually coming to a consensus on its validation status.¹⁰ Unfortunately, even if a method is validated, ICCVAM does not have the power to require agencies to adopt it.

Panels meet from time to time to discuss the evaluation process and suggest new procedures. These deliberations are

ICCVAM's Validated Alternatives

In the ten years since its inception, the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) has validated only six alternative methods and recommended them for use to the scientific community. While none of these methods permanently replace the utilization of animals in a particular study, they do reduce and refine their use.

- Corrositex® — An *in vitro* test to determine skin corrosion, Corrositex® uses a biomembrane and chemical detection system that changes color when in contact with corrosive substances. In some cases, this could replace the use of rabbits in corrosivity research; however, ICCVAM concluded that in certain cases Corrositex® should be used in conjunction with animal tests.

- EPIKIN™ — A model of reconstructed human epithelium, developed to test skin corrosion. This method was first validated by the European Centre on the Validation of Alternative Methods (ECVAM) as a complete replacement for animal tests. In contrast, ICCVAM has validated EPIKIN™ for reduction purposes, suggesting that some substances may need to be tested on animals after using this method.

- EpiDerm™ — Used in the study of skin corrosion and toxicology, EpiDerm™ is a layered model of human-derived epidermal keratinocytes. This method was first approved by ECVAM for use as a stand-alone assay. However, ICCVAM recommended that EpiDerm™ be used only as part of a tiered assessment strategy, which may or may not involve animals.

- Rat Skin Transcutaneous Electrical Resistance (TER) Assay — Replacing the use of rabbits in skin corrosivity tests, the Rat Skin TER Assay utilizes rat skin samples instead. Despite the fact that ECVAM recommended the Rat Skin TER Assay for use in all corrosivity tests, ICCVAM deemed this method unreliable in testing certain classes of chemicals, and suggested that traditional animal studies still be used.

- Murine Local Lymph Node Assay (LLNA) — The Murine LLNA is used as an alternative to guinea pig tests that screen for allergic reactions on the skin. Unfortunately, the Murine LLNA uses mice as a substitute to test substances topically.

- Up-and-Down Procedure (UDP) — Used to estimate acute oral toxicity, the UDP is an *in vivo* test that reduces the number of rodents used.

In addition to these approved methods, ICCVAM is also in the final stages of approving two more alternative methods. Because these methods have already been approved by the European Centre on the Validation of Alternative Methods (ECVAM) and have passed scrutiny in ICCVAM's final peer review report published last year, they are expected to pass with flying colors. However, final ICCVAM recommendations have yet to be transmitted to federal agencies.

- Bovine Corneal Opacity and Permeability (BCOP) Test Method — An *in vitro* test for detecting eye irritants, the BCOP Test Method uses tissues obtained from slaughterhouses to replace the use of live animals.

- Isolated Chicken Eye (ICE) Test Method — The ICE Test Method uses tissue obtained from slaughterhouses, which would otherwise be discarded, to detect ocular irritants. **AV**

RESOURCES

ICCVAM website. General Information About NICEATM Test Method Evaluation Areas. Retrieved August 9, 2007, from <http://iccvam.niehs.nih.gov/methods/methods/htm>.

Public comments submitted by the Humane Society Legislative Fund on behalf of the Doris Day Animal League, Humane Society Legislative Fund, People for the Ethical Treatment of Animals, Physicians Committee for Responsible Medicine, Alternatives Research and Development Foundation, and American Anti-Vivisection Society on June 7, 2007, concerning the Draft NICEATM-ICCVAM 5-year plan; 72 FR 23832; May 1, 2007.

conducted in public sessions with the opportunity for public comment.¹¹

However, ICCVAM's process for reviewing alternatives has been cumbersome and slow. There is growing frustration within the animal protection community, industry, and the general public with how ICCVAM operates, and many feel that significant changes are needed. Such dissatisfaction is not surprising when one looks at ICCVAM's track record for the development, validation, and acceptance of alternatives.

In the 10 years since ICCVAM has been in existence, it has initiated and completed the validation of just three test methods.¹² Another five test methods validated by the European Centre for the Validation of Alternative Methods (ECVAM) have been or are being reviewed by ICCVAM. The review processes have been invariably long and resource-consuming yet have resulted in only limited acceptance of the alternative methods in the best cases.¹³

In the meantime, another 13 test

methods have been endorsed by ECVAM's Scientific Advisory Committee (ESAC), none of which have yet been reviewed by ICCVAM. In contrast, all three of ICCVAM's validated methods have been quickly endorsed by ESAC.¹⁴

While ECVAM is applying enormous resources and making great strides in Europe, many people are questioning why ICCVAM has not made similar progress. The animal welfare community was initially enthusiastic about the formation of ICCVAM and, in fact, instrumental in encouraging Congressional support for its establishment, but AAVS and others now have serious concerns about ICCVAM's ability to advance alternatives adequately to meet the urgent challenge for a new testing paradigm that does not use animals.

ICCVAM's Five-Year Plan

In 2006, the Congressional Appropriations Committee asked NICEATM/ICCVAM to create a Five-Year Plan outlining how it will advance the use of alternatives in the U.S.¹⁵ NICEATM/ICCVAM needs to seize this opportunity to re-strategize and develop new approaches to create a path forward for alternatives.

NICEATM/ICCVAM proceeded by gathering information from its member agencies and the public to aid in the formulation of the Five-Year Plan (the Plan), due by November 15, 2007.¹⁶ It announced that a Draft Plan was available for public comment on May 7, 2007.¹⁷

AAVS and our affiliate, the Alternatives Research & Development Foundation (ARDF), reviewed ICCVAM's Draft Plan and attended several public meetings discussing the Plan. The Draft Plan as presented, unfortunately, did little to alleviate our concerns with ICCVAM. Instead, it was a compilation of ICCVAM's past activities, with indications that it will do more of the same. Given that these approaches have not been demonstrated to be effective during the past decade,

there is no reason to believe they will be more successful in the future.

AAVS and ARDF submitted comments with several other animal protection groups detailing our concerns and suggestions for improvement.¹⁸ Even ICCVAM's own Scientific Advisory Committee (SACATM) expressed significant concerns with the Draft Plan, encouraging ICCVAM to use this opportunity to take leadership in the alternatives field.¹⁹

ICCVAM's Priority Areas

The Draft Five-Year Plan begins by outlining four key challenges, which include:

- Identifying priorities and conducting and facilitating alternative test method activities.
- Incorporating new science and technology.
- Fostering regulatory acceptance and use of alternative methods.
- Developing partnerships and strengthening interactions with ICCVAM stakeholders.²⁰

AAVS, as well as other organizations and animal advocates, fully supports the strengthening of ICCVAM relationships, particularly regarding the sharing of resources and scientific expertise, maximizing validation efficiency, and minimizing duplication of tests.

Next, ICCVAM identified priority areas on which to focus its efforts for the next five years. Based on the potential impact on reducing, refining, or replacing animals for testing; applicability to multiple agencies; and potential to provide improved prediction of adverse health or environmental effects, ICCVAM selected eight different toxicity testing areas:²¹

Acute Toxicity – Measures hazards arising from accidental exposure to a substance, either from ingestion, inhalation, or contact on skin.

Ocular Toxicity – Measures ability of a substance to cause temporary or permanent eye damage.

Biologics/Vaccines – Measures vaccine potency.

Dermal Toxicity – Measures ability of a substance to cause temporary or permanent skin irritation/damage.

Immunotoxicity – Measures ability of a substance to cause an allergic reaction, particularly when applied to the skin.

Endocrine Disruption – Measures ability of a substance to interfere with the endocrine system (hormones).

Pyrogenicity – Measures ability of a substance or device to induce fever.

Chronic Toxicity/Carcinogenicity – Measures hazards arising from long-term exposure to a substance, particularly the substance's ability to damage cellular DNA and/or cause cancer.

ICCVAM also identified Neurotoxicity Testing and Reproductive and Developmental Toxicity Testing as areas of interest.

ICCVAM's plan, however, fails to provide any overview, description, or analysis of how the above criteria apply to its stated priorities. For example, the Plan gives no indication of how many animals are used in each testing area and would therefore be spared by the alternatives work that ICCVAM is prioritizing. There is also no indication of which agencies require what kind of testing and when. Additionally, the ability of the animal tests currently used to predict adverse health or environmental effects has not been reported.

This kind of information is basic and necessary if alternatives are going to be developed and adopted in any coordinated and meaningful way. Yet such information is exceedingly difficult to obtain in the U.S., and this lack of transparency is just one reason why alternatives research here has lagged behind Europe.

The Draft Plan continues with a list of activities that ICCVAM plans to pursue in each of its identified priority areas. However, the Plan provides no indication that ICCVAM will conduct its activities in any way that will improve its past underperformance in advancing alternatives in the U.S.

Recommendations for advancing the use of alternatives

In general, progress in the European Union (EU) on developing and validating alternatives for toxicity testing has far surpassed the U.S. AAVS, ARDF, and several other animal protection organizations want ICCVAM's Five-Year Plan to include an expedited review process so that it can act swiftly to take advantage of the progress that has been made in the EU, rather than going through the long, duplicative, and largely ineffective approach currently used by ICCVAM.

The Plan also needs to demonstrate that ICCVAM will focus more of its resources on the development and adoption of alternatives that will lead to the replacement of animals in toxicity tests, rather than just refinement and reduction alternatives. Given the limited resources it has, ICCVAM would be a far more effective leader in the alternatives field if it made replacement a priority.

ICCVAM Mission

"ICCVAM's mission is to facilitate development, validation, and regulatory acceptance of new and revised regulatory test methods that reduce, refine, and replace the use of animals in testing while maintaining and promoting scientific quality and the protection of human health, animal health, and the environment."

http://iccvam.niehs.nih.gov/about/ni_Mission.htm

Alternatives Under Consideration by ICCVAM

Three sets of alternative test methods have been nominated to ICCVAM for review and validation:

Local Lymph Node Assay (LLNA) for Classification of Skin Sensitizers

The LLNA was initially validated by ICCVAM in 1999 as a reduction and refinement alternative for assessing the ability of certain substances to cause an allergic skin reaction. This nomination requests an expansion of the applications for which the LLNA can be used. In particular, ICCVAM is requested to review the applicability of:

- LLNA as a stand-alone assay for potency determinations (including severity) for classification purposes
- Non-radioactive LLNA protocols
- LLNA "cut-down" or "limit" test
- Use of LLNA to test mixtures, aqueous solutions, and metals
- Current applicability domain for LLNA

Sponsor: Consumer Product Safety Commission

Toxicity Testing Area: Immunotoxicity

Status: Currently under evaluation by ICCVAM.

In addition to the feedback provided by AAVS and other animal protection organizations, ICCVAM received several other constructive criticisms on its Draft Plan. These included a call for ICCVAM to specify clearly defined deliverables with timelines so that the Plan can serve as a blueprint for moving forward. It was also suggested that ICCVAM should implement a web-based scorecard to clarify the development and validation process for each alternative under review and to track the progress being made.²²

SACATM's Five-Year Plan Working Group (FYPWG) delivered a critical analysis of ICCVAM's Plan and identified several ways in which the Plan could be made stronger and more useful. The FYPWG echoed many of the same observations and suggestions made by the animal protection community, including an emphasis on the need for a more comprehensive Plan, the need to describe how priority criteria apply to testing areas, and the need for a Plan that addresses the frustrations felt by many stakeholders with the slow pace of progress being made by ICCVAM.²³

The FYPWG specifically stated that, "the Draft Five-Year Plan falls short in articulating a clear vision and strategic perspective," and suggested that ICCVAM open a dialogue with the scientific, stakeholder, and regulatory committees to identify barriers to progress and ways to overcome them. The FYPWG further suggested that ICCVAM move its focus

MCF-7 Estrogenic Activity Cell Proliferation Assay

This nomination requests ICCVAM to review a high throughput, *in vitro* alternative for assessing the ability of a chemical to disrupt the endocrine (hormone) system by affecting estrogenic activity.

Sponsor: CertiChem, Inc.

Toxicity Testing Area: Endocrine Disruption

Status: Recommended for validation studies.

In Vitro Pyrogenicity Test Methods

This nomination requests ICCVAM to review five alternative test methods validated by ECVAM for assessing the ability of a vaccine or other biologic to induce fever.

Sponsor: ECVAM

Toxicity Testing Area: Biologics/Vaccines

Status: Peer Review complete, suggesting additional studies and limited acceptance of methods.

ICCVAM is also providing input on the National Toxicology Program's High Throughput Screening Initiative. For more information about ICCVAM's past, present, and future activities, please visit <http://iccvam.niehs.nih.gov>. **AV**

beyond research and development activities and more towards activities that will lead to translation, validation, and adoption of alternatives by regulatory agencies. The FYPWG also called on ICCVAM to "fully embrace the 3Rs and exert the leadership needed...."²⁴

Summary

It is clear that ICCVAM's Draft Five-Year Plan fell short of the hopes and expectations of many for a comprehensive, specific plan that outlines how ICCVAM will advance alternatives in the U.S. and that will have a maximal impact on replacing and reducing animal use.

However, ICCVAM expressed its intention to take the suggestions made by the animal protection community, SACATM, and other stakeholders into consideration. The Final Five-Year Plan has the potential to make substantive changes to ICCVAM operations in order to accomplish more meaningful and rapid progress in the alternatives field, which was the intent of Congress in establishing ICCVAM.

AAVS and our affiliate, ARDF, will continue to monitor ICCVAM's activities and work to boost the promotion and adoption of alternatives to animal use by ICCVAM and federal agencies. This is a long and tedious struggle, but AAVS and ARDF are committed to advocating for the implementation of non-animal methods in research and testing. **AV**

RESOURCES

¹ Pub. L. No. 103-43 (1993).

² ICCVAM website. *About the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM)*. Retrieved July 23, 2007, from http://iccvam.niehs.nih.gov/about/about_ICCVAM.htm.

³ ICCVAM. "Validation and Regulatory Acceptance of Toxicological Test Methods: A report of the ad hoc Interagency Coordinating Committee on the Validation of Alternative Methods." Retrieved on August 7, 2007, from http://iccvam.niehs.nih.gov/about/about_ICCVAM.htm.

⁴ See *supra* note 2.

⁵ See *supra* note 2.

⁶ Pub. L. No. 106-545, 114 Stat. 2721 (2000).

⁷ See *supra* note 6.

⁸ See *supra* note 6.

⁹ The current representative from an animal advocacy group is Dr. June Bradlaw of the International Foundation for Ethical Research. National Toxicology Program website. *SACATM Members (February, 2007)*. Retrieved August 7, 2007, from <http://ntp-server.niehs.nih.gov/ntpweb/index.cfm?objectid=7201660B-BDB7-CEBA-FD-4C95354AF0C7FF>.

¹⁰ See *supra* note 2.

¹¹ See *supra* note 2.

¹² Public comments filed June 7, 2008 by Humane Society Legislative Fund on behalf of Doris Day Animal League, Humane Society Legislative Fund, People for the Ethical Treatment of Animals, Physicians Committee for Responsible Medicine, Alternatives Research & Development Foundation, and American Anti-Vivisection Society regarding Draft NICEATM-ICCVAM Five-Year Plan (2008-2012) (72 FR 23832). Available at http://iccvam.niehs.nih.gov/pubcomment/5YP_draft/HSLF-ICCVAM5YrPlan.pdf.

¹³ See *supra* note 12.

¹⁴ See *supra* note 12.

¹⁵ ICCVAM/NICEATM. "The NICEATM-ICCVAM Five-Year Plan (2008-2012). Draft: May 4, 2007." Available at: http://iccvam.niehs.nih.gov/docs/about_docs/5YrPlan04May07FD.pdf.

¹⁶ See *supra* note 15.

¹⁷ 72 FR 23832; May 1, 2007.

¹⁸ See *supra* note 12.

¹⁹ SACATM Working Group for the NICEATM-ICCVAM Five-Year Plan (2007). "Review of the Draft NICEATM-ICCVAM Five-Year Plan." Available at: <http://ntp.niehs.nih.gov/index.cfm?objectid=498AFC7E-F1F6-975E-7751AAB67107B677>.

²⁰ See *supra* note 15.

²¹ See *supra* note 15.

²² Scala, R. (2007). "NICEATM-ICCVAM Town Meeting Summary." Presented June 12, 2007 at SACATM Meeting. Available at <http://iccvam.niehs.nih.gov/meetings/5YrPlanTM/TownMtg-Sum11Jun07fd-dw.pdf>.

²³ See *supra* note 19.

²⁴ See *supra* note 19.²³ See *supra* note 19.

WITH A LITTLE HELP FROM MY FRIENDS...

The European Centre for the Validation of Alternative Methods (ECVAM) is the agency charged with promoting and validating alternatives in the European Union (EU).

It is not often that scientific developments in Europe advance faster than the U.S. In the case of alternatives to animal experiments, however, this appears to be the case. But a more detailed analysis shows that the situation is not that simple, and the difference in EU and U.S. approaches offers opportunities to push and strengthen each other.

The support of animal welfare organizations from Europe and, increasingly, from the U.S. has always been instrumental to our work: directly, through collaboration and, indirectly, by raising public awareness and political support. No mentally sane person enjoys carrying out experiments that entail the suffering of animals, and through the 3R principles (reduce, refine, replace, as the formula to systematically reduce animal use and suffering), a compromise formula was found between the societal need to advance research and to limit animal use, which now is gaining acceptance within both scientific and animal welfare organizations. This 3R concept requires the continuous development of science toward less animal use and suffering, and animal welfare organizations play a central role in maintaining the drive of this process.

The 3Rs as a concept was first introduced in 1959 in the UK, when William Russell and Rex Burch published their famous book, *Principles of Humane Experimental Technique*. The

a transatlantic view on the collaboration to make validated alternatives to animal experiments available

**By Thomas Hartung,
ECVAM, EU Joint Research Centre,
Institute for Health and
Consumer Protection**

oldest organization active in the field of alternatives, FRAME (Fund for the Replacement of Animals in Medical Experiments) is based in the UK. In the U.S., the Johns Hopkins Center for Alternatives to Animal Testing (CAAT) was launched in Baltimore, Maryland, in 1981, giving U.S. scientists a competent resource for information on alternatives.

Remarkably, the full integration of an alternative resource entity into a renowned university such as Johns Hopkins is a model that has not been followed very much in Europe, with the recent much smaller exceptions of Utrecht, The Netherlands, and Konstanz, Germany. However, this integration into the education of the next generation of researchers is a crucial means to further alternative methods into becoming an integral part of the scientific repertoire.

Legislation

The legislative situation regarding alternatives is very different on both sides of the Atlantic. In the U.S., the federal Animal Welfare Act (AWA) sets minimum standards of animal care for experimental laboratories, animal dealers, and others. In 1970, the AWA was specifically amended to protect all "warm-blooded animals" used in research, but regulations

promulgated the exclusion of rats, mice, and birds. However, these makeup well over 95 percent of all animals used in the U.S. (Rats, mice, and birds constitute about 80 percent of the animals used in the UK.)

Animal welfare standards differed among European countries until 1986 when Directive 86/609/EEC established common standards, which were implemented in 1989 by all member states (today, 27 countries with about 500 million inhabitants).

Two articles are especially important in the context of this piece:

Article 7.2. An experiment shall not be performed if another scientifically satisfactory method of obtaining the result sought, not entailing the use of an animal, is reasonably and practicably available.

Article 23.1. The Commission and Member States should encourage research into the development and validation of alternative techniques which could provide the same level of information as that obtained in experiments using animals but which involve fewer animals or which entail less painful procedures, and shall take such other steps as they consider appropriate to encourage research in this field. The Commission and Member States shall monitor trends in experimental methods.

The articles laid the foundation for the creation of ECVAM in 1991, which followed the launch of the European Research Group for Alternatives in Toxicity Testing (ERGATT) in 1986 that established the principles of validation that were incorporated into ECVAM's procedures. The articles also form the basis for an extensive funding program for the development of alternative methods

(about \$300 million by the EU since 1986, and an estimated \$100 million by the member states in national programs). For example, today ECVAM is involved in 13 research projects with 260 partner organizations and receives \$110 million in funding from the EU Commission (EC) Directorate-General for Research.

In 1993, the U.S. NIH Revitalization Act included statements drafted and supported by animal protection organizations and several large corporations that promote the concept of alternatives. In particular, the Act authorized the establishment of an Applied Toxicology Program within the National Institute of Environmental Health Sciences (NIEHS), which eventually developed into the Interagency Coordinating Committee for the Validation of Alternative Methods (ICCVAM). A framework for validation and implementation of *in vitro* toxicity tests was developed by CAAT,¹ and contributed to the development of the ICCVAM principles for validation.

In 2004, ECVAM was further developed by involving U.S. colleagues in its Modular Approach to validation, opening the door for the use of new approaches. Based on both the ECVAM and ICCVAM principles, consensus on an OECD (Organisation for Economic Co-operation and Development) level was achieved, and methods to validate alternatives were agreed upon.² Overall, there is no difference in principle between ECVAM and ICCVAM, but there is difference in the details—how validation of alternatives is carried out and, perhaps, even more important, how this is funded.

ECVAM is involved in the tailored development of alternatives and has its own laboratories, with about half of the 60 staff members working experimentally both to further develop tests and to carry out validations. The project management of ECVAM systematically develops testing strategies and coordinates validation efforts involving flexible taskforces and validation management groups with external experts. Suggestions for tests to be considered can be made from the public via the ECVAM website.

After a dossier of a validation (using existing data as well as validation study results) is completed and quality checked, the ECVAM Scientific Advisory Committee (ESAC) carries out the peer-review and issues a statement of validity. Notably, regulatory bodies are not represented on the ESAC (except where member states have nominated such representatives) and the European Chemicals Bureau, which is coordinating regulatory functions of the member states.

The U.S. situation is different. The closest equivalent to ECVAM is actually NICEATM (the National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods). ICCVAM is part of NICEATM and support consists mainly of background review documents versus the active coordination of programs developing and validating methods. However, in recent years, ECVAM and NICEATM have overlapped by expanding their respective instruments and coordinated approach. For example, ECVAM introduced retrospective validation, i.e. the compilation of dossiers of existing information to enable a peer-review, and NICEATM started the coordination of prospective validation studies. This has enormously contributed to sharing the work burden in areas such as eye irritation and endocrine disrupters.

The differences between the agencies today are more in the amount of available funding than in approach. A higher staff number and budget allow ECVAM to evaluate about 170 test methods, of which 37 are at the late stages of validation. The program is very much driven by demanding EU legislation, such as the 7th Amendment of the Cosmetics Directive from 2003 and REACH (Registration, Evaluation, and Authorisation of Chemicals) from 2006.

ICCVAM as a peer-reviewing committee issuing final statements on validity, much more resembles the ESAC. However, being composed of 15 federal agencies, it includes far more regulators than ESAC. ICCVAM is obviously more the driving force of the process than ESAC, but attempts to strengthen the independence and role of ESAC are ongoing. Notably, the difference in composition is somehow compensated by the complementary composition of the Scientific Advisory Committee on Alternative Toxicological Methods (SACATM) and the current establishment of the ECVAM Regulatory Advisory Panel.

Collaboration

The existing collaboration between ECVAM and ICCVAM in the field of alternative testing methods has been strengthened during the last four years and comprises the following activities: 1) ICCVAM has observer status on the ECVAM Scientific Advisory Committee, 2) the head of ECVAM became a member of SACATM, 3) ESAC and ICCVAM collaborate in the parallel ongoing peer-reviews (pyrogen tests, haematotoxicity, eye irritation, micronucleus test, skin irritation, etc.), and 4) Several studies (acute toxicity, endocrine disrupters,

mutagenicity) and six workshops were and are jointly being carried out. Additionally, ICCVAM and ECVAM have discussed the creation of an International Council of Validation Bodies to coordinate validation studies at the level of the OECD, and discussion about formal collaboration with the OECD has been initiated. About 20 visits of ICCVAM members or ICCVAM-nominated experts to ECVAM taskforces, workshops, and validation management groups take place per year.

The framework of political collaboration with the U.S. has developed very favorably. The EU – U.S. Guidelines for Regulatory Co-operation and Transparency were finalised in 2002. In November 2002, a road map containing five initial “pilot projects” to implement the Guidelines was agreed upon, among them:

“Cosmetics: DG ENTR and the U.S. Food and Drug Administration (“FDA”) have agreed to co-operate in a pilot project concerning the validation of non-animal testing methods. The co-operation aims at early exchange of information and joint efforts to facilitate the OECD process in this area. The U.S. ICCVAM (Interagency Co-ordinating Committee on the Validation of Alternative Methods) and its European counter-part ECVAM (European Centre for the Validation of Alternative Methods) will collaborate among others on scientific evaluation of proposed methods. Contacts between ECVAM and ICCVAM work well. Intensified co-operation is envisaged.”

The collaboration was again reinforced at the April 2007 EU – U.S. Summit.

Conclusion

In recent years, the EU collaboration with the U.S. has been considerably enlarged and strengthened. We succeeded in anticipating discussions on differences in view, which would have been necessary anyway at the stage of international acceptance of validated results. At this early stage, however, the needs and concerns of the partners can still be accommodated in a study design and communication about concerns has been sufficient to clarify and overcome these hurdles.

To learn more about ECVAM, please visit ecvam.jrc.it/index.htm. **AV**

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1 Goldberg et al., 1993. *Xenobiotica* 23, 563-572.

2 OECD TG No. 34 Guidance document on the validation and international acceptance of new or updated test methods for hazard assessment.

Alternatives in Action: The Changing Face of Cosmetics



**By Vicki Katrinak,
AAVS Policy Analyst**

Much of the recent success in alternatives research, development, and use has been focused on the testing of personal care and household products and their component ingredients. The availability of non-animal alternatives for this type of testing has proliferated due to consumer and company demand as well as new regulatory requirements imposed by the European Union (EU). Without a doubt, the use of animals in product testing remains the subject of widespread criticism given the relatively inane purpose that these animal-tested products and ingredients serve. However, there still remains much confusion about the requirements for testing these finished products and their component ingredients, which leads to the continued use of outdated animal testing methods.

The Past of the Matter

In the United States, testing of personal care products on animals began in the 1930s with the passage of the Food, Drug, and Cosmetic (FD&C) Act of 1938. Before then, these products were not tested at all, allowing substances that caused severe effects in unsuspecting

consumers to reach the market.¹ The FD&C Act gave the United States Food and Drug Administration (FDA) regulatory authority over cosmetics, and FDA scientists were heavily involved in the development of the animal testing techniques still in use today by the cosmetic testing industry. However, there is no regulatory requirement either by the FDA or the Consumer Product Safety Commission, which regulates household products, that animal tests must be performed. The cruelty of common animal test methods, most notoriously the Draize eye and skin tests, which require the placement of chemicals into the eyes or on the skin of live animals, and the Lethal Dose 50 test, which determines the amount of chemical needed to kill 50 percent of the animals in a test group, were first exposed to the public in the late 1970s. Consumers were outraged by the use of such gruesome animal tests to make products like shampoo and lipstick and advocated for an end to such activities.

Consumer demand pushed many companies to take a proactive stand on the issue of animal testing and the development of alternative methods. In fact, the Cosmetic, Toiletry, and Fragrance Association, the trade group representing

the major manufacturers of personal care and household products, developed the Johns Hopkins Center for Alternatives to Animal Testing (CAAT) in 1981. At that time, CAAT was "to develop basic scientific knowledge necessary to create innovative non-whole animal methods for evaluating the safety and efficacy of commercial and therapeutic products."² While some companies have looked to CAAT to assist in the creation of appropriate non-animal alternative test methods, others made the decision to abandon animal testing ingredients and products entirely.

Present Day Success

Despite many companies' efforts to make positive changes, a great amount of animal testing of personal care and household products (most often their ingredients) continues to occur. Fortunately, animal advocates have decided to push for legislative change, and in some cases, they have been largely successful. The United Kingdom stopped licensing animal testing for cosmetic products and ingredients in 1998. A small number of other European countries such as Austria, Belgium, The Netherlands, and Germany have passed cosmetic testing bans. In May of this year, Israel passed a law banning the use of animals for testing of cosmetic and cleaning products³ and is also considering legislation to ban the import and sale of products that have been tested on animals.⁴

In 2004, the European Union passed the seventh amendment of the Cosmetics Directive (76/768/EEC) that sets a series of deadlines for animal testing bans and bans on the sale of cosmetics containing animal tested ingredients (see box on opposite page). Most of these deadlines are tied to the availability of non-animal testing methods. This legislation will have an enormous impact on the cosmetics industry both in the EU and abroad, since the law sets specific deadlines not just for the production but also for the sale of products that have been tested on animals or contain animal-tested ingredients. In today's global economy, companies based in the United States depend on profits from their European markets. This dependence will inevitably require these companies to more aggressively pursue non-animal alternatives for product testing.

In 2006, the EU also passed legislation that will require the safety testing of nearly 30,000 chemicals in an effort to protect human health and the environment. This legislation, Registration, Evaluation, Authorization and Restriction of Chemicals (REACH), requires the generation of safety data for all chemical

substances produced or imported into the EU at a rate higher than 1 ton per year.⁵ Because of the concerns raised by animal advocates, REACH was amended prior to final passage both to promote the use of currently available non-animal alternative test methods and to encourage the development of new alternatives.

Faced with the new testing requirements through REACH and the impending testing ban imposed by the cosmetics directive, cosmetic companies are now pushing harder than ever for the development of appropriate alternative methods. Some companies have decided to take on this new challenge by being directly involved in the development of these alternatives. For example, L'Oreal recently saw its human skin model, EPISKIN®, validated by the European Centre for the Validation of Alternative Methods (ECVAM) as an alternative to skin irritation tests performed on animals. "The EPISKIN® method will completely replace the regulatory Draize skin irritation test, a classic test introduced into safety tests for drugs and chemicals 60 years ago and involves applying the product to a rabbit's skin."⁶ Previously, this alternative had been validated only to replace skin corrosivity testing. The acceptance of this alternative is expected to allow L'Oreal to test 10,000 different chemicals required under REACH without the use of animals.⁷ The cosmetic giant seemed to decide the best way to handle these new regulatory requirements was to stay ahead of the game. Now that EPISKIN® has been validated for use, other companies will have to use this alternative method, allowing L'Oreal to boost its bottom line.

Looking to the Future

The use of alternatives in the product testing industry will help to alleviate the needless suffering of millions of animals each year. As alternatives become more sophisticated and prove to be more accurate and beneficial than traditional animal models, other industries will likely push for the regulatory acceptance of these new approaches. Certainly the use of non-animal alternatives to test personal care and household products is long overdue. But the ultimate success of efforts to change how these products are made will likely have lasting repercussions in other areas of animal testing. Pushing for alternatives in cosmetic testing appeals to the public's sense of responsibility to animals and will enable these alternative methods to gain the credibility and acceptance they need to affect change on an even larger scale. **AV**

RESOURCES

- ¹ Institute for Laboratory Animal Research (2004). Safety Testing. In *Science, Medicine, and Animals*. (p. 21-28). Retrieved November 27, 2006, from <http://newton.nap.edu/books/0309088941/html/21.html>.
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Seventh Amendment to the Cosmetics Directive (76/768/EEC) Animal Testing Deadlines in Europe

SEPTEMBER 11, 2004:

- Ban on animal testing of finished cosmetic products in the EU.
- Ban on the sale of cosmetic products and ingredients tested on animals outside the EU where validated alternative tests exist.

MARCH 11, 2009:

- Ban on animal testing of cosmetic ingredients or formulations in the EU.
- Ban on the sale of cosmetic products and ingredients tested on animals for all but a few test areas.

MARCH 11, 2013:

- Ban on the sale of cosmetic products or ingredients tested on animals for the remaining test areas.
- The ban could be delayed by new legislation if non-animal tests have not been made available. **AV**

Tom's of Maine

Leading the Way to Non-Animal Alternatives

While many companies use regulatory requirements to justify their continued use of animal testing, some companies have pushed the government to change policies to bring consumers the products they desire without the use of cruel and needless animal tests. Tom's of Maine, a company that manufactures personal care products such as toothpaste, deodorant, and soap, is one such company. Instead of relying on animal-based tests to prove the safety and efficacy of its fluoride toothpastes, Tom's urged the Food and Drug Administration (FDA) to accept data from non-animal alternatives.

In 1995, the FDA established final rules, referred to as a monograph, for over-the-counter anti-cavity products. At that time, FDA specified the use of certain biological testing requirements for such products: an animal caries (cavity) reduction and either an enamel solubility reduction or a fluoride enamel uptake.¹ In the animal caries reduction test, "rats are superinfected with cariogenic bacteria and, unlike clinical subjects, swallow the fluoride toothpaste."² In these tests, steel clamps force the rats' jaws apart so that the anti-cavity chemicals can be swabbed onto their teeth. After three weeks, the rats are killed, and their teeth are examined.

Committed to manufacturing products without the use of animal testing, Tom's of

Maine petitioned the FDA to instead permit the use of non-animal alternatives to prove that its fluoride toothpastes are both safe and effective. In 1996, FDA granted Tom's petition to use Intraoral Appliance models, which use small pieces of tooth enamel mounted to dentures worn by human subjects.³

Tom's of Maine was one of the first companies to be approved by the Leaping Bunny Program, which is administered by the Coalition for Consumer Information on Cosmetics. Approved companies pledge to manufacture products free of new animal testing, both for final products and ingredients. Tom's of Maine's efforts to gain regulatory acceptance of non-animal tests demonstrates its true commitment to cruelty-free products and sets the company apart as a leader in bringing about change for animals in the product testing industry.

RESOURCES

- ¹ Anticaries Drug Products for Over-the-Counter Human Use; Final Monograph." Federal Register 60 (6 October 1995): 52474-52510.
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MANY VIABLE ALTERNATIVES TO ANIMAL RESEARCH EXIST, AND SEVERAL HAVE BEEN VALIDATED. IN ADDITION, OTHER METHODS OF INVESTIGATION SUCH AS CLINICAL AND EPIDEMIOLOGICAL RESEARCH PRODUCE DATA THAT ARE DIRECTLY APPLICABLE TO HUMANS.

By Crystal Schaeffer, M.A. Ed., AAVS Outreach Director

ANIMAL RESEARCH FAILINGS: UNRELIABILITY, WELFARE, AND ETHICS

The history of scientific investigation using animals dates back for centuries, and as such, it has an ideology deeply rooted in tradition, which is instilled in young would-be scientists while they are still in school. Because there is such a strong tie to the past, it is sometimes difficult for new non-animal methods of research and testing to be accepted and utilized.

However, the use of animals as models of human disease in research and testing is flawed both ethically and scientifically. Assessing the safety and effectiveness of new drugs and products is an inevitable part of modern commerce and government, but it would benefit all concerned if testing was not done using animals. Efficient, cost-effective, *in vitro* alternatives exist, and other methods of investigation, from computer simulations to clinical research, are viable investigative tools. Indeed, animal experimentation is unreliable and unethical and it threatens animal welfare.

Unreliability

Due to anatomical, physiological, and metabolic differences between all animal species, data gathered from research and testing studies that utilize animals are not easily extrapolated to human conditions, and are often not applicable. Additionally, unlike many *in vitro* alternatives, animal experiments are not typically subject to the same scrutiny of a validation process to show whether they can produce reliable and reproducible data.

Research

Animals are used as models for human diseases, injuries, psychology, and medical treatments. In biomedical research, because animals are not generally susceptible to the same diseases as humans or do not react in similar ways, scientists have to unnaturally induce diseases (often using genetic engineering) to attempt to circumvent the natural differences between humans and other animals. Despite such drastic measures, the resulting animal models are still frequently neither appropriate nor applicable in investigating human diseases.

For example, in the 1980s, a massive push to find a cure for HIV/AIDS led to the creation of several animal models of the disease (mice, rabbits, monkeys, to list a few). However, in the decade that followed, AIDS in animal models differed from human AIDS in viral structure, disease symptoms, and disease progression. In contrast, non-animal alternative research methods have had far greater success. "Candidate antivirals have been screened using *in vitro* systems and those with acceptable safety profiles have gone directly into humans with little supportive efficacy data in any *in vivo* [animal] system," said animal researcher Michael Wyand. "The reasons for this are complex but certainly include...the persistent view held by many that there is no predictive animal model for HIV infection in humans."¹ Since the first HIV vaccine clinical trial in humans, more than 80 vaccines that successfully prevented HIV/AIDS in primates failed in human trials.² Human clinical research using patients infected with HIV/AIDS is a much more promising source of applicable data that be can analyzed to learn more about the disease and develop treatments.

An example of a unique, rather innovative research alternative is the bioengineered human skin construct (BHSC), a three-dimensional human skin equivalent that is used as a tissue

culture model to help develop treatments for burn victims. The developer of the BHSC, Charles Hewitt, Ph.D., reported that a literary search from 1987-1997 uncovered over 1,400 animal studies investigating burn trauma, and estimated that these experiments involved more than 59,000 animals over that period.³ Pigs are most commonly used in burn research, enduring excruciating pain from second and third degree burns. "[O]ur experiments would have a potentially dramatic and significant impact upon reducing the number of animals utilized for burn science,"⁴ stated Dr. Hewitt. "We feel that the reduction in pain and suffering alone is a worthwhile pursuit."⁵

Testing

Animals are used in a number of ways to test the irritancy, corrosivity, and toxicity of various substances, including personal care and household products, chemicals, drugs, and vaccines. Two of the most commonly used animals in testing are mice and rats bred for research, neither of whom are covered by the Animal Welfare Act and, therefore, may not be afforded even the minimal standards of care and treatment offered other animals who are covered, such as cats, guinea pigs, and monkeys.

Mice are commonly used in assessing carcinogenicity. However, some scientists are questioning the reliability of their use. A review examining over 500 rodent carcinogenicity studies concluded that rodent cancer assays are scientifically invalid as well as economically unfeasible.⁶ Conversely, a combination of *in vitro* tests can reproduce data similar to existing carcinogenicity databases and cost less than animal tests.⁷

The U.S. National Cancer Institute (NCI) recognized the inappropriateness of using mouse models to test drugs and carcinogenicity in 1987 when findings showed that the data were not applicable to human conditions. As a result, NCI decided to phase out its mouse research and moved in favor of using human cell lines and cultures instead.^{8,9}

Animal welfare

According to U.S. Department of Agriculture statistics, 1,177,566 animals,¹⁰ including cats, dogs, rabbits, sheep, and primates, were utilized in laboratory experiments in 2005, the most recent year with available data.¹¹ Of those, nearly half were reported by the researchers themselves to have experienced pain and distress associated with experimental protocols, and it is likely that this figure could be even higher given the subjective nature of the reporting. Additionally,

over 84,600 were used in research that caused pain but they received no analgesic relief.¹²

The suffering that animals used in research and testing endure is both physical and psychological in nature. For example, animals used in chronic toxicology and carcinogenicity testing are typically administered the test substance every day, seven days a week, for up to two years.¹³ Also, according to the National Institute of Environmental Sciences, as 'few' as 25 percent to as many as 75 percent of rats utilized in such studies die before the end of two years.¹⁴ Typical clinical signs of animal suffering in toxicology testing include: difficulty breathing, tremors, abnormal vocalization, diarrhea, vomiting, bleeding, abdominal rigidity, and swollen joints.¹⁵

It is also important to note that 'routine' laboratory handling and practices can cause animals great stress. In fact, such duress can cause increases in heart rate and blood pressure, and hormone levels that can be 20-100 percent higher than normal levels and last up to one hour.¹⁶ Not only does such handling cause the animal stress and discomfort, but it can also distort research data.¹⁷ Additionally, just as animals who live in zoos and circuses exhibit stereotypic behaviors such as repetitive rocking and pacing, bar chewing, and head banging, prompted by poor environmental living conditions, so do those in laboratories. Animals living in tight confinement can also engage in other psychotic behaviors like self mutilation and hair pulling.

Ethics

Many of those who are involved in animal research and testing will try to justify their use of animals by claiming that the human benefits derived from their research trump concerns of animal suffering. They may believe that animals are inferior to humans and lack intelligence, language, relationships, and altruism. However, this line of thinking could not be further from the truth. There is, in fact, mounting evidence that many animals experience the same range of emotions as humans.^{18,19,20} For example, mice are known to show empathy for cage mates who are suffering and in pain,²¹ and chimpanzees and gorillas can not only be taught human sign language, but they will use it to communicate with their own kind.²²

Animals should not be utilized in research and testing because they have the capacity to suffer, just as we do. Unfortunately, some scientists lose sight of this as they become desensitized to animal suffering and/or try and justify their use.

In the 1980s, a massive push to find a cure for HIV/AIDS led to the creation of several animal models of the disease (mice, rabbits, monkeys, to list a few.)



For example, a sociologist conducted an ethnographic study of animal researchers and asserted that "Scientists interviewed for this study agreed readily that animals are capable of feeling pain, but such assertions were muted by an overriding view of lab animals as creatures existing solely for the purposes of research." The author concluded that this view facilitated an environment where animals in their laboratories were often not properly administered anesthesia and rarely given analgesics.²³

One area of animal research which is particularly disturbing is experimental psychology, wherein animals are subjected to painful stimuli to analyze their behavior, purposely addicted to drugs, or placed in maternal deprivation studies in which infant monkeys are taken from their mothers soon after birth and kept in total isolation. Originally made infamous by Harry Harlow in the 1950s and 1960s, maternal deprivation instigates severe psychosis and these types of experiments continue today, despite literature dating back to the 1940s that show similar responses in human studies.^{24,25,26}

Conclusion

The use of animals in research and testing is scientifically unsound and unethical. Because the physiology and metabolism of animals and humans differ, data extrapolated from animal research cannot be easily or reliably applied to human conditions. Many viable alternatives to animal research exist, and several have been validated. In addition, other methods of investigation such as clinical and epidemiological research produce data that are directly applicable to humans.

Animals in laboratories suffer tremendously, both physically and psychologically.

As sentient beings, animals have the capacity to feel pain and suffer, and because of this, their use in research and testing cannot be justified. **AV**

RESOURCES

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Alternatives in Education: Revolutionizing Today's Classrooms

**By Laura Ducceschi,
AAVS Education Director
& Nicole Green,
AAVS Associate Director of Education**

The realm of alternatives in education is providing numerous options for educators and students who want to teach and learn without harming animals while studying disciplines like biology, anatomy, physiology, and psychology. Free loan programs like Animalearn's The Science Bank, which provides over 400 humane science-teaching tools, have made the process of obtaining alternatives for the classroom quick, convenient, and, most importantly, just as or even more effective than using dead specimens.

Humane Education

For over 15 years, Animalearn, AAVS's education program, has been working to make a difference for animals used in research, testing, and education. Our main focus is to eliminate the use of animals in education and replace their use with viable humane alternatives that are educationally effective and stimulate students' study of life. Today we are living in the age of advanced technology, and Animalearn's The Science Bank includes a wealth of innovative CD-ROMs, realistic animal models, charts, posters, and videos that give teachers the ability to modernize their classrooms. The Science Bank houses dissection alternatives not only for anatomy but also for anesthesia and critical care, biochemistry and cell biology, clinical skills and surgery, embryology and developmental biology, histology, pathology, pharmacology, physiology, and psychology.

Due to the abundance of alternative methods available in The Science Bank that help teach and learn science, Animalearn representatives empower parents and students so that they can make a significant difference for animals who are being used in the classroom. A highly recommended and beneficial resource for parents and students who are opposed to dissection is the Animalearn Resource Kit, which can be given to teachers. This comprehensive Kit includes a copy of The Science Bank catalog, in addition to a plethora of dissection-related materials such as a cost comparison sheet, which breaks down the cost effectiveness of alternatives compared to dissection specimens over a three-year time period.

Also inside the Kit is a list of comparative studies of student performance, which confirms that students who are trained using humane teaching methods perform at least as well as or better than those who utilize animals.

Animalearn representatives travel worldwide to showcase the viable and cutting-edge alternatives available in The Science Bank and to give presentations to educators who are interested in knowing more about the digital classroom. We offer tutorials to help teachers learn how to use the technology in their classrooms for a seamless transition from traditional animal dissection.



Instilling Respect for Animals

Animalearn's most recent endeavor to educate K-6 students about the plight of animals used in education has been to create our own *Animal Profiles*, which includes five informative fact sheets and colorful stickers of some of the most commonly dissected animals in classrooms today: cats, crayfish, earthworms, pigs, and rats. Along with our popular *Frog Fact Kit*, which comes with fact sheets, a poster, and stickers, we aim to give younger students a better appreciation and respect for animals, which we hope will lead them to choose alternatives when faced with dissection in the higher grades.

Student Rights

Students can sometimes run into challenges when requesting to use a dissection alternative. Animalearn receives numerous calls from students who want to know how to approach a teacher or professor with their concerns on this sensitive topic. Fortunately, students from K-12 who live in California, Florida, Illinois, New Jersey, New York, Oregon, Pennsylvania, Rhode Island, and Virginia have the legal right to choose a humane alternative to dissection. Louisiana, Maine, Maryland, and Massachusetts offer informal policies, and other states, like Michigan, are trying to pass similar legislation for students.

**Fortunately, students
from K-12 who live in California,
Florida, Illinois, New Jersey,
New York, Oregon, Pennsylvania,
Rhode Island, and Virginia
have the legal right to choose a
humane alternative to dissection.**

Those students who live in states that do not have a legal student choice policy in place still have the right to object to dissection. In many cases, students living in states without protective policies have been successful in encouraging their teachers and/or school districts to allow them to use dissection alternatives. In states such as California and Maryland, one student's objection set the creation of a law or policy in motion!

College and university students need to follow a different path to obtain student choice, since in most cases, they do not have an overriding school code that is dictated by a state or overarching governing body. As a result, individual institutions prescribe their own guidelines on issues such as dissection and vivisection in the classroom. Fortunately, many students and student animal protection groups have successfully been able to secure student choice policies at their colleges/universities, including Harvard University, Sarah Lawrence College, the University of Illinois, and Hofstra University, just to name a few.

Student choice policies are important in assisting those students who do not want to dissect because it conflicts with their value systems, but in many cases students are unaware that these policies are even in place. Animalearn works closely with students in K-12, college/university, and veterinary medicine to help them successfully obtain and use alternatives in their education. We believe that humane educators are critical to making school districts, colleges, and universities aware that these policies exist and request that their students are also made aware of their options.

Conclusion

Traditional dissections can be a thing of the past if more educators, students, and other compassionate individuals spread the word about the abundance of alternatives in education, the cost effectiveness and quality of these products, and, most importantly, their ability to provide today's students with a more progressive and humane education. **AV**

The Science Bank Top Five for 2007

Animalearn's The Science Bank has over 400 alternatives to using animals in education, ranging from CD-ROMs to realistic models. We offer products for every education level, from grades K-12, to college/university, and veterinary medicine.



The alternatives to dissection and animal experimentation in The Science Bank fit in well with national and state public education requirements as well as university requirements for science education, and are excellent substitutes to the dissection of animals. The Science Bank is helping to revolutionize dissection, moving it out of the antiquated wet lab and into the modern computer lab.

Every year, Animalearn picks its top five alternatives in terms of their popularity with borrowers using The Science Bank loan program. This year, the top picks are:

1. BioLab Cat

Perfect for junior and senior high school level biology education, BioLab Cat is an interactive CD-ROM that turns the student's computer mouse into a virtual scalpel, probe, and magnifying glass, for a high tech dissection that will not harm any cats. With realistic imagery, BioLab Cat allows students to learn about external features, musculature, internal organs, and the skeletal system through dissection and anatomy lessons.



Public Opinion

As Animalearn reaches out to educators, we try to incorporate feedback received in order to improve the quality of the programs and services we offer. In most cases, borrowers are pleased with the alternatives in The Science Bank and share their thoughts with us.

Thank you so much for sending all the models, CD-ROMs, and information for my daughter Jessica to use for her biology dissection

2. DryLab Plus Fetal Pig

A visually accurate Fetal Pig CD-ROM dissection for junior through senior high and college level biology education. This alternative provides quality photography that examines the complex internal and external anatomy of the fetal pig and includes detailed diagrams, slides, animation, and over 100 photos at eight different stages of gestation. Sound and video keep students fully engaged, and over 400 questions test their knowledge.

3. The Digital Frog 2.5

An excellent quality CD-ROM dissection of the frog, Digital Frog 2.5 combines realistic imagery with animation, and allows students to make 'incisions' with their computer mice. If the 'incisions' are made incorrectly, the student is prompted to repeat them correctly. Perfect for junior through senior high school and college biology education, Digital Frog 2.5 combines anatomy, physiology, dissection, and a unique ecology section that allows students to relate the study of physiology to the habitat, lifestyle, and challenges of frog populations, promoting critical thinking skills. The Digital Frog 2.5 encourages kindness toward frogs, while promoting excellence in anatomy and physiology education.

4. Pregnant Cat Realistic Model

The Pregnant Cat Realistic Model is a

life-size dissection model featuring over 100 individual anatomical details, and is the perfect complement for CD-ROM dissection alternatives such as BioLab Cat. This model, which can be used by students from junior high through college, includes a cross-sectioned kidney showing the cortex and medulla, major arteries and veins, muscle groups of the fore and hind limbs, and the open uterus, exposing a developing fetus. Along with a key identifying 136 structures, this model also has an open mouth cavity detailing the teeth and nasopharynx.

5. Critical Care Jerry

Critical Care Jerry is a realistic, full-size canine mannikin, approximating a 60-70 lb. dog. Jerry is perfect for use in colleges, veterinary and medical schools, or veterinary technician schools. Jerry features an artificial pulse and realistic airway, with representations of the trachea, esophagus, and epiglottis. This mannikin also has working lungs and can be used in endotracheal placement, compressions, and mouth-to-snout resuscitation. Students have the ability to aspirate air and fluid from the thoracic cavity to simulate trauma, as well as jugular vascular access. Students also have the opportunity to perform IV draw and injections with Jerry. This mannikin can be used to demonstrate splinting and bandaging, and features disposable and cleanable parts. Along with Critical Care Jerry, students and educators can also borrow Critical Care Fluffy, a feline mannikin. **AV**

"requirement" at school. Thank you, too, for sending your information packets for me to distribute to the school districts.

I applaud your company on the outstanding alternatives you have designed for teachers and students to use, both the models and the CDs.

Melanie Blake
Houston, TX

Thank you very much for the use of Critical Care Jerry. He was very useful in our CPR class. It was great for our staff to have a hands-on experience before a crisis situation actually occurs. Our training program for employees is extensive, 5 days initially and then 2 days every 90 days for 1 year. It's wonderful to have alternatives, like the products in your lending library, for our staff. I highly recommend your services to all of our referring hospitals.

Sara Beebe
Animal Emergency Hospital
Grand Rapids, MI

Just a quick note to say thank you so much for all you and your staff do at Animalearn. You have all been so helpful, with a great attitude and giving spirit. I have used your dissection alternatives for two years now in my Homeschool Co-op biology classes. I have had students who were very apprehensive about taking biology class, because they thought it meant that they had to dissect animals. Your top-of-the-line alternatives have been invaluable in making biology accessible, and not uncomfortable, for many of my students. Thank you for helping me show young students that animals' biology, and their amazing anatomy, can be taught with kindness, and without harming any more animals.

Kathy McGovern
Biology: Outschoollers Co-operative
Buxton, ME

AAVS Steps on World Stage to Promote Alternatives

This past summer, Animalearn, AAVS's education division, was proud to be a poster presenter at the 6th World Congress on Alternatives & Animal Use in the Life Sciences, a biannual conference where scientists, policy makers, and advocates meet and discuss alternatives and their development and implementation. AAVS Education Director Laura Ducceschi presented research on the attitudes of students and professors regarding student choice policies at five different U.S. universities.



Guidelines for the Development of Student Choice Policies Regarding Dissection in Colleges and Universities: An Ethnographic Analysis of Faculty and Student Concerns

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Lynette Hart, Ph.D., School of Veterinary Medicine, University of California, Davis

Nicole Green, Associate Director, Animalearn, Jenkintown, PA

challenging. Our ethnographic analyses represent faculty and students at six U.S. colleges and universities working toward current and/or proposed formalized student choice policies and reveal five key factors of concern arising among both faculty members and students: 1) specific academic requirements and learning objectives; 2) administrative responsibilities for staffing, scheduling, and supplies; 3) student access to alternatives and disclosure of animal use; 4) identifying and acquiring effective alternatives; and 5) constructive dialogue among students, faculty, and administration. We present the typical concerns and recommendations of students, faculty, and administrators working for the creation of formalized student choice policies, and offer a template of guidelines for colleges and universities seeking to formalize student choice.

Method

Individual interviews were held with six students and six faculty members who had been seeking to develop a student choice policy. Five interviews were conducted in-person, six were by telephone, and two were interactive interviews via the internet with a duration averaging 35 minutes (range of 20 -70 minutes). There were eleven individual interviews and one group interview. A series of open-

ended questions focused on the interviewee's experiences in developing a new policy and concerns. Detailed written notes were made during each interview. Each interviewee had experience in the establishment, implementation, and/or utilization of student choice at his or her university. The six U.S. colleges and universities were selected to be diverse in demographics, curriculum, geography, and educational focus. Colleges and universities represented were: Bryn Mawr College (Pennsylvania); Hofstra University (New York); Sarah Lawrence College (New York); University of Illinois Champaign-Urbana (Illinois); Virginia Commonwealth University (Virginia); and Worcester Polytechnic Institute (Massachusetts).

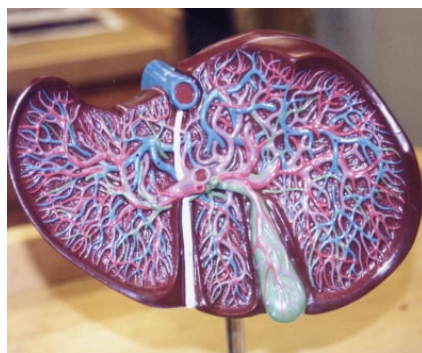
For the ethnographic analysis, concerns mentioned in each interview were summarized and tabulated separately for faculty members and students.

Results

Both faculty members and students expressed five key areas of concern:

1. Specific Academic Requirements and Learning Objectives

- Students expected to review other universities' existing student choice policies, assessing effects on existing



academic course requirements. Top ranked universities were of special interest to demonstrate pedagogical efficacy.



Abstract

Legislation in 15 states relating to animal use in K-12 education offers elementary and secondary students the option to decline participating in dissection. Similar provisions do not exist for college students. Recently, however, some college students and universities have developed policies offering alternatives to students who object to dissection on ethical grounds. The process of initiating such policies affects students, faculty, and administrators and often proves

- Usually the implementation of choice only in required and some elective courses, limiting selection of courses for students with alternatives.

- Faculty concern with academic freedom to use animals in instruction as well as concern for quality of alternatives. Sometimes just to avoid conflict, faculty eliminated animal use from specific classes.

- Ambiguous requirement for an 'equivalent' experience with alternatives. Learning objectives from classes using animals may be applied to classes with alternative learning objectives and experiences.

- Faculty support for student choice, but also value of dissection, especially for future surgeons, science educators, and medical professionals. Some question the value for undergraduates.

2. Administrative Responsibilities for Staffing, Scheduling, and Supplies

- Effect of student choice policy on staffing and course scheduling. "Can we do this?" "Do we have enough faculty and resources to implement alternatives?" An 'alternatives' lab course can be required for students choosing alternatives, perhaps in alternating semesters from a conventional course.

- Campus units affected by the policy. Most such policies are university-wide, but a student choice policy can be specific to departments, retaining their autonomy.

3. Student Access to Alternatives and Disclosure of Animal Use

- Informal (unwritten) student choice policy leading to uneven implementation, with some allowed alternatives and others not. Disparity in access to alternatives was a rationale for seeking a formal student choice policy.

- Advance disclosure in courses of required animal use. Students would like the option to either discuss alternatives or avoid the class, perhaps by disclosure on the syllabus.

4. Identifying and Acquiring Effective Alternatives

- Faculty expectation that few students would utilize a student choice policy.

- Efficacy of available alternatives. Faculty had not assessed all available alternatives. Some students were displeased with the alternatives selected for courses. Some felt that undue effort was required when using selected alternatives, or that there was still some pressure to participate in dissection.

- Assigning responsibility to someone for identifying and providing effective and suitable alternatives. Students can

facilitate with options for alternatives. Education departments from animal protection organizations helped some students, assisting them in presenting appropriate alternatives. Faculty often were involved in selection of alternatives for certain courses.

5. Constructive Dialogue Among Students, Faculty, and Administration

- Supportive faculty member (not necessarily life science) for involvement in the creation, negotiation, implementation, and follow-up of student choice. Coordination with senior administrators ensures long-term success.

- Testimony from respected professional(s) in related field to support the use of alternatives.

- Defined outcomes rather than a moving target. If it seems endless, faculty may ask, "What can students ask for now, that all animal research cease?" It can seem to be a slippery slope. Student advocates are inclined to want more, asking, "What else might succeed in the future?"

- Student-led initiatives as source of pride. At one campus, students involved in a social change project focused on a student choice policy, establishing on-campus hearings about animal use and meeting with biology faculty, lending credibility to efforts. Faculty valued involvement in project.

- Animal advocates viewed as naïve, uninformed, and unreasonable. Well-researched, balanced, and accurate presentations with professional manners to key decision makers counteract that perception. In a chain reaction process, one faculty advocate promotes others to listen. A hostile atmosphere results in polarization and defensiveness.

- Limited power of student government to affect change. As helpful allies, student government support, as in a referendum election for student choice, can send a message to the university.

Conclusions

Recommended best practices for success in student choice efforts are:

1. Address academic requirements and curricular issues.

- Review existing student choice policies at major universities for supporting documentation.

- Identify specific courses that will be affected by the policy.

- Assess whether it will be more effective to offer alternatives in affected courses or to offer 'alternatives-only' courses in specific semesters.

2. Define the administrative scope of the policy and which units will be affected by the policy.

3. Clarify students' options for choice and clearly designate classes with animal use.

4. Assign responsibility and a method to identify and acquire effective alternatives for courses where needed.

5. Identify a supportive faculty member to spearhead policy efforts for initiation, implementation, and follow-up, also fostering a collegial environment. **AV**

CCIC Recognizes Young Scientist

Last year, in an effort to promote the use and development of non-animal alternatives in research, testing, and education, the Coalition for Consumer Information on Cosmetics (CCIC), established the Dr. Ethel Thurston Memorial Scholarship in recognition of Ethel Thurston, Ph.D., a respected educator and pioneer of alternatives development. A scholarship was awarded to a deserving



AAVS President Sue Leary with Dr. Ethel Thurston Memorial Scholarship winner Finance Dechsakulthorn.

graduate student who had demonstrated a proficiency toward alternatives development and their use in research. The money provided was for a travel grant so the recipient could attend the World Congress on Alternatives & Animal Use in the Life Sciences.

The recipient of the Dr. Ethel Thurston Memorial Scholarship is Finance Dechsakulthorn, who attends the University of New South Wales in Sydney, Australia. Mr. Dechsakulthorn's primary area of research involves nanotechnology, and he is currently investigating the cell toxicity of selective substances using human skin cells.

As the Chair of CCIC, AAVS representatives President Sue Leary and Education Director Laura Ducceschi, were able to meet with Mr. Dechsakulthorn and discuss the importance of alternative research methods. **AV**



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USPTO Accepts Challenge on Legality of Animal Patent Advocacy Groups Applaud Move that Could Open Debate on Patenting Animals

Jenkintown, PA—This week the United States Patent and Trademark Office (USPTO) announced a decision to open an investigation into whether rabbits and other animals whose eyes have been purposefully damaged can be patented. The patent (#6,924,413) which is being challenged by the American Anti-Vivisection Society (AAVS), the Alternatives Research & Development Foundation (ARDF), and PatentWatch, argues that animals are not patentable subjects and that, in fact, animal patents provide an incentive to harm animals for economic gain.

In addition, the patent challenge highlighted numerous instances of prior scientific publications that should invalidate the patent. The USPTO agreed that “substantial new questions of patentability” were raised.

The groups’ first challenge to an animal patent succeeded in having the University of Texas drop its patent claims on beagles who were severely sickened and infected with mold. In addition, the Canadian Supreme Court ruled in 2002 that animals could not be patented, further challenging the legitimacy of animal patents in the U.S.

“Animal patents have no place in our society and are an inappropriate application of U.S. patent law. A rabbit with damaged eyes is still a rabbit,” said Tracie Letterman, an attorney and Executive Director of AAVS.

Results from a 2004 Opinion Research Corp. survey of 1,008 U.S. adults commissioned by AAVS found that two out of three people consider it unethical to issue patents on animals as if they were human inventions. Further, 85 percent of those surveyed were not even aware that universities and corporations are getting patents on animals.

More than 660 patents have been issued on animals since the Patent Office granted its first animal patent in 1988. Interestingly, approximately one-third of all animal patents granted to date are issued to foreign companies. The Japanese-owned Biochemical and Pharmacological Laboratories, Inc., filed the patent that is the subject of this challenge.

“Allowing foreign or domestic corporations to patent animals who have been intentionally injured, sickened, or genetically altered provides an incentive to harm animals for economic gain,” said Sue Leary, President of ARDF. “This directly conflicts with laws encouraging the replacement of animals in experiments with alternatives.”

“We’re pleased with the Patent Office for re-opening this patent application and hope that they will do the right thing by denying this patent,” said Andy Kimbrell of PatentWatch. “Our legal challenge and the poll numbers showing widespread public opposition to animal patenting should send a strong message to the Patent Office that this patent is neither legally valid nor morally acceptable.”

Look her in the eye.... Could you profit from her pain?

Rabbits' eyes are being purposefully injured to develop new treatments for dry eye. In 2005, the U.S. government issued a patent on rabbits to a Japanese company, allowing it to profit from animal suffering.

animals are NOT inventions



www.StopAnimalPatents.org

(800)SAY-AAVS • aavs@aavs.org

ANIMALEARN HONORS ART TEACHER WHO INSPIRES

In August, the staff of Animalearn was thrilled to participate in the creation of a mural promoting non-violence towards animals at a Philadelphia elementary school. The *South Philly Review* published a story highlighting the student designed mural and the work of art teacher and AAVS member Maria Pandolfi. Animalearn publicly acknowledged Pandolfi for her ongoing efforts to instill compassion and respect for all animals in her students by awarding her with its annual Humane Educators Award.

"We think that Maria's efforts of teaching kindness and actually relating it not only to the animal community, but to humans, was criteria for why we selected her for the Award," said Laura Ducceschi, AAVS Education Director.

Praising Pandolfi's dedication, AAVS Associate Director of Education Nicole Green added, "She definitely just goes above and beyond what any teacher I've seen does for her students and really instills that message of kindness to animals and compassion towards all creatures."

Pandolfi was gracious in receiving her honor. "I do things because I really love being with the kids. I don't even think about getting paid for this stuff, but it feels good when someone recognizes what you do." **AV**

South Philly Review
Caitlin Meals
August 9, 2007

Animalearn Shows its Expertise

As a leader in the humane education community, Animalearn was recently approached by the editor of *The Animals Voice* magazine and asked to write about the environmental impacts of dissection. Nicole Green, AAVS Associate Director of Education, was given the task and poignantly discussed this issue.

"There are many ways that dissection negatively impacts our environment," Green wrote. "Frogs are the most commonly dissected species in classrooms today and are typically taken from the wild. These creatures play an integral role in the world's ecosystems, mainly because they regulate

populations of insects, who can decimate crops."

Ms. Green also discussed the link between dissection and environmental pollution. Chemicals used to preserve dead specimens are not only respiratory irritants and known to cause cancer in humans, but they are also environmental pollutants. "Careless or irresponsible disposal of these preservatives or animal remains can contaminate water and soil and potentially harm wildlife and the health of human beings," she wrote. In addition, Green noted that Ken Roy, Chairperson for the National Science Teacher Association, has spoken out against using preserved animals in the classroom due to the many dangerous properties of these chemicals. He has specifically stated that "no specimens that

are preserved in formaldehyde should be used in middle school science."

Additionally, the ways in which animals are used in the classroom can negatively shape student value systems towards animals and the environment. "The removal of animals from their natural habitats for use in classrooms disrupts ecosystems and sets a negative example for wildlife conservation and environmental protection—two vital concepts for future scientists," said Green.

"The most environmentally friendly way to learn anatomy is to cut out dissection from the classroom," Green continued. "There are hundreds of viable, non-animal, state of the art alternatives available from organizations like Animalearn." **AV**



RABBIT CLONED IN HUNGARY

Hungarian researchers have announced the birth of Tapsilla, the first rabbit cloned in the country. Four other teams worldwide have also cloned rabbits with the intention of using them in toxicity testing and to study human disease. In addition, rabbits in France were cloned to produce proteins in their milk that treat kidney cancer and Hodgkin's disease.

Tapsilla, which is equivalent to "Thumpella" in English, had actually been a twin, but her sibling died shortly after birth. Unfortunately, clones have a very high mortality rate, if they are even born at all. According to numerous scientific studies, over 95 percent of

cloning attempts fail. Birth defects, physiological impairments, illness, and premature death are the norm, not the exception, when cloning.

The rabbits were born at Hungary's Agricultural Biotechnology Research Center and were delivered by caesarean section. Professor Andras Dinnyes, head of the Center's research team, said he hoped cloned rabbits like Tapsilla will play a role in developing new medications. In reality, non-human animals, cloned or otherwise, are not effective models for studying the human condition for the simple fact that their physiology and metabolism is very different from humans'. **AV**



NRC Report Calls for New Approach to Testing Chemicals that Will Greatly Reduce the Numbers of Animals Used

This year, the National Research Council (NRC) released a report titled "Toxicity Testing in the Twenty-First Century: A Vision and a Strategy," which advocates the use of non-animal *in vitro* test methods. NRC is affiliated with the National Academy of Sciences, which advises Congress on scientific matters.

According to the

report, "animal toxicity tests are time-consuming and resource-intensive," and are not always useful in testing human responses. The authors give a classic example of an animal-tested drug that had serious consequences when applied to humans. Thalidomide, prescribed in the 1950s and 1960s to treat sleeplessness and morning sickness, produced no abnormal

effects in rats; however, the drug was responsible for the birth defects of nearly 10,000 children.

The report also questions the practice of administering high doses of chemicals to animals when, traditionally, humans would be exposed to much lower concentrations. As an alternative, the authors recommend using human cells in

'high-throughput assays,' which could test thousands of chemicals in many different concentrations to determine the chemicals' effects.

The study, requested by the Environmental Protection Agency, concluded that "human cell systems have the potential to largely supplant testing in animals." **AV**

Scientists Use Computers to Map Immune Systems



At a recent meeting of computer scientists in Cambridge, UK, researchers discussed the possibility of using computers to test various substances in lieu of animals or humans. Computer models, they said, will soon become so advanced that they will be able to predict human response to any drug.

The event was hosted by Microsoft Research in Cambridge, which planned the affair in honor of its 10th birthday. In attendance were such scholars as David Harel, professor of computer science and applied mathematics at the Weizmann Institute of Science, who demonstrated a computer model of a worm who shares various systems in common with

humans. "Biological systems can be modeled and analyzed using man-made computerized systems," he said. "What this means is that the smartest approach to new drugs may not be to design a new drug at all, but instead to understand the way a biological system works in its environment."

Stephen Emmott, a visiting professor of neural biology at University College in London and also the head of computational biology at Microsoft Research Cambridge, explained this theory further. "This work, which is called 'systems biology,' will make it possible to test drugs on computers and not animals," he said. "It's also about developing novel therapies for curing disease by finding ways to trigger an immune response, which the body wasn't capable of producing without using the blunt instrument of drugs."

Utilizing computers for drug research instead of humans and animals may be more reliable and cost effective. Drug trials are extremely expensive, and even if they do reach phase three human clinical trials, positive results are not always guaranteed. For example, last year, six volunteers testing an anti-inflammatory drug fell ill and were admitted to the intensive care unit of a London hospital. The drug had previously been tested on animals and showed no serious side effects. **AV**

Breast Cancer Model Could Replace Animal Tests

Researchers at Queen Mary's School of Medicine and Dentistry in London have developed a new alternative to investigate breast cancer that could



halt the use of hundreds of animals in painful experiments each year. The research was funded by the Dr. Hadwen Trust, a UK charity that promotes non-animal medical research.

Mice are commonly used when researching treatments for breast cancer and endure painful procedures, such as the insertion of cancerous cells and harvesting of tumors. Hundreds of animals may be used in each series of tests. However, because mice differ so greatly from humans, they make poor models for studying human disease.

Fortunately, there has been a growing interest in the use of alternatives. As the researchers in London have demonstrated, using human cell cultures is much more relevant to the human condition.

The researchers began by culturing three different types of breast cells from normal and cancerous tissues. Cultivated in a collagen gel, the cells formed three-dimensional structures that closely resemble the glandular form they take in the breast.

The cell cultures are now being used to investigate ductal carcinoma *in situ* (DCIS), a common pre-cancerous condition that leads to 20 percent of all breast cancers. It develops when some cells in the breast ducts become cancerous but have not yet invaded the rest of the breast. Now, with this human-relevant model, researchers can learn more about the early developments of the disease, its progression, and potential treatments in a way that is far more reliable than using cells from other species.

Professor Louise Jones, one of the researchers on the team, hopes this unique model will create strides in breast cancer research. "Our test tube models of DCIS breast cancer are exciting and extremely novel... Developing more realistic test tube models of human breast cancer can provide an alternative to animal experiments," she said. **AV**

U.S. and EU Harmonize Testing Regulations

The U.S. Food and Drug Administration (FDA) and the European Commission recently collaborated at a meeting in Brussels to discuss increased communication between countries on matters of animal testing. The new arrangement will allow for easier trade of cosmetics between the U.S. and the European Union (EU) and comes on the heels of the EU ban on animal testing for cosmetics, which began in 2004 and will come into full effect by 2013.

With the trade value of U.S. cosmetic exports to the EU amounting to almost \$2 billion per year, and imports from the states to the EU amounting to nearly \$4 billion per year, cooperation between the two regions is required for the cosmetic industry to stay afloat.

As the new regulations mandate, confidential information regarding the safety of cosmetics and medical devices will now be more freely shared. In addition, advance drafts of pertinent legislation will also be exchanged, and any ongoing or emerging health and safety issues will be discussed between the two regions.

The two agencies intend to work together to find alternatives to animal testing, a move that could eventually end the process altogether. The more uniform the two regions' regulations are, the greater the opportunity for trade in personal care products between them. **AV**

MESSAGE TO MEMBERS

Dear Friends,

I have been a girly-girl my whole life. I love jewelry, pretty dresses, shopping and make-up. As soon as I could hold a lipstick tube, I was wearing it—wherever it landed. Over time, and with the help of my mother, another fabulous girly-girl, I came to master the art of make-up application, and I relish time spent pouring over the seemingly endless array of eye, lip, cheek, and nail colors offered in drug and department store make-up counters.

But I never thought about what went into making my perfect shade of lip gloss and mascara, the two staples of my vanity diet, until I began working with AAVS. They opened my eyes—literally—to the world of animal testing on cosmetics and household products. I was horrified and immediately felt guilty for being so thoughtless in my product selections. I just couldn't believe it. Do we really need to test to see if mascara hurts when placed directly on the eye? I've done it enough times myself to prove that test positive.

Over the past four years, I have consciously changed my make-up and household product choices to include cruelty-free products—all thanks to AAVS. I feel better about myself and my cruelty-free choices and I proudly share this information with my friends and family, most of whom were under the delusion that most make-up is not tested on animals anymore. I'm sure many of you have experienced the same phenomenon.

It also makes me very proud to share with people that AAVS is the Chair of the Coalition for Consumer Information on Cosmetics, and is currently making significant strides in promoting the importance of shopping with compassion, which includes the introduction of a brand new website currently under construction. Also, let's not forget the *Compassionate Shopping Guide*. Where would I be without it? I'll tell you: finding myself standing in the middle of my favorite make-up mecca wondering where do I start, and unknowingly choosing brands that test on animals.

But no more! With the help of that itty bitty *Guide* I walked into the light without looking back, and discovered a wonderful, cruelty-free world full of all the mascara and lip gloss this girly-girl could ever dream of! Not to mention laundry detergent and a myriad of household cleaning products. (Yes, believe it or not, I do enjoy cleaning!)

If you take away nothing from my letter other than this I'll have done my job: I urge you to please carry your *Guide* with you wherever you go. It's designed to fit into the smallest wallet—something I have yet to master—and is easily passed along to friends and family. I've even (subtly) placed a *Guide* or two in cosmetic gifts I've given to friends for birthdays and holidays. So start sharing the love and pass along a *Guide* today. You'll feel so much better you did. Take my word for it.



Happy Shopping,

Heather Gaghan

Director of Development & Member Services

Tina Nelson Sanctuary Fund

This fund was established to honor the memory of Tina Nelson, AAVS's Executive Director from 1995-2005. Sanctuaries and their work to provide a safe haven for animals who were once used in laboratories or exploited in other ways were a cause very dear to Tina's heart. She was a constant champion for all animals and was especially drawn to the plight of primates used in research. This fund will provide support for sanctuaries that provide homes for animals in need, and will also provide a lasting legacy for Tina's vision and AAVS's mission to end experiments on animals. If you would like more information on the Fund, please feel free to visit us at www.aavs.org and click on the Support AAVS tab to learn more about the woman who inspired the Fund, and how to make a donation.

AAVS Memorial Fund

A unique way of remembering kindred animals and animal lovers while making a gift in their name to help stop animal suffering. All AAVS tributes are used for continuing our mission's work of ending the use of animals in biomedical research, product testing, and education.

Memorial donations of any amount are greatly appreciated, and with a donation of \$50 or more, your tribute will be acknowledged in an upcoming issue of the *AV Magazine* as well as in a special recognition section of AAVS's Annual Report. Additionally, at your request, we will notify the family member or other individual you have remembered as a memorial gift to AAVS.



TRIBUTES

In loving memory of Rajah Oey.
Aimee Oey
Brooklyn, NY

In memory of Valentine, Brandy, and Smokey. We will always love you.

Bruce and Cozy Smoller
Potomac, MD

In memory of Missy. Thank you for your mothering of us all, your suffering to be with us, and your unfailing loyalty and love. I miss you.

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Santa Fe, NM

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Cathy Cook
New York, NY

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In memory of my cat, Jasmine. Thank you for being my furry little soulmate for 14 years. You taught me the purest meaning of love, compassion, and friendship.

Patty Smith
Port Ewen, NY

In memory of Millie. She was my beloved friend and companion.

Rosemary A. Broecker
Chicago, IL

In memory of Gwen Miller, a long-lived life, marking an end to an era. Love always until we meet again, love Momma and Dad.

Christina Miller
Haverford, PA



Innovation has its Awards

ARDF IS PLEASED TO ANNOUNCE THE RECIPIENTS OF THE 2007 ALTERNATIVES RESEARCH GRANTS

In this issue of the *AV Magazine*, readers have been exposed to the promise of alternatives to the use of animals in scientific research. AAVS established the Alternatives Research & Development Foundation (ARDF) in 1993 in order to fulfill that promise. ARDF's annual Alternatives Research Grant program is the hallmark activity of ARDF, with approximately \$1.5 million awarded to date.

To respond to an urgent and constant need for new methods development in a rapidly-changing scientific landscape, ARDF invites applications from a broad range of researchers. The proposals are evaluated and systematically rated by qualified reviewers experienced in the respective fields of study. The reviewers look at the potential for helping replace animals in the near future, and they also evaluate the scientific merit of the proposals, for which a number of technical questions must be addressed.

The following are just three of the six grantees for 2007. We will highlight the remaining three in the next issue of the *AV Magazine*.

Frank A. Barile, Ph.D.

St. John's University, Queens, NY

In Vitro Model for Cytotoxicity Using Mouse Embryonic Stem Cells

In 2001, an International Workshop on In Vitro Methods for Assessing Acute Systemic Toxicity pointed out the need for a simple predictive system for passage of chemicals through biological membranes, such as dermal, gastrointestinal, or blood-brain barrier. Dr. Barile, a toxicologist who is an expert in *in vitro* toxicological methods, plans a series of studies, the aim of which is to develop a cell culture model with the potential not only to screen chemicals for their effect on paracellular permeability, that is, passive transport of chemicals through intact membranes, but also to measure acute cytotoxicity. The fundamental principal of cyto[cell]toxicity tests is that most chemical injury is caused by a basal cytotoxic mechanism. This means that a toxic effect on cells can be observed because a basic function ceases or is damaged to a point that can be measured. Certain cell processes do not differ fundamentally among cell types and so are good to select for measurement if the test is intended to have a broad application.

Dr. Barile's team is tackling a stubborn sticking point in an area that has been a target of alternatives development for 20 years. Scientists have developed a number of *in vitro* models as alternative methods to acute systemic toxicity testing, but there are still no validated procedures in the U.S. for full replacement. While to some extent, this may be a policy failure, it also

reflects a scientific problem. Cell culture alternatives have tended to be focused on acute end points such as skin or eye toxicity, and the consensus is that in order to further reduce the use of animals in acute lethality assays, it is necessary to develop several simple *in vitro* models whose results can be combined to provide accurate predictions of human and animal acute systemic toxicity.

Due to the federal prohibitions and costs associated with acquiring and maintaining human embryonic stem cells, the experiments target the use of mouse embryonic stem cells (mESC), which are commercially available as an already established line. With the regulatory restrictions applied to human ESCs, Dr. Barile's judgment is that these cells are the most expedient way to move forward to replace the acute toxicity testing on living animals. The excitement about ESCs derives from their ability to differentiate to many cell types and tissues. Good cell culture practice permits virtually unlimited proliferation of these cells *in vitro*, and so, in accordance with ARDF's grant conditions, this study does not include any procedures on mice.

Dr. Barile's team will use the mESCs to establish selectively permeable monolayers of cells on cell culture inserts, followed by cytotoxicity testing. It is anticipated that establishment of *in vitro* models using mESC cells will enhance the potential for: 1) the construction of biologically active membranes, 2) the evolution of suitable replacement tissues, 3) use in drug development, and 4) validation against currently used animal tests.

UPDATE

Wenbing Deng, Ph.D.

University of California, Davis, CA
ES Cell-Derived Human
Oligodendrocytes for Assessment of
Neurotoxicity In Vitro

This study will test whether the human ES (Embryonic Stem) cell-derived oligodendroglia (neurological tissue associated with myelin formation) are a valid alternative for the assessment of neurotoxicity.

Because ES cells replicate indefinitely in culture, they have the potential to greatly reduce the use of animals in testing for neurotoxicity. Dr. Deng's lab has previously demonstrated, using cultured brain cells, that environmentally relevant, low-level lead can disturb the survival, proliferation and differentiation of oligodendroglia at critical windows of development. The previous study identified receptors that are strong targets for lead-induced toxicity, and the ARDF-funded study will use measurements of these targets and others to detect early stages of lead toxicity *in vitro*.

Developmental neurotoxicity is an area of increasing regulatory agency interest and touches on many fields of research and testing. It presents a unique challenge for alternatives development, and large numbers of animals continue to be used, involving many females and embryos at various stages of growth.

This project—which uses a federally-sanctioned human stem cell line - aims to fill the need for a simple and general *in vitro* protocol. Ultimately, it may be able to lay the foundation for future investigations into nerve cell development, screening of drugs and assessment of chemical toxicity, and even cell-based therapy for diseases in which oligodendroglia are injured or lost.

Anne Raub Greenlee, Ph.D.

Oregon Health & Science University, La
Grande, OR

Human Embryonic Stem Cell Model
to Predict Risk of Neural Tube Birth
Defects

Because of the urgent need for alternatives to highly invasive animal use in developmental toxicology, ARDF is funding another study in this area. It also explores the potential of using human ESC's (a federally-sanctioned human stem cell line).

Neural tube defects (NTDs), including anencephaly (absence of the brain) and spina bifida, are severe malformations occurring when the brain or spinal cord fail to close during early pregnancy. Each year, approximately 1 in 1,000 pregnancies in the U.S. and an estimated 300,000 newborns worldwide are afflicted. While prenatal folate supplements have been associated with a decline in occurrence, treatments are ineffective once the neural tube fails to close. Therefore, prevention is crucial. Genetic, nutritional, and environmental factors contribute. However, the mechanism of disease remains poorly understood, and many animals, especially mice, have been used to identify agents that may pose a risk of NTD formation. Long-term, Dr. Greenlee and her team want to establish cell-based screening methods to rapidly assess neurotoxic chemical risks, but, first, she wants to address the problem of extrapolation of findings from animals to humans by developing a model using human cells.

This study funded by ARDF will test whether neural tube structures can be formed *in vitro* from differentiation of human embryonic stem (hES) cells and then be used to predict chemical risks of NTDs. Dr. Greenlee's specific aims are to: 1) develop undifferentiated hES cells

into neural tube structures *in vitro*; 2) predict risk of NTDs by altering hES cell differentiation into neural tube structures using a known agent; and 3) test folic acid for its ability to prevent VPS-induced NTDs.

Findings should help establish alternative methodology for identifying hazardous agents capable of inducing NTDs. Further validation studies have the potential to yield a robust alternative to animal experimentation for developmental neurotoxicology testing. **AV**

ARDF congratulates all the grant recipients and thanks Dr. Rodger Curren, President of the Institute for In Vitro Sciences, for coordinating the grant review process again this year.

If you wish to support ARDF's work to develop alternative methods of conducting high quality scientific research, your tax-deductible contributions are welcome and may be sent to: ARDF, 801 Old York Rd., #316, Jenkintown, PA 19046.

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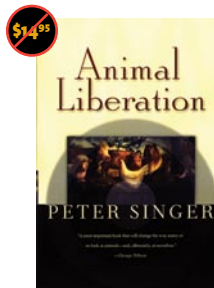
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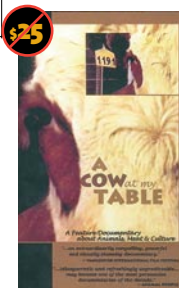
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Nearly 125 years ago, AAVS was founded by social visionary Caroline Earle White. Knowing that small acts of kindness can make a difference for animals, she tirelessly worked to improve the lives of those who were in need of loving homes, labored on city streets, and suffered in laboratories.

Make her legacy yours.

You can help ensure that Caroline Earle White's vision and the work of AAVS continues far into the future. For information on estate planning and becoming a member of the Caroline Earle White Society, please return the attached form, or call (215)887-0816.



Caroline Earle White Society

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To recognize the thoughtfulness and generosity of those who have chosen to provide for AAVS in their estate plans, we have created The Caroline Earle White Society, named in honor of our founder. If you are interested in becoming a member of The Caroline Earle White Society, please contact Heather Gaghan, Director of Development & Member Services at (215)887-0816.

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